POSTER SESSION 1
Hair/Alopecia .........................................................100 – 105
Infectious Diseases ...................................................106 – 135
Inflammatory Diseases ..............................................136 – 220
Lymphoproliferative ...............................................221 – 263
Melanocytic Neoplasms .........................................264 – 293

POSTER SESSION 2
Neoplasia, Carcinogenesis, Tumor Biology .......................500 – 625
Other ........................................................................626 – 681
POSTER SESSION 1

Hair/Alopecia

100  
Wooly Hair Nevus: Rare Histopathologic Finding
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Wooly Hair Nevus is a rare disorder of hair resulting in a circumscribed patch of short curly hair. About half the time these lesions are associated with an epidermal nevus. Trichoscopy usually shows short intervals of waves which has been likened to that of a “crawling snake”. Histopathology of these lesions is only reported in case reports with no formal studies on these lesions performed. Here-in we report a case of an 11 year old female with a circumscribed patch of shortened hairs on the anterior scalp. Trichoscopy revealed no abnormalities. Histology was only significant for a twist in the hair shaft at the follicular infundibulum after exiting the follicle with no curving of the follicle itself. The case shows a novel finding of twisting of the hair without involvement of the follicle. This is also the first case of wooly hair nevus associated with leukonychia and ulerythema ophryogenes.

101  
Sarcoidosis Arising Within Frontal Fibrosing Alopecia
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Sarcoidosis is a multisystem disorder of unknown etiology that commonly affects the skin. Development of cutaneous sarcoidosis within areas of prior tissue damage including tattoos, dermal filler injection sites, herpes zoster, and scars from mechanical injury is a well-documented phenomenon. Sarcoidosis has also been reported to koeberize within sites of skin trauma including venipuncture sites in intravenous drug users following interferon-a therapy for hepatitis C. We report a case of sarcoidosis arising on the scalp within the scar of frontal fibrosing alopecia. A review of the English language literature reviewed no prior such reports. Our patient is a 73-year-old female who presented with regression of the frontal hairline and scaly erythematous papules and plaques overlying a circumferential scarred atrophic plaque along the frontal hairline. Scalp biopsy demonstrated epithelioid granulomas, diminished terminal hair follicles, and focal perifollicular lymphocytic infiltrate with interface change and dyskeratotic keratinocytes. Infectious stains were negative and Movat stain demonstrated a loss of elastic fibers. Angiotensin converting enzyme level was elevated supporting a diagnosis of sarcoidosis. While cutaneous disease occurs frequently, alopecia is a rare manifestation of sarcoidosis that usually affects African American females in their 4th and 5th decades of life. It is important to consider sarcoidosis within the differential diagnosis of cicatricial alopecia as 80% of patients with scalp involvement have systemic disease.
A Case of Co-localization of Alopecia Areata and Vitiligo on the Scalp
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Alopecia areata and vitiligo are two cutaneous diseases that are believed to be primarily autoimmune in pathogenesis. The coexistence of these two conditions in the same patient has been well described, but there are few reports of the two disease processes occurring in the same location. We report the case of a patient with a history of discoid lupus who presented with new patches of hair loss on her scalp for the past year that had been worsening over the last few months despite treatment with hydroxychloroquine and topical minoxidil. Her exam revealed two well-circumscribed depigmented alopecic patches with few short white hairs on the frontal hairline and left scalp that were accentuated with Wood’s lamp exam. These patches differed from the hypopigmented scars along her occipital scalp related to her discoid lupus that did not accentuate with Wood’s lamp exam. A punch biopsy of the depigmented patch on her left scalp revealed features consistent with both vitiligo and alopecia areata without evidence of discoid lupus. The rarity of co-localization of alopecia areata and vitiligo raises the question of whether this phenomenon is underdiagnosed, underreported, truly rare, or coincidental. It is important to continue to gain understanding of underlying pathogenesis of these diseases so that more definitive treatment modalities may be offered.

Characterizing the Inflammatory Microenvironment of Frontal Fibrosing Alopecia
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Introduction: Frontal fibrosing alopecia (FFA) is a cicatricial alopecia typically occurring in postmenopausal women. The etiology and pathophysiology of FFA is poorly understood but thought to be immune mediated. This study aims to further explore the extent of fibrosis and the inflammatory microenvironment by characterizing the role of Langerhans cells (LCs), helper T cells, cytotoxic T cells, and B cells around the involved follicles in FFA. Methods: 11 paraffin-embedded tissues from patients with a clinical and histopathologic diagnosis of FFA were selected for immunohistochemical studies using CD3, CD4, CD8, CD1a, and CD20. The lymphocytes and LCs were analyzed around the affected follicles. The CD4/CD8 T lymphocyte ratios were calculated in each case and compared to the infiltrate CD4/CD8 T lymphocyte ratios in uninvolved areas. Results: On histopathologic review, at least 35% of follicles in each case were affected by the disease with concentric perifollicular fibrosis surrounded by a perifollicular lichenoid lymphocytic infiltrate around the infundibulioisthmic portion of the hair follicle. There is an increase of perifollicular LCs (mean of 18, standard deviation of 5.5) and intrafollicular LCs (mean of 14, standard deviation of 4.3) in FFA involved follicles when compared to normal follicles (p<0.0001). The involved follicles also show a relative decrease in CD4/8 ratio indicating an increased CD8+ T cell population, significantly distinct from a CD4 dominant population in normal follicles (p<0.0001). Conclusion: The inflammatory characterization of FFA shows a CD8 predominant T lymphocytic infiltrate with increased numbers of LCs at the infundibuloisthmic region. The increased LCs may illustrate an aberrantly persistent antigen presentation that leads to a CD8+ T cell response.
104
Follicular Induction and CK20+ Merkel Cells Overlying Lesions of Focal Dermal Mucinosis
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Focal dermal mucinosis (FDM), or cutaneous focal mucinosis, is a benign reactive process categorized as a primary mucinosis. Skin biopsy is essential for diagnosis, as the clinical appearance is often non-specific, typically presenting in adults as a solitary, asymptomatic skin-colored papule. Histopathologically, it is characterized by a localized area of mucin deposition associated with fibroblasts in the dermis. Follicular induction is a phenomenon whereby the epidermis is induced by an underlying process to form primitive or mature hair follicles and sebaceous glands. Follicular induction has been reported overlying various benign and malignant dermal neoplasms, including dermatofibroma and neurofibroma. Follicular induction has been rarely described in FDM. Here, we performed a retrospective histologic review of lesions of FDM confirmed by skin biopsy from 2010 to 2015 in our department. We found that 11% (11/98) of FDM lesions demonstrated follicular induction. CK20 staining was performed on 4 of these biopsies and highlighted an increased density of CK20+ Merkel cells within the basaloid epidermal proliferations, supporting follicular differentiation. Since superficial basal cell carcinomas (BCC) often demonstrate a mucinous stroma around the basaloid islands, FDM with follicular induction may closely mimic a BCC histologically, particularly in superficial shave biopsies. Therefore, it is important that dermatopathologists be aware of this phenomenon. Furthermore, positive CK20 staining within the basaloid epithelial proliferations may be helpful in differentiating follicular induction overlying FDM from a basal cell carcinoma.

105
Drug-induced Psoriasiform Alopecia, a Known Side Effect of Anti-TNF Agents, Identified in a Patient on the PDE-4 Inhibitor Apremilast for Scalp Psoriasis
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Psoriasiform alopecia is a known side effect of the tumor necrosis factor- alpha inhibitors (anti-TNFs) used for autoimmune disorders. Another FDA-approved treatment for psoriasis and psoriatic arthritis is apremilast (Otezla®; Celgene, Summit, NJ, USA), an oral small molecule inhibitor of the enzyme phosphodiesterase 4 (PDE-4) which decreases the pro-inflammatory cytokines TNF-alpha, IFN-gamma, IL-17, and IL-23. Known adverse effects of apremilast include diarrhea, nausea, and nasopharyngitis. We present the case of a 37-year-old woman who developed alopecia during treatment with apremilast for severe scalp psoriasis. Four years earlier, she was diagnosed with inverse and limited plaque psoriasis. She received neither anti-TNFs nor other systemic therapy. Within six weeks of starting apremilast, she presented with non-scarring alopecia characterized by severely decreased hair density of the inferior vertex and occipital scalp with minimal scale and erythema. A 4-mm punch biopsy from an area of alopecia at the right vertex was performed. Histologic examination of transverse (horizontal) sections showed superficial features of psoriasis including psoriasiform epidermal hyperplasia with parakeratosis containing neutrophils and marked atrophy of sebaceous glands. There were deeper
features of alopecia areata such as increased catagen/telogen and miniaturized hairs. A superficial perivascular and deep perifollicular lymphoid infiltrate with some plasma cells and eosinophils supported a drug reaction over psoriatic alopecia. A Periodic acid-Schiff (PAS) stain was negative for fungal forms. Apremilast was discontinued. The hair loss stabilized after treatment with intralesional triamcinolone and a topical steroid. To our knowledge, a drug-induced psoriasiform alopecia has not previously been reported in a patient on apremilast. This case provides evidence that the psoriatic alopecia/alopecia areata-like reaction is not limited to the anti-TNF biologic agents.

**Infectious Diseases**

106 **FELLOW**

Artifactual Immunohistochemical Staining of Mycobacterium Leprae with Treponema pallidum Antibody

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Immunohistochemistry is widely used in diagnosing infectious diseases in dermatopathology. One of the most commonly utilized immunostains is a rabbit polyclonal antibody against Treponema pallidum. Treponemal immunostain has been shown to have increased sensitivity (71%) and specificity when compared to silver stain. However, several recent reports have identified that T. pallidum immunostain can falsly recognize and label several mycobacterial species including M. marinum, M. tuberculosis, as well as M. leprae. Here we report ten cases of artifactual staining of Mycobacterium spp. with predilute T. pallidum antibody (Biocare). We noted staining of mycobacteria with T. pallidum antibody in several examined specimens. Thus, artifactual staining of mycobacteria with widely utilized T. pallidum antibody represents an important histopathologic pitfall. We suggest that caution must be exercised when interpreting T. pallidum immunohistochemical staining. It may be prudent to utilize additional anti-mycobacterial tissue stains along with clinical and serologic data to diagnose mycobacterial or treponemal infection with certainty.

107

Arrector Pili Muscle Involvement In Leprosy: An Under Appreciated Finding

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Leprosy is a chronic infectious disease caused by Mycobacterium leprae. Histology plays a pivotal role in this difficult-to-diagnose condition. A 54-year-old man originally from Brazil presented to his dermatologist with a longstanding generalized eruption of annular plaques and nodules over his trunk and extremities. In the past he had been diagnosed with sarcoid following a biopsy that revealed a granulomatus dermatitis. Eight years later, a repeat biopsy from the trunk revealed a superficial and deep perivascular lymphohistocytic infiltrate with sparse perineural involvement. However, the dermatopathologist noted prominent infiltration of an arrector pili muscle with foamy histiocytes, allowing a diagnosis of leprosy despite two negative Fite stains. While emphasis has been placed on perineural inflammation in leprosy, dermatopathologists should consider this diagnosis when seeing inflammation of arrector pili muscles. In fact, C.G.S lyer theorized that involvement of arrector pili...
muscles is due to infiltration along the nerve innervating the smooth muscle. In addition, a recent study from India identified alterations in arrector pili muscles in otherwise unaffected areas of skin in those with all types of leprosy.

108
Human Polyoma Virus 7 Associated Pruritus: Second Reported Case
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A 47 year old white male, who received a cardiac transplant thirteen years previously followed by a re-transplant two years later due to organ rejection, presented with worsening pruritus primarily on the trunk and extremities since the past year. The patient was on chronic immunosuppressive therapy with mycophenolate mofetil, tacrolimus, and everolimus. The pruritic dermatosis manifested as hypo- and hyperpigmented macules, and generalized xerosis with lichenification of the trunk and extremities. Histological examination of skin from affected sites revealed abnormalities in the stratum corneum and superficial epidermis. Numerous keratinocytes prematurely keratinizing within the epidermis were identified. The stratum corneum contained areas of eosinophilic somewhat epithelioid aggregates of parakeratosis. The lesional areas had a similar appearance to molluscum bodies. This pattern has previously been described as peacock plume. Additional studies were performed and immunohistochemical studies were positive for SV40, human polyoma virus T antigen, and capsid VP1 suggesting HPyV7 associated pruritic eruption. This is a rare and recently described entity in which very little is still known and it is likely under recognized.

109
A Case of the Immune Reconstitution Inflammatory Syndrome in Treated Whipple’s Disease
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Introduction: Whipple’s disease (WD) is a rare (incidence 1:1,000,000), progressive, infectious disease caused by the gram-positive bacterium Tropheryma whippelii (TW). Approximately 10% of patients with WD being treated with antibiotics will develop a complication known as the immune reconstitution inflammatory syndrome (IRIS). Case Presentation: A 51-year-old male presented to the dermatologist with a six-month history of myalgias and widely distributed erythematous subcutaneous nodules. There were no surface changes and the lesions were non-tender and non-pruritic. He had been diagnosed with WD three months before the onset of symptoms, and had been treated with one month of IV ceftriaxone followed by two months of Septra. He was switched to doxycycline and hydroxychloroquine once the symptoms developed, as it was felt to be a drug eruption. He had also been on prednisone of various dosages for the previous 2 years while being worked up for WD. This was increased from 2 mg to 15 mg after the appearance of the rash. Cutaneous biopsy revealed a focal nodular to diffuse inflammatory reaction in the dermis and subcutis containing lymphocytes and histiocytes, some of which had foamy cytoplasm. PAS and GMS positive eosinophilic granules were noted in scattered histiocytes, morphologically similar to what was observed in the original duodenal biopsy. However,
while PCR was positive in the duodenum, confirming WD, it returned negative for TW in the skin. Nevertheless, electron microscopy (EM) revealed structures resembling rod-shaped bacilli. At last follow-up, all cutaneous symptoms had resolved, and he was otherwise well. He was changed back to Septra, with which he will require 1 year of treatment. Conclusion: IRIS is a pathological inflammatory response to antigens from a replicating infection or persistent non-replicating antigen, most well known for occurring in patients being treated for HIV or tuberculosis. It can also occur during treatment of WD; however, there are very few cases reported given the rarity of this disease. While PCR was negative for the cutaneous biopsy, we believe this presentation is in keeping with IRIS on the basis of the microscopic, histochemical and EM findings.

110
Achilles Cyst in a Cirrhotic Patient, Not Always What it Seems.
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“Phaeohyphomycosis” encompasses infections caused by pigmented, melanin producing fungi commonly found in soil. Over 100 species of dematiaceous fungi can cause phaeohyphomycosis (1), and they can produce severe disease in the immunocompromised. Manifestations of infection include subcutaneous nodules, brain abscesses, and disseminated disease (2). Cystic variants of infection are typically associated with immunocompromised states as has been reported by Herschel et al (3) and Xiaowei et al (4). We present a 70-year-old male with type II diabetes, coronary artery disease, Hepatitis B, cirrhosis (MELD score 11), and skin cancer who was seen for basal cell carcinoma. He complained of a cystic nodule on the left Achilles present for several years, and was previously lanced but had recurred. On exam, a 3x3cm cystic nodule was noted on the left Achilles. Due to pain, recurrence, and an unusual location for cysts, an excision was performed. Histology was notable for a granulomatous inflammatory pattern surrounding cystic cavities, and closer inspection unveiled golden-brown pigmented fungal organisms with hyphal and yeast forms consistent with phaeohyphomycosis. Despite the relatively increased risk associated with mycotic infections (diabetes, cirrhosis), excision was sufficient to resolve the symptoms without utilization of systemic antifungals, and no evidence of recurrence or dissemination was noted on follow-up. This case highlights some valuable learning objectives that include: identifying lesions presenting in atypical locations; broadening a differential for cystic nodules; resolution after excision without systemic therapy; adequate follow-up and treatment in immunocompromised hosts to reduce the potential of secondary dissemination and associated complications.

111
Cutaneous Cryptococcosis Misdiagnosed as Histoplasmosis: A Potential Pitfall
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We present a case of a 65-year-old Caucasian male who presented with a 6 week history of a pruritic, painful rash on the upper back consisting of rounded, erythematous plaques with central clearing and discharge. The patient had a history of cardiac transplantation and chronic immunosuppressant
therapy. He was empirically treated for herpes zoster without resolution. Subsequent biopsies of the rash from an outside facility were diagnosed as histoplasmosis. Biopsy was repeated at our institution. Histologic sections demonstrated an ulcerated epidermis overlying a superficial and deep dermis altered by broad areas of clearing surrounding pleomorphic yeast forms in clusters. The yeast were highlighted by PASD, GMS, and mucicarmine stains, consistent with cryptococcal infection. Fite and AFB stains were negative. Skin culture grew Cryptococcus neoformans. Cutaneous manifestations of disseminated cryptococcal infections are relatively rare (10-15% of patients) and often precede central nervous system involvement, highlighting the importance of early and accurate diagnosis. The characteristic feature of Cryptococcus is the thick polysaccharide capsule creating a clear space around the organism and staining with mucicarmine. When the capsule is poorly formed or in the setting of a gelatinous histologic pattern relatively devoid of inflammation, however, misdiagnosis may ensue. Then, cryptococci may resemble yeast of similar size, such as Histoplasma and Candida and may result in negative cryptococcal antigen tests, which detect antigens present in the capsule. Fontana-Masson staining may help to distinguish Cryptococcus from other yeast due to the presence of melanin in its capsule. Furthermore, co-infection with Cryptococcus and Histoplasma in a single skin lesion has been reported and should be considered. Biopsies and culture remain essential for the accurate diagnosis of any unusual skin lesion in an immunocompromised patient.

112
Septolobular Panniculitis in Disseminated Lyme Borreliosis
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Recognized by the Infectious Disease Society of America criteria as the only independently diagnostic clinical feature of Lyme disease, erythema migrans is well-known by clinicians as the prototypical cutaneous manifestation of the condition. The full spectrum of skin manifestations of Lyme borreliosis, however, is less well appreciated, but equally important for clinical recognition. Erythema migrans itself may present as vesicular, indurated, necrotic, purpuric, solid, or targetoid, and other established manifestations of Lyme borreliosis include acrodermatitis chronica atrophicans and borrelial lymphocytoma cutis. Panniculitis represents an unusual cutaneous manifestation of Lyme disease, which developing following dissemination of the spirochete. We present such a case of Lyme panniculitis in a patient who was initially treated for cellulitis as well as neck and radicular leg pain. Our patient’s unique presentation emphasizes the importance of recognition of this rare clinical and pathologic inflammatory pattern as a sign of Lyme disease.

113
Cutaneous Cryptococcosis Mimicking Non-melanoma Skin Cancer
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Cutaneous Cryptococcus is a fairly rare and usually opportunistic infection caused by the yeast Cryptococcus neoformans. Cutaneous lesions have been seen in 10-15% of patients with disseminated
disease. These lesions may exhibit variable morphology from acneiform papules and pustules to cellulitis or pyoderma gangrenosum-like lesions, thus imitating common clinical lesions. Here we present a case of cutaneous cryptococcosis mimicking non-melanoma skin cancer. A 54 year old Caucasian male with a history of psoriasis, presented with a solitary erythematous, scaly lesion on the scalp which did not resolve with cryotherapy. Clinically, the lesion was suspicious for non-melanoma skin cancer. A shave biopsy of the lesion demonstrated an ulcerated lesion with extensive serum/inflammatory crust and reactive epidermis. In the subjacent dermis was a collection of histiocytes containing refractile, round, fungal organisms, consistent with Cryptococcus. A GMS stain highlighted the broad range in size of the organisms, as well as the narrow-based budding; and a mucicarmine stain highlighted the capsules around the organisms. Cutaneous cryptococcosis is classified into primary and secondary forms, with the primary ones still being controversial. Many specific criterion have been established in order to diagnose primary cutaneous cryptococcosis, which in and of themselves, essentially preclude making the diagnosis. The prevailing opinion is that cutaneous cryptococcosis does not exist without systemic involvement. However, some believe that there is evidence that skin should be recognized as a portal of entry for Cryptococcus and as such, primary cutaneous cryptococcosis is a distinct and actual entity. While some claim there are features which differentiate primary from secondary cutaneous cryptococcosis, only thorough investigation will establish the diagnosis. Our case exemplifies a rare and unusual entity mimicking one that is universal in our clinics; emphasizing the importance of early biopsy and thorough histologic examination.

114  FELLOW
Imported Fire Ant Envenomation: A Histopathologic Study of a Recognizable Form of Arthropod Reaction
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Background: Skin reactions to the sting of the imported fire ant have characteristic clinicopathological features, not mentioned in the recent dermatological literature. Because the habitat of the imported fire ant is expanding, dermatologists and dermatopathologists will benefit from becoming familiar with this condition. Objective: We sought to evaluate the clinicopathological features in an induced typical lesion and in a series of regular biopsies. Methods: One case of experimental envenomation was prospectively followed for 48 hours with biopsies. In addition, six cases from our laboratory were evaluated histologically. Results: The typical lesion follows a very distinctive clinical and histologic evolution over 48 hours, with the formation of a subepidermal pustule overlying a wedge shaped area of dermal collagen basophilic degeneration. In the six cases retrieved from our files, the main features were a superficial and deep dermal, perivascular, periannexal and interstitial infiltrate consisting of neutrophils with basophilic degeneration of the collagen. A subepidermal pustule was noted in half of the cases. Conclusions: From biopsies taken in a clinical setting, even in the absence of the characteristic subepidermal pustule, the diagnosis of imported fire ant sting can be suspected if there is a superficial and deep perivascular, periannexal and interstitial infiltrate composed of neutrophils, with some basophilic denaturation of collagen.
A Case of Misdiagnosed Syphilitic Proctitis

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A 31-year-old white-collar worker presented with his wife to our proctology clinic complaining of bowel habit change with tenesmus, mucous discharge and hematochezia. Stool occult blood test was positive. Sigmoidoscopy showed a pachymucosa with multiple superficial ulcerations of the lower colon. Histologic findings of rectal biopsies showed chronic inflammation with erosion and hyperplasia of lymphoid tissue. Laboratory tests including HIV antibody test and serum RPR/TPPA test were all negative. Patient was treated as “proctitis” with Mesalazine for one month without any improvement of symptoms. The patient went to the dermatologist afterwards by himself requiring another syphilis and HIV test. The result of serum RPR test was 1:128 and TPPA test was positive. An HIV antibody test was negative. Further questioning revealed rectal intercourse with different sex partners. To confirm the relationship between the proctitis and syphilis, dermatologist requested an immunohistochemical staining of the rectal biopsy specimen with anti-Treponema antibody, which demonstrated numerous spirochetes in rectal mucosa. Hence, for clinically and histologically nonspecific proctitis, even with negative syphilis test, an immunohistochemical staining of Treponema is necessary.

Making a new diagnosis of Hansen’s disease can be difficult, especially when the findings may be subtle or mimic another more common disease process. From an assortment of 42 United States-based cases, we present a few cases with unusual histologic findings. Among these, a surprising case that was clinically thought to be granuloma annulare in a 69-year-old woman. A second case had a lymphocyte predominant infiltrate more suggestive of lupus erythematosus in an 83-year-old woman. A third case had many parallel linear foamy granulomas in a zebra-striped pattern. While there is significant clinical and histologic overlap between some variants of leprosy and other more commonly recognized disease entities, we will present some pathologic clues that raise suspicion for this diagnosis. Besides the well-known clue of foamy histiocytes, the presence of plasma cells can be helpful. These cases highlight the need to consider Hansen’s disease in the differential diagnosis, particularly in locales where local 9-banded armadillos may harbor the disease.

Unusual Histologic Patterns in Hansen’s Disease
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Making a new diagnosis of Hansen’s disease can be difficult, especially when the findings may be subtle or mimic another more common disease process. From an assortment of 42 United States-based cases, we present a few cases with unusual histologic findings. Among these, a surprising case that was clinically thought to be granuloma annulare in a 69-year-old woman. A second case had a lymphocyte predominant infiltrate more suggestive of lupus erythematosus in an 83-year-old woman. A third case had many parallel linear foamy granulomas in a zebra-striped pattern.

While there is significant clinical and histologic overlap between some variants of leprosy and other more commonly recognized disease entities, we will present some pathologic clues that raise suspicion for this diagnosis. Besides the well-known clue of foamy histiocytes, the presence of plasma cells can be helpful. These cases highlight the need to consider Hansen’s disease in the differential diagnosis, particularly in locales where local 9-banded armadillos may harbor the disease.
Two Cases of Cutaneous Nocardiosis in Immunocompromised Patients
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Cutaneous nocardiosis can develop from direct inoculation or hematogenous dissemination from another end organ site. We present two cases of iatrogenically immunosuppressed patients who presented with cutaneous nocardiosis. One case mimicked eruptive non-melanoma skin cancer clinically, but histopathology demonstrated a lobular panniculic abscess. The other case presented with conventional supplicative papulonodules that histopathologically revealed a dermal abscess. Gram stain in both cases revealed rare filamentous gram positive rods but AFB stain was negative. Tissue culture identified Nocardia Amikacinintolerans and Nocardia brasiliensis isolates. Superficial abscess formation was associated with direct traumatic inoculation, while focal panniculic abscesses formation corresponded to hematologic spread. Pulmonary involvement was ultimately established in both cases highlighting the importance of altering clinicians to the possibility of extra-cutaneous involvement. Negative AFB staining in formalin fixed specimens does not exclude a diagnosis of Nocardi as, as the classic dual Gram-positive, AFB-positive staining is more likely to be present with fresh tissue culture specimens.

Old World Leishmaniasis: An Ancient Disease with a Non-Standardized Microscopic and Clinical Classifications
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Background: Microscopic and clinical classifications of cutaneous leishmania (CL) have been set in the 1980’s. Since then, they have been used invariably on assumption that the progression of the disease has remained the same. Lebanon, a nonendemic country, is suffering from a CL epidemic due to the massive population influx from endemic Syria. Design: Patients diagnosed and speciated with CL (n=169) using molecular and microscopic analysis on punch biopsies/scrapings were studied. General demographic data (age, gender, country of residence, lesion age), microscopic data [Ridley’s (RP) and microscopic (MP) patterns and Parasitic index (PI)] and clinical stage (CS) were documented. MP was scored as: 1: superficial; 2: superficial and deep; 3: diffuse and 4: nodular dermatitis. CS was scored as: 1: inflammatory; 2: proliferative/reorganization; 3: healed phases. The 3 patterns were studied in comparison to the lesion age and PI. Results: At low PI, CS and MP showed healing scores (scores 4 and 3, respectively). In contrast, RP showed variable distribution at low PI. The same pattern is noted when correlating the different patterns with high PI. In comparison to lesion age, none of the three patterns showed the predicted linear correlation with lesion progression. Thirteen patients defeated the term "annual sore" and were sampled at 12 - 36 months. Most of those patients were in the pediatric category (77%) and showed low PI. In the aforementioned cases, no trend was noted in CP and RP whereas the MP showed advanced scores. Conclusion: In the studied population, the previously adopted classifications did not correlate with the disease progression. Such findings may raise the possibility of evolving disease. The proposed CP and MP showed better correlation with the disease progression, however, other interplaying factors may be affecting the manifestation of this disease. 
Florid Fusarium Infection of Immunocompetent Woman with Non-Healing Leg Wound

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Fusarium comprises a large genus of filamentous fungi ubiquitous in soil and plant material. In humans, Fusarium is associated with a broad spectrum of infections ranging from keratitis and onychomycosis to fungemia and disseminated cutaneous lesions. Advanced disease almost exclusively manifests within immunocompromised individuals, particularly those with prolonged neutropenia. We present an 81 year-old woman with no significant past medical history admitted for debridement of non-healing leg wound. Three weeks prior to admission, the patient suffered a partial degloving injury down to bone of the right lower leg after falling on a tree trunk in a Central American swamp. At a local hospital, skin and subcutaneous tissue was replanted and tacked over the wound. She was treated with a course of Levofloxacin. On return to the United States, our patient presented to wound clinic with a large, non-healing, V-shaped skin tear with patchy purple discoloration at the edges. No fluctuance or purulence was appreciated. Hematoxylin and eosin stain from debridement specimen revealed fungal elements within a necrotic epidermis and throughout the dermis and subcutis. Grocott's methenamine silver and Periodic acid–Schiff staining further demonstrated abundant septate, branching hyaline hyphae with intravascular fungal invasion. Tissue culture confirmed fusarium. The patient continues to follow with surgery and infectious disease. She continues to improve with serial debridement and a prolonged course of voriconazole and IV ertapenem. This case of extensive fusarial infection following a degloving injury highlights the prevalence of fusarium within our environment and the importance of maintaining a high suspicion for deep fungal infection following trauma with organic material.
A Case of Hand-foot-mouth Disease Presenting with Erythema Multiforme-like Histologic Features
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Hand-foot-mouth disease (HFMD) is a viral exanthem and enanthem characterized by elliptical vesicles on the hands and feet along with painful erosions in the oral mucosa secondary to infection with enteroviruses. While rarely biopsied given the distinct clinical presentation, well developed vesicles on histology may display a lymphocytic infiltrate, epidermal dyskeratosis, and epidermal and dermal edema with intraepidermal vesiculation. However, biopsies of early-stage lesions may show a lymphocytic infiltrate with epidermal necrosis that is very similar to erythema multiforme (EM) or Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN). Recent studies on T-cell mediated cytotoxic mechanisms have shown that these three distinct diseases may share a common pathway leading to epidermal cell death and necrosis found on histologic examination. We present a case of 53-year-old male who presented with an acral, vesicular eruption. Histologic examination showed confluent epidermal necrosis, dyskeratosis, and marked papillary dermal edema suggestive of a bullous variant of EM. However, follow-up clinical information revealed that the patient's wife had recently been diagnosed with HFMD, necessitating reevaluation of the initial diagnosis. When presented with the previously mentioned histologic findings, a broad differential diagnosis, which includes HFMD, should be considered. Given that the clinical morphology, treatment, and prognosis of HFMD, EM and SJS/TEN are very distinct, clinicopathologic correlation is crucial.

WITHDRAWN

WITHDRAWN
A 74-year-old woman presented with a one-month history of a solitary nodule on a long-standing plaque that has been existing for about 50 years on his face. Physical examination revealed a dull red plaque with a diameter of 15 cm on her left face and neck. On the edge of the plaque, there was a dome-shaped nodule with centrical keratic surface, and the diameter of the nodule was about 3 cm. Histopathology analysis of the plaque showed granulomatous inflammation composed of epithelioid histiocytes and multinuclear giant cells, but caseation necrosis was not prominent. These characteristics suggested the diagnosis of lupus vulgaris, which was validated by subsequent T-spot assay. Meanwhile, the histopathology analysis on the totally excised nodule suggested the diagnosis of keratoacanthoma. The patient was then treated with quadruple anti-tuberculosis therapy. Unexpectedly, the tumor recurred at 2 months after excision and enlarged rapidly, and after the secondary surgery, non-healing ulcers appeared. Although PET-CT analysis showed no systemic metastasis, the patient gave up advanced therapy and died 1 year later probably because of malnutrition. The case indicates that keratoacanthoma arising on the lesion of lupus vulgaris may have a poor prognosis.
125

**Cutaneous Leishmaniasis in a Traveler Mimicking Squamous Cell Carcinoma**

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A 48 year old female presented to an outside facility with an ulcerated nodule on the left dorsal forearm. A punch biopsy demonstrated irregular epidermal hyperplasia and atypical squamous epithelium adjacent to ulcer, with dense dermal inflammation. Cytokeratin immunostain demonstrated infiltrative islands of squamous epithelium within the upper dermis. A diagnosis of poorly differentiated squamous cell carcinoma was rendered, and the patient subsequently underwent Mohs micrographic surgery, three stages of which were unable to clear what was believed to be tumor-associated inflammation. The patient was referred to our institution for further management options. Additional history revealed that the patient had recently traveled to Panama and developed many arthropod bite reactions. Each had spontaneously resolved, except one persistent lump on her left forearm, which subsequently ulcerated. Physical examination in our clinic revealed new subcutaneous nodules of the left extensor elbow and left antecubital fossa. Re-review of the original biopsy specimen demonstrated, beneath the squamous proliferation, tuberculoid granulomatous dermatitis with admixed plasma cells. Giemsa staining highlighted rare intracellular amastigotes, confirming the diagnosis of cutaneous leishmaniasis. This case highlights the pitfall of pseudocarcinomatous hyperplasia associated with cutaneous leishmaniasis, and the crucial nature of clinical-pathologic correlation, especially for travelers residing in non-endemic areas.

126

**Case Report: Disseminated Cysticercosis Mimicking Kaposi Sarcoma in an HIV Infected Child**

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A 4 year old HIV positive male in rural Tanzania presented for evaluation of violaceous skin and genital lesions, as well as few flesh colored subcutaneous nodules which rapidly grew after initiation of antiretroviral therapy, 8 weeks earlier. His presentation was notable for a circumferential violaceous and necrotic penile lesion and more than 30 other papules, plaques, and nodules over his trunk and extremities. The patient was clinically diagnosed with Kaposi sarcoma and started on chemotherapy, which was intensified later due to a failure to achieve complete clinical remission. At initial induction of antiviral therapy, his baseline CD4 count was 32 cells/mm\(^3\) (3%), and while receiving chemotherapy, he achieved full viral suppression with a rise in CD4 count to 455 cells/mm\(^3\) (45%). Despite therapy, his subcutaneous nodules failed to regress and continued to increase in size and number. There was now clinical concern for resistant Kaposi sarcoma or another process. Biopsy of a scapular subcutaneous nodule was obtained. Microscopic sections demonstrated a cyst composed of 3 layers—an outer cuticular layer, a middle cellular layer and an inner fibrillary layer which showed a characteristic racemose pattern, consistent with the encysted larval stage of pork tapeworm Taenia solium. The cyst was surrounded by a fibrous pseudocapsule, which showed host response in the form of chronic
inflammatory infiltrate composed of histiocytes, lymphocytes, plasma cells and numerous eosinophils. The patient was diagnosed with disseminated cysticercosis. His chemotherapy was stopped and he was started on praziquantel and albendazole for 10 days, and prednisone due to the potential for neural involvement. After completing 10 days of anti-helminthic therapy, there was a dramatic reduction in the size and number of subcutaneous nodules. Immunocompromise from HIV, as well as chemotherapy, can put patients at risk for severe/disseminated infection, and the patients’ environment may predispose them to conditions restricted to certain geographic locations. In order to ensure quality care of these patients, access to histopathology is often essential in order to accurately diagnose and manage these patients’ critical conditions.

127

**Scabies Mimicking Bullous Pemphigoid on Direct Immunofluorescence**

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We report a case of an 87-year-old ill appearing male with a history of dementia and exposure to several people treated with scabies as well as a possible history of his own scabies infection. Physical exam demonstrated edematous pink papules and scattered pustules on the back, abdomen, chest, and arms. Included in the clinical differential diagnosis were urticarial phase bullous pemphigoid, Grover’s disease, eczema, and hypersensitivity reaction. On H&E, initial sections showed focal epidermal necrosis, neutrophilic pustule, and superficial perivascular inflammation with eosinophils. Deeper sections showed focal unequivocal scabies mite parts at the surface, associated with necrosis and pustules. The biopsy sent for direct immunofluorescence showed moderate intensity, linear IgG fluorescence at the dermal-epidermal junction, non-specific dermal IgG reactivity, and negative reactivity for C3, IgA, IgM, and fibrinogen. Evidence is abundant in support of the body mounting a humoral response to scabies infection. Rise and fall of serum IgG, IgM, and particularly IgE levels all correlate with infection and treatment of scabies infection. In skin, direct immunofluorescence of scabies lesions has been reported to show various epidermal, vascular and dermal patterns of positivity with IgM, IgA, IgG, C3, and fibrin. Direct Immunofluorescence is often requested for itchy blistering skin rash particularly when bullous pemphigoid is in the clinical differential diagnosis. Case studies have shown this false positive reaction is most common in bullous scabies lesions, but clinical bullae do not have to be present to give a false positive DIF, as demonstrated in this case. H&E will be non-specific in most cases, as mite parts are only seen up to 20% of cases, even when serial sections are performed. Regardless, the H&E and clinical history were most helpful in making the correct diagnosis. It is important to recognize scabies infection can produce a false positive linear IgG fluorescent pattern on direct immunofluorescence.

128

**Neural Presentation of Systemic Blastomycosis Diagnosed by Skin Biopsy**

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Blastomyces dermatitidis is a thermally dimorphic fungus endemic to the Midwest, Ohio and Mississippi River valleys, and the Great Lakes and St. Lawrence River basins. The infection is caused by inhalation of conidia, with cutaneous and pulmonary primary sites of involvement. In immunocompromised patients,
dissemination to the skin, bone, and central nervous system can occur. We present a case of a 57-year-old Caucasian female with a history of cirrhosis secondary to non-alcoholic fatty liver disease and pancytopenia who was admitted with new onset numbness of the saddle region with bowel and bladder incontinence. Radiologic examination revealed an enhancing lesion in the conus medullaris in addition to enhancing lesions in the brain. During the workup, it was also noted that she had a one month history of non-healing skin lesions. Two punch biopsies of skin were performed and submitted for histopathology and microbiology. Histologically, the punch biopsy consisted of dermal granulation tissue with dense mixed inflammatory infiltrate and ill-defined granulomas with foreign body-type giant cells. PAS stain highlighted broad based, budding yeast forms with a double contoured cell wall and ranging in size from 8-15 µm. Microbiology culture confirmed the diagnosis of Blastomyces dermatitidis. The patient was diagnosed with disseminated Blastomycosis with CNS involvement and was started on Amphotericin B based on the dermopathology result. She was subsequently switched to voriconazole due to acute kidney injury and experienced resolution of her neurologic symptoms after 10 days of treatment. She was discharged home and placed on oral voriconazole for 12 months.

129
Mycobacterial Spindle Cell Pseudotumor
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Mycobacterial spindle cell pseudotumor is a rare benign lesion composed of spindled cells containing mycobacteria. It typically occurs in immunocompromised patients and it has been reported in multiple organ systems including the skin, lymph nodes, spleen, lung and brain. A 66 year old female presented to our clinic for a new painful 1.5 cm subcutaneous nodule on the left buttock. Her past medical history was significant for multiple skin cancers including a recent squamous cell carcinoma on the left leg treated with mohs surgery and dermatomyositis managed with two immunosuppressing medications, mycophenolate mofetil and prednisone. The nodule was excised and submitted for histologic examination. The pathology showed a large, unencapsulated subcutaneous nodule composed of spindled cells with scattered foci of histiocytes. Fite and auramine rhodamine stains revealed numerous rod shaped structures. PCR identified mycobacterium avium DNA. The patient was referred to infectious disease and she is being treated with a two to three month course of clarithromycin and ethambutol. Mycobacterial spindle cell pseudotumor is an uncommon manifestation of a mycobacterial infection in which there is a benign proliferation of spindled cells containing mycobacteria. It occurs almost exclusively in immunocompromised patients, especially in patients with AIDS. While multiple mycobacterial species have been identified in these pseudotumors, mycobacterium avium intracellulare complex is the most common cause. Mycobacterial spindle cell pseudotumor has been reported in various organ systems including the skin where it can mimic other cutaneous spindled cell or mesenchymal neoplasms such as dermatofibroma, nodular fasciitis, xanthogranuloma and Kaposi’s sarcoma. This is an important entity to consider in the differential of a cutaneous spindle-cell neoplasm, especially in patients who are immunocompromised.
Disseminated Acid-Fast Bacilli Infection in a Patient with Metastatic Melanoma Treated with a PD-1 Inhibitor
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We report a case of a 76 year old woman with periorbital melanoma that subsequently metastasized and was treated with surgery, radiation, pembrolizumab and ipilimumab, who developed nonpruritic painless raised erythematous lesions over the extremities and chest for 3 weeks. Examination of the biopsy showed histiocytes, poorly formed granulomas and acute inflammatory cells in the subcutaneous fat. Staining revealed numerous gram positive, FITE stain positive, acid fast bacilli (AFB) throughout the subcutaneous infiltrate. Blood cultures grew acid fast bacilli in 8 days on both aerobic and anaerobic plates. Samples have been sent for Next Generation Sequencing for speciation. This is the first time an association between disseminated acid fast bacilli and pembrolizumab therapy has been documented. The patient had previously developed pembrolizumab-induced hepatitis, and had been treated with corticosteroids; therefore, it is also possible that the infection was secondary to steroid use. Pembrolizumab works primarily by inhibiting Programmed Cell Death Protein-1 (PD-1). PD-1 is an immunomodulator, promoting apoptosis of antigen-specific T cells while preventing apoptosis of helper T cells. Melanomas often express PD-1, inhibiting the activation and proliferation of CD8+ T cells. Numerous studies have demonstrated that PD-1 inhibited mice are exquisitely sensitive to AFB infection. Ours is the first documented case of disseminated AFB infection in a melanoma patient treated with anti-PD1 therapy. A causal relationship between the two cannot be established by this case alone. However, this experience, in conjunction with data from animal models and the underlying biochemistry, provides compelling evidence to investigate the possible relationship between PD-1 inhibitors and susceptibility to disseminated AFB infection.

Atypical Cutaneous CMV Infections in Non-AIDS Patients; A Report of 2 Cases
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Cytomegalovirus (CMV) is a DNA virus belonging to the herpes virus group. The infection from this virus is increasing in the immunocompromised patients, especially AIDS or organ transplant recipients. Nevertheless, the skin lesion is uncommon. We present two cases of atypical cutaneous CMV infection. The first case was a 66 year-old Thai woman with overlapping syndrome, on treatment with multiple immunosuppressants. She presented with high grade fever and asymptomatic purpuric papules and pustules on her forearms and legs. Laboratory investigations showed bicytopenia from complete blood count. Chest radiography and high-resolution computed tomography of the chest revealed lung nodules. The second case was a 49-year-old Thai woman with systemic lupus erythematosus (SLE) and obtained multiple immunosuppressants. She presented with fever and multiple erythematous papules with ulcers of the extremities and trunk. Basic laboratory investigations were normal. The skin biopsies from both cases showed perivascular infiltration with inflammatory cells and numerous large round eosinophilic intranuclear inclusion bodies (owl's eye appearance) in the dermis. The CMV antigen stained the cytoplasm of owl's eye cells. Further investigations presented high level CMV viral load in both cases. Finally, the diagnosis CMV infection was made. In conclusion, we presented the cases with
cutaneous CMV infection in immunocompromised host. This group of patients is susceptible to variety of infections and presented with atypical manifestations. Cutaneous manifestations with skin biopsy in some cases may play a major role for the correct diagnosis and prompt treatment.

132
Interstitial Granuloma Annulare-like Secondary Syphilis
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Secondary syphilis, also known as the “Great Imitator,” has various clinical and histopathologic manifestations. Herein we report a case of secondary syphilis with distinctively unusual histologic findings simulating interstitial granuloma annulare. In addition, the pathophysiology of granulomatous formation in secondary syphilis will be discussed. A 50-year-old man presented to the Teledermatology Clinic with a one-month history of a non-pruritic eruption which started on his chest and spread to his abdomen, back, and neck but spared his palms and soles. On investigation, he previously developed a non-painful ulcer in his glans penis for which he attributed to trauma during sexual activity. Teledermatologic photos showed numerous erythematous papules with urticarial-to-granulomatous-like appearance. Upon further evaluation in the Dermatology Clinic, the patient reported unprotected homosexual encounters. Histologic examination of a representative red papule showed superficial and deep perivascular and periadnexal lymphohistiocytic plasmacellular infiltrate diffusely between collagen bundles. Immunohistochemistry with antibodies to Treponema pallidum confirmed the diagnosis of syphilis. Further work-up revealed a RPR titer of 1:132 and a negative HIV antibody test. Adding this unique case to the literature, we conclude that secondary syphilis should be included in the differential diagnosis of “atypical” interstitial granuloma annulare especially when a dense perivascular lymphocytic infiltrate with plasma cells is present.

133
Recrudescence of Syphilis: Increasing Incidence at a Tertiary Center and Description of a Unique Presentation
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Introduction: The incidence of syphilis has been increasing in the United States since 2001. We quantified the incidence of syphilis from 2008-2016 at Mount Sinai Division of Dermatopathology and assessed the histologic, immunohistochemical, and clinical features in a subset of cases. Methods: We performed keyword searches for "syphilis" and "lues" in the Mount Sinai Dermatopathology database, spanning from 2008-2016. Only positive or highly suspicious biopsies by anti-treponemal immunohistochemistry (IHC) were considered true positives. Results: The incidence of syphilis increased annually after 2009, reaching 15.1 per 100,000 cases accessioned (95% CI 28.4-86.2). From 2014-2016 the incidence (16.4 per 100,000 cases; 95% CI 7.1-20.4) is >2-fold higher than the two prior three-year periods. From 2014-2016, all 13 patients were male and seven (54%) had a clinical differential of syphilis. Five cases (30.8%) had 6 or more of the common histologic features; perivascular inflammation
with endothelial cell swelling was the most common (12/13 cases). Neutrophil exocytosis without neutrophils in the stratum corneum was a unique finding in four cases (30.7%). Two of these lacked plasma cells and clinical suspicion. Conclusion: Our database shows an increased incidence of secondary syphilis since 2009. While no single histologic pattern was sensitive or specific, neutrophilic exocytosis was a unique finding when both plasma cells and clinical suspicion were absent. Dermatopathologists must remain suspicious of syphilis when reading inflammatory biopsies with a range of features, and screening by anti-treponemal IHC should be strongly considered.

134
Blastomycosis-like Mucocutaneous Candidiasis: A Case Report
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An 88-year-old male with diabetes mellitus and obesity presented with a 6-month history of slowly enlarging, verrucous plaque of the nasal ala, tip, and upper lip. Histopathologic examination of the skin lesion showed pseudoepitheliomatous hyperplasia, infiltrative appearing squamous islands in the dermis, and dense chronic lymphocytic and granulomatous inflammation in the dermis. There was overlying hyperkeratosis, hemorrhagic crust and serous crusting. Grocott’s methenamine silver stain demonstrated numerous intracorneal yeast and pseudohyphae and culture revealed Candida albicans/dubliniensis. These histopathologic changes were most consistent with blastomycosis-like pyoderma. A review of the literature reveals that the majority of previously reported cases of blastomycosis-like pyoderma are caused by bacterial infection rather than fungal infection. We report a case of blastomycosis-like mucocutaneous candidiasis.

135
Correlation Between Histopathologic Features and Likelihood of Identifying Superficial Dermatophytosis with Periodic Acid Schiff-Diastase Stain: A Case-control Study
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Background: Periodic Acid Schiff-Diastase (PAS-D) stains are used routinely in dermatopathology, even when superficial dermatophytosis is absent from the diagnostic impression. Conventional teaching is that parakeratosis or intracorneal neutrophils justify the use of PAS-D stain to identify possible dermatophytosis. However, these beliefs have not been rigorously tested. This study investigates the correlation of histopathological features with the likelihood of identifying superficial dermatophytosis on PAS-D stain. Methods: Skin biopsy cases in which a PAS-D stain was ordered in routine practice were retrospectively reviewed by a dermatopathologist blinded to clinicopathologic information and initial stain interpretation. We compared histopathologic findings of cases with dermatophytosis to those without. Results: Dermatophytes were identified on H&E staining in 49 (77.8%) of the 63 total positive cases. Diffuse compact orthokeratosis (p<0.001) and focal parakeratosis (p=0.03) were significantly more frequent in dermatophytosis. Neutrophils in stratum corneum and spongiosis did not differ between the groups significantly. When present, fungal elements were most frequently observed within compact orthokeratosis (62.0%) and parakeratosis (31.8%) but rarely within intracorneal pustules (12.7%). In some dermatophyte cases, intracorneal neutrophils (47.6%) or parakeratosis (17.5%) were
entirely absent. Conclusions: In the appropriate clinical setting, the presence of compact orthokeratosis or focal parakeratosis justifies PAS-D staining. The absence of intracorneal neutrophils or parakeratosis is insufficient to exclude the possibility of dermatophytosis. Given the variability of stratum corneum changes in dermatophytosis, a low threshold to perform a PAS-D stain appears to be reasonable. These data may contribute to discussions regarding appropriate use criteria of the PAS-D stain in dermatopathology.

Inflammotry Diseases

136

Follicular Psoriasis: A Rare Variant of Psoriasis
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Follicular psoriasis is a clinicopathologic variant of psoriasis. There are very few cases reported in the literature, possibly due to the lack of awareness of this unusual type of psoriasis. Psoriasis is a chronic autoimmune T-cell mediated skin disorder. There are several clinical variants. The most common variant is psoriasis vulgaris which commonly involves the extensor surfaces. Here we report an unusual case of a 66 year old female who presented with multiple variably sized circumscribed areas of scaly erythematous follicular papules on the trunk. The lesions had some clinical features of eruptive psoriasis but also had a decidedly follicular pattern. The clinical differential diagnosis included eruptive psoriasis, parapsoriasis, mycosis fungoides and pityriasis rubra pilaris. Punch biopsies of the lesions showed dilated follicular infundibula with marked parakeratotic plugging and Munro microabssceses, hypogranulosis, and small spongiform pustules involving the follicular infundibulum. There was associated confluent “shoulder” parakeratosis with hypogranulosis. Other areas showed features of eruptive psoriasis. The histologic findings were consistent with a follicular variant of psoriasis, which at least in this case may be a subtype of eruptive psoriasis.

137

Histiocytoid Sweet Syndrome: An Overlooked Histological Variant of Neutrophilic Dermatosis
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Histiocytoid Sweet Syndrome (HSS) is a variant of Sweet syndrome that is known as an acute febrile neutrophilic dermatosis. HSS clinically presents as a classic sweet syndrome with tender cutaneous erythematous plaques and nodules in patients with fever and neutrophilia that may be triggered by infection, autoimmune disease or malignancy. However, HSS will histologically show a histiocytoid dermal infiltrate instead of a neutrophilic infiltrate. Herein, we describe a case of HSS in a 45 year old woman who developed painful, erythematous plaques and nodules on trunk and extremities after an upper respiratory infection. Skin biopsy revealed a diffuse mononuclear and histiocytoid infiltrate in the dermis and subcutaneous fat. The pattern of immunohistochemical staining with CD68, CD163, and
myeloperoxidase stains confirmed our impression of HSS. This case demonstrates that clinicopathologic correlation is critical for the diagnosis of HSS so that this entity may not be histologically mistaken for other mononuclear/histiocytic inflammatory conditions.

138

**Necrobiotic Interstitial Granulomatous Dermatitis with Granuloma Annulare-like Pattern Following Liposuction**

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A 41 year old female presented with bilateral 1 cm erythematous tender recurring nodules for the past 6 months underlying liposuction scars on the thigh. The clinical differential diagnosis included panniculitis, tumid lupus, and infection. A punch biopsy was performed. Histopathologic findings demonstrated an interstitial to palisading granulomatous infiltrate with necrobiosis and dermal mucin deposition involving the reticular dermis and extending into subcutaneous tissue. Special stains for microorganisms where negative. There was no evidence of foreign material. The histopathologic pattern of interstitial granulomatous inflammation with prominent necrobiosis/mucin deposition was felt to be most consistent with a granuloma annulare-like pattern. Necrobiotic granulomatous dermatitis is seen in association with granuloma annulare, necrobiosis lipoidica, necrobiotic xanthogranuloma, rheumatoid nodules, rheumatic fever nodules, and in reactions to foreign material or vaccines. There are some relatively well know adverse effects of liposuction which include allergic contact dermatitis to the surgical site, seroma, post inflammatory changes, and infection. This is the first report to our knowledge of necrobiotic interstitial granulomatous dermatitis with a granuloma annulare-like pattern following liposuction.

WITHDRAWN
Juvenile xanthogranuloma (JXG) is a well-documented self-limited disease of histiocytes and giant cells. There is a lack of literature describing the histologic evolution of this disease. We present a case of an early JXG and the histologic changes following excision. Our patient was a 7 month old male with a past medical history significant for atopic dermatitis who presented to our office for a follow up. On exam there was a 0.8 x 0.7 cm red, umbilicated papule on his abdomen which had been growing for the past month was noted. Given the atypical appearance of the lesion and rapid enlargement, a shave biopsy was performed. Histological sections revealed an irregular epidermis with a cellular dermal neoplasm composed of spindle shaped plump cells arranged in fascicles. The cells had elongated nuclei with amphophilic cytoplasm. There were numerous infiltrating lymphocytes with scattered eosinophils. The lesional cells were positive for CD68, Factor XIII and negative for CD1a, S100. Histological sections from the re-excision revealed a dermal neoplasm with infiltrative borders composed of polygonal cells arranged in vague fascicles with indistinct borders, pale, foamy cytoplasm and round to oval nuclei. Numerous eosinophils with Touton giant cells were seen. Although the etiology of JXG is unknown, the self-limiting nature and characteristic histologic progression as seen in this patient argues that it is an inflammatory reactive process. Dermatopathologists should also be aware of the absence of Touton giant cells in early JXG.

Programmed cell death 1 receptor (PD-1) is an inhibitory receptor present on activated T cells. The interaction between PD-1 and its ligands (PD-L1), which are often expressed on tumor cells, inhibits the ability of the activated T cell to produce an immune response. This leads to inhibition of the antitumor activity of cytotoxic T cells. Nivolumab and pembrolizumab are monoclonal antibodies that target PD-1. They have been FDA approved to treat unresectable or metastatic melanoma. Cutaneous adverse events occurred in about 50% of patients treated with PD-1 inhibitors and were categorized as maculopapular eruption, vitiligo, pruritus, acne, or mucositis. Interestingly, patients who developed
cutaneous adverse events had significantly longer progression-free intervals compared with patients who did not develop cutaneous adverse events. Psoriasiform eruptions have not been reported except for a few recently published case reports. We report a series of three patients treated with PD-1 inhibitors for different malignancies who all developed a psoriasiform eruption. The exact pathogenesis of a psoriasiform eruption with PD-1 receptor inhibition is not well understood. A recent study examined PD-1 knockout mice and showed that these mice had increased levels of IL-17A and IL-22, leading to a psoriasis phenotype. The study then treated wildtype mice with a PD-1 antibody and showed an increase in IL-17A and IL-22 levels as well as exacerbation of psoriatic disease. Therefore, a proposed mechanism of psoriasiform eruptions with PD-1 inhibitors is that the blockade of immune-checkpoint receptors augments TH1 and TH17 cell activities. Although this immunologic shift may lead to a psoriasiform eruption, enhanced TH1 activity may also correlate with a higher antitumor effect, leading to an improved overall survival. Nonetheless, further studies are needed to elucidate the exact mechanism and implications of psoriasiform eruptions in patients treated with PD-1 inhibitors.

142
Acute Mucocutaneous Methotrexate Toxicity With Marked Eosinophilic Infiltrate
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Methotrexate toxicity in mucocutaneous areas is not usually associated with tissue eosinophilia. We describe a case of acute methotrexate-induced pancytopenia and mucocutaneous erosions with interface dermatitis and eosinophils. A 76-year-old African American female with a history of bullous pemphigoid and chronic kidney disease on methotrexate therapy presented with lower extremity cellulitis, developing erosions of the oral mucosa, axillae, and inguinal areas during hospitalization after daily dosage of methotrexate. Physical examination displayed oral erosions and shallow circular cutaneous erosions on neck, back, chest, abdomen, arms, legs, and feet. Laboratory results showed pancytopenia and elevated liver function test. A lesional skin biopsy revealed an irregular acanthotic epidermis with interface dermatitis, individual dyskeratotic cells at all levels of the epidermis, focal confluent dyskeratosis, focal acantholysis and a superficial perivascular and interstitial lymphocytic infiltrate with numerous eosinophils. Direct Immunofluorescence results were negative. Methotrexate was stopped, and the patient was given leucovorin, leading to improvement of anemia, liver function test and cutaneous lesions. The patient subsequently died from infectious complications. The histopathologic changes in acute mucocutaneous toxicity range from pauci-inflammatory erosions with dyskeratotic keratinocytes to interface dermatitis and infrequently seen eosinophils. This case exemplifies that interface dermatitis with marked eosinophilic infiltrate can be found in the setting of acute mucocutaneous methotrexate toxicity.
143
**Vaccine Associated Eruptive Psoriasis with Tissue Eosinophilia**
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Psoriasis is a chronic inflammatory, immune-mediated disease with multiple known triggers including stress, infections and medications. The influenza and tetanus and diptheria (Td) vaccines have both been reported in association with new-onset and flares of existing psoriasis. We present a 50 year-old male with new-onset erythematous scaly plaques on the scalp, face, trunk and extremities with vesicular pustules and desquamation on hands and feet. He had a history of untreated scaling of the scalp but no previous medical history of psoriasis. The patient was on no medications or supplements, but had received MMR, polio and HBV vaccines 3 weeks prior to presentation. Histology revealed spongiotic and psoriasiform dermatitis with focal spongiform pustulation and overlying psoriatic scale, as well as dermal inflammatory infiltrates containing scattered eosinophils; peripheral eosinophilia was absent. Although it is unclear which vaccine triggered the eruption, MMR, polio and HBV vaccines have not been previously reported in the literature as a cause of eruptive psoriasis.

144
**Cornstarch: An Indicator of Occult Drug Use**
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We report the case of a 30-year-old female with a remote history of intravenous (IV) drug abuse, presenting with episodic, multicentric forearm lesions previously attributed to e. coli infected cat scratches. The most recent presentation began as a base of thumb papule which was self-treated with incision and reported to express purulent material. In contrast, a subsequent base of thumb biopsy demonstrated milky-white, non-purulent material. Histologic examination revealed a granulomatous inflammation with giant cells reacting to particulates. These crystalline, birefringent particles, ranging in size from 7 to 30 microns, were suggestive of cornstarch and small amounts of talc. Immunohistochemical stains and cultures were negative for infectious etiologies. Skin-popping, the subcutaneous injection of an illicit substance, is a last resort for many addicts with damaged veins and often results in abscess formation. Filler compounds like talc, cornstarch, flour, and other toxic substances, which are commonly mixed into these injected illicit substances, likely potentiate irritation. Historically, both talc and cornstarch have induced granulomatous peritoneal reactions; however, case reports of similar cutaneous reactions are scant. In this case, identification of cornstarch particles accompanying the granulomatous inflammation was imperative. Due to its relatively quick degradation and metabolism, corn starch is considered an indicator of recent drug use. We present this case as an example of histologic particulate identification as a method of confirmation for clinically occult drug use.
Pseudolymphomatous folliculitis is an uncommon inflammatory condition of the skin characterized by an intradermal and perifollicular inflammatory infiltrate that may histologically resemble primary cutaneous extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma). T and B cell clones can be detected in cases of pseudolymphomatous folliculitis, while clonality cannot be demonstrated in a significant number of MALT lymphomas (up to 30%). Our patient was a 69-year-old woman who presented with a solitary pruritic, pink papule on the left lower eyelid that did not respond to doxycycline treatment. Histologic sections of the excisional biopsy showed a dense perivascular, perifollicular, and interstitial lymphohistiocytic infiltrate with an infiltrative to nodular appearance that raised concern for a low grade lymphoproliferative disorder. As previously described, numerous CD1a+ dendritic cells (DCs) were noted within the involved hair follicles and throughout the intradermal lymphocytic infiltrate, findings uncharacteristic of MALT lymphoma. Langerin staining revealed an increased population of Langerhans cells within the epidermis and follicular epithelium as well as within the dermis. However, the number of CD1a+/langerin- dermal DCs significantly outnumbered the total langerin+ population in both the epidermal, follicular, and dermal compartments. Immunohistochemical evaluation for CD163 revealed an additional population of histiocytic cells that appeared to be CD1a+/langerin-. A PD-1 immunostain highlighted a subset of T cells present throughout the biopsy, including expression within B cell clusters. A PD-L1 immunostain highlighted clusters of weakly PD-L1+ cells concentrated within the B cell aggregates. It has previously been suggested that pseudolymphomatous folliculitis may be distinguished from cutaneous marginal zone lymphoma based on presence of CD1a and PD-1-expressing cells. Our findings support this, although they indicate that the DC prominence in this disorder is primarily mediated by non-Langerhans cell dermal indeterminate cells with a CD1a+/langerin- immunophenotype.

Heparin is well known for inducing a variety of dermatoses, including localized cutaneous allergic reactions, ecchymoses, skin necrosis, and rare heparin-induced hemorrhagic bullae. Both unfractionated heparin and low-molecular weight heparin formulations have been implicated. We present a case of heparin induced edematous bullous dermatosis in a 65-year-old woman with acute promyelocytic leukemia and a history of disseminated intravascular coagulation. The patient underwent IV infusion of unfractionated heparin in the left antecubital fossa after the development of stroke like symptoms. Several painful, flaccid bullae developed on the upper forearm, extending downstream of the injection site, ranging from a few millimeters up to three centimeters. These bullae arose 3 days after the heparin infusion. Bullae exhibited a positive Absoe-Hansen sign and contained clear serous fluid without purulence or hemorrhage. Biopsy revealed a large bulla with re-epithelialization, aged degeneration of the epidermis, focal subepidermal hemorrhagic blister and prominent papillary dermal edema. Small amounts of red cells and neutrophils were present in the bulla. No thromboembolism
was identified. The patient’s bullae improved in 7 days with discontinuation of heparin and a short course of oral prednisone. In summary, we report a case of heparin induced bullous dermatosis adjacent to the injection site on the forearm without significant hemorrhage, thrombosis, or necrosis.

147

148  RESIDENT
Florid Granuloma Annulare-Like Reaction in Regional Lymph Nodes Following "Regression" of Red Pigment in Tattoo
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A healthy 50-year-old woman had a tattoo performed on the posterior aspect of her neck. Shortly thereafter she noted redness and tenderness at the tattoo site. On examination, she was also found to have enlargement of the draining lymph nodes. Treatment with cephalaxin and hydrocortisone cream was instituted, without success. Within a few months the red pigment had disappeared from the tattoo
We report a case of hydroa vacciniforme in a 20 year old woman who presented with a 13 month history of recurrent vesicular eruptions on the nose, forearms, hands, and feet. The lesions appeared 8-12 hours following prolonged sun exposure during the late spring and summer months, unassociated with sunburn, pain, or pruritis. Most vesicles persisted for 5 to 7 days followed by crusting and healing without scarring. No exposure to a photosensitizing agent could be identified. The patient denied experiencing any similar reaction in the past. Physical exam revealed multiple tense vesicles (2-5 mm) on an erythematous base, on the nasal dorsum, dorsal hands, and left 4th-5th toes. Exam was otherwise unremarkable. CBC with differential count was within normal limits, as well as liver and renal function tests, antinuclear antibody, and erythrocyte sedimentation rate. EBNA-IgG and viral capsid antigen (VCA)-IgG antibodies were found to be positive while VCA-IgM and IgD early antigen were negative, suggesting latent infection. Sections showed ballooning vesiculation with papillary dermal edema and a mononuclear cell infiltrate including enlarged cells. The cells exhibited irregularly-shaped and angulated nuclei. Immunohistochemistry for EBER was positive in these nuclei. Direct immunofluorescence performed was negative. Findings were consistent with a diagnosis of hydroa vacciniforme. The patient was started on beta-carotene (Lumitene) 15mg daily and advised to avoid direct exposure to sunlight. Exam at 1 month follow-up showed no new vesicle formation. Hydroa vacciniforme is a rare chronic photodermatosis of unknown etiology characterized by recurrent vesicles occurring within 1-2 days of sun exposure that heal with varioliform scarring. As onset typically occurs in childhood and resolves by late teens, this case is unusual. Diagnosis is based on history, histopathology, and normal lab findings to differentiate from polymorphous light eruption and porphyrias, among others. Confirmation with UVA phototesting may be performed. Sun protection and avoidance are mainstays of management, and carotenoids have been used as a treatment modality, though data pertaining to efficacy is sparse.
150

**Gottron Papules of Dermatomyositis Show Histopathological Features Similar to Localized Lymphedema**

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Background: Although Gottron papules are a classic finding in dermatomyositis, they are only reported in very few papers in the literature, and the largest series on the subject only includes 11 cases.

Objective: To study the main histopathological features of Gottron papules in a series of twelve patients with confirmed dermatomyositis. Also, to evaluate which of such findings could be explained in the context of localized lymphedema.

Methods: We evaluated hematoxylin & eosin (H&E) stains on all cases. We also performed histochemical stains to evaluate for dermal deposition of mucin. Finally, we studied the CD123+ cell population in the inflammatory infiltrate by immunohistochemistry.

Results: We found that the epidermis was either acanthotic or hyperplastic in all cases. Edema of the papillary dermis was a remarkable feature in four cases. We found a significant dermal inflammatory infiltrate in all cases but one, and this infiltrate was primarily composed of lymphocytes and histiocytes. A few scattered neutrophils and eosinophils were found in some cases. Mucin deposition in the reticular dermis was an inconstant feature, only found in six of our cases. Vacuolization of the basal layer was also a frequent finding, although it was not found in three of the cases. Basement membrane thickening was difficult to identify by H&E stains, although it was seen on PAS-D stains in most cases. We identified CD123+ cells in all cases but two; in nine cases, they were found in clusters of up to 12 cells. Intraepidermal CD123+ cells were also found in eight cases. All cases but one showed lymphangiectasia in the upper part of the dermis, including the papillary and reticular dermis. In addition, collapsed lymphatics were evident underlying the dermal sclerosis.

Conclusions: We conclude that Gottron papules show features similar to those seen in localized lymphedema.

151

WITHDRAWN
Acquired Macular Hyperpigmentation: A Case Report of Early Erythema Dyschromicum Perstans

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Erythema Dyschromicum Perstans (EDP) is a rare acquired macular hyperpigmentation disorder of unknown etiology usually affecting young adults of Central and South American populations. The histopathological findings are non-specific and can be subdivided into early and late. We report a case of a 35-year-old El Salvadoran male with a 3 month history of pruritic lesions involving his back, which spread to his chest and axillae. Dermatologic exam was significant for hyperpigmented, heterogeneous blue-black plaques and macules diffusely involving the back and torso. His axillae showed areas of erythema with central darkening. Punch biopsy showed vacuolar change and patchy lichenoid interface dermatitis with superficial perivascular lymphohistiocytic inflammation, and prominent dermal melanophages. The histopathologic findings of EDP vary depending on the time of the biopsy in relation to the activity of the lesion. EDP is commonly biopsied in its late stage and demonstrates sparse inflammatory infiltrate with prominent dermal melanophages, which may suggest a resolving lichenoid dermatitis such as lichen planus (LP). The lack of histopathologic findings such as hypergranulosis and basilar squamatization, combined with the clinical findings, favored a diagnosis of EDP. In our case, the inflammatory infiltrate was more than usually observed in EDP and likely represents the early phase, which is often not biopsied. EDP is part of a spectrum of acquired hyperpigmentation disorders that can have significant cosmetic morbidity. Early lesions are uncommonly encountered in dermatopathology and are clinically characterized by large areas of hyperpigmentation with erythematous borders. Pathology demonstrates patchy lichenoid lymphohistiocytic and perivascular inflammation with scattered dermal melanophages. The case presented here highlights the clinical and histopathology findings in the early phase of EDP.
Flame Figures in Bullous Pemphigoid: A Case Report and Review of the Literature

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Importance: Flame figures are a histological finding seen in eosinophilic cellulitis (Wells syndrome) and several other conditions. They consist of deposition of eosinophil granules around collagen bundles, giving a stellate, bright eosinophilic appearance. In addition to Wells syndrome, they may be seen in dermatophytosis, eczema, insect bites, and parasitic infections. Even though Wells and colleagues first noted in 1979 the presence of flame figures in bullous pemphigoid (BP), only few cases have been reported to date in the literature documenting this phenomenon. Observations: The patient was a 66-year-old female with erythematous papules and plaques on both arms and legs, previously diagnosed with scabies. A tense vesicle on an erythematous base on the right posterior thigh was biopsied. Histological examination revealed a subepidermal vesicle with numerous eosinophils and neutrophils. The dermis showed a diffuse eosinophilic infiltrate with flame figures. Direct immunofluorescence (IgG and C3) and a serology panel (180 and 230 IgG antibodies) were positive for bullous pemphigoid. A thorough search brought up only six prior cases of BP with flame figures in the English language literature. Conclusion: This is seventh reported case of BP with flame figures. It highlights that flame figures are not exclusively seen in Wells syndrome, and may be seen in other conditions as well, including BP uncommonly. Awareness of this finding can help prevent misdiagnosis.
Background: Erythroderma is defined as generalized erythema involving >90% of body surface area accompanied by a variable degree of scaling. Most commonly, erythroderma is the result of exacerbation of a pre-existing dermatosis, drugs or cutaneous T-cell lymphoma. Correct diagnosis is essential to direct therapy, yet the value of skin biopsy in this scenario has been debated. We present a case of de novo erythroderma of unique cause in which skin biopsy and careful clinical correlation were essential to elucidation of the etiology. Case Report: A 63-year-old Cambodian woman with no history of previous dermatosis presented with a 4-day history of a diffuse rash. She denied new contacts or products, or any new medications. Physical examination revealed diffuse erythema with fine scale confluent on the back, face, scalp, and chest. Her abdomen and lower extremities had erythematous, blanching macules. No mucosal involvement was noted. Vital signs were normal. A punch biopsy revealed a mild interface dermatitis with scattered dyskeratotic keratinocytes and lymphocyte exocytosis. Peripheral flow cytometry and T-cell rearrangement studies were negative. A positive HSV IgM antibody was the only laboratory abnormality. The diagnosis of Herpes simplex virus-associated erythema multiforme (HAEM) with an erythrodermic presentation was made. The patient was started on topical corticosteroids with good response and plans to follow up as an outpatient. Conclusion: Interface dermatitis is a rare finding in skin biopsies of erythroderma. Although the role of skin biopsy in diagnosis of erythroderma has been questioned, this case illustrates that histopathological findings may be central in establishing its cause. An erythema multiforme-like histology, combined with serologic evidence of recent herpesvirus exposure, lead to the accurate identification of the etiology in this case. We believe that this represents the first case of HAEM presenting as erythroderma reported in the literature.

A Case of Interstitial Granulomatous Dermatitis Due to Systemic Lupus Erythematosus in a Pediatric Patient
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A twelve year old female with systemic lupus erythematosus developed violaceous, semi-firm, papules and plaques on the symmetrical trunk and upper arms. Lesions were moderately pruritic. Systemic therapy for her lupus included prednisone and hydroxychloroquine, and cyclophosphamide infusions had been added for lupus nephritis six months prior to skin eruption. Lesions were intermittent, lasting 1-2 weeks, and self-resolved with hyperpigmentation. There was no improvement with topical steroids. She presented to dermatology, and skin biopsy showed superficial and deep mixed inflammatory infiltrate, with CD68 stain highlighting a predominance of histiocytes. There was no evidence of vasculitis, panniculitis, or findings specific to lupus erythematosus. Therefore, a diagnosis of interstitial granulomatous dermatitis was made. Her systemic immunosuppressive therapy was modified;
Drug reaction with eosinophilia and systemic symptoms (DRESS) is a rare but potentially life-threatening drug-induced hypersensitivity reaction. This syndrome is characterized by a late-appearing, slow-progressing diffuse maculopapular rash accompanied by atypical lymphocytes, eosinophilia, and systemic symptoms such as fever, lymphadenopathy, hepatic compromise, and renal dysfunction. DRESS is most commonly caused by exposure to antiepileptic agents and allopurinol, but has also been associated with sulfonamides, some antibiotics, raltegravir, and vemurafenib. We report a case of a 46-year-old female on pentoxifylline for four weeks for cirrhosis presenting with a painful whole-body rash, desquamation, and eosinophilia with hepatorenal syndrome. A skin biopsy showed chronic spongiosis and interface dermatitis with perivascular and interstitial chronic inflammatory infiltrate with eosinophils. Based on clinical and histological findings, the patient was diagnosed with DRESS. To our knowledge, this is the second reported case of DRESS syndrome following pentoxifylline exposure.

Nail Histopathology in Refractory Classical Adult (Type I) Pityriasis Rubra Pilaris
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Histopathologic nail findings in pityriasis rubra pilaris (PRP) are rarely described in the literature. We present a patient with refractory classical adult (type I) PRP who presented to our facility at age 45 with a two-year history of a rash that started as a small patch on her chest and progressed into confluent plaques and eventually erythroderma. On physical exam, the patient had orange-yellow scaly plaques with islands of sparing involving the face, trunk, and upper extremities as well as palmoplantar keratoderma. All fingernails were markedly dystrophic and tender to palpation with distal hyperkeratosis, yellow discoloration, onycholysis and subungual debris. Pincer nail deformity and joint swelling of the distal interphalangeal joints were also present. She underwent four nail biopsies over several years to document extent and severity of disease before ultimately having all fingernails removed due to treatment refractory pain. Biopsies exhibited epidermal hyperplasia of the nail plate with overlying columns of parakeratosis alternating with compact orthokeratosis, focal spongiosis and intermittent collections of serum. The earliest specimen showed a mild focal acute inflammatory infiltrate within a pocket of serum; no other specimen had a significant inflammatory infiltrate. Special
stains performed in three specimens revealed bacterial colonization yet no microbial infection. Dilated, tortuous dermal capillaries and a confluent granular layer, characteristic of psoriatic nails, were not present in any specimen. We present this case to highlight the histopathologic nail findings of classical adult (type I) PRP.

159
Histopathologic Characterization of Lichen Sclerosus
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Lichen Sclerosus (LS) is an inflammatory skin condition more common in women characterized clinically by pruritic white plaques with overlying atrophic epidermis imparting a “cigarette paper” quality to skin. Classically found in peri-genital regions, it can also occur at extragenital sites. Overall, the pathogenesis of LS is poorly understood. While the histopathologic features of LS are similar at the different sites, genital lesions may have a risk of progressing to carcinoma, suggesting the possibility of different underlying mechanisms. In an effort to better characterize LS, we compared the histopathologic features and staining patterns of extragenital and genital LS. METHODS: We retrieved archival slides from patients diagnosed with LS from 2009-2014, confirmed the diagnosis histologically, and evaluated histologic features, elastic fiber distribution, and MMP-9 expression. RESULTS: 42 cases of genital LS and 41 cases of extragenital LS were compared. Both types were more common in women, and most biopsies displayed common features including atrophy of the epidermis, attenuation of rete ridges, homogenization of the papillary dermis, and loss of superficial dermal elastic fibers. All cases expressed MMP-9 in histiocytes. However, giant cells, elastophagocytosis (ingestion of elastic fibers by macrophage-derived cells) and interstitial granulomatous infiltrate were observed significantly more commonly in extragenital LS. Genital LS, in contrast, was more likely (in a subset of cases) to exhibit a previously undescribed increase in mid and deep dermal elastic fibers. CONCLUSION: Our study is the first to comprehensively describe elastophagocytosis in LS and link it to extragenital LS specifically. This is also the first study to characterize MMP-9 staining patterns of LS. Our results suggest diverging mechanisms in the development of extragenital and genital LS, and offer new avenues of study for this debilitating disease.

160
Cutaneous Crohn Disease with Superimposed Psoriasis: A Unique Case with Overlapping Histology
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Crohn disease is an idiopathic, chronic inflammatory disorder of the gastrointestinal tract. The diagnosis rests on a combination of radiologic, endoscopic, and histopathologic features. Sterile granulomatous inflammation is a common histopathological finding in Crohn disease, and when present, is helpful in making the diagnosis. Patients with Crohn disease are more prone to developing a number of cutaneous inflammatory eruptions, which include both granulomatous and non-granulomatous processes. Granulomas appearing in nodular, ulcerated or plaque-like lesions, at sites well removed from involved mucosal surfaces, is often referred to as “metastatic” Crohn disease. We recently encountered a unique case in which a patient with Crohn disease presented with skin lesions with histopathologic features of
both pustular psoriasis and granulomatous inflammation of cutaneous Crohn disease. To our knowledge, this may represent the first reported case in which such findings were seen concomitantly in the same patient, in the same lesions. Review of the literature suggests that the intersection of these two histopathological reaction patterns may not be pure coincidence. Clinical-pathologic correlation of this case will be discussed, along with a review of the potential mechanisms of this unique disease presentation.

161

**Annular Lichenoid Dermatitis of Youth in New York City.**

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A 35 year-old female from Israel, with no significant past medical history, presented with a one month history of four asymptomatic round to oval patches over the left abdomen and ipsilateral inguinal fold. The lesions appeared to be in different stages, some exhibiting mild erythema and some appeared to be fading, resulting in patches with a brown border and a hypopigmented center. A punch biopsy from one of the lesions revealed a lichenoid dermatitis, with a bandlike inflammatory cell infiltrate which tended to favor the tips of the rete ridges and spare the interpapillary plates, composed of small and monomorphous lymphocytes. After clinicopathologic correlation, the diagnosis of annular lichenoid dermatitis of youth (ALDY) was established. ALDY is a newly described entity, first reported by Annessi et al in 23 patients with ages ranging between 5 and 22 years, and has since been described in adults, with a total of 43 cases in the international literature. Its pathophysiology has not yet been elucidated but interestingly, most of the patients are either Mediterranean based or have history of travelling to that area. To our knowledge, this is the second case of ALDY in New York City, and the third that has been reported in the US.

162

**Cutaneous Noninfectious Granulomas Serve as Diagnostic Clue to Primary Immunodeficiency Disorders in Children**

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Background: Primary immunodeficiencies (PID) constitute a large group of diseases, and the incidence of PID is unexpectedly high. Noninfectious granulomas could be presented in 7%–19% common variable immunodeficiencies (CVID) patients, 8% ataxia telangiectasia, severe combined immunodeficiencies, Blau syndrome, and Wiskott–Aldrich syndrome etc.. This histological feature may serve as a clue to early diagnosis of PID. Methods: Here, we presented three pediatric cases with skin lesions of generalized papules or multiple ulcers and other systemic symptoms. Further workups were performed based on the histology features of skin biopsies and lead to the final diagnoses. Results: Case 1. 6 year old female presented with recurrent multiple skin ulcers and painful joints for over a year. The patient
was born healthy but then developed intermittent diarrhea and pneumonia. No similar family history was reported. A skin biopsy performed and tuberculoid granulomas was noted. Further workup identified decreased IgA in serum, thus, the diagnosis of CVID was made. Case 2. 3 year old male presented with generalized papules since 1 month old. He also complained of joints weakness and short vision. Focal epitheloid granulomas around hair follicle was noted in skin biopsy specimen. Further tests revealed intermittent hypertension, renal anomaly and uveitis. The diagnosis of Blau syndrome was made with detection of CARD15 mutation. Case 3. 3 year old male, presented with intermittent fever, swelling joints of extremities for 2 years and multiple plaques on skin proceeding to ulcers for a year. He was born healthy and no family history was recorded. Systemic workup detected persistent anemia, elevated peripheral IgE, bone deformity and multiple cysts. Skin biopsy revealed florid granulomatous dermatitis with neutrophilic infiltration. Blau syndrome was made with CARD15 gene mutation. Conclusions Noninfectious cutaneous granulomas could serve as diagnostic clue to PID in pediatric cases. Timely diagnosis and treatment of PID will prevent progression and a better prognosis.
A woman in her 50s presented with a 6-week history of arthralgias, photosensitivity, and a progressive, painful mucocutaneous eruption. There were no provoking medication-related or infectious factors identified. On physical exam, she had lesions suggestive of erythema multiforme (EM) including numerous targetoid lesions on the trunk & extremities, desquamating patches on the face, and oral erosions. She also had severe chilblains of the hands & feet. Biopsy showed histologic features overlapping within the spectra of EM and some forms of acute cutaneous lupus (ACL), including vacuolar interface dermatitis with subepidermal clefting, apoptotic keratinocytes, and epidermal necrosis. Laboratory testing was notable for pancytopenia in addition to markedly elevated ANA (with speckled pattern), rheumatoid factor, anti-Sm, and anti-Ro antibodies. The patient met several diagnostic criteria for systemic lupus erythematosus, and further fulfilled all major and minor criteria for the diagnosis of Rowell’s Syndrome. Rowell’s syndrome in an extremely rare presentation of lupus erythematosus that manifests with EM-like lesions, perniosis of the hands & feet, and characteristic serologies. This case is unique in that it fulfilled all major and minor criteria for diagnosis, which is uncommon among the 25 cases of Rowell’s Syndrome reported in the literature. Furthermore, it highlights the importance of obtaining connective tissue disease serologies in patients that present with EM and lack identifiable causes, particularly when histopathology shows overlap between EM and ACL.
166

**Vulvar Lupus Erythematosus: A Rare Event**

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Vulvar involvement occurs in only 5% of patients suffering from lupus erythematosus (LE). The literature in LE involving the genitalia is minimal. Herein, we described a 32-year-old woman diagnosed with LE in 2001 based on photosensitive malar rash, moderately high dsDNA titer and low complements. Since that time, she has been treated with steroids resulting in good control of skin lesions and no evidence of systemic manifestations. In the last three years, the patient has complained of progressive pain, burning and malodorous genital discharge. Clinical examination revealed an ulcerated erythematous area involving the left labium minor. A punch biopsy showed squamous epithelium with vacuolar changes of the basal layer and dyskeratotic cells. Colloidal iron highlighted increased dermal mucin. Direct immunofluorescence (DIF) detected diffuse granular IgG, IgA, IgM, C3 and fibrin with linear accentuation. The diagnosis of LE was rendered. The most frequently described clinical presentations of LE in the vulva, as seen in our patient, are erosions/ulcers and erosive plaques. The absence of a specific clinical presentation makes vulvar LE to be confused with other infectious, inflammatory and neoplastic diseases. Increase awareness of its occurrence would trigger activation of autoimmune work-up in suspicious lesions and consideration of LE when confronted with a genital biopsy showing interface dermatitis. Early diagnosis and treatment of vulvar LE may avoid significant morbidity in these patients.

167

**Cutaneous Malakoplakia of the Neck: A Dermatopathologic Rarity and a Potential Pitfall for the Misdiagnosis of a Deep Fungal Infection**

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We present a case of a 70-year-old man with a 10 month history of recurrent neck abscesses and acute onset altered mental status and tachycardia. CT imaging of a right neck mass revealed a multilobulated enhancing lesion extending from the submandibular gland to the thyroid in the anterior neck. Tissue from his subsequent debridement as well as blood cultures showed growth of E. coli. Histopathology revealed sheets of histiocytes with foamy to granular cytoplasm admixed with numerous neutrophils and lesser numbers of lymphocytes and plasma cells. Intra- and extracellular pale staining, round to ovoid inclusions were identified, raising concern for the possibility of a fungal infection. However, these proved to be positive by Perl's (iron) and by von Kossa (calcium) stains as well as PAS, consistent with Michaelis-Gutmann bodies. A diagnosis of E. coli sepsis with cutaneous malakoplakia was made. Malakoplakia is an uncommon chronic granulomatous disease usually arising in the genitourinary tract of immunosuppressed individuals, and now known to occur in a variety of organ systems, including the skin. An association with bacterial infection, particularly E. coli, has been well documented, and although the mechanism remains unclear, the disease is thought to result from an acquired defect in phagolysosome function resulting in incomplete bacterial clearance. Since first reported in 1972, approximately 70 cases of cutaneous malakoplakia have been described, most in patients with a known cause for immunosuppression such as organ transplantation or treatment for autoimmune disease. In 20% of cases reported, as in our patient, there is no known cause of underlying immunosuppression.
Although the largest subset of cutaneous cases involved the perineum, buttocks, peri-anal or inguinal skin (43%), an updated review of the literature reveals that significant proportion of cases have involved the head and neck (25%), as in this case. We highlight a case of cutaneous malakoplakia with subsequent E. coli sepsis as a rarity seen in the practice of dermatopathology, and emphasize a potential pitfall of mistaking Michaelis-Gutmann bodies for a deep fungal infection with a granulomatous inflammatory reaction.

168

WITHDRAWN

169

Significant Dermal Mucin in Pityriasis Lichenoides Chronica: Comparison with Cutaneous Lupus Erythematosus and Other Interface Dermatitides

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Pityriasis lichenoides chronica is an uncommon dermatitis with uncertain histogenesis. Although its clinical and histological features are well documented, the presence of dermal mucin is not well characterized. We collected thirty-two skin biopsy specimens, comprising pityriasis lichenoides chronica, cutaneous lupus erythematosus and other interface dermatitides, including drug reactions,
erythema multiforme and lichen planus, from patients with no known history of lupus erythematosus. These were assessed by three independent dermatopathologists and analyzed using a quantitative pathology imaging system to quantify dermal mucin. We show that the image analysis system could provide an accurate quantification of dermal mucin that corresponded closely with the estimations made by pathologists. Interestingly, we observed that a higher proportion of pityriasis lichenoides chronica showed significant dermal mucin compared to lupus erythematosus. The dermal mucin in pityriasis lichenoides chronica appeared to be concentrated in the superficial dermis, whereas very high levels of mucin in the deep dermis were seen in several cases of cutaneous lupus erythematosus. The group of other interface dermatitides had the lowest proportion of cases with significant dermal mucin amongst the three diagnostic groups. Although there was substantial overlap in the range of dermal mucin levels encountered in the three groups, the highest levels of dermal mucin in both the superficial and deep dermis were encountered in cutaneous lupus erythematosus.

170

Clinicopathologic Features of Pazopanib-Associated Dermatitis
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The development of various novel targeted chemotherapy agents has introduced a wide spectrum of dermatologic toxicities. Pazopanib is a multi-targeted tyrosine kinase inhibitor with anti-angiogenic properties used in the treatment of renal cell carcinoma and some soft tissue tumors. While it has been reported to cause various dermatologic manifestations, the pathologic features are poorly characterized. We present a case of an 86 year-old man with history of clear cell renal cell carcinoma seven years prior who was treated with radical nephrectomy and multiple excised cutaneous squamous cell carcinomas. He presented with low-volume metastatic renal cell carcinoma to the lungs and failed initial treatment with nivolumab after developing severe arthritis. Dexamethasone was started and, upon resolution of the arthritis four weeks later, pazopanib was initiated. With re-introduction of therapy, he developed a pruritic rash evolving into dry, scaling lesions after two weeks. A shave biopsy was performed. Pathologic examination demonstrated hyperkeratosis with focal parakeratosis, verrucous epidermal hyperplasia, brisk lichenoid interface dermatitis, Civatte bodies, eosinophils, and erythrocyte extravasation consistent with an erythema multiforme-like drug reaction. PAS-staining was negative for fungal organisms. To our knowledge, we are first to describe some of these features of pazopanib-associated dermatitis. Recognition of this entity is important as clinicopathologic correlation may help implicate this or a similar agent and provide guidance for optimization of chemotherapy for patient quality of life.
A Case of Thymoma-associated Multiorgan Autoimmunity with Pityriasis Lichenoides Chronica-like Eruption as an Early Manifestation

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A 60-year-old, otherwise-healthy Japanese female presented with 9-month history of erythroderma. The early manifestations were itchy, scaly erythematous papules on lower limbs. A skin biopsy specimen showed interface vacuolar dermatitis with many necrotic keratinocytes in the epidermis with slight acanthosis and parakeratosis. She was diagnosed as pityriasis lichenoides chronica (PLC) in several dermatology clinics and hospitals. Her eruptions were refractory to treatments including topical corticosteroid, narrow-band UVB phototherapy and oral etretinate and she became erythrodermic in subsequent 4 months despite these treatments. She was referred to our department presenting with generalized erythroderma. We performed a re-biopsy and histopathological examination displayed similar findings. We considered it the skin manifestation of thymoma-associated multiorgan autoimmunity (TAMA) in the differential diagnosis and a computed tomography scan revealed 11 x 9.5 x 7 cm sized thymoma in the mediastinum. The laboratory analysis also revealed hypogammaglobulinemia and positive anti-acetylcholine receptor antibody titer without muscle weakness, which are typical findings of TAMA. Our case highlights that TAMA can be preceded by PLC-like eruption as an initial manifestation. Although it is a rare condition, dermatologists and dermatopathologists should be aware of TAMA as differential diagnosis of PLC.

Sclerodermatomyositis with Associated Lichen Amyloidosis

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Sclerodermatomyositis is a rare connective tissue disease demonstrating overlapping clinical and histologic features of both systemic sclerosis and dermatomyositis. Herein, we present a 72 year-old woman with severe pruritus, sclerotic changes of her arms and legs, progressive salt-and-pepper skin dyspigmentation, and proximal muscle weakness. Laboratory evaluation was significant for positive ANA, anti-SSA, and anti-RNP antibodies. Skin biopsies demonstrated thickened dermal collagen bundles with atrophy and vacuolar degeneration of the overlying epidermis. However, in some areas, the epidermis was hyperkeratotic and amyloid was present in the subjacent papillary dermis. This case illustrates the range of clinical and histopathologic findings of sclerodermatomyositis with the additional and unusual feature of lichen amyloidosis, and we propose that lichen amyloidosis may be an underreported association with this uncommon condition.
An Unusual Case of Plaque-type Multinucleate Cell Angiohistiocytoma Following Traumatic Injury in a Male Patient
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We present a case of a 56-year-old male patient who developed a well demarcated, erythematous, indurated, round plaque on the forehead after sustaining a traumatic injury to the same area in a motor vehicle accident. Histology was notable for the presence of bizarre, multinucleated giant cells and a proliferation of blood vessels in the background of a fibrohistiocytic-rich stroma. On follow up the lesion was found to have resolved spontaneously. Multinucleate cell angiohistiocytoma (MCAH) is thought to be a rare, benign, fibrohistiocytic and vascular proliferation possibly in response to trauma to the distal extremities, although in many cases the exact etiology is unclear. It has been suggested that the inciting factor causes mast cells to interact with fibrohistiocytic cells leading to a release of proangiogenic cytokines. It is typically seen in middle aged female patients and characterized by erythematous to violaceous grouped papules on the acral surfaces. Lesions typically persist indefinitely and are resistant to treatment. Our case of this rarely described entity, through the clinical history and disease course, suggests that MCAH is indeed a vasculoproliferative response to an inciting factor, such as trauma, but further investigation will be required to elucidate the exact pathophysiology.

Calciphylaxis Associated with Warfarin Use
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Calciphylaxis is an often fatal syndrome of microvascular calcification classically associated with end-stage renal disease, dialysis, and/or hyperparathyroidism. The characteristic histologic features include calcification of small and medium-sized arteries with thrombosis within the subcutis. Recently, calciphylaxis in the setting of normal renal and parathyroid function has been described. In this setting, risk factors for its development include warfarin use, obesity, liver disease, white race, female gender, diabetes, infection, and malignancy, among others. We present a case of a Caucasian female in her 70's who was evaluated in the dermatology clinic with an 8 week history of an enlarging, exquisitely tender, retiform ulceration on the lower leg. She had no history of kidney or parathyroid disease. Her past medical history was significant for atrial fibrillation, with warfarin use for more than five years. Biopsy demonstrated calcification of the medium sized vessels within the subcutis, with focal fat necrosis and stromal calcification. Blood urea nitrogen, creatinine, calcium, phosphorus, and parathyroid hormone were normal prior to her presentation, and remained normal throughout her disease course. Extensive workup for an underlying trigger was negative. She responded well to intravenous and intralesional sodium thiosulfate and is slowly making a full recovery. This case is unique and relevant because it demonstrates an uncommon instance of calciphylaxis triggered by anticoagulant use. Additionally, it demonstrates less commonly seen histologic features of calciphylaxis including fat necrosis and dermal stromal calcification.
Histologic Features of Intraliesional Bleomycin Induced Changes Simulating Lymphocytic Vasculitis
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Intraliesional bleomycin sulfate is a highly effective treatment option for recalcitrant warts. Its mechanism of action includes inhibiting DNA synthesis. Local side effects include erythema, edema, and pain at the injection site, and Raynaud’s symptoms. Development of a black eschar is a delayed finding. Histologic features of bleomycin-injected verruca have rarely been reported. After 48 hours, keratinocytes and eccrine ductal epithelium are in various stages of apoptosis, which may become confluent necrosis, resulting in a sub or intra-epidermal blister. Neutrophils may accumulate in the granular layer or eccrine coils, simulating neutrophilic eccrine hidradenitis. Subepidermal/intraepithelial hemorrhage may be seen. Cytolysis, nuclear disruption, and vacuolization are ultrastructural features. Post-treatment biopsies are not usually performed, but may cause concern if one is not aware of the clinical history and/or expected biopsy findings. We report additional histologic features of intraliesional bleomycin. A 61 year old male presented with a 6 mm warty papule on his left forearm that was biopsied to rule out persistent wart versus carcinoma after 3 months of intraliesional bleomycin (every three weeks). Histologically, there were zones of dermal necrosis and perforating collagenesis, with a remnant of necrotic epithelium. A medium caliber vessel near the dermal-subcutaneous junction was infiltrated by lymphocytes, and surrounded by extravasated erythrocytes, mild fat necrosis, and hyalinization of the subcutaneous tissue. Occasional eosinophils were seen. To our knowledge, this is the first report of intraliesional bleomycin simulating lymphocytic vasculitis.
177

Farxiga Induced Sweet’s Syndrome
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Sweet’s syndrome (Acute febrile neutrophilic dermatosis) can be induced by medications, in addition to a variety of other causes. Sweet’s syndrome is characterized by fever, leukocytosis, and tender red plaques often localized to the upper extremity. Microscopic evaluation reveals a dense dermal neutrophilic infiltrate without vasculitis and papillary dermal edema. Farxiga (dapagliflozin), is a new type II diabetes drug approved by the U.S. Food and Drug Administration in January 2014, that belongs to the Gliflozin class. We describe a 75 year-old-woman who developed a fine papular rash in a photo-distributed area on her neck and chest, and associated malaise within one week of beginning Farxiga. Over the following two weeks the rash progressively worsened and she also developed painful hemorrhagic bullous plaques bilaterally on the dorsum of her hands. The histopathology of the hand lesions was consistent with Sweet’s syndrome. It consisted of a nodular infiltrate of neutrophils, papillary dermal edema, and leukocytoclastic debris. Once the patient stopped taking Farxiga, the lesions on her neck and chest began to fade within one week; her hands, however, showed only minimal improvement. Only after a more aggressive treatment with Celestone, high dose systemic steroids, and topical Clobetasol ointment did her hand lesions slowly heal. To our knowledge this is the first report of drug-induced Sweet’s syndrome associated with this new diabetes medication.

178

Erythema Elevatum Diutinum and Celiac Disease
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Erythema Elevatum Diutinum (EED) is a rare form of localized fibrosing small-vessel vasculitis characterized by red to violaceous persistent soft papules, nodules and plaques, which later become yellow-brown and firm. It has predilection for extensor surfaces of the extremities. Histologically EED differs based on the stage of the disease. In the early stages it demonstrates non-specific leukocytoclastic vasculitis. Granulation tissue, fibrosis, and a diffuse mixed inflammatory infiltrate consisting predominantly of neutrophils, develop in later stages. EED has multiple possible etiologies, from infectious to immune complex-mediated. Three cases of EED in association with celiac disease (CD) have been reported in English literature to date. We present yet another case of EED in a patient with previously undiagnosed celiac disease with no gastrointestinal complaints. The patient was treated with a gluten-free diet which resulted in a complete resolution of the lesions.
Cutaneous infections and foreign body reactions are common skin manifestations of intravenous drug abuse. As intravenous drug abusers enter treatment, they sometimes divert their maintenance therapy via injection to induce a faster, more intense opioid effect. Buprenorphine, a semi-synthetic partial opioid agonist used as an oral maintenance treatment for patients with a history of opioid dependence, has become associated with an increased risk of diversion. We report on a 43-year-old man with a who presented to the infectious disease clinic with a 2-week history of recurrent, painful skin lesions. He complained of concurrent fevers and noted the eruption of the lesions during times of extreme stress. He reported a past history of drug and alcohol abuse for which he was prescribed sublingual buprenorphine. On physical exam, the patient was well-appearing with numerous erythematous nodules and fluctuant subcutaneous abscesses on the upper and lower extremities, sparing the back, trunk, and torso. Skin punch biopsy revealed a prominent collection of neutrophils in the deep reticular dermis. Polarization microscopy was used to assess the abscess for the presence of inorganic material that may have been responsible for the necrotic subcutis. Polarizable material was seen among the inflammatory elements of the abscess and was noted to form small, round, birefringent particles with Maltese Cross morphology. This material was subtly highlighted by PAS stain. Otherwise, special stains were negative for mycobacteria, fungus, and bacteria. Prior reports have documented the presence of birefringent material with Maltese Cross morphology in association with subcutaneous injection of buprenorphine. This case highlights the importance of clinical history in as well as the undervalued utility of polarization microscopy in the histopathological evaluation of atypical skin abscesses.

A 55-year-old woman with an established history of celiac disease and poor adherence to a gluten-free diet presented with a 2 month history of intensely pruritic pink papules over her knees, arms, back, and abdomen. Serum anti-tissue transglutaminase antibodies measured 119 μ/mL (reference range 0.1 - 10.0 μ/mL). A punch biopsy from the right lateral knee revealed superficial dermal perivascular lymphocytic inflammation and small intracorneal pustules. Direct immunofluorescence (DIF) revealed strong fibrillar deposition of IgA and IgG along the basement membrane. A presumptive diagnosis of dermatitis herpetiformis (DH) was made in light of the clinical, serologic, and DIF findings. The patient was treated with Dapsone and encouraged to resume her gluten-free diet. She experienced gradual improvement over the subsequent months. A fibrillar pattern of IgA deposition has been described in a rare subset of patients with DH. Our case is remarkable for exhibiting these unusual DIF findings in addition to nonspecific histologic features that are similar to those previously described in another rare subset of patients with DH and more classic DIF findings. This case report underscores the importance of incorporating clinical, serologic and DIF data in establishing the diagnosis of DH. Furthermore, it raises awareness of an atypical and possibly underreported DIF pattern that allowed us to make the correct diagnosis in the absence of classic histologic findings.
181
Hand-foot Syndrome Due to Cabozantinib Presenting as Spongiotic Dermatitis
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A woman in her 50s with a history of medullary thyroid cancer received therapy with cabozantinib. Within several weeks of treatment, she developed painful plaques and bullae on her dorsal and volar hands and feet. Histopathology demonstrated an acute spongiotic dermatitis with eosinophils. Upon discontinuation of cabozantinib, the acral cutaneous lesions resolved. Hand-foot syndrome, or palmoplantar dysesthesia, is a cutaneous adverse effect of chemotherapy. Hand-foot syndrome presents with painful erythema, edema, bullae, and desquamative plaques of the palmoplantar but also dorsal acral surfaces. Causative agents include doxorubicin, 5-fluorouracil, capecitabine, and tyrosine kinase inhibitors. The histology of hand-foot syndrome has classically been described as vacuolar interface dermatitis, often with epidermal dysmaturation and keratinocyte atypia. Cabozantinib is an inhibitor of the tyrosine kinases C-met and VEGFR2 and has recently been FDA-approved for the treatment of medullary thyroid carcinoma and advanced renal cell carcinoma. Hand-foot syndrome due to cabozantinib has been clinically reported, but the histology has not yet been described. The case described herein demonstrates the classic clinical features of hand-foot syndrome but with a surprising tissue reaction pattern, that of a spongiotic dermatitis. Given the increasing use of this chemotherapeutic agent and the morbidity related to this cutaneous adverse effect, it is helpful for dermatopathologists to be aware that a spongiotic reaction pattern may be seen in hand-foot syndrome due to cabozantinib.

182
Pseudoherpetic Grover's Disease
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Acantholytic disorders such as pemphigus may occasionally produce pseudoherpetic histologic changes. These changes may be mistakenly interpreted as viral cytopathic effect due to herpesvirus. Herein, three cases of Grover's disease with pseudoherpetic changes are described. In all three cases, the clinical appearance is that of a chronic, pruritic, papulovesicular eruption on the trunk and abdomen. Histology in all three cases demonstrates a focus of acantholysis with variable necrosis and multiple individual keratinocytes with pseudoherpetic change. True nuclear molding and multinucleation were absent. Immunoperoxidase for varicella zoster virus and herpes simplex virus 1 and 2 were negative. Grover's disease (transient acantholytic dermatosis) is a common inflammatory dermatosis, and the classic histology mimics that of Darier's disease with focal acantholysis and dyskeratosis. Other histologic variants resemble Hailey-hailey disease, pemphigus vulgaris and foliaceus, and spongiotic dermatitis. Dermatopathologists should also be aware of pseudoherpetic changes in Grover's, to avoid interpretation as herpesvirus infection and to recognize an additional variant of a common inflammatory dermatosis.
183
Ipilimumab-induced Sarcoidosis in a Patient with Metastatic Melanoma
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Immune-related adverse events secondary to ipilimumab, an immunotherapy now often used for metastatic melanoma, are important to recognize. We report a case of a 60-year old female with metastatic melanoma who developed sarcoidosis in the setting of ipilimumab therapy. Her primary left ankle superficial spreading melanoma was notable for a depth of 14 mm (anatomic level V), ulceration, 3 mitoses/mm², lymphovascular invasion, and a focus suspicious for perineural invasion. Three months after completing one year of adjuvant interferon therapy, she developed multiple palpable left leg nodules and inguinal lymphadenopathy. Biopsies revealed metastatic melanoma. She was started on a phase 2 trial of nivolumab plus ipilimumab. Imaging studies showed a 40% reduction in disease burden and no new metastatic lesions after six doses of nivolumab (3mg/kg). She was subsequently started on ipilimumab (3mg/kg). After dose #3, she developed numerous subcutaneous nodules on her bilateral forearms and right knee. Biopsy of a left forearm nodule showed numerous epithelioid granulomas with multinucleated giant cells and asteroid bodies. As special stains did not detect any microorganisms, the findings were consistent with a granulomatous dermatitis, such as sarcoidosis. Imaging studies showed continued decrease in size of the left leg subcutaneous nodules. Given the presence of bilateral mediastinal and hilar lymphadenopathy, the patient underwent endobronchial ultrasound biopsy of mediastinal lymph nodes, which showed non-necrotizing granulomas, without evidence of malignancy or microorganisms. Treatment with ipilimumab was discontinued, and her subcutaneous nodules regressed spontaneously. Repeat imaging showed improvement in mediastinal and hilar lymphadenopathy. We describe a unique case of a patient with metastatic melanoma treated with ipilimumab who developed subcutaneous and pulmonary sarcoidosis to increase awareness of this potential complication of ipilimumab therapy.

184
Chronic Penile Lymphedema
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Chronic penile lymphedema is a rare entity that results from damage to lymphatic vessels. We report a case of a 38-year old male with penile edema for 8 months. He had no urinary symptoms or sexual dysfunction and no history of penile trauma, urinary tract infections, or sexually-transmitted diseases. He had been sexually active and monogamous with his wife. Physical examination revealed an uncircumcised penis with swelling of the phallus and foreskin with some erythema. No overlying epidermal changes, phimosis, or inguinal lymphadenopathy were present. Imaging studies revealed no hydronephrosis, stones, or renal lesions; slightly enlarged mesenteric lymph nodes were noted and stable on repeat scans. A penile skin biopsy showed mild hyperkeratosis, superficial and deep dermal lymphohistiocytic and plasma cell infiltrate with rare eosinophils, dermal fibrosis, superficial edema, and slight telangiectasia. Trichrome and elastic stains highlighted thickened collagen bundles and reticular elastic fibers, respectively. No amyloid deposition or increased dermal mucin were present on Congo red and colloidal iron stains, respectively. A spirochete stain was negative. Overall, the clinicopathological findings were most consistent with chronic lymphedema. The patient was given a 3-week course of
Ciprofloxacin and prednisolone and subsequently reported significant improvement in penile swelling and erythema. As mild swelling of the foreskin remained on exam, he was prescribed a second therapeutic course and consideration has been given to circumcision. Chronic penile lymphedema is a reactive condition, with no identifiable infectious cause, that can be distressing and may cause sexual or urinary dysfunction. It occurs secondary to persistent lymphatic irritation and scarring and no definitive treatment is available. Awareness of this entity can facilitate the diagnosis in the appropriate clinical context as histopathological findings can be non-specific.

185
Leukocytoclastic Debris - A Clue to Diagnosis in Non-classical Presentations of Dermatitis Herpetiformis.
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Dermatitis herpetiformis (DH) is a subepidermal vesicular disorder that is characterized by a pruritic papulovesicular eruption and is often associated with gluten-sensitive enteropathy (GSE). Classically, biopsies of DH show papillary dermal neutrophilic microabscesses, and direct immunofluorescence (DIF) reveals granular deposition of IgA in the dermal papillae. Occasionally, biopsies of DH may demonstrate less classical findings resulting in diagnostic difficulties. We identified 15 cases of DH through a retrospective review of our medical records. DIF was performed in 10 cases, all of which showed granular deposition of IgA in the dermal papillae. High clinical suspicion for DH was noted in the remaining 5 cases. Three patients had a confirmed diagnosis of GSE. On histopathological review of the 15 cases, all showed variable numbers of neutrophils within the infiltrate, however, 3 showed only rare neutrophils. All cases demonstrated leukocytoclastic debris within the superficial dermis and in 6, the debris was as prominent as or more prominent than the collections of neutrophils. Intracorneal leukocytoclastic debris was seen in 2 cases, and other 2 cases demonstrated intracorneal collections of intact neutrophils. A well-developed subepidermal bulla was present in 8 cases including one which showed minimal inflammation, but demonstrated a collection of leukocytoclastic debris in the superficial dermis. The diagnosis of DH was initially suspected neither clinically nor histopathologically in this case, but was later confirmed by a DIF. Twelve cases showed admixed eosinophils, of which two demonstrated a dense eosinophil-rich infiltrate, mimicking eosinophil-rich bullous disorders. DH is a subepidermal vesicular dermatitis that is characterized by neutrophilic microabscesses and a granular deposition of IgA in the dermal papillae. We describe a collection of cases that, in addition to classical findings, also showed less frequently described features such as prominent eosinophils, well-developed subepidermal bullae, and leukocytoclastic debris. In one of the described cases, the bullous presentation and pauci-inflammatory infiltrate were misleading and the presence of intradermal leukocytoclastic debris ultimately served as a clue to the correct diagnosis.
Utility of Ancillary ELISA Testing and Immunohistochemistry in Distinguishing Pseudo-vesicular Pemphigoid Gestationis from other Pregnancy-related Dermatoses

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We describe two cases of pemphigoid gestationis (PG) that presented with pseudo-vesicular lesions and a non-bullous histopathology. ELISA testing for autoantibodies to bullous pemphigoid antigens (BP180 and BP230) was helpful in confirming the diagnosis in both cases. Additionally, C3d immunohistochemistry may have diagnostic utility. A 24-year-old gravida 1 woman at 30 weeks gestation (case 1) and a 39-year-old gravida 2 woman at 26 weeks gestation (case 2) presented with pruritic, edematous, erythematous papules and plaques on the trunk and extremities. Blisters were minimal to absent. In both cases, biopsy for H&E showed a superficial and deep perivascular inflammatory cell infiltrate with eosinophils. DIF showed linear C3 deposition along the basement membrane in the first case but was not performed in the second. ELISA was performed in both cases and was positive for elevated circulating autoantibodies to BP180 and negative to BP230. C3d immunohistochemistry was performed on case 1 and showed strong linear staining at the basal cell layer, although this was negative in case 2. Case 1 improved on prednisone and topical steroids. Case 2 improved on topical steroids alone. Both women subsequently delivered healthy babies. The utility of ancillary diagnostic tests lies in the differentiation between pemphigoid gestationis and other pregnancy-related dermatosis, in particular, polymorphic urticarial papules and plaques of pregnancy (PUPPP). Clinically and histologically, PUPPP resembles non-bullous PG; however unlike PUPPP, PG is associated with adverse fetal outcomes. DIF, ELISA, and/or C3d immunohistochemistry may be helpful in distinguishing PG from other pregnancy dermatoses, in particular PUPPP, especially in non-bullous presentations of PG.

Polarized Immune Infiltrates in Morphea and Eosinophilic Fasciitis Offer Novel Insights for Differentiation and Treatment Strategy

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Morphea and eosinophilic fasciitis (EF) are rare fibrosing disorders and may present a diagnostic challenge. While histopathologic features are often distinct, in some cases, there may be overlap. Clinicopathological differentiation is necessary for guiding patient management. Given that both are inflammatory/autoimmune connective tissue diseases, T-cells contribute to their pathogenesis. We sought to determine whether T cell immune polarization enables histopathologic distinction. We retrospectively examined clinicopathologically confirmed cases of Morphea (n=12) and EF (n=8) using immunohistochemistry methods to characterize the T cell infiltrate. Immunohistochemical staining for CD3, CD8, and T-bet and GATA-3 (transcription factors reported to be specific and mutually exclusive for Th1 and Th2 cells, respectively) with dual staining for CD4, were evaluated. Positively stained cells were counted manually in three high power fields by two dermatopathologists. Statistical analyses were performed with p<0.05 considered significant. No significant difference in CD3+ cells was identified (p=0.19), however, the ratio of CD4:CD8+ T-cells was significantly greater in morphea compared to EF.
(1.15 and 0.64, respectively; p=0.034). The Th1/Th2 ratio was significantly lower in morphea compared to EF (1.68 and 2.66, respectively; p=0.027). Morphea and EF may be histopathologically distinguished based on the relative constitution of helper T-cell subtype. These findings offer novel insight into our understanding of disease pathogenesis and support a potential role for Th2 inhibition in anti-fibrotic therapeutic strategy.

188
Conjunctival Churg-Strauss Syndrome in a Young Adult Male With Persistent Ptosis
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Ocular involvement in Churg-Strauss syndrome is an exceedingly rare phenomenon with only isolated case reports in the literature. Previous cases have been categorized into two distinct forms with vastly different prognoses, orbital inflammatory pseudotumor and ischemic vasculitis. The former presentation is characterized by conjunctival involvement, orbital abnormalities on MRI, absence of ANCA positivity, lack of cranial neuropathies and indolent progression with a good response to treatment. In contrast, the ischemic vasculitic variant exhibits histologic evidence of vasculitis, ANCA positivity, cranial nerve neuropathies and a more rapid course with poor visual outcome. Here, we present a 24-year-old male with a remote history of childhood asthma who developed right-sided ptosis with associated hypereosinophilia in Fall 2013. One year later, he developed left-sided Bell’s palsy treated successfully with valacyclovir and prednisone. Three months following a right-sided blepharoplasty, ipsilateral small white nodules erupted over palpebral and bulbar conjunctiva. Biopsy revealed changes characteristic of ANCA-negative Churg-Strauss syndrome, including palisading necrotizing eosinophil-rich granulomas without concomitant vasculitic changes. He was treated with tobramycin and dexamethasone ophthalmic suspensions as well as triamcinolone acetonide injections into sub-Tenon’s space with subsequent resolution of lesions. A second repair was performed to correct persistent ptosis and direct immunofluorescent studies of the excised material failed to show immunoreactant deposition. His ocular pathology has now nearly resolved without any evidence of visual loss or systemic progression. This case is remarkable given the development of neuropathy in the absence of frank vasculitis, suggesting that an alternate mechanism such as eosinophil degranulation may be implicated.

189
Eosinophilic Angiocentric Fibrosis Co-Existing with Granuloma Faciale: A Rare Form of Tumefactive Fibrosing Vasculitis Presenting as an Orbital Pseudotumor
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Eosinophilic angiocentric fibrosis (EAF) is recognized by many as a mucosal variant of granuloma faciale (GF) localized to the orbit and the upper respiratory tract. Both processes are characterized by small vessel vasculitis and perivascular fibrosis, with accentuation of the former in GF and the later in EAF. Occasionally, the two processes occur simultaneously in the same patient. We present a 67-year-old male who developed a persistent pseudotumor of the left orbit beginning in 1996 associated with chronic sinusitis. Treatment with chemotherapy and corticosteroids was ineffective. After an initial
excision, the tumor recurred requiring five additional rounds of debulking. Of note, in 2015 he also developed granuloma faciale of the right cheek. Histologic examination of the orbital tissue revealed an obliterate tumefactive fibrosing process with concentric perivascular onion skin and storiform fibroplasia. Focal leukocytoclasis, red cell extravasation and mural fibrin were also noted. Immunohistochemical studies revealed a lymphocyte populace comprised predominantly of CD4+ T cells of the Th2 subset (GATA3+). Numerous plasma cells were seen with many staining positively for IgG4. The findings were held to be diagnostic of eosinophilic angiocentric fibrosis with co-existing granuloma faciale. In general, EAF responds poorly to oral medications including steroids, often requiring repeated surgical intervention. The abundance of plasma cells within these lesions and the recent association of EAF with IgG4-related systemic disease may support the use of agents such as rituximab for the future treatment of this condition.

190
A Clinicopathologic and Immunophenotypic Comparison Between Eosinophilic Fasciitis and Morphea Profunda
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Background: Eosinophilic fasciitis (EF) and morphea profunda (MP) are inflammatory and sclerosing disorders of the subcutis that may exhibit overlap in clinical and pathological presentations. Factors differentiating these two disorders are not well-defined. Objective: To identify clinicopathological and immunophenotypic features distinguishing EF and MP. Methods: We evaluated H&E, CD123, CD34, VVG, and mast cell tryptase stains on sections from deep skin biopsies (extending to fascia) from 16 patients with clinical diagnosis of EF and 11 patients with MP. Results: Patients with EF were significantly more likely to be male, have involvement of the forearms, and have a peripheral eosinophilia. The fascia was more likely to contain eosinophils in EF compared to MP (p=0.003), though eosinophils were absent in 3 (19%) of EF cases. Focal absence of CD34 staining was more prominent in EF (p=0.04). Inflammation, sclerosis, and CD123-positive cells in fascia were more often features of EF than morphea (no statistically significant differences). The extent of VVG and tryptase staining did not differ between the two groups. Because there was no dermal sclerosis in many cases of EF and MP (56% and 36%, respectively), our data emphasize the importance of obtaining deep biopsies for microscopic evaluation. Conclusion: We did not identify significant pathological differences between patients diagnosed clinically as eosinophilic fasciitis versus morphea profunda. Due to overlapping microscopic and immunophenotypic features, clinical correlation remains critical in differentiating these two disorders.
191

FELLOW

Lichenoid Dermatoses with Pseudomelanocytic or Benign Melanocytic Nests Versus Melanoma in Situ with Lichenoid Inflammation: A Comparative Study

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Pseudomelanocytic / melanocytic nests (PMNs) positive for MITF arising in lichenoid inflammation are a known diagnostic pitfall for melanoma in situ (MIS), especially on chronically sun damaged skin. We sought to evaluate histopathologic findings in biopsies with “pseudomelanocytic nests” (PMNs) to identify features helpful in distinguishing this benign process from MIS. Eight biopsies from seven patients containing PMNs within lichenoid dermatoses and twenty cases of MIS with lichenoid inflammation were evaluated for histopathologic features including pagetoid scatter, lentiginous junctional melanocytic proliferation, cytologic atypia, and pigmentation. Clinically, 6/8 cases of PMNs represented either a rash or a discrete lesion not thought to be a melanocytic neoplasm, with a range of clinical diagnoses including lichen planus, erythema dyschromicum perstans, lupus, melasma, and inflamed keratosis. The two cases in which the clinical differential included a melanocytic lesion were from non-sun damaged skin. Twenty cases diagnosed as MIS or severely atypical junctional melanocytic neoplasm, with lichenoid inflammation were reviewed for comparison. All eight specimens of PMNs showed at least one nest of MITF positive cells at the dermo-epidermal junction with interface change and dermal lichenoid infiltrate. Cytologic atypia, pagetoid scatter and confluence of junctional melanocytes was not seen in any of these cases. In contrast, all cases of MIS had at least focal proliferation of lentiginous melanocytes in a confluent pattern with varying degrees of cytologic atypia, and 8/20 cases of MIS showed pagetoid scatter of melanocytes. Multinucleated melanocytes within the epidermis were present in 6/20 of cases of MIS and 0/8 cases of PMNs. In conclusion, confluent proliferation of atypical junctional melanocytes, pagetoid scatter and multinucleated melanocytes are helpful features in differentiating between benign pseudomelanocytic nests arising in lichenoid dermatoses and inflamed MIS.

192

RESIDENT

Unilateral Localized Bullous Pemphigoid Without Known Trigger

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Bullous pemphigoid (BP) is a well-known autoimmune blistering dermatosis secondary to autoantibodies to the epidermal basement membrane. A localized unilateral variant of BP has been described and this is often associated with an underlying cause. Common triggers for this unique unilateral presentation include: localized damage to the skin by physical or chemical agents, neurological disorders, prior radiation, and chronic lymphedema. We report two cases of localized unilateral BP without a known trigger. Patients presented with a similar history of questionable cellulitis with associated blisters that were unresponsive to multiple courses of antibiotics. The clinical lesions were classic for BP but the distribution and course made this a diagnostic challenge. Biopsies, serologies, and immunofluorescent studies on both patients were positive confirming a diagnosis of BP. One of the patients responded to systemic steroids which were tapered after starting Doxycycline. This patient was disease free after 3 months of treatment. The other patient required both oral steroids and Cellcept and had a prolonged course of disease. Unfortunately, the patient subsequently expired from other comorbidities. Although
both patients had similar disease at onset, their different clinical courses exemplify the complexity of treatment as well as need for individualized care in patients with BP. Localized unilateral BP without a known trigger has never been described in the English literature. The dermatology community should be aware of this rare presentation of BP. Given its unique clinical presentation a high index of suspicion as well as dermatopathologic correlation is needed for an accurate diagnosis.

193
A Unique Presentation of Lupus Miliaris Disseminatus Faciei
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Lupus miliaris disseminatus faciei is a rare cutaneous disorder most commonly presenting as red-brown papules on the central face with a characteristic tendency to involve the eyelids. Extrafacial manifestations have been reported to occur but almost always coexist with facial involvement. Classically, an apple-jelly color is seen with diascopy of the papules. Histopathology reveals epitheloid cell granulomas with variable caseation depending on the timing of the biopsy. While its etiology is unknown, its association with rosacea, sarcoidosis, and mycobacterial infection has been disputed, but most believe this is an unrelated and distinct clinical entity. Numerous variably successful treatments have been reported in the literature, but no established treatment guidelines exist. We present a case of lupus miliaris disseminatus faciei presenting exclusively on the posterior neck to remind clinicians that LMDF can occur anywhere on the body without concurrent facial involvement. To our knowledge, this is the first reported case of lupus miliaris disseminatus faciei occurring solely on the posterior neck without facial involvement.

194
Spontaneously Resolving Figurate Erythema
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A 55-year-old man with a history of neuroblastoma presented with a pruritic eruption on his trunk, arms, and legs for two months consisting of erythematous annular plaques with collarettes of scale and central clearing. He denied any new medications or travel. Histopathology of a punch biopsy showed spongiotic dermatitis, dyskeratotic keratinocytes, and superficial and deep perivascular lympho-eosinophilic infiltrate. No fungal organisms, granulomas, nor flame figures were identified. Clinical pathologic correlation was most consistent with a diagnosis of eosinophilic annular erythema (EAE). A 1-week trial of clobetasol ointment resulted in no improvement of the lesions. Three months later, he noted improvement without treatment in most lesions. However, he noted new asymptomatic annular lesions on his leg and back. The patient deferred further treatment. Initially described in children, EAE is a rare benign dermatosis of unknown etiology and pathogenesis. It is typically asymptomatic and tends to resolve spontaneously over months or years. Clinically it presents as figurate erythema and histologically it is characterized by superficial and deep perivascular lymphocytic and eosinophilic
infiltrates. Treatment may include topical steroids or antimalarials. However lesions often spontaneously resolve.

195
Pembrolizumab Induced Bullous Pemphigoid
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Pembrolizumab is a highly selective, humanized monoclonal immunoglobulin G4-kappa isotype antibody against programmed cell death-1 (PD-1) that is designated to block the negative immune-regulatory signaling of the PD-1 receptor expressed by T-cells, B-cells and macrophages. The blockade of immune checkpoints has showed revolutionized durable responses in patients with unresectable or metastatic melanoma after immunotherapy. Herein, we report a case of bullous pemphigus induced by pembrolizumab. The patient is an 80 year old man with stage pt3b N2c M1 melanoma. Mutation testing of tumor excluded the BRAF mutation. Patient was started on pembrolizumab. He developed ruptured and intact blisters and erythematous papules which were first noticed on the thighs and progressed to posterior legs and trunk and proximal upper extremities. The obtained punch biopsy showed subepidermal vesiculobullous formation with mixed inflammation including neutrophils and eosinophils. Direct immunofluorescence study (DIF) demonstrated linear staining of the epidermal basement membrane zone for IgG and C3 and the diagnosis of bullous pemphigus was rendered. He was treated with tapering oral prednisone, resulting in tremendous improvement of the skin rash. However a secondary fare up limited to proximal upper and lower extremities occurs following complete stopping of the prednisone. The common dermatologic side effects of pembrolizumab include nonspecific rash, itching and flushing. However, due to the potential risk of immune related adverse events close monitoring of these patients is recommended.

196
Characterization of Cell-type Specific Expression of CXCR3 Ligands in Morphea
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Morphea is a disease of dermal inflammation and resultant sclerosis with considerable functional and cosmetic consequences. Cellular and molecular events in pathogenesis of morphea remain poorly elucidated. Preliminary studies using genome-wide gene expression analysis support the role of gamma interferon mediated pathways in the early pathogenesis of morphea. Specifically, CXCL-9 and 10, known ligands of CXCR3 receptor, were shown to be strongly upregulated in morphea. In this study, we characterized inflammatory infiltrate in morphea and investigated cell-type specific expression of CXCR3 ligands in morphea using immunohistochemistry (IHC). Our data show that cellular infiltrate of early inflammatory morphea lesions consists of predominantly T lymphocytes with significantly increased CD4 T helper cell population. The immune cell infiltrate of early morphea was enriched in CXCR3+ immune cells, which co-localizes with CD4+ cells, but not CD8+ lymphocytes. We demonstrate that CXCL9 is expressed by a small subset of cell of varying morphologies within perivascular, periadnexal, and interstitial infiltrates. CXCL9 expression co-localized with CD68, but not CD20, CD34, CD123, or SMA,
suggesting that dermal macrophages may secrete CXCL9 ligand. Moreover, CXCL9 expression was detected in close proximity to CXCR3 expressing immune cells. Based on our findings, we suggest that expression of CXCR3 ligands, specifically CXCL9, in morphea may enhance recruitment of CXCR-3 expressing activated T lymphocytes into the lesional skin and propagate early stages of inflammation.

197
Childhood Granulomatous Periorificial Dermatitis With Extra-facial Involvement
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Childhood granulomatous periorificial dermatitis (CGPD) is a rare yet well described subtype of periorificial dermatitis typically seen in prepubertal children of darker skin types. Perioral and periocular papules are typical but rare reports also describe extra-facial involvement. We report the challenging case of a 5-year-old female of Indian descent who presented to dermatology with a 6-month history of innumerable tiny red-brown papules in perioral and periocular distribution. Additionally, there were many small brown macules consistent with post-inflammatory hyperpigmentation as well as small, pitted scars on her central back. No travel history was reported. After a 4-day course of prenisone, a biopsy of the back was performed, which showed a well-demarcated cluster of “naked” granulomas in the mid dermis. A diagnosis of sarcoidosis was favored and further workup and treatment was started including predisone 30 mg daily and methotrexate 10 mg weekly. After the patient was referred to our institution, deeper sections of the block were obtained and a distinct perifollicular granulomatous pattern was observed. Special stains including PAS, AFB, and FITE were negative. Further workup of the patient included normal CBC, CMP, CRP, ESR, and C3, a negative dsDNA, and angiotensin converting enzyme, and only weakly positive ANA at 1:80. No uveitis was seen during examination by an ophthalmologist. Based on clinical morphology, characteristic histopathology, and lack of systemic involvement, a diagnosis of CGPD with extra-facial involvement was favored over sarcoidosis. Distinguishing between CGPD and sarcoidosis is important as several studies show that steroids are an important factor in precipitating or worsening CGPD, but are commonly used to treat sarcoidosis. Also, sarcoidosis in this age group is often associated with systemic disease whereas CGPD is self-limiting. We suspect this case lacks the more characteristic lymphocytic infiltrate described in the literature because of systemic steroid administered before the biopsy. Regardless, the perifollicular pattern is very conspicuous. Because sarcoidosis, infection, and granulomatous rosacea, are included in the differential, strong clinical correlation and special stains will aid in making the diagnosis.

198
CHILD Syndrome with Verruciform Xanthomas
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Background: Congenital hemidysplasia with ichthyosiform erythroderma and limb defects (CHILD) syndrome is an uncommon X linked dominant disease manifesting as skin abnormalities, erythematous plaques, dermatosis, and skeletal hypoplasia on one side of the body. A rare cutaneous trait
encountered in CHILD syndrome is verruciform xanthomas. Verruciform xanthomas are typically solitary, erythematous plaques with a characteristic histologic appearance affecting the perioral and anogenital areas. They may represent an immune reaction to local trauma or inflammation. The presence of verruciform xanthomas may be seen in association with various disorders, including CHILD syndrome, or may develop independently. This case presents a 57 year old female with CHILD syndrome with a two year history of extensive verrucous plaques on the right earlobe and right elbow. Methods and Results: A transverse biopsy of the right earlobe was taken, followed several months later by a transverse biopsy of the right elbow. Hematoxylin and eosin stains were performed. Histology revealed parakeratosis with elongated rete ridges. Foamy cell infiltrates were seen within the dermal papillae. This confirmed a diagnosis of verruciform xanthomas in the setting of CHILD syndrome in both biopsy specimens. Conclusion: Cutaneous verruciform xanthomas presenting in the setting of CHILD syndrome is a rare phenomenon of this condition. This unique case is presented as an example of extragenital verruciform xanthomas occurring in a patient with CHILD syndrome.

A Unique Case of Dermatitis Herpetiformis Demonstrating Eosinophilic Spongiosis as the Predominant Histologic Pattern
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Dermatitis herpetiformis is an uncommon subepidermal blistering disorder characterized by pruritic papulovesicular eruptions with a predilection for extensor surfaces, an association with autoimmune disorders and gluten-sensitive enteropathy, and a defining immunofluorescence pattern of granular IgA deposition within the dermal papillae. Histologic findings include neutrophilic microabscesses largely confined to the dermal papillae, dermal papillary edema and a neutrophil-rich subepidermal bulla. To our knowledge, dermatitis herpetiformis has not been previously reported with eosinophilic spongiosis as the predominant histologic pattern. A 54-year old man with serology-confirmed gluten intolerance diagnosed at an outside institution presented with a 2 year history of an intermittent, generalized pruritic rash which was refractory to a gluten-free diet. Laboratory investigation revealed a serum IgA tissue transglutaminase antibody level of 5.7 U/mL (reference range < 4.0 U/mL) and slight elevation of the erythrocyte sedimentation rate. Physical examination showed a papular eruption involving the bilateral elbows, hips, inguinal region and knees, as well as the upper buttocks, with the right elbow demonstrating mild excoriation. Punch biopsy of the right inguinal region demonstrated prominent eosinophilic spongiosis, neutrophilic papillitis and mixed dermal inflammation composed of neutrophils and eosinophils. Perilesional direct immunofluorescence demonstrated strong granular IgA deposition along the basement membrane zone and strong stippled IgA deposition within the dermal papillae. This case demonstrates that dermatitis herpetiformis may show a predominant histologic pattern of eosinophilic spongiosis and underscores the importance of histopathologic correlation with clinical and immunofluorescence findings.
200

An Unusual Manifestation of Systemic Amyloidosis
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Primary systemic amyloidosis commonly presents with mucocutaneous findings. Cutaneous manifestations can include purpura, waxy papules, nodules or plaques, macroglossia, pigmentary changes, scleroderma-like thickening of the skin, bullous lesions, alopecia, and nail dystrophy. The latter finding is a rare symptom of systemic amyloidosis and the nail typically shows longitudinal ridging, onychorrhexis, and onychoschizia. A 61-year-old caucasian gentleman presented to our clinic for evaluation of onychodystrophy. He had a known history of lambda light chain amyloidosis with cardiac and renal involvement diagnosed in April 2012, but his disease had been stable with treatment. Physical exam showed nail plate atrophy, onychoschizia, pronounced onychorrhexis, onychoatrophy, and mild periungual erythema affecting all ten fingernails. Bilateral halluces also showed similar physical exam findings but to a lesser degree. Nail biopsy revealed underlying deposits of amorphous pale pink material in the superficial dermis and surrounding superficial vessels. Congo Red Stain highlighted these deposits and demonstrated the distinguishing apple-green birefringence on polarization. The findings are consistent with cutaneous amyloidosis secondary to systemic disease. Systemic amyloidosis is an uncommon cause of nail dystrophy; however, our case underscores the importance of biopsy and histopathologic evaluation in the undifferentiated patient for accurate diagnosis.

201

Signs of Danger: Cutaneous Manifestations of Graft Versus Host Disease in a Liver Transplant Recipient
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We report the case of a 62 y/o male who underwent an orthotopic liver transplant 3 months prior and subsequently presented to our hospital with a 3 day history of non-painful, non-pruritic macropapular rash. The rash began on his palms and soles and spread upwards across his arms and legs. The patient reported no other symptoms, no medication changes, and had no similar prior eruption. A 2 mm punch biopsy was performed, and several classic histopathologic signs of development of Graft-Versus-Host Disease (GVHD) were seen including a lymphocytic infiltrate, epidermal necrosis including keratinocyte necrosis and areas of basement membrane hydropic changes. This dermatopathologic diagnosis lead to rapid detection of GVHD and appropriate treatment was initiated for our patient. Liver transplants are less commonly associated with GVHD reaction, which most often occur after a bone marrow or stem cell transplant. However the primary organ systems involved in GVHD manifestation are the skin, GI tract and liver. Our patient had no other signs and symptoms of acute GVHD which can include nausea, emesis, abdominal cramping, and diarrhea. This macropapular rash was his only presenting symptom and knowledge of cutaneous manifestations of both acute and chronic GVHD can result in a life-saving diagnosis for the transplant patient. The differential diagnosis can also include drug eruption for acute GVHD and lichen planus for chronic GVHD. Therefore it is critical for all physicians participating in the care of transplant recipients to be familiar with the cutaneous manifestations of GVHD.
A 79 year-old man presented with a rash of five months duration. Physical exam demonstrated diffuse shallow, erosions with overlying scale and crust on his periocular face and cheeks, neck, arms, chest, axillae, buttocks, groin, low back, and legs. There was minor conjunctival erythema and discharge without erosion. Pertinently, the oral mucosa and lips were spared. Biopsy revealed acantholysis within the granular layer, overlying thin parakeratosis and scattered dyskeratotic keratinocytes in a suprabasal distribution. The acantholysis extended down follicular epithelium. There was minimal spongiosis and focal areas of mild vacuolar interface change and superficial perivascular lymphohistiocytic infiltrate with scattered eosinophils and melanophages. Direct immunofluorescent antibodies were positive for IgG and complement C3 in net-like intracellular pattern within the epidermis. Additionally, there was weak linear and granular staining for complement C3 along the basement membrane zone. Furthermore, epidermal antibody testing revealed positive intercellular substance antibodies and negative basement membrane zone antibodies. Given the overall clinical picture, the diagnosis was felt to be most consistent with pemphigus foliaceus (PF), an autoimmune blistering disease caused by autoantibodies targeting the keratinocyte protein desmoglein 1. This case demonstrates an unusual immunofluorescent staining pattern in PF exhibiting both intracellular and basement membrane immunofluorescent positivity, further highlighting the heterogeneous features of vesiculobullous disease. It is important for the pathologist to be aware of the variable immunofluorescent patterns in order to make an expeditious and accurate diagnosis.
cryoglobulins (801 ug/mL). Remote hepatitis panel and HIV were negative. Serum and urine electrophoresis revealed positive M protein with atypical restriction bands present in the IgG and kappa regions consistent with IgG kappa monoclonal gammopathy. A bone marrow biopsy was performed and showed no immunophenotypic evidence of lymphoproliferative disorder. CT scans of the chest, abdomen, and pelvis did not reveal neoplastic disease. Given the results of work-up, the patient was given a diagnosis of plasma cell proliferative monoclonal gammopathy associated cryoglobulinemia. He was treated with 5 sessions of plasmapheresis and subsequent Rituximab with mild gradual improvement of his digital ischemia. This case demonstrates the importance of skin biopsy to diagnose and guide treatment for a rare cause of digital ischemia.

204
A Case of Cutaneous Crospovidone Deposition: A Clue to Potential Injectable Drug Use
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Crospovidone, a polymer of poly N-vinyl-2-pyrrolidone, is an insoluble disintegrant found in pharmaceutical tablets. This material has been encountered in the lungs of intravenous drug users embolized with other components such as talc and microcrystalline cellulose. Crospovidone histologically appears as basophilic, dense, irregular, non-birefringent, and coral-like, resembling calcification. Crospovidone’s histochemical staining profile is distinct. The material appears violet-blue (H&E), red (Mucicarmine, Fontana Masson, Prussian blue and Congo red), and negative (von Kossa). Alcian blue and Movat pentachrome stains have variable staining, highlighting phagocytized and naked crospovidone blue and red to yellow-orange respectively. We present a case of primary cutaneous crospovidone deposition. A 31 year-old woman with a past history of drug use, presented with a wound at the popliteal fossa forming a necrotic eschar. Clinically, the differential diagnoses included vasculitis and levamisole necrosis, although the patient denied recent drug use. Biopsy examination disclosed dermal deposits of basophilic material with an irregular, jagged surface contour reminiscent of coral. Calcium von Kossa stain did not highlight this material. A background granulomatous reaction was present with the same material seen within giant cells. Alcian blue stained phagocytized crospovidone blue, and crospovidone appeared red with Mucicarmine and Congo red. Additional polarizable “Maltese cross” particles were present, consistent with talc. These findings, in the absence of vasculitis/vasculopathy, suggested the wound site was an injection site. Crospovidone is used in a variety of pharmaceutical tablets and does not point to a specific drug. However, histologic recognition of this material is important so potential injectable drug use gets considered in the overall clinical picture.
205

Neutrophilic Eccrine Hidradenitis in Association with Abiraterone

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A 90-year-old male with a history of prostate cancer metastatic to the bone, managed with Lupron, abiraterone (Zytiga), and denosumab (Xgeva), developed two discrete painless skin lesions on the left upper arm and left leg. The lesions were both 3 cm, raised, and erythematous with central necrosis. Histopathologic findings demonstrated interface dermatitis and neutrophilic inflammation involving eccrine glands with associated necrosis of eccrine glands. The histologic findings were felt to be consistent with the diagnosis of neutrophilic eccrine hidradenitis (NEH). NEH typically presents as asymptomatic to pruritic plaques and nodules on the trunk following induction chemotherapy in patients with acute myelogenous leukemia, and has also been described in patients with other hematologic malignancies, or more rarely, in patients with solid tumors. NEH has also been rarely associated with HIV infection and bacterial infection. NEH is typically associated with cytotoxic drugs, with the most common being cytarabine. Our patient had recently begun treatment with abiraterone. Abiraterone is an androgen synthesis inhibitor. This is to our knowledge the first reported case of NEH in association with this class of medication.

206

Necrotic Arthropod Bite in a Young Woman

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We present the case of a 17-year-old girl who developed a draining nodule on her right great toe after walking barefoot in the grass in Massachusetts and feeling what she thought was a bug bite. She presented for evaluation after several days, whereupon examination revealed a one centimeter white nodule with three millimeters of surrounding erythema on the dorsal right hallux. Serous fluid was drained, but the nodule persisted despite lancing. Gram stain and culture were negative. Deep shave biopsy revealed extensive liquefactive necrosis, marked edema, and an eosinophil-rich inflammatory infiltrate. Immunohistochemistry for HSV-1 and 2 was negative, and no bacteria or fungi were seen on Brown-Brenn and PAS stains. Levels through the block ultimately revealed a punctum containing an arthropod hypostome with surrounding microabscess. The brown recluse spider (Loxosceles reclusa) is well-known for its ability to produce a necrotic lesion and is often credited to be the perpetrator of necrotizing bites. Dermal necrosis, however, can also develop following a bite or sting by black flies (family Simuliidae), mosquitoes (family Culicidae), honey bees (genus Apis), soft ticks (genus Argasidae), centipedes (class Chilopoda), mites (subclass Acari), rove beetle (family Staphylinidae), fire ants (Solenopsis invicta), South African sand spiders (Sicarius hahni), and scorpions (order Scorpiones). In addition, exaggerated reactions with necrosis can occur in immunodeficient patients bitten by bed bugs (Cimex lectularius) and mosquitoes. We present this case to demonstrate the value of careful histopathologic examination to assess the etiology of necrotic nodules and to discuss the range of arthropods that can induce necrosis when they bite.
A 51-year-old woman with recurrent acute myeloid leukemia and a history of leukemia cutis, status post allogeneic transplant one year prior, complicated by graft-versus-host disease (GVHD), was admitted for fatigue and a temperature of 100.1°F. She reported a new, pruritic and mildly tender rash on her bilateral distal extremities present for one week. Physical examination was notable for scattered pink-to-violaceous, indurated papules with central excoriations on her bilateral lower extremities, distinct from the patient’s background GVHD. Her white blood cell count was 15.4. Punch biopsy of the right lateral calf revealed a neutrophilic infiltrate within the mid-dermal arteriolar walls and adjacent dermis.

Large intravascular thrombi containing neutrophils were present. This distinctive feature suggested a septic etiology, prompting performance of special stains for microorganisms. PAS, GMS, and Fite stains were negative for fungi and acid fast bacilli. Brown-Brenn stain revealed abundant Gram positive cocci within the thrombus and adjacent dermis, consistent with septic vasculitis. No leukemic cells were present (CD34 and CD177 immunostains examined). Bacteremia with septic vasculitis had not been suspected by the treating physicians. Etiologic evaluation of acute necrotizing vasculitis requires clinicopathologic correlation and often serology for autoantibodies. In the setting of active arteritis, the findings of intravascular thrombi with neutrophilic aggregates and adjacent interstitial dermal neutrophilic infiltrate are clues to an infectious etiology. This case illustrates the importance of nuanced histologic evaluation of vasculitis to elucidate etiology and provide timely, appropriate treatment for improved patient outcome.

Chronic cutaneous graft versus-host disease (GVHD) typically presents as a diffuse process. Rare cases of localized eruptions that follow Blashko's lines or dermatomal distribution have been described. Such a linear or dermatomal lichenoid GVHD (DL-GVHD) may appear on normal skin or in association with previous viral infections. In fact, GVHD may develop in varicella zoster scars and rarely in areas of measles exanthem, consistent with an isotopic phenomenon. Rarely, diffuse pattern chronic GVHD may be preceded by viral infection. While the exact causative relationship is not yet elucidated, unmasking of new self-antigens (cellular mosaicism) and generation of keratinocytic neoantigens have been attributed to the triggering and/or exaggeration of host immune response. We report a case of DL-GVHD in a 35-year-old woman with relapsed acute myeloid leukemia who underwent a haploidentical stem cell transplant. Her post-transplant course was complicated by hepatic GVHD and CMV reactivation, but she had been weaned off of immunosuppressive therapy for more than 18 months with undetectable CMV levels. Three years post transplant, the patient presented with asymptomatic progressively enlarging
Transient Acantholytic Dermatosis of Chemotherapy

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Grover’s disease-like eruption has been described in the setting of chemotherapy, usually with a combination of several chemotherapeutic agents in patients with malignancies. We present such a case with cytarabine as the sole agent. A 72 year old Caucasian man with recently diagnosed acute myelogenous leukemia developed a widespread erythematous papular eruption on the trunk, shoulders, arms, and lower extremities seven days after infusion of cytarabine and idarubicin. The rash persisted for three weeks. The patient was then infused with cytarabine alone and within eight days, again developed lesions in a similar distribution and morphology. The lesions again resolved in less than 3 weeks. Histologically, the lesions showed suprabasal/mid epidermal acantholysis forming a large lacuna with confluent dyskeratotic cells above the vesicle and rare dyskeratotic cells below the vesicle. Darier’s disease-like changes were present, with the presence of corps ronds and corps grains. Prominent extravasated red blood cells were seen in the papillary dermis, with numerous foamy histiocytes and perivascular lymphocytes in the upper dermis. From our case and a literature review, we noted that, in comparison to typical Grover’s disease, many of these Grover’s disease-like eruptions in the setting of chemotherapy demonstrate: a. wider distribution of the eruption, often extending to upper and lower extremities and feet, b. shorter duration of the eruption from days to weeks, c. larger intra-epidermal lacuna, and d. chemotherapeutic effects such as the presence of necrotic keratinocytes, large atypical cells and red cell extravasation.

Linear (Blaschkoid) Lichen Planus: A Rare Presentation During Infancy

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Lichen Planus (LP) is an uncommon entity in children and its presentation varies based on morphology and distribution of lesion. Linear LP is an extremely rare form of LP, in which linear lesions follow lines of Blaschko. We present a rare variant during infancy, an uncommon age group for this disease. A healthy 19 m.o. Indian male presented to dermatology clinic with a non-pruritic rash on his left flank for 3-4 months. Review of system was negative for symptoms of infection with no significant family history and his vaccinations were up to date. On physical examination, a single linear array of small brown to purple papules following the lines of Blaschko was present in the left mid-flank and mid-back. The clinical
A 78 y.o. man with metastatic melanoma developed a diffuse pruritic rash upon treatment with ipilimumab. The patient was skin type II with poorly defined confluent scaly red blanching papules with superficial crusting involving the face, neck, and extremities with sparing of the ventral arms and bathing suit area. There were no oral-mucosal lesions. Biopsy was performed to exclude erythema multiforme, vasculitis, SJS and TEN. Histopathology revealed mild spongiotic dermatitis with hyperkeratosis, slight acanthosis, dyskeratotic keratinocytes, and superficial perivascular lymphohistiocytic infiltrate with eosinophils. There was no evidence of acute vasculitis. The clinicopathologic findings were consistent with a Grade 3 ipilimumab-induced eczematous rash in a photo recall-type distribution. Ipilimumab was discontinued and the patient was treated with oral and topical steroids. There was mild improvement, but the rash persisted for 6 months until the patient's demise from melanoma. Ipilimumab is known to produce an eczematous dermatitis due to the presence of CD3+, CD4+, CD8+ T-cell and eosinophilic inflammatory infiltrate. An interesting feature of this case is the photo recall-type distribution, with marked sparing of the bathing suit area and ventral arms, suggesting a recall effect in areas of chronic sun exposure. Photo or UV recall dermatitis is a phototoxic eruption occurring in a previously sunburnt area following administration of drug. It is characterized by spongiosis, vesiculation, and apoptotic keratinocytes. It has been described in association with methotrexate, docetaxel/cyclophosphamide, and various antibiotics. To our knowledge, this is the first report of ipilimumab-induced photo recall dermatitis.

Prior studies have shown that inflammatory dermatoses of the vulva cause significant diagnostic difficulty for general pathologists and that dermatopathologists are more adept at rendering a specific and clinically actionable diagnosis in this setting. We sought to investigate diagnostic differences for non-neoplastic vulvar biopsies between gynecologic subspecialty pathologists and dermatopathologists.
at a large tertiary referral center. A search of our pathology database for all vulvar biopsies from July 2010-July 2015 identified 2138 cases. Neoplastic diagnoses were excluded, leaving 1127 non-neoplastic, inflammatory cases. We focused on 378 cases with nonspecific top line diagnoses that did not discretely communicate a specific diagnosis or inflammatory pattern (e.g. spongiosis), after excluding excisions, cases that lacked epithelium, and cases clinically suspicious for neoplasms. The cases were reviewed by 5 dermatopathologists blinded to the prior diagnosis and clinical history. The utilization of ancillary testing was evaluated by comparing what the dermatopathologist would have requested versus what was requested at time of signout. A discrete diagnosis/reaction pattern was able to be diagnosed in 305/378 cases (81%). The most common diagnoses were spongiosi mucositis/dermatitis, lichen sclerosus, and interface mucositis/dermatitis. Sixty-eight cases were identified as neoplasms, including squamous papilloma, benign keratosis and 6 cases of in situ carcinoma. In terms of ancillary tests, dermatopathologists would have requested ancillary testing in 48/378 (13%) versus 86/378 (23%) cases that had ancillary tests performed at the initial evaluation. These results support the value of dermatopathologist consultation. Consultation by dermatopathologists has the potential to improve individual patient care and to effect the nomenclature standardization that facilitates large-scale, population-based research.

213
Aminoquinoline Exacerbated Cutaneous Lupus Erythematosus

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We report a case of a 45-year-old female with a recent diagnosis of subacute cutaneous lupus erythematosus who developed a widespread pruritic rash after starting hydroxychloroquine. She denied signs and symptoms of systemic involvement and any other new medications prior to this eruption. Physical exam revealed a well-nourished female in no apparent distress, with over 90% body surface area involvement by annular, polycyclic plaques, some with dusky centers and some with a collarette of scale lining the inner ring of atypical target lesions. Lab results revealed leukocytosis, thrombocytosis, mildly elevated AST, low C4, >1:320 ANA titer, and positive rheumatoid factor and anti-SS-A. Histopathologic examination of a biopsy revealed widespread keratinocyte apoptosis, interface dermatitis, superficial perivascular lymphohistocytes inflammation with occasional admixed eosinophils and some increased dermal mucin. The patient was started on oral prednisone and clobetasol cream. Hydroxychloroquine was held, and her rash resolved in the ensuing weeks. Aminoquinoline induction of lichenoid drug eruptions has been well documented. However, at today’s doses, these agents have a favorable safety profile and are currently first line systemic therapy for cutaneous lupus erythematosus (CLE). Nevertheless, their historical tendency to damage basal keratinocytes persists and may be the inciting event in predisposed individuals for aminoquinoline induced or exacerbated CLE. Clinical hints of aminoquinoline induced or exacerbated CLE lesions include pruritus and a wider rash distribution. Though the distinction between idiopathic and aminoquinoline induced CLE frequently cannot be distinguished, eosinophils, acrosyringium homing lymphocytes, and alternating paucicellular interface dermatitis with lichenoid dermatitis are cited as possible histopathologic discriminators. Lesions ultimately resolve with hydroxychloroquine withdrawal.
215

**Giant Granuloma Annulare**

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Granuloma annulare is a dermatosis of unclear etiology for which three histological patterns have been described: 1) necrobiotic granulomas, 2) epithelioid granulomas, and 3) an interstitial pattern. All three histological patterns are focal and, with the exception of deep/subcutaneous granuloma annulare, are localized to the superficial or mid dermis. We describe a distinct clinical and histological subtype of granuloma annulare characterized by the unusually large size of at least 1 cm that to our knowledge has not been reported. Two patients presented for excision of a large dermal nodule; one was a 2.5 cm mass on the forearm and the other a 1.3 cm mass at the elbow. Histologically, aggregates of palisading necrobiotic granulomas containing mucin occupied the entire dermis and superficial subcutaneous tissue. Mitotically active histiocytes were present in one case. Special stains for infectious organisms (PAS, GMS, AFB) were performed on one case and were negative. These lesions were diagnostically difficult, as they could be mistaken for both benign and malignant entities such as rheumatoid nodule and epithelioid sarcoma.
The Spectrum of Immunohistochemical Staining of Non-melanocytic Lesions with Mart-1 and MITF
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Melan-A and MITF staining can be seen in both non-melanocytic neoplasms and inflammatory processes. Our aim was to establish the range of diagnoses in which spurious MITF and Mart-1 staining occurs. A variety of inflammatory and neoplastic cases were studied with a dual immunohistochemical stain, including post-inflammatory pigmented alteration, cutaneous sarcoidosis, discoid lupus erythematosus, dermatofibroma, a selection of other histiocytic lesions, and lymph nodes from non-melanoma patients. Mart-1 positive cells were identified in cases of post-inflammatory pigmented alteration (3/5 cases, 60%) and discoid lupus erythematosus (1/4 cases, 25%). Rare dual staining dermal cells were observed in discoid lupus erythematosus (3/4 cases, 75%). Diffuse MITF positivity was seen in a wide range of histiocytic lesions (22/26 cases, 85%) that included granulomatous, xanthomatous, and neoplastic entities, and scattered MITF positivity was seen in lymph nodes (2/10 cases, 20%). Finally, rare Mart-1 and dual staining cells were seen in lymph nodes without capsular nevus (2/10, 20% and 1/10, 10%, respectively). These results are consistent with previous reports of Melan-A and MITF staining cells occurring in interface dermatitis, however this study indicates that such staining may also occur in other inflammatory dermatoses and anatomic sites. Importantly, diffuse immunopositivity of histiocytes with MITF suggests that dual staining cells are histiocytes with spurious Mart-1 staining. The presence of Mart-1 and/or MITF staining cells in lymph node parenchyma is of unknown significance.

Acute Phototoxic Reaction Secondary to Topical Vitamin D3 and Tanning Bed Use
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We report a 31-year-old otherwise healthy female admitted with acute onset of severe skin pain and erythema. The eruption occurred one day after the patient applied a vitamin D3 moisturizing cream to her upper body and subsequently used a tanning bed. Physical exam showed large, confluent patches of erythema with associated edema and scattered vesicles involving the face, neck, chest, arms, and back. There was sheet-like sloughing of the epidermis of the central chest and upper back, with a positive Nikolsky’s sign of the adjacent skin. Well demarcated, geographic areas of sparing corresponded to areas where the patient did not apply the vitamin D3 cream. Biopsy revealed numerous necrotic keratinocytes extending throughout the epidermis with sparing of the dermal portion of eccrine ducts. There was subepidermal clefting with an underlying mild superficial perivascular and interstitial infiltrate composed of lymphocytes, histiocytes, and rare neutrophils. The involved skin was gently debrided and the patient discharged with antibiotics, ibuprofen, and acetaminophen. Phototoxic reactions are acute cutaneous eruptions characterized by cutaneous inflammation and cell damage following cutaneous and/or systemic exposure to both a photoactive agent and a sufficient amount of UV radiation, typically UVA. Most tanning bed sources utilize UVA radiation. The combination of the two induces delayed cutaneous erythema 24-36 hours after exposure. The severity of phototoxic eruptions is dose-dependent and sheet-like epidermal necrosis correlates with exposure to high dosage of UVA radiation from tanning bed use. This effect has also been seen in patients applying calcipotriene to affected areas immediately prior to phototherapy, a combination often utilized in the treatment of psoriasis.
Treatment of this condition is primarily supportive. NSAIDs and topical steroids may help decrease erythema and discomfort, particularly during the active phase of erythema after UVA exposure.

218

Linear Psoriasis: A Case Report of a 71-Year-Old Female

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A 71-year-old woman presented with an one-month history of pruritus, burning, flaky, and erythematous plaques. The lesions were in a very narrow lineal distribution, extending from the lateral left sole to the left popliteal region. The right leg also had similar erythematous plaques at pretibial region. She had no other lesions nor previous history of psoriasis. Microscopically, the skin biopsy revealed orthokeratosis, parakeratosis and traumatized Koebnerization. Elongation of rete ridges was not prominent. The PAS and the DIF stains were negative. The histology was difficult to distinguish from pustular dermatoses. Together with the clinical presentation, a diagnosis of psoriasis was favored. The patient had good clinical response to oral prednisone. Linear psoriasis is a very rare variant of psoriasis, characterized by a linear distribution of the psoriatic lesions along Blaschko’s lines. It usually response well to local treatment. The etiology is not known, but may be due to genetic mosaicism. Only about 23 reports have been published in the English literature. It typically occurs in the lower extremities of older individual. The main differential diagnosis is Inflammatory linear verrucous epidermal nevus (ILVEN). A few immunohistochemical markers have been shown to be helpful in the diagnosis; Ki-67 index is usual high in linear psoriasis such as in this case, but remains low in ILVEN. However, clinical presentation, histological findings and response to treatment are all needed to be taken into consideration to diagnose this rare form of psoriasis.

219

Lichen Planus Pigmentosus Coexisting with Frontal Fibrosing Alopecia, A case Report of a 69-Year-Old Caucasian Woman

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Lichen planus pigmentosus (LPPig) is a rare variant of lichen planus, most commonly described in Indians. An association with scarring alopecia has not been well documented. Herein, we present a case of a 69-year-old Caucasian woman with an established history of lichen planopilaris (LPP) and new lesions classical for LPPig. On presentation, there was a 4 month history of diffuse hyperpigmentation with mild erythema of the left axilla. The lesions were asymptomatic. Lesions of lichen planus were not seen. On biopsy, the epidermis was mildly atrophic, and there was a lichenoid inflammatory infiltrate associated with dermal melanin deposits and melanophages. Scattered neutrophils were seen in the stratum corneum and rare eosinophils in the dermis. Taken together with the clinical setting, a late
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A Rare Case of Pemphigus with IgC and IgA Antibodies to Desmocollins

A 77-year-old Caucasian male presented with one year of a painful pustular rash that began in his axillae and progressed to his trunk and extremities. Based on a previous biopsy from an outside institution reporting psoriasiform changes; he had been treated for presumed generalized pustular psoriasis with cyclosporine, methotrexate and acitretin, none of which improved his symptoms. A subsequent biopsy on the thigh performed at our hospital demonstrated subcorneal vesiculopustular dermatitis with focal acantholysis in the granular layer. Although IgA pemphigus was suspected based on the clinical and histologic features, on direct immunofluorescence, there was intercellular deposition of IgG and C3 in the upper epidermis with sparing of the basal layer, compatible with pemphigus foliaceus. A diagnosis of the pustular variant of pemphigus foliaceus was made. However, surprisingly, a subsequent ELISA performed in our laboratory was negative for IgG autoantibodies to desmogleins 1 and 3. Given the histologic and immunofluorescent findings, we suspect this to be a case of superficial pemphigus with IgG autoantibodies to desmocollins or other non-desmoglein proteins, as has been described in rare case reports of superficial IgG/IgA or variants of IgG pemphigus. Further ELISA studies are pending in a research laboratory to investigate this hypothesis.

Lymphoproliferative

Cutaneous Plasmacytosis: The Great Mimicker of Syphilis

Jennifer Bares, BS

Primary cutaneous plasmacytosis (PCP) is a rare lymphoplasmatocytic disorder of unknown etiology primarily seen in middle-aged men of Japanese descent that mostly follows a chronic indolent course. Increased serum level of interleukin 6 (IL-6) has been hypothesized to contribute to cutaneous and systemic plasmacytosis along with multicentric Castleman disease. We report a case of a 66-year-old Caucasian female with a two-year history of asymptomatic violaceous to erythematous scattered truncal thin papules without scale that follow skin tension lines. These lesions gradually spread to involve the upper back, chest, abdomen, and axilla and were refractory to treatment with doxycycline and clobetasol ointment. Pathologic examination revealed perivascular infiltrates of abundant plasma cells and lymphocytes with polyclonal kappa and lambda light chains. Immunohistochemical studies were negative for EBER, HHV-8, and spirochetes. Given no systemic involvement and negative work up
including ANA, anti-SSA/SSB, FTA-ABS, SPEP, UPEP IFE, and IL-6 levels, our patient was diagnosed with primary cutaneous plasmacytosis. With approximately 10 cases of PCP in the Caucasian population found in the literature, we herein highlight a rare case of PCP in a non-Asian descent and a great syphilis mimicker clinically and histopathologically.

222
Leukemia Cutis Presenting as Symmetric Panniculitis
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Leukemia cutis (LC) is a rare cutaneous manifestation of leukemia that portends a poor prognosis with an average life expectancy of 8.3 months. LC is most commonly observed in the setting of acute myelogenous leukemia (AML), afflicting 2.9% of patients with neither an age nor gender predilection. Lesions are most commonly seen on the head, neck and trunk. Histopathologic examination characteristically shows medium to large, leukemic cells infiltrating the dermis and often extending to subcutaneous adipose tissue. A 44-year-old woman with a history of AML status post matched unrelated donor peripheral stem cell transplantation presented to clinic for evaluation of erythematous nodules on the bilateral lower extremities of several weeks duration. Physical exam revealed three ill-defined, erythematous, thin nodules on each lower extremity. Differential diagnosis included erythema nodosum, infection and leukemia cutis given the patient’s known history of AML. Wedge biopsy revealed numerous atypical mononuclear cells with abundant cytoplasm within the lobules and septae of the subcutaneous adipose tissue consistent with leukemia cutis. A subsequent bone marrow biopsy showed a hypocellular marrow with panhypoplasia, but no evidence of leukemia. The patient was admitted to the hospital and started on salvage chemotherapy with fludarabine, cytarabine and granulocyte colony-stimulating factor (FLAG-IDA) in addition to field radiation of the bilateral lower extremities. Leukemia cutis presenting as bilateral lower extremity panniculitis with histologic correlate has yet to be reported. This case demonstrates an atypical clinical and histologic presentation of a rare disease. Given the poor prognostication associated with LC, it is of paramount importance to identify LC early and consider it in the differential diagnosis of bilateral lower extremity panniculitis.

223
Cutaneous Involvement as an Initial Presentation of Systemic CLL
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We report the case of a 62-year-old Caucasian male presenting with a one year history of bilateral, erythematous, patchy, upper arm rashes. Histologic examination demonstrated a diffuse, sheet-like infiltration of the superficial and deep dermis, separated from the epidermis by a grenz zone. Further examination revealed intervening pale regions, suggestive of proliferation centers, composed of a mixed lymphocytic population amid a background of hyperchromatic, small lymphocytes with round nuclei. The mixed population was comprised of small to intermediate sized hyperchromatic lymphocytes with scant cytoplasm (prolymphocytes) and larger lymphocytes with vesicular nuclei and central eosinophilic nucleoli (paraimmunoblasts). Immunohistochemical staining revealed a CD20, CD5, and CD23 positive neoplastic B-cell population with mild BCL-6 positivity. The totality of the findings was diagnostic of
cutaneous involvement by Chronic Lymphocytic Leukemia/ Small Lymphocytic Leukemia (CLL/SLL). Subsequent peripheral blood flow cytometry confirmed this diagnosis, demonstrating a B-cell population with lambda light chain restriction and an identical immunophenotype to the cutaneous infiltrate. CLL is the most common adult leukemia. Relative to other adult leukemias, such as Acute Myelogenous Leukemia, CLL infrequently involves the skin. Rarer still does CLL initially manifest via cutaneous involvement. We share this case as a learning opportunity for those who may not have encountered cutaneous CLL in their training.

224

Adult T-cell Leukemia Presenting Histologically as Mycosis Fungoides

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Adult T-Cell Leukemia involves the skin 50-70% of the time. Clinically, it has a diverse diagnostic differential. The manner of HTLV integration into host DNA may contribute towards the heterogeneity of clinical manifestations. Therefore, it is important to refine the histological criteria of cutaneous ATLL manifestations and its mimickers. We present a 29-year-old female from Haiti with hypercalcemia and bone lesions. Peripheral smear showed 25% atypical T cells positive for CD3, CD4, CD25, and negative for CD8 and CD7. Bone marrow flow cytometry confirmed the same aberrant T cell population. HTLV serology was positive and chromosomal analysis showed a complex, abnormal female karyotype. She was diagnosed with Adult T cell leukemia/lymphoma (ATLL) and began Hyper-CVAD chemotherapy. Few weeks later, she developed a diffuse rash with differential diagnoses that included molluscum contagiosum, allergic contact dermatitis, cryptococcus, penicilliosis, and varicella zoster. Skin biopsy morphology appeared similar to mycosis fungoides (MF) with microabscesses but with lesser than anticipated spongiosis. Cells of interest were immunopositive for CD3, CD5, CD25, and CD30, with loss of CD7. She was subsequently diagnosed with cutaneous Adult T-Cell Leukemia. MF is the most common mimicker, especially if the patient lacks a prior diagnosis. Histologically, in comparison, ATLL tends to have more apoptotic bodies, more extensive dermal infiltrate, less extensive epidermotropism, and a higher likelihood of giant cells with irregular nuclei. We are presenting this case to emphasize the potential histological similarities between MF and ATLL. It is imperative to consider demographics, clinical history, and special non-routine test results such as HTLV PCR or serology, immunohistochemistry pattern, and TCR clonal gene rearrangement in the diagnosis.

225

Secondary Cutaneous EBV Associated Diffuse Large B-Cell Lymphoma with Hodgkin/Reed-Sternberg-like Cells Development in a Patient with Angioimmunoblastic T-Cell Lymphoma

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Two different types of lymphoma occurs in the same patient is very rare. Here, we reported a 49-year-old Chinese female who developed cutaneous EBV-associated diffuse large B-cell lymphoma (DLBCL)
after the treatment of nodal angioimmunoblastic T-cell lymphoma (AITL). At the time of initial stage, microscopic examination of lymph node was consistent with AITL, and the EBV positive B-cells was not found. Twenty-one months later, the patient had multiple plaques and nodules on skin, whereas the biopsy of skin lesion featured as cutaneous AITL with EBV positive Hodgkin/Reed-Sternberg-like (HRS-L) B-cells proliferation. Most lesions were disappeared after a three-weeks treatment, however, one refractory lesion showed the histologic features of EBV-associated DLBCL. With the available data of previously reports, we found that extranodal involvement by secondary EBV-associated DLBCL and without detected EBV-infected B cell in AITL might be two negative factors for prognosis of this disease.

RESIDENT

A Case of Pediatric Primary Cutaneous Gamma-Delta T-Cell Lymphoma with an Indolent Presentation Mimicking CD8+ Mycosis Fungoides

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Mycosis fungoides (MF) is the most common subtype of cutaneous T-cell lymphoma (CTCL) in both adults and children. Most adult cases show a CD4(+), αβ T cell receptor (TCR)(+) phenotype and a slowly progressive disease course with evolution of patches into plaques and tumors. Pediatric cases tend to present as patches with an overrepresentation of CD8(+) phenotype and a good response rate to phototherapy. Primary cutaneous gamma-delta (γδ) T-cell lymphoma (PCGD-TCL) is a much rarer subtype of CTCL that is defined by γδ TCR expression. In both adults and children, it typically manifests as disseminated ulceronecrotic plaques and nodules on the extremities and exhibits an aggressive disease course. However, rare indolent presentations have been reported in both age groups. Herein, we describe the case of a 9 year old boy who presented with a one year history of progressive, slightly scaly, light brown patches that started on his abdomen and spread to his buttocks, legs, arms, and groin. There was no palpable lymphadenopathy. Bloodwork revealed normal CBC, CMP, and LDH values. Histopathology exhibited superficial lymphocytic infiltrates with epidermotropism but no dermal or subcutaneous involvement. Lymphocytes showed cytologic atypia, including hyperchromasia and irregular nuclear contours. Immunohistochemistry revealed a CD3(+), CD8(+), γδ TCR(+), CD56(+), CD4(-), CD7(-), CD30(-), and αβ TCR(-) phenotype. In situ hybridization for EBV was negative. The patient is currently being treated with narrow-band UVB phototherapy. To our knowledge, this is the first case report of pediatric CD8(+) MF with γδ T-cell phenotype. Our findings suggest that this subset of pediatric CD8(+) MF should be re-classified as PCGD-TCL. We will be undertaking a multi-institutional study to define the frequency of this CTCL phenotype in the pediatric population.
227

Lymphomatoid Papulosis Type E: An Angioinvasive Lymphoproliferative E Disorder with an Indolent Clinical Course
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Lymphomatoid papulosis (LyP) is a chronic lymphoproliferative disorder that belongs to the spectrum of primary cutaneous CD30+ lymphoproliferative disorders. It typically shows a waxing and waning clinical course and has been categorized into 5 subtypes by histomorphology. LyP type E (LyP-E), the most recently described variant, is characterized by angioinvasive behavior. Here, we describe a 42-year-old woman with a 1-year history of scattered recurrent papules on the trunk and extremities that healed spontaneously. Histologic examination of biopsies from three separate lesions revealed variably CD30+ atypical lymphocytes with CD8 predominance arranged in a perivascular and a periadnexal distribution. In addition, angioinvasion/angiodestruction with adjacent tissue necrosis was also present. In situ hybridization analysis for Epstein–Barr virus-encoded small RNA (EBER) was negative. Molecular analysis revealed monoclonal T-cell receptor gene rearrangement. The indolent clinical behavior and the above histopathologic findings are consistent with lymphomatoid papulosis, type-E. Due to the rarity of this entity and its histomorphologic resemblance to other angiocentric and angiodestructive lymphomas that require aggressive treatment, it is important to recognize this entity for proper clinical management.

228

A Hydroa Vacciniforme-like Eruption Associated with EBV in the Patient of NK/T Cell Lymphoma
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Compared to typical hydroa vacciniforme, Epstein-Barr virus (EBV)-associated hydroa vacciniforme-like eruption shows more variable clinical manifestations and prognosis. Some patients were reported to progress to malignant hematologic disorders such as lymphoma and leukemia. The hematologic disorders reported in the patients with EBV-associated hydroa vacciniforme-like eruption can be characterized by T-cell immunophenotype. Here we report a case of EBV-associated hydroa vacciniforme-like eruption in the patient of NK/T cell lymphoma. A 32-year-old Korean man presented with recurrent necrotic papules on the face. The symptoms developed at late-adolescent. The patient was diagnosed as EBV-associated NK/T cell lymphoma from the oral cavity. The patient also stated he had mosquito type hypersensitivity from childhood. A skin biopsy at his face showed EBV-associated hydroa vacciniforme-like eruption. However, provocation by UV irradiation did not reproduce skin lesion. EBV viral loading was detected but low at peripheral blood level. The patient was treated systemic chemotherapeutic treatment and showed complete response for lymphoma, but facial EBV-associated hydroa vacciniforme-like eruption still remained ups and downs.
Synchronous Type E Lymphomatoid Papulosis and Folliculotropic Mycosis Fungoides: A Rare Clinicopathologic Presentation

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Lymphomatoid papulosis (LyP) is a CD30+ primary cutaneous T-cell lymphoproliferative disorder. It usually presents as multiple ulcerated skin papules and nodules that eventually heal without treatment. Although it has been shown that patients with LyP tend to develop other types of lymphomas, including mycosis fungoides (MF) and classical Hodgkin lymphoma, either before or after the diagnosis of LyP, the presence of both LyP and MF synchronously is rare. Here we present an interesting case of an elderly patient who developed LyP and folliculotropic MF simultaneously. A 73 year old Caucasian male presented with nonhealing ulcerated nodules on his trunk and upper extremities of several months duration. The skin lesions started as nodules that eventually ulcerated and left a crater-shaped area. Some of the nodules healed on their own while others remain relatively unchanged. The physical exam
revealed plaque-like areas of induration on the forehead and forearms of at least 1-year duration. An excisional biopsy of one of the crateriform lesion revealed a large ulcer with an angiotropic CD4-positive and partially CD30 positive infiltrate and clonal T-cell receptor rearrangement. A biopsy from the forehead showed a distinctive folliculotropic infiltrate with relative absence of epidermotropism and focal follicular mucinosis. The majority of the lymphocytes were small to medium in size with irregular nuclear contours. Immunophenotypically, these lymphocytes demonstrated aberrant loss of CD7 expression and increased CD4/CD8 ratio. The above histological and clinical findings were consistent with a diagnosis of folliculotropic MF with synchronous/superimposed type E LyP. The occurrence of LyP and MF in a synchronous fashion poses a diagnostic change. Multiple biopsies may be necessary to reach the correct diagnosis. Awareness of this rare but important presentation of both entities is necessary for a prompt diagnosis.

231
Evolution of Lymphocytoma Cutis into Follicular B-Cell Lymphoma
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Lymphocytoma cutis is a cutaneous “pseudolymphoma” with immunophenotypic and molecular characteristics of a polytypic, reactive inflammatory infiltrate in the majority of cases despite histomorphologic features reminiscent of true lymphoma. Many environmental and iatrogenic insults have been implicated as drivers of this lymphoid hyperplasia in the skin, including exposure to precious metals and tattoo ink, infection with Borrelia burgdorferi and other microorganisms, vaccinations, trauma, and a wide list of drugs, but details of its pathogenesis and relation to malignant lymphoma remain controversial. In most cases, its course is benign, resolving spontaneously or with topical corticosteroids. However, local aggression and malignant transformation have been very rarely reported. We report a case of a 64 year old female with a one-year history of idiopathic, multifocal lymphocytoma cutis and previously negative IHC and flow cytometric studies who developed systemic, strongly bcl-2-positive, follicular B-cell lymphoma (WHO grade 1-2 of 3) with scalp involvement. In a 2002 series by Kulow et al, four patients with lymphocytoma cutis showed evolution to primary cutaneous B-cell lymphoma, however, systemic involvement was not identified at 14 months average follow-up. The following year, Nihal and colleagues reported 2 cases of cutaneous B-cell lymphoma transformed from lymphoid hyperplasia. Our case is unusual both for the evolution of cutaneous lymphoid hyperplasia to follicle center lymphoma of the skin, and for the systemic nature of the follicle center lymphoma. More work is required toward understanding systemic lymphomagenesis in the context of these possible precursor lesions in the skin, specifying their staging, and developing coordinated management strategies.
232

Langerhans Cell Histiocytosis Presenting as a Solitary Cutaneous Lesion in a 36 Year-Old
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Langerhans cell histiocytosis (LCH) is a rare disorder of proliferating clonal histiocytes. LCH presentation can span a wide spectrum from localized cutaneous lesions to widespread multorgan disease. Most commonly, LCH involves the bones, lungs, skin, or reticuloendothelial system. Adult onset of this disease is incredibly unusual, as most cases present in the pediatric population. We present a case of Langerhans cell histiocytosis occurring in a 36 year old man. The lesion appeared as a slightly tender and pruritic, 8 mm pink papule on the lower back. No other skin lesions were noted on examination. Clinically, the lesion was felt to be most compatible with non-melanoma skin cancer, with the differential diagnosis including basal cell carcinoma, Spitz nevus, and cyst. Histologic examination revealed irregular psoriasiform hyperplasia with confluent parakeratosis and moderate papillary dermal edema. Additionally, within the papillary and superficial reticular dermis was a mixed inflammatory infiltrate consisting of neutrophils, eosinophils, lymphocytes and histiocytes with reniform shaped nuclei. These histiocytes seemed strangely abundant and monotonous-appearing. A CD1a immunohistochemical stain demonstrated diffuse positivity in this cell population and highlighted the large quantity of Langerhans cells within the infiltrate. Further work up failed to reveal any evidence of systemic disease or the presence of BRAF mutations.

LCH presenting in adults may account for up to 30% of cases; however, LCH presenting only as cutaneous disease in adults is rare. While cutaneous LCH usually portends an indolent course, in some adults, a second hematological malignancy may present later in life. Because of this, guidelines for staging, treatment, and follow-up are important, but do not exist in the adult population as they do in pediatrics. Recognizing and diagnosing cutaneous LCH in adults can be difficult, but is necessary in order to investigate for systemic disease and monitor for potential future malignancies.

233

Unique Histopathological Finding of Prominent Mucin in Primary Cutaneous Anaplastic Large Cell Lymphoma
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Primary cutaneous anaplastic large cell lymphoma (pcALCL) is histologically characterized by a dense dermal infiltrate of large CD30-positive tumor cells and stains negative for expression of epithelial membrane antigen (EMA) and anaplastic lymphoma kinase (ALK), distinguishing it from systemic ALCL. Reactive lymphocytes, histiocytes, eosinophils, and neutrophils are commonly present in the periphery and in ulcerating lesions with epidermal hyperplasia. We present two cases of pcALCL with a unique histopathological finding of mucin. Case 1 is a 30-year-old female who presented with a 2-week history of multiple, large ulcerating nodular lesions on her neck, abdomen, chest, and shoulders. Case 2 is 55-year-old female who presented with a 3-week history of a single 1 cm lacquer-colored nodule on her right arm. The skin biopsies of both patients showed enlarged, atypical and pleomorphic-appearing lymphoid cells in the dermis with prominent mucin, and stained positive for CD30 and negative for ALK.
and EMA. Both patients underwent PET/CT scans, which showed no systemic involvement. To our knowledge, there are only a few other case reports with mucin in systemic ALCL, but none reported with pcALCL.

234  
**Plasmablastic Lymphoma: A Case Report**  
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Plasmablastic lymphoma is a rare neoplasm of blastic cells that displays morphological and immunophenotypic features of terminal B-cell differentiation. We present an interesting case of a 53 year-old man with HIV that was evaluated due to multiple asymptomatic bleeding violaceous-erythematous nodules on his left lower leg which had developed during the last year. The clinical findings were concerning for an HIV-related neoplastic or infectious process. A skin biopsy showed sheets of atypical enlarged lymphoid cells in the deep dermis with immunoblastic features, eccentric nuclei with prominent nucleoli and perinuclear hof. Mitotic index was high and apoptotic cells were present. Tumors cells were positive for CD138, CD38, MUM1, and CD56. EBV in situ hybridization was positive along with kappa light chain restriction, supporting the diagnosis of plasmablastic lymphoma. No lymph node or bone marrow involvement were found. The patient was started on chemotherapy due to rapid increase of cutaneous lesions. Plasmablastic lymphoma is seen most frequently in HIV-positive individuals. The oral mucosa is the most common site of presentation, but one half of cases can arise on extra-oral locations such as skin, anus, and gastrointestinal tract. Cutaneous involvement manifests as solitary or grouped, purple/erythematous nodules or plaques on the extremities. Immunohistochemistry is essential for the diagnosis. Characteristically tumor cells are positive for CD138, CD38, MUM1 and negative or weakly positive for CD45, CD20 and pax5. Staining for bcl-6 and CD56 are usually negative, although CD56 can be positive in cases showing plasmacytic differentiation, as in our case. Cytoplasmatic immunoglobulins can be demonstrated in about 50% of cases, with either kappa or lambda light chain restriction. Differential diagnosis includes other blastic lymphomas showing plasmablastic or plasmacytic differentiation. The prognosis is poor, as most patients die within 1 year of diagnosis.

235  
**Cutaneous Plasmacytosis: A Rare Entity with Classic Presentation**  
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Cutaneous plasmacytosis is a rare disease characterized by multiple plasma-cell rich infiltrates in the skin and an associated hypergammaglobulinemia. We present a classic example of cutaneous plasmacytosis in a 46-year-old Korean male. The patient presented with disseminated well-demarcated brown plaques on the face, neck, chest, and back in the absence of systemic symptoms (no fevers, chills, weight loss, or lymphadenopathy). Peripheral blood analysis identified hypergammaglobulinemia with elevated IgG but no indication of an associated lymphoproliferative process. CT and PET scans were negative for systemic disease. Skin biopsy showed a prominent superficial and deep perivascular and periadnexal
lymphoplasmacytic infiltrate. An immunohistochemical stain for CD138+ highlighted a predominant population of plasma cells, while CD20 and CD79a showed an intermingled B-cell population. Kappa and lambda in situ hybridization showed a polytypic plasma cell population with a slight kappa predominance. The findings were compatible with cutaneous plasmacytosis. Cutaneous and systemic plasmacytosis, originally considered variants of Castleman’s disease, are thought to be reactive processes which occur largely in Japanese males between 20 and 55 years old. Systemic plasmacytosis, defined by involvement of two organ systems in addition to the skin, might rarely progress to lymphoma, but overall, the course of cutaneous plasmacytosis is chronic and benign. Significant differential diagnostic considerations include infection, collagen vascular disease, pseudolymphoma and marginal zone lymphoma. The disease albeit rare should always be considered in the aforementioned patient demographic.

236
Blastic Plasmacytoid Dendritic Cell Neoplasm and A Potential Mimicker: A Retrospective Analysis of Registered Cases from Two Hospitals
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Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare hematologic aggressive malignancy. It has a M/F ratio of 3.3:1, with a mean age in the sixth decade. Two-thirds of patients have an abnormal karyotype. It has a predilection for skin and rapidly develops involvement of the bone marrow (BM), peripheral blood and lymph nodes. Five cases of BPDCN were gathered from the files of La Paz University Hospital in Madrid, Spain, and Wake Forest Baptist Medical Center (WFBMC) in Winston-Salem, NC. There were 4 males and 1 female, all Caucasian. The mean age at diagnosis was 63 years. All cases had cutaneous and BM involvement at diagnosis. Histologic examination from both sites showed proliferation of medium-sized blastoid cells. Immunohistochemical (IHC) stains and flow cytometric analysis showed CD45+, CD4+, CD56+, and CD123+. TCL1+ in 2 cases. All cases were negative for CD34 and lineage-specific markers. One of the male patients had monosomy 15. The female patient had trisomy 8 with a diagnosis of acute myelomonocytic leukemia and persistent plasmacytoid dendritic cell (pDC) aggregates in the BM biopsy taken 4 months after diagnosis. One additional case was included from WFBMC because it was considered as a potential clinical and histological mimicker in the skin. The patient was a 66 yo white male with a plaque on left flank. The skin biopsy showed medium-sized blastoid cells in subpapillary dermis, around blood vessels and in subcutaneous lobules. IHC showed CD3+, CD4+, CD123+, TdT+, CD34-, CD117-, and MPO-, raising the possibility of BPDCN, but the immunostains of the identical cells in the BM were CD4+, CD123+, CD34+ and CD56-, TCL1-, CD117- and lineage-specific markers-. Based on the CD34+, CD56- and TCL1-, the neoplasm was finally classified as an acute undifferentiated leukemia with cutaneous involvement. A less probable diagnosis could have been a BPDCN with an immature phenotype: CD34+/-, CD117-/dim+ pDC that are negative for CD56 and they coexist with non-pDC lineage blastoid cells; but this subgroup has a significantly lower rate of extramedullary involvement at presentation. In conclusion, it is important to perform a broad immunohistochemical and/or genetic analysis for a definitive diagnosis of BPDCN and to be aware of the maturational profile of pDC blasts in BPDCN and potential mimickers.
Hydroa vacciniforme-like Lymphoma in a 19 Year-Old Man Born in the United States

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Hydroa vacciniforme (HV) is a rare, chronic photodermatosis in children associated with Epstein-Barr Virus (EBV). Hydroa vacciniforme-like lymphoma (HVLL) is an aggressive EBV-positive T- or NK-cell lymphoma clinically resembling HV found in Asian and indigenous Latin American children. We present the case of a 19-year-old US-born male of K’iche’ (indigenous Guatemalan) ancestry who developed bilateral bullous and ulcerating lesions on sun-exposed areas of his lip and upper extremities accompanied by lymphadenopathy and low-grade fevers. The patient presented with a two-year history of isolated recurrent labial lesions that were presumed to be herpetic despite negative viral cultures. The patient’s condition progressed and eventually required admission when he developed lesions on the upper extremities. Laboratory studies revealed elevated AST, ALT, CRP, ESR, and LDH as well as normocytic anemia with reactive lymphocytes on smear. Titers for EBV viral capsule antigen IgG and EBV early antigen IgG were positive. EBV VCA IgM and EBV nuclear antigen IgG were negative. Histologic examination of the lesions displayed epidermal and dermal infiltration by hyperchromatic lymphocytes with large nuclei. Some fibrinoid necrosis was noted in deep dermal vessels. On immunostaining, lesional lymphocytes were positive for CD3 and CD8 and negative for CD4, CD10, CD56, CD79a, TdT and gm3. In-situ hybridization for EBV was positive. A stain for Beta-F1 was focally positive. A diagnosis of HVLL was made. This is one of the first cases of HVLL reported in the US. This patient exhibited many of the commonly reported manifestations of HVLL: recurrent bullous and ulcerating lesions, potential chronic EBV infection, and lymphadenopathy, as well as elevated LDH, transaminases, and inflammatory markers. Though the pathogenesis of HV and HVLL are unknown, it is suspected that HVLL may represent a more severe, malignant form of HV. Compared to HV, HVLL lesions can appear outside sun-exposed areas, tend to be larger, have a denser infiltrate, and present with systemic symptoms. Our case is unique in its 2-year history of isolated labial lesions, a manifestation only seen in this patient to our knowledge. Lastly, our case underlines the importance of obtaining a thorough social history, including ancestry.

Adult Onset Multiple Xanthogranulomas with Associated Monoclonal Gammapathy

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A 53-year-old male presented to the clinic for evaluation of a 3 year history of multiple progressively enlarging nodules scattered diffusely on his neck, torso and extremities. His past medical history was unremarkable, and he did not take any medications. Review of systems was negative for fevers, fatigue, night sweats and weight changes. On exam, there were numerous red-brown firm nodules and plaques on the bilateral median cubital fossae, axilla, arms, thorax, right posterior auricular neck, posterior thighs and ankles. A shave and a punch biopsy of nodules of the right and left arm were performed;
The diagnosis of multiple adult xanthogranulomas (MAXG) prompted a hematologic evaluation. Lab studies including blood counts, chemistries, urine protein electrophoresis, and serum free light chains were normal. Serum protein electrophoresis (SPEP) was notable for an elevated monoclonal immunoglobulin (M protein) of 1.00g/dL and immunofixation showed the presence of lambda monoclonal paraprotein. A skeletal survey showed no lytic bone lesions. Overall the patient’s risk of progression to multiple myeloma was calculated at 5% over 20 years. Discussion: MAXG is a rare condition whose etiology is poorly understood. The association between MAXG and lymphoproliferative diseases was not recognized until recently, with associated lymphoproliferative disorders reported in 25% of cases. Our case represents only the second reported case of MAXG in association with monoclonal gammopathy, and adds to the handful of cases associated with lymphoproliferative disorders.

239

**Primary Cutaneous Lymphomatoid Granulomatosis: An Unusual Presentation**

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Lymphomatoid granulomatosis (LYG) is a rare Epstein-Barr virus (EBV)-associated B-cell lymphoproliferative disorder characterized by polymorphic cellular infiltrates producing nodular mass lesions in affected organs; commonly the lungs, kidney, liver, and brain. Skin involvement may be seen in 25-50% of cases. We report a case of a 41-year-old woman with a history of sarcoidosis who presented with an isolated 3.8 x 4.0 cm annular ulcerated lesion of the left buttock, clinically concerning for ulcerative sarcoidosis versus pyoderma gangrenosum. A punch biopsy showed perivascular and periadnexal lymphoid infiltrates, extending from the superficial dermis to the subcutaneous adipose tissue. The cellular composition included abundant small lymphocytes, fewer histiocytes and plasma cells, and patchy clusters of large atypical lymphocytes with irregular nuclear contours, open granular chromatin with prominent nucleoli, and variable amounts of cytoplasm. The smaller lymphocytes predominated in the papillary dermis, where there was focal abutment with the dermal-epidermal junction, mild vacuolar interface change, and mild lymphoid exocytosis. The larger lymphocytes predominated in the reticular dermis and subcutaneous fat, associated with vascular damage and patchy areas of coagulative necrosis. No adipocyte rimming by lymphocytes was seen. Background T-cells were abundant, mostly positive for TCR-α/β, had CD4>CD8 expression, and maintained pan-T-cell marker expression. The large B-cells expressed EBER (>50/hpf), CD20, CD30, MUM1, PAX5, and had a Ki-67 index of 70-80%. CD10, CD21, and PD-1 were negative. AFB and GMS stains were negative for organisms. Based on the histology and immunophenotype, the patient was diagnosed with Grade 3 LYG which is considered a variant of diffuse large B-cell lymphoma. Staging work up with PET/CT and bone marrow biopsy was negative, confirming primary cutaneous LYG. She is currently undergoing treatment with multi-agent chemotherapy.
240

**Angioimmunoblastic T-cell Lymphoma Presenting with Cutaneous Medium-vessel Vasculitis**

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Angioimmunoblastic T-cell lymphoma (AITL) is a T-helper peripheral T-cell lymphoma that usually presents with lymphadenopathy and autoimmune phenomenon. Skin manifestations are common in AITL (40-50%); however, the clinical and histologic features are often nonspecific. We report an unusual type of a medium vessel cutaneous vasculitis in a previously undiagnosed case of AITL. A 54-year-old woman presented with an 8-week history of malaise, fever, oral ulcers, bilateral painful lower leg ulcers, and lymphadenopathy. On exam, large stellate ulcers with necrotic black eschar were seen on the anterior shins. Laboratory work up revealed autoimmune hemolytic anemia with positive Coombs test, leukopenia, polyclonal hypergammaglobulinemia, and high EBV titers. Anti-nuclear antigen, anti-neutrophil cytoplasmic antibody, and cryoglobulins were negative. Computerized tomography showed axillary and extensive mediastinal lymphadenopathy. Axillary lymph node biopsy revealed complete effacement by a polymorphous infiltrate of small to intermediate lymphocytes, polytypic plasma cells, and histiocytes. The lymphocytes were predominantly CD3+/CD4+ T cells showing variable positivity for BCL6 and PD-1 with partial loss of CD7, compatible with a follicular helper T-cell origin. CD21 highlighted expanded follicular dendritic meshwork. T-cell receptor gene rearrangement showed an identical T-cell clone in the lymph node and bone marrow. Biopsy of the lower leg ulcer and peri-ulcer skin showed epidermal necrosis overlying superficial and deep perivascular infiltrate of lymphocytes, plasma cells and neutrophils. There was fibrinoid necrosis of vessel walls with fibrin thrombi, consistent with small to medium vessel vasculitis. Based on the combination of lymph node and bone marrow findings, the patient was diagnosed with advanced AITL with associated paraneoplastic vasculitis. Rapid healing of her ulcers happened after chemotherapy and wound care. She is status post autologous stem cell transplant and remains without evidence of recurrence of her AITL or vasculitis.

241

**Relapsed EBV-associated Polymorphic B-cell Posttransplant Lymphoproliferative Disorder Presenting as a Solitary Subcutaneous Nodule: Report of a Case**

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Posttransplant lymphoproliferative disorder (PLTD) is a well-known complication of solid organ or allogeneic stem cell transplantation. Despite proclivity for multiorgan involvement, cutaneous PTLD is rarely encountered. A 35-year-old woman with a history of papillary renal cell carcinoma underwent renal transplantation in 2010. Approximately one-year later, she was diagnosed with nodal polymorphic B-cell PTLD. Complete response was achieved with IV Rituximab and remission ensued. Five-years later, while on oral tacrolimus and prednisone, she presented with a firm 1.5cm violaceous subcutaneous nodule on the left lower back. The clinical interpretation was cutaneous metastasis versus angiolipoma. Histopathologic examination revealed a large, lymphoid neoplasm with a deep center of gravity. Immunophenotyping showed a partially T-cell rich infiltrate with large sheets of B-cells, labeling with CD3 and PAX5, respectively. Intertwining pale zones comprised of small to medium-sized plasmacytoid
cells and scattered atypical large cells lacked CD3/PAX5 expression. These cells co-expressed CD79a and MUM-1, but lacked CD138 and CD56 expression. Kappa light chain restriction was also evident with diffuse EBV-encoded RNA expression. A diagnosis of cutaneous polymorphic B-cell PTLD was rendered. Our case highlights a rare subcutaneous presentation of relapsed polymorphic B-cell PTLD status post Rituximab. Cutaneous B-cell PTLD may be misconstrued as ‘atypical’ marginal zone lymphoma, particularly if T-cell rich, plasmacytic differentiation, and/or light-chain restriction is evident, or more simply, if a history of immunosuppression is not conveyed. Dermatopathologists and dermatologists alike should have heightened awareness of cutaneous PTLD to avoid misdiagnosis and subsequent life threatening disease progression.

242
Papillomatous Mycosis Fungoides Mimicking Inflamed Seborrheic Keratosis: A Rare Diagnosis
Confirmed via High-Throughput Sequencing
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Mycosis fungoides is the most common subtype of cutaneous lymphoma. Although a few disease variants have been accepted in the WHO Classification, many rare presentations have been described. We report a case of a 47 year-old male with an asymptomatic large cluster of brownish-pink, papillomatous plaques on the left hip and upper thigh for approximately 10 years. A biopsy done at an outside institution was diagnosed as a seborrheic keratosis. Due to increasing size, subsequent biopsies were performed and demonstrated similar epidermal changes previously seen, associated with a dense lymphocytic infiltrate and only focal epidermotropism. Immunohistochemistry showed CD3 and CD4 positivity in the lesional cells, with a marginally skewed CD4:CD8. High throughput sequencing showed shared dominant clonal sequences in TCR beta and gamma accounting for >60% of all sequences across multiple biopsy specimens, supporting the diagnosis of mycosis fungoides. Papillomatous/vegetating mycosis fungoides is a rare variant of an uncommon disease, with few similar cases in the literature. Some cases have been described as seborrheic keratoses arising in the setting of mycosis fungoides in a collision fashion, but the current patient’s physical exam suggests that the observed epidermal changes are induced by the tumor itself. The case’s limited epidermotropism and inconclusive IHC stains proved challenging, but the concerning clinical findings led to the use of high throughput sequencing. By demonstrating the exact TCR sequence and its proportion of all sequences in a given biopsy, high throughput sequencing can provide convincing evidence of clonality in ambiguous lesions, with accuracy comparable to or greater than traditional PCR. Although a case of seborrheic keratosis associated with mycosis fungoides in a collision fashion has been previously described, we believe that, the epidermal changes seen, in this case, are an epidermal response induced by the tumor.
Development of Primary Cutaneous Gamma Delta T-Cell Lymphoma 8 years After Chemotherapy and Radiation for Metastatic Colon Cancer
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T-cell lymphomas (TCL) that express γδ receptors are more aggressive than their αβ counterparts and are exceedingly rare. The primary cutaneous γδ TCLs (PCGDTCL) can present with prominent epidermal involvement or with a subcutaneous panniculitis-like histology. We report a 92 year old female with a history of stage III colorectal cancer in 2006, treated with chemo and radiation therapy, who presented to her dermatologist at an outside institution in 2014 with pruritic and flaky skin lesions on her ears, face and chest. A biopsy of the left ear in 01/2015 revealed a cutaneous TCL which was confirmed to be confined to the skin and subcutis by a PET/CT scan. On 08/2015 a second biopsy of a cutaneous chest wall lesion was performed at our institution which revealed diffuse sheets of medium to large sized neoplastic lymphocytes. Some of the neoplastic cells were rimming adipocytes and had a panniculitis-like pattern. The cells expressed CD3, CD26, CD45, CLA (cutaneous lymphocyte-associated antigen), TCR γδ, Granzyme B and TIA-1 by flow cytometry. These findings led to the diagnosis of a PCGDTCL. The γδ variant of cutaneous T-cell lymphoma is rarely diagnosed because the prevalence of non-neoplastic γδ T cells residing in the skin, the supposed precursors to this malignancy, is very low. Also, this diagnosis may be overlooked because many T-cell lymphomas are not worked up to see the type of receptor expression. The poor prognosis of PCGDTCL makes identifying this entity as early as possible very important since a more aggressive course of therapy is needed due to its poor response to conventional chemo and radiation therapy. The relationship between the onset of PCGDTCL and the chemotherapy and radiation for metastatic colon cancer in this case remains unclear.

Mycosis Fungoides with Strong Intraepidermal CD30 Staining
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Large cell transformation (LCT) occurs in a minority of patients with mycosis fungoides (MF), and is associated with a more aggressive course. LCT is defined histologically as the presence of large (nuclei 4x the size of typical) lymphocytes that comprise >25% of the atypical lymphocytes. CD30-positivity has been associated with LCT, but CD30 is not required. When CD30 is present in LCT, staining is usually limited to the dermis. We describe a case of MF with strong intraepidermal CD30 staining. A 60 yo male presented with 9mo history of psoriasiform rash involving 30% body surface area. Prior to referral to our center, his rash had been diagnosed clinically as psoriasis and apremilast was started; however, his rash progressed, with the sudden development of a painful, ulcerated plaque of the left arm. Skin biopsies of the ulcerated plaque and background psoriasiform lesions demonstrated an atypical epidermotropic, folliculotrop, and syringotrop lymphoid infiltrate of medium-sized, hyperchromatic lymphocytes with an elevated CD4:CD8 ratio, and loss of CD7. Strong CD30-positivity was noted in the epidermis, as well as scattered in the superficial dermis, though the dermal component was not otherwise diagnostic of LCT. Molecular studies demonstrated a T-cell clone; staging was negative for systemic involvement. Intraepidermal CD30 positivity is a rare finding in MF, and the clinical significance is currently unclear.
Intraepidermal CD30 positivity can be seen in other lymphoproliferative disorders, including lymphomatoid papulosis and pagetoid reticulosis, neither of which was a good clinicopathologic fit in our case. Earlier literature suggested that when intraepidermal CD30 is seen in early MF, clinical behavior is identical to early MF without CD30; however, more recent literature suggests that intraepidermal CD30 may be associated with a higher maximal stage. In our patient’s case, intraepidermal CD30 may be indicative of a more aggressive course, although his history is complicated by the use of an immunosuppressant medication. Our case emphasizes the need for more data on prognostic factors in MF.

245
Two Cases of Cutaneous Post-Transplant Lymphoproliferative Disorder
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By definition of the World Health Organization, post-transplant lymphoproliferative disorders (PTLD) are lymphoid or plasmacytic proliferations which develop in recipients of solid organ, bone marrow, or stem cell allografts as a result of immunosuppression. Most cases of PTLD are associated with Epstein-Barr virus (EBV) infection. PTLD frequently involves the internal organs to include lymph nodes, liver, gastrointestinal tract, central nervous system, and often the transplanted organ. Cutaneous involvement of PTLD is exceedingly rare. We report two new case of PTLD presenting as multiple nodules and plaques on the lower legs of transplant recipients. Our first patient is a 59-year-old male kidney transplant recipient. Histopathologic examination and immunohistochemical (IHC) studies performed on one of the nodules revealed an atypical plasmacytoid and plasmablastic proliferation that showed lambda light chain restriction, CD138 positivity, and EBV positivity. These findings are diagnostic of plasmablastic PTLD, an uncommon variant of monomorphic PTLD. Our second patient is a 60-year-old male lung transplant recipient. Histopathologic examination and IHC studies performed on one of the lesions showed CD30, CD45, and in situ hybridization for EBV RNA (EBER) positivity. In situ hybridization for kappa and lambda light chain RNA showed kappa light chain restriction. IHC studies for CD3 and CD20 were negative. Although CD20 was negative, the kappa light chain restriction indicates a B-cell lineage. These findings demonstrate a monomorphic PTLD most consistent with a diffuse large B-cell lymphoma.

246
Spindle Cell Variant of Primary Cutaneous B-Cell Lymphoma
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Primary cutaneous spindle cell lymphoma is a rare variant of primary cutaneous B-cell lymphoma (PCBCL), although not represented in WHO–EORTC classification, it needs to be distinguished from other malignant spindle cell tumors including spindle cell melanoma, sarcomatoid squamous cell carcinoma, atypical fibroxanthoma, and soft tissue sarcomas. We report 3 cases of primary cutaneous spindle cell lymphoma in 2 males and 1 female (age range 66-76 years). The patients presented with solitary skin lesions, distributed in the head and neck area and the chest. One patient had been diagnosed with
Unilesional Follicular Mycosis Fungoides: Report of Five Cases and Review of the Literature

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Unilesional follicular mycosis fungoides (UMFM) is a rare variant of cutaneous T-cell lymphoma (CTCL) characterized by selective involvement of the hair follicles by neoplastic T cells presenting as a solitary lesion occupying less than 5% of the body surface. We describe 5 patients (all males, age range 14-64 years, mean: 35) who presented with a solitary lesion on the trunk or head and neck for a period of time. The lesions were indurated erythematous and scaly patches and plaques associated with follicular prominence and hair loss. The biopsies showed an atypical folliculotropin lymphocytic infiltrate accompanied by follicular mucinosis in certain cases. The folliculotropic infiltrate extended to involve the lower isthmatic part of the follicle and in 1 case there was an alopecia areata-like lymphomatoid bulbitis. There was no evidence of large cell transformation nor was there a significant degree of infiltration of the interfollicular dermis or epidermis. Higher magnification disclosed marked cerebriform atypia amidst the lymphocytes. Phenotypic studies demonstrated a high CD4 to CD8 ratio in excess of 5 with a significant loss of CD7. The differential diagnosis was largely with a prelymphomatous T-cell dyscrasia be it in the context of folliculotropic T-cell lymphocytosis or alopecia mucinosa. Based on the depth of lymphocytic infiltration (involvement of the entire follicle), the degree of lymphoid atypia and the significantly abnormal phenotypic profile, the process was categorized as UFMF. In all cases the patients received either light treatment or complete radiation. One patient developed additional similar lesions involving the thigh and buttock after a period of 3-4 years of untreated unilesional MF; other patients in whom the duration of the lesion was less than 1 year were cured with local extirpative therapy. Our experience is similar to the most recently reported series of 7 patients in terms of demographics, site localization, clinical presentation, and excellent treatment response. The first reported case was in 1999 by Marzano and co-workers. 8 subsequent additional cases have been
reported. In summation UFMF is a potentially curable form of MF showing a younger male predilection. Early diagnosis and treatment intervention likely define a cornerstone for ensuring the best patient outcome.

248 RESIDENT
Leukemia Cutis as the Presenting Symptom of Acute Leukemia: Clinical and Histologic Spectrum in a Series of Four Patients
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Leukemia cutis (LC), a rare cutaneous manifestation of leukemia, can precede, follow, occur concurrently with, or present in the absence of (aleukemic) systemic leukemia. Thus, identification can be important for early diagnosis of systemic disease and prognostic assessment. LC is especially rare as the presenting symptom of leukemia, and is associated with a poor prognosis. Although more commonly seen in acute leukemias of myeloid and monocytic lineage, LC has also been seen in chronic leukemia. Here we review four patients who presented with diverse skin lesions ranging from an erythematous rash to violaceous macules and papules to subcutaneous nodules. Specifically, one case clinically mimicked a fixed drug eruption in a patient treated with antibiotics one week before presentation, and one case clinically mimicked miliaria rubra. Three of the four patients were diagnosed with acute myeloid leukemia (AML); one patient was diagnosed with chronic lymphocytic leukemia. Histologically, the lesions showed two overarching morphologic patterns: atypical perivascular lymphocytic inflammation or nodular dermal inflammation composed of histiocyte-like cells with prominent nucleoli. In the patient with clinically suspected miliaria rubra, there was a distinct perieccrine leukemic infiltrate. In cases of acute myeloid leukemia, tumoral cells were positive for myeloperoxidase (MPO), a helpful marker to distinguish myeloid from nonmyeloid cells, and CD68, a marker expressed on monocytes that is frequently positive in AML. The cells were negative for CD14, a marker helpful for evaluation of monocyte maturity. In the absence of systemic leukemia, common diagnostic tools for hematologic malignancies such as bone marrow biopsy and flow cytometry are non-contributory, making morphologic and immunohistochemical analysis of the skin lesions key to diagnosis. In conclusion, in cases of aleukemic LC, the varied clinical presentation correlates closely with histologic presentation.

WITHDRAWN
250
Cystic and Comedonal Mycosis Fungoides with Folliculotropism
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Mycosis Fungoides (MF) is the most common form of primary cutaneous T-cell lymphoma (CTCL). Classically, this disease presents as irregularly shaped, scaly, erythematous macules and patches that may progress to plaques and tumors commonly involving the buttocks, breasts, and flexures of extremities. Folliculotropic MF (FMF) is a rare, more aggressive variant that commonly presents as erythematous indurated plaques or tumors with comedo-like papules, acneiform lesions, plugged hair follicles, or cysts affecting the head and neck. We present a 29 year old woman with a 1 year history of right thigh cysts. Surgical excision revealed follicular cysts with FMF. She then presented to our clinic at which time there were asymptomatic ill-defined few cm erythematous indurated non-scaly plaques with several open comedones on the right buttock and gluteal cleft. Histological examination of a skin biopsy revealed a follicular cyst with a moderately dense infiltrate of small to medium atypical lymphocytes which were CD3 positive with loss of CD7 expression and CD4 to CD8 ratio of approximately 3.5:1. T-cell gene rearrangement studies showed monoclonality identical to the patient’s previous cyst excision. The patient was started on triamcinolone 0.1% ointment in the morning and tazarotene 0.1% cream at night which provided clinical improvement. This case highlights the importance of integrating clinical morphology, histopathology and immunophenotypic findings of a rare variant of cutaneous lymphoma.
Cutaneous CD4+ small/medium sized pleomorphic T-cell lymphoma is a relatively rare subtype of cutaneous lymphoproliferative disorder with an indolent clinical behavior. It is a provisional entity in the World Health Organization (WHO) classification of cutaneous lymphomas. Herein, we report a case of solitary erythematous nodule in the left infraorbital area in a 56-year-old white female. The lesion was not itchy or painful and was present for 2 months at presentation. The patient denied any fever, night sweats, weight loss or fatigue. A shave biopsy was done to rule out basal cell carcinoma. The histology revealed a moderately dense perifollicular and peradnexal lymphohistiocytic infiltrate compatible with a lymphoproliferative process. Subsequently a punch biopsy of the lesion was investigated and the microscopy revealed a dense nodular lymphoid infiltrate distributed throughout the superficial and deep dermis without any epidermotropism or folliculotropism. The infiltrate was composed of pleomorphic small to medium sized lymphocytes. Immunohistochemical stains demonstrated the predominance of CD3+, CD4+ T-cells and a minor component of CD20+ B-cells. PD1 highlighted a significant subset of cells. Kappa and lambda light chain stains revealed a scant population of polytypic plasma cells. CD30, CD56, MUM-1, TIA-1, CXCL-13, bcl-6 and cyclin-D1 highlighted rare cells. EBER in-situ hybridization and ALK-1 stains were negative. The T-cell clonality study revealed a monoclonal T-cell population with clonal peaks in both TCR beta and gamma tubes. A primary cutaneous CD4-positive small/medium T-cell lymphoma was highly considered. In the meantime, the patient underwent root canal process for her toothache due to some chronic dental inflammatory process. The skin lesion started subsiding following the procedure and is almost resolved. This case highlights an unusual course of a so-called clonal disease and hence differentiating it from other lymphoproliferative process remains a challenge.

Hypopigmented mycosis fungoides (HMF) is a rare subtype of mycosis fungoides (MF) but relatively common in children. Large cell transformation in HMF is exceptionally rare. Herein, we report a case of HMF in an 8-year-old middle-eastern male who presented to us with a 6 year history of hypopigmented patches. The lesion started as a small hypopigmented patch in the lower back at an age of 2 years. At presentation, there were well-demarcated hypopigmented smooth patches involving bilateral arms, lower back, buttocks, posterior thighs, and lower legs. Few of these patches revealed background erythema and pink papules at the periphery. The differential of pityriasis alba, HMF, and vitiligo were considered at this point. The punch biopsy revealed an abnormal epidermotropic T-cell infiltrate with the lymphocytes immunoexpressing CD2, CD3, and CD5. The intraepidermal lymphocytes demonstrated predominant expression of CD8. The T-cell clonality study was positive with clonal peaks in both TCR beta (A and C) and TCR gamma (A and B) tubes. The findings were most compatible with HMF stage IB.
Patients infected with human immunodeficiency virus type I (HIV-1) are more likely to develop cutaneous malignancies from oncogenic viruses such as human herpesvirus 8 (HHV-8), Epstein-Barr virus (EBV), and human papillomavirus (HPV). Of lymphoid neoplasms, B-cell non-Hodgkin lymphomas are more common in HIV patients. While HIV and HTLV-I co-infection is known to occur, Adult T-cell leukemia/lymphoma associated with this co-infection presenting cutaneously appears quite uncommon. We report an unusual case of a 61-year-old male with history of HIV on HAART, with painful pink papules and macules on distal fingers, and innumerable pink, edematous, discrete papules on the lower to mid back for more than a year with waxing and waning course. Biopsy of the back showed a dense atypical lymphocytic infiltrate in the dermis with perivascular accentuation and focal epidermotropism. Immunohistochemistry demonstrated a markedly increased CD4:CD8 ratio and CD25 expression. T-cell receptor gene rearrangement analysis of the biopsy and an earlier blood sample revealed an identical clonal population. The patient tested positive for HTLV-I antibodies and peripheral blood smear showed atypical lymphocytes. His HIV viral count remained undetectable. His WBC count at presentation was 23.3 with a CD4:CD8 ratio of 20:1. These findings support the diagnosis of HTLV-I associated T-cell lymphoma/leukemia with cutaneous involvement. Retrospective review of peripheral blood tests revealed a sharp increase in WBC and absolute CD4 counts as well as CD4:CD8 ratio about a year prior to presenting to dermatology, corresponding strikingly to rash onset. Few HIV-associated peripheral or cutaneous T-cell lymphomas have been reported. Literature search revealed only one case of HTLV-I associated CD4+ T-cell lymphoma/leukemia in an HIV-2 positive patient who presented with erythroderma. Similarly, HTLV-II is associated with rare cases of neoplasia in HIV patients, particularly large granular lymphocytic (LGL) leukemia, and cutaneous CD8+ T-cell lymphoma. This case demonstrates a rare case of HTLV-I associated CD4+ T-cell lymphoma in an HIV patient with a singularly unique presentation of non-diffuse, papular, waxing and waning cutaneous eruptions.
Primary cutaneous anaplastic large cell lymphoma (pcALCL) is generally regarded as an indolent CD30+ proliferation with a good prognosis. However, patients with extensive limb disease (ELD) have a more aggressive course that is often refractory to common treatments. We report a 73 year old gentleman who presented to clinic with indurated scaling nodules of his left leg. These began as small, asymptomatic, raised lesions that over six months had enlarged and become tender and pruritic. New growths were still appearing throughout the affected limb. Biopsy revealed a diffuse infiltrate of large, atypical lymphoid cells extending through the dermis and subcutis. These cells expressed CD2, CD3, CD4, vimentin, and TCR-beta. More than 75% of these cells were CD30 positive, and many also co-expressed CD45. PET-CT scans showed no signs of lymphatic spread or other systemic involvement. The patient was diagnosed with pcALCL-ELD stage T2bN0M0, and treatment was initiated with local radiotherapy. He was found to be mildly anemic and leukopenic; bone marrow biopsy identified hypercellularity consistent with myelodysplastic syndrome. It is unclear what relationship—if any—exists between his hematopoietic disorder and the cutaneous lymphoma. Case reports have described the synchronous occurrence of cutaneous lymphomas and myelodysplasia, but often in the context of immunosuppressive treatments or chemotherapeutics. This case raises awareness of the pcALCL-ELD subtype as a particularly malignant variation of an otherwise relatively benign lymphoma.

Mycosis fungoides (MF) is the most common type of cutaneous T-cell lymphoma (CTCL) and is well known for its wide variety of clinical presentations. The classic presentation is characterized by variably sized erythematous patches with fine scale, which may progress to plaques and tumors. The variants of MF can be difficult to diagnose as the classic features may be absent or obscured. We present a 50 year-old Caucasian female with small, scaly pink macules and papules on the lower legs of 2 years duration. The lesions were asymptomatic and stable. The clinical differential diagnosis included pityriasis lichenoides, guttate psoriasis, and papular eczema. She was treated with empiric topical steroids, but given her lack of improvement by three month follow-up a punch biopsy was performed. The biopsy consisted of an infiltrate of enlarged, atypical lymphocytes with hyperchromatic, convoluted nuclei exhibiting marked epidermotropism and focal syringotropism. The lymphocytes were predominantly CD3(+), CD8(+), CD4(-), CD7(-), and CD30(-). The clinical and morphologic features were consistent with the papular variant of MF. The patient was transitioned to clobetasol and mechlorethamine, and her eruption has remained stable. The papular variant of MF was first described in 2005. It presents as a chronic papular eruption without conventional features of MF. The lesions are generally localized to the trunk and extremities. The 15 cases of papular MF described in the literature have generally shown a
good clinical prognosis, similar to early, conventional MF. However, some patients progress to typical MF so close clinical follow-up is essential.

256

Neutrophil-rich Cutaneous T-lymphoproliferative Disorders: An Uncommon Mimicker of Neutrophilic Dermatoses and Infections

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Some cutaneous lymphomas, such as anaplastic large cell lymphoma and angioimmunoblastic T-cell lymphoma, are known to have a mixed inflammatory infiltrate, including neutrophils. While others, such as mycosis fungoides (MF) and peripheral T-cell lymphoma, not otherwise specified (PTCL NOS) are not. A review of one institution’s files for cases of MF and PTCL NOS with a dense neutrophil infiltrate yielded 9 cases over 20 years. Four patients already had a diagnosis of cutaneous T-cell lymphoma. In 5 patients, these neutrophil-rich biopsies were their initial lymphoma diagnosis and the clinical impression was either pyoderma gangrenosum, impetiginized drug eruption, infection, eczema or cutaneous lymphoma. In the de-novo lymphoma cases, T-cell gene rearrangement studies were positive in 4 of 5 cases. One de-novo case had a negative T-cell gene rearrangement study, but had significant loss of CD7 and persistent mycosis fungoides on repeat biopsy. All cases were CD4 positive, with loss of CD7 and none co-expressed CD8. One case showed rare scattered CD30 positive cells and was classified as mycosis fungoides with CD30 positive large cell transformation. The remaining cases had either negative or weak/equivocal CD30 expression. None of these cases were positive for ALK. Cultures and/or stains for infectious organisms were negative in 7 patients. Two patients had positive bacterial cultures, one of which had septic shock. This patient also had involvement of PTCL NOS in an inguinal lymph node, with an associated neutrophil-rich infiltrate. One patient died of sepsis and one patient progressed to generalized erythroderma within 3 months. Six patients were alive and tolerating topical therapies, methotrexate, photo or radiation therapy at 3-12 months. One patient was lost to follow-up. The etiology of these neutrophil-rich infiltrates is unclear: they could be a reaction to a superimposed infection, a treatment effect, or possibly an inherent component of the lymphoma. Regardless of the etiology, these cases highlight an uncommon histologic feature of cutaneous T-lymphoproliferative disorders, which can mimic several non-neoplastic conditions, including infections.

257

A Rare Lesion on the Nose: Primary Cutaneous Acral CD8-Positive T-cell Lymphoma

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A 32-year-old female was evaluated for a pedunculated, long-standing, and unchanged papule on her nose. A punch biopsy demonstrated a diffuse dermal atypical lymphoid infiltrate comprised of medium to large cells accompanied by mild epidermotropism and folliculotropism. The infiltrate demonstrated immunoreactivity for CD3 and BCL-6. The CD8 to CD4 ratio was approximately 10:1. Cells stained positively for granzyme B and TIA-1 while CD30 and perforin were negative. CD20, CD21, and BCL2 highlighted only scattered cells within the inflammatory infiltrate. Given the histology, immunoreactivity pattern, and clinical history, a diagnosis of primary cutaneous acral CD8-positive T cell
lymphoma was rendered. This rarely reported entity has predilection for the ear and acral sites. Less than ten cases have been reported on the nose, and our patient is the youngest to date. The time course of the lesion is additionally quite remarkable. A twenty-year retrospective search through archives at our institution yielded no similar cases. Our patient is currently undergoing close clinical monitoring without recurrence of the lesion. Despite WHO provisional reclassification as a lymphoma, recognition and appropriate management are of this entity are of utmost importance to limit morbidity associated with therapies used to treat more aggressive cutaneous lymphomas.

258
Cutaneous T-cell Lymphomas (CTCL) in the Setting of Biologic Agents

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A 67-year-old woman presented with a few erythematous, scale patches and plaques on the extremities/trunk and a violaceous 2x3 cm tumor on her right forearm. Past medical history revealed a clinical diagnosis of plaque psoriasis for 20 years and historical medications included topical steroids and methotrexate. Due to treatment failure, she had been placed on secukinumab, an IL-17 inhibitor, 5 weeks prior to presentation. The IL-17 inhibitor resulted in marked improvement of her patches/plaques but rapid growth of the tumor. The tumor was diagnosed as primary cutaneous aggressive epidermotropic CD8+ T-cell lymphoma (PC AECTCL) based on the immunophenotype of the neoplastic cells. At presentation, a biopsy form a scaly plaque was obtained and the arm tumor was rebiopsied. Both specimens showed an atypical epidermotropic T-cell infiltrate with a T-cytotoxic phenotype (CD3+/CD4-/CD8+). The histologic differential diagnosis included mycosis fungoides with a T-cytotoxic phenotype, PC AECTCL, and less likely, gamma/delta T-cell lymphoma. PET/CT showed soft tissue thickening in the area of the right forearm tumor and two soft tissue nodules in the subcutaneous fat of the posterior thigh and left humerus all with increased FDG uptake concerning for involvement by the patients lymphoma; but normal lymph nodes. Secukinumab was discontinued. Quickly after discontinuation there was complete regression of the tumor and some recurrence of the patches/plaques. It is unclear what role the IL-17 antagonist played in the stimulation of this patient’s CTCL. IL-17 has been shown to both inhibit and promote the growth of mycosis fungoides. This case highlights the importance of incorporation of all concurrent medications, in particular new biologic agents designed to target cytokines involved in immune regulation, into the diagnosis of cutaneous lymphoma with a cautionary note of diagnosing an aggressive lymphoma in the setting of immunomodulatory therapy.

259
Primary Cutaneous ALK+ Anaplastic Large Cell Lymphoma in a 12 Year-Old Girl

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Anaplastic large cell lymphoma (ALCL) was first described in 1985 by Stein et al and is a clinically, morphologically and immunophenotypically heterogeneous neoplasm characterized by ALK expression, rearrangement of the ALK gene, and most characteristically its occurrence in children. Clinically, cutaneous ALK+ALCL can be divided into primary (cutaneous forms) and more typically secondary
Primary cutaneous follicle center lymphoma (PCFCL) commonly presents as solitary or grouped lesions on the scalp, head and neck. We have observed a high prevalence of men with limited scalp involvement and concomitant androgenetic alopecia among our patients with PCFCL. In order to further investigate this observation, we performed a retrospective review of patients diagnosed with PCFCL at our institution from 2006 to 2016. Clinical data and skin biopsies of all eligible patients were collected and reviewed. We identified 52 of 87 PCFCL patients in our database with scalp involvement. We were able to evaluate 48 of these patients for the presence of androgenetic alopecia (AA). Thirty were noted to have AA (26M, 4F). This group had a median age of 54 years (range=31-82), which was slightly younger than the entire PCFCL group (56.5). Most of these patients had limited and localized disease (T1=17, T2=7, T3=2) and most patients achieved a complete response (13/17) with skin directed therapies (surgery, IL steroids or radiation). Only one patient had nodal involvement and splenomegaly, which resolved with systemic therapy. Skin biopsies showed a predominance of a nodular pattern (21/26) with a mixture of centrocytes and centroblasts, while a diffuse pattern with large cells was noted in 5/26 biopsies. None of the patients with AA had disease progression with a median follow-up of 38 months (range=2-19 years). We concluded that PCFCL is significantly associated with scalp involvement and androgenetic alopecia in men (p=0.01). In our cases, this presentation tended to be indolent with no evidence of significant disease progression.
Double-negative Early Stage Mycosis Fungoides in a Pediatric Patient
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Mycosis fungoides is the most common form of cutaneous T cell lymphoma. It has several clinical and histopathological variants. Most variants of mycosis fungoides display a CD-4 predominant phenotype; however, hypopigmented and pagetoid reticulosis variants are known to have CD-8 predominance. Other immunohistochemical findings include frequent loss of CD-7. So-called “double-negative” mycosis fungoides is a histopathologic variant of mycosis fungoides that displays loss of both markers CD-4 and CD-8 as well as CD-7, retaining CD-45 and CD-3 positivity. Clinical presentation is often atypical, including localized, hypopigmented and ichthyosiform types, and this aberrant immunophenotype does not appear to have prognostic significance. We describe the case of a 13 year old female presenting with a 1 year history of progressive, asymptomatic annular hypopigmented patches of the neck and left upper back and arm, previously diagnosed as vitiligo, but minimally responsive to therapy with topical steroids. Biopsy revealed a superficial lymphocytic infiltrate with epidermotropism and predilection for the dermoeidermal junction, displaying marked “tagging” along the basement membrane. Immunohistochemistry revealed CD-45 and CD-3 positivity of the epidermotropic cells, but these cells stained negative for CD-4, CD-7 and CD-8. MITF was also examined, revealing normal numbers of melanocytes, and the lymphocytes were also negative for CD-20. The patient was diagnosed with double-negative hypopigmented patch-stage mycosis fungoides. Less than 20 cases of this entity has been reported in the literature, and this is only the sixth known report in a pediatric patient. We aim to remind pathologists and clinicians of this rare form of mycosis fungoides, and the need to distinguish it from other malignancies in the differential diagnosis.

Transdifferentiation from Systemic Follicular Lymphoma to Cutaneous Langerhans Cell Histiocytosis
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Classically, the differentiation of lymphoid and myeloid elements from pluripotent stem cells to mature, lineage committed hematopoietic cells is considered to be a unidirectional process. Follicular lymphoma (FL) is a mature B-cell lymphoma of germinal center B-cells with the translocation t(14;18)(q32;21) and BCL2 gene rearrangements. We received a case in consultation of a 57 year-old woman with a history of systemic FL, treated with rituximab, who presented with multiple scalp nodules. Punch biopsy revealed a diffuse infiltrate of atypical lymphohistiocytic cells involving the dermis and superficial subcutis, with patchy epidermotropism. Eosinophils were not conspicuous. Neoplastic cells contained abundant pale eosinophilic cytoplasm with occasional vacuoles, and enlarged nuclei with oval to reniform, polygonal and multilobate nuclear contours, vesicular chromatin, occasional nuclear grooves and variably prominent nucleoli. Mitotic figures were conspicuous. Immunohistochemical staining showed the lesional cells to be positive for CD4, CD43, CD1a, Langerin, S100 (pale), and Bcl2. The cells were negative for CD20, CD79a, PAX5, CD30, and CD3. Mutant BRAFV600E staining was negative. Fluorescence in-situ hybridization studies identified the same t(14;18)(q32;21) translocation within
lesional cells, found in the original follicular lymphoma specimen, confirming a clonal relationship. Langerhans cell histiocytosis (LCH) has been reported to arise in association with other hematolymphoid malignancies; and one case of clonally related, synchronous, FL and LCH was recently described along with a metachronous FL and Langerhans cell sarcoma. We present this case due to its unique evolution from a mature B-cell malignancy which transformed and transdifferentiated to cutaneous LCH; and to encourage dermatopathologists to approach similar cases with an open mind and broad differential diagnosis.

263

WITHDRAWN
Melanocytic Neoplasms

Antigen Negative Metastatic Melanoma

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Introduction: Melanocytic markers including S-100 are expressed in nearly all cases of metastatic melanoma. Although rare, metastatic melanoma can lose positivity for all antigens making definitive diagnosis challenging. Methods: We retrospectively reviewed metastatic melanoma cases from 1/2010-3/2016 at our institution to evaluate the incidence and characteristics of antigen negative metastatic melanoma. Results: Of 113 patients with metastatic melanoma, 3 (2.7%) metastases were negative for S-100 in addition to other melanoma markers tested. The mean patient age was 74.6 years (range 59-84) with a M:F ratio 2:1. In one case, the patient presented with a metastasis with positivity for melanocytic markers, and his subsequent metastasis was antigen negative. All cases showed epithelioid morphology with negative sentinel lymph node biopsy (performed in two cases). Two cases were BRAF V600E mutation negative. In the patient with positive BRAF V600E mutation, the patient died before initiating BRAF inhibitor therapy. One patient received immunotherapy. The average time lapse between antigen positive tumor and antigen negative tumor was 20.6 months. One patient died a month after the diagnosis of antigen negative metastatic melanoma, while 2 patients are alive at 2 and 28 months respectively. Conclusions: Definitive diagnosis in these difficult cases is largely based on clinical history and morphological comparison. Interestingly, all sentinel lymph nodes were negative for metastatic melanoma, and the majority of cases showed epithelioid morphology and lack BRAF V600E mutation. While it might be postulated that antigen loss could be secondary to treatment effect, only one patient in our series received immunotherapy.

265

Lentigo Maligna: A Potentially Challenging Diagnosis in the Young

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Dermatopathologists are taught to be wary of atypical junctional melanocytic proliferations on heavilysun damaged skin of the elderly because these changes usually signify melanoma in situ of lentigomaligna type. When junctional proliferation with minimal atypia is noted on the skin of young adults,pathologists often suspect a nevus. We review the case of a lentigo maligna in a young woman that wasoriginally classified as a junctional nevus. Clinical correlation led to the diagnosis of melanoma in situ of lentigo maligna type. With the increased incidence of melanoma, dermatopathologists must becomeaware of atypical presentations of melanoma in individuals of all ages. Diagnostic criteria for melanomain situ will be reviewed.
Primary mucosal melanoma is a rare malignancy that arises from mucosal melanocytes and is commonly associated with a prominent lymphocytic response. Although significantly less common than cutaneous melanoma, the prognosis for mucosal melanoma is appreciably worse, with overall death rates approaching 30% for all patients (compared to less than 10% for cutaneous melanoma). Using immunohistochemistry, we assayed 18 in situ and invasive mucosal melanomas and 14 metastases (from several primary sites including head and neck, the female genital tract, and the gastrointestinal tract) for PD-1 and PD-L1 expression. A total of 5 of 11 in situ lesions showed significant expression of PD-L1 (>1% of tumor cells) compared to 0 of 7 primary invasive tumors and 2 of 14 metastases (p = 0.0318, Fisher's exact test). Within tumor-associated immune cells, the majority of both in situ lesions (7 of 11) and invasive and metastatic tumors (12 of 21) exhibited significant (>5% of cells) PD-L1 expression. Additionally, a significant (>5%) PD-1-positive lymphocyte population was identified in 10 of 11 in situ melanomas, 3 of 7 primary invasive tumors, and 10 of 14 metastases. As PD-L1 expression in tumor-associated immune cells was recently shown to be an even better predictor of response to an immune checkpoint inhibitor targeting the PD-1 pathway than actual tumor cell expression of PD-L1, our results suggest that some metastatic mucosal melanomas may respond well to these therapies. Furthermore, the expression of PD-L1 by in situ lesions may relate to the tendency for mucosal melanomas to show extensive and occasionally multifocal radial growth phase components despite evidence of robust immune responses.

Melanoma may uncommonly undergo sarcomatous transformation and dedifferentiation into spindle cell morphology with loss of melanocytic markers. Dedifferentiated melanoma may very rarely form true rhabdomyoblasts with skeletal muscle immunophenotype (rhabdomyosarcomatous heterologous component). A 52-year-old woman was diagnosed with invasive melanoma (Breslow depth 0.83 mm) of the right upper back in 2012. This was treated by wide local excision without sentinel lymph node biopsy. In 2013, she developed a right axillary mass that was excised to show metastatic melanoma with two zones: epithelioid cell zones expressing S100 protein and MART-1 and spindle cell zones with overall loss of melanocytic markers but strong expression of desmin. BRAF V600E was mutated in this axillary mass including in the S100 protein negative, desmin positive zone. In 2015, a thoracic epidural mass biopsy showed atypical spindle cells with focal HMB-45 but essentially no S100 protein expression. Numerous rhabdomyoblasts, some with striations, were present; these were strongly positive for desmin and myogenin. In 2016, a right nephrectomy was performed for tumor metastasis to the kidney. The renal mass showed sheets of spindle cells and rhabdomyoblasts expressing desmin and myogenin but not S100 protein; only focal areas still retained expression of HMB-45 and SOX-10 supporting the
Follicular Malignant Melanoma: A Rare Morphological Variant of Melanoma: Report of a Case
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Follicular malignant melanoma (FMM) is a rare and recently described variant of melanoma. Here, we report a case of this unusual disease and comment on current literature. A 59 year old male with a history of melanoma in-situ and basal cell carcinoma presented to clinic for evaluation of a lesion on the chest. During a full-body skin exam, he was incidentally noted to have a 2mm flesh-colored papule on the dorsal left forearm. Clinically, the differential diagnosis included nevus, basal cell carcinoma and cyst. A shave biopsy was obtained and histological evaluation performed. Hematoxylin and eosin staining showed a dermal proliferation of atypical melanocytes extending from the follicular infundibulum to the adjacent reticular dermis. Immunohistochemical staining for Melan-A and HMB45 highlighted the tumor cells. 10% of the tumor cells were positive for Ki67. No epidermal changes were noted nor were signs of regression. The patient was diagnosed with follicular malignant melanoma with a Breslow depth of 1.1mm and Clark level IV. He underwent wide local excision and sentinel lymph node biopsy. Pathology revealed no residual melanoma and negative lymph node biopsy. FMM is histologically distinct from lentigo maligna (LM) and lentigo maligna melanoma (LMM) and clinically distinct from metastatic folliculotropic melanoma. Like LM, FMM occurs on sun-damaged skin. However, unlike LM, FMM does not have to include an epidermal component. Histologically, metastatic folliculotropic melanoma may be indistinguishable from FMM. Even more challenging may be achieving a clinical suspicion high enough for biopsy as the reported cases often look like an unremarkable comedone or cyst. Only through a coordinated effort between the clinician and the pathologist may the correct diagnosis be made and appropriate treatment sought.

Rosette-like Structures in an Atypical Spitz Compound Melanocytic Nevus
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INTRODUCTION Rosette-like structures (RLS) are rare histologic features seen in melanocytic lesions. There has been 1 other known reported case of these structures in atypical Spitz tumors (ASTs) and 3 others spitzoid tumors with RLS to undergo neural immunohistochemical staining.1 CASE An 11 year-old female presents with a lesion of the left ear. Gross specimen reveals 0.7 x 0.6 x 0.3 cm dome-shaped, white-tan and firm papule. Microscopic evaluation: -Nests of epithelioid and slightly spindled melanocytes w/ surrounding clefting along DEJ -Focal aggregates of eosinophilic basement membrane material (Kamino bodies) -In dermis, melanocytes forming RLS with peripheralized cells and central
ALK Expression is Found Lacking in Deep Penetrating Nevi

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INTRODUCTION: Recent studies have identified the presence of kinase fusions in Spitzoid neoplasms. Approximately 10% of Spitzoid neoplasms were found to harbor anaplastic lymphoma kinase (ALK) rearrangements, with corresponding strong diffuse ALK immunoreactivity. Deep penetrating nevi (DPN) are a subset of melanocytic neoplasms with features of wedge-shaped dermal proliferation with extension along adnexal structures. Their histologic features of primarily dermal growth, increased pigmentation, and HMB45 positivity have historically supported a classification scheme that grouped DPN with blue nevi while being separate from the Spitz family of tumors. However, a recent molecular study identified rare HRAS mutations in a subset of DPN, a mutation that is also present in a subset of Spitz nevi. The purpose of this study is to see if DPN possess ALK rearrangements, thereby providing more evidence that DPN may be pathogenetically related to Spitzoid neoplasms.

METHODS: 19 cases of DPN were evaluated by three dermatopathologists. Formalin-fixed, paraffin-embedded sections were stained with antibodies ALK. Cases with immunoreactivity for ALK will undergo fluorescent in situ hybridization (FISH) to investigate for the presence of a kinase rearrangement. RESULTS: Patchy and focal ALK expression was found in only 1 case of DPN (1/19, 5%). This case had been signed out as an “atypical melanocytic neoplasm with features of cellular blue nevus and deep penetrating nevus”. This patchy immunoreactivity is different than the diffuse immunoreactivity reported in ALK-rearranged Spitzoid neoplasms. Confirmatory molecular testing is still pending. All other reviewed DPN were negative for ALK immunohistochemistry. CONCLUSION: Initial studies suggest that most DPN lack ALK immunoreactivity, which does not support their classification in the family of Spitzoid neoplasms. Future studies will expand our sample size and investigate the expression of other kinases in DPN.
Melanoma with a Unique Pattern of Metastastic Locoregional Disease
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An 84-year-old white male initially presented to his local physician for evaluation of a pigmented skin lesion. His past medical history was significant for metabolic syndrome and cardiac-related comorbidities, but negative for any self or family history of cancer. On exam, there was a single, ulcerated, darkly pigmented lesion (1.8 cm) over his left dorsal forearm. A biopsy was performed and histopathologic evaluation revealed an asymmetric melanocytic proliferation consisting of irregularly distributed nests within the epidermis with extension into the deep reticular dermis. A prominent single cell population with confluence along the dermal-epidermal junction and extensive adnexal involvement was noted in the background of marked solar damage. The lesion measured to a Breslow depth of 1.56mm, Clark’s level IV with ulceration and no regression. The subsequent re-excision with sentinel node biopsy failed to show any residual melanoma. He subsequently presented multiple times over the next 3-4 years with erythematous, well-demarcated plaques containing numerous (~50-70) punctate black papules and nodules. Biopsies confirmed these to be locoregional metastatic recurrences of melanoma with dermal lymphatic infiltration. Therapy included additional forearm surgeries, radiation therapy and intralesional injections of talimogene laherparepvec with ultimate resolution of any active melanoma in the forearm or distant spread. This presentation of erythematous plaques as the initial spread of metastatic melanoma is a rather unusual and under reported presentation.

Tumoral Melanosis as a Therapeutic Response to PD-1 Inhibitor in Advanced Melanoma: Report of Three Cases
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Tumoral melanosis is defined as nodular aggregates of pigment-laden macrophages without melanocytes on histopathology. Although there is lack of consensus, tumoral melanosis adjacent to primary melanoma is considered as a sign of a tumor regression with the potential for metastasis and poor prognosis. Occasionally tumor melanosis is also reported as a consequence of pigmented epithelial neoplastic growth and trauma. The significance of tumoral melanosis in the setting of advanced melanoma treatment, especially in the era of emerging immunotherapy, has not been well documented. Herein we have observed tumoral melanosis in three patients with metastatic melanoma who underwent treatment with immune checkpoint PD-1 inhibitor (pembrolizumab). All patients had initial diagnosis of stage III to stage IV metastatic melanoma, and two of them received other unsuccessful treatment regimens including BRAF inhibitor and CTLA-4 inhibitor (ipilimumab) prior to pembrolizumab. The tumoral melanosis was found at the area of in-transit metastasis, axillary lymph nodes, and the area adjacent to the primary excision site, respectively. Immunohistochecmical stain to Melan-A was negative in all cases confirming the absence of melanocytes. All patients had significant clinical and radiologic response to the treatment with rapid resolution of metastatic diseases based on PET/CT imaging. All three patients remain clinically free of disease after follow-up time of 19 months, 12 months and 3 months, respectively. In conclusion, we speculate that tumoral melanosis can be observed as the pathologic treatment effect to PD-1 inhibitor in melanoma patients and possibly indicates optimal response to the treatment with rapid resolution of metastatic diseases based on PET/CT imaging. All three patients remain clinically free of disease after follow-up time of 19 months, 12 months and 3 months, respectively. In conclusion, we speculate that tumoral melanosis can be observed as the pathologic treatment effect to PD-1 inhibitor in melanoma patients and possibly indicates optimal.
response. Long-term follow-up and larger-scale study are needed to further elucidate the significance of tumoral melanosis as it correlates with clinical response and prognosis in patients treated with PD-1 inhibitor.

273

Acquired Blue Nevus of the Nail Bed

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Blue nevi are dermal melanocytic proliferations histologically characterized by dermal spindle-shaped and pigmented bipolar dendritic cells. This generally benign skin tumor can be congenital or acquired. The nevi usually present as gray-blue or brown-blue solitary nodules or plaques, often found on the skin of the head and neck, dorsum of distal extremities, and pre-sacral regions and occasionally in the oral cavity and mucosal surfaces. We report on a 47-year-old Japanese man who presented with a 2 mm blue circular macule on the nail bed immediately distal to the lunula of the right first toe. A punch biopsy of the nail bed revealed dendritic melanocytes containing fine melanin and numerous polygonal macrophages containing abundant coarse melanin throughout a fibrotic reticular dermis. A MART-1 immunohistochemical stain was positive for dermal melanocytes and a Fontana-Masson stain was positive for dermal pigment. The patient was diagnosed with an acquired common blue nevus on the nail bed, which was completely removed by punch biopsy. Melanocytic nevi of the nail apparatus are extremely rare simply due to a low number of melanocytes in the nail as compared to skin. Our case is truly unique because our patient’s nevus involved the nail bed, where melanocytes are often completely absent or dormant. For this reason, melanocytic nevi of the nail bed are rarely observed in clinical practice. Our report of a nail bed nevus is only the third such report in the literature, and the sole case of an acquired blue nevus of the toenail bed.

274

Diagnostic Distinction of Malignant Melanoma and Benign Nevi by a Gene Expression Signature and Correlation to Clinical Outcomes

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Background: Biomarker gene expression quantification shows utility as a diagnostic adjunct for ambiguous melanocytic lesions. A clinically validated 23-gene signature showed greater than 90% diagnostic accuracy compared to expert consensus histopathologic diagnosis. Here the sensitivity and specificity of this molecular test was additionally tested against clinical outcome based classification of melanocytic lesions.
Design: Expression of 23 genes was measured (qRT-PCR from FFPE biopsies) from 99 primary melanomas that ultimately metastasized and 83 benign nevi. A weighted algorithm was applied to the expression levels to produce a single numeric score, and the sensitivity and specificity of the score was determined based on clinical outcome-proven diagnosis.

Results: Malignant melanoma subtypes included superficial spreading, nodular, acral, desmoplastic and others, and all had proven distant metastasis (median follow-up 16.7 months). Nevi included banal, dysplastic (mild to severe dysplasia), Spitz and rare cases of "atypical melanocytic proliferations" of uncertain potential, and all had no adverse events (median follow-up 74.9 months). The gene expression score differentiated malignant melanoma from benign nevi with a sensitivity of 93.8% and a specificity of 96.2%.

Conclusions: The gene expression score distinguishes melanoma from nevi with a high degree of accuracy as compared to the diagnostic standard of clinical outcome. Additional studies evaluating potential causes of false negative and false positive results may contribute to improved utilization of the test as an adjunct to histopathology.

275
Rethinking Melanoma of Unknown Primary by Targeted Next Generation Sequencing: A Case of "Primary Melanoma of the Adrenal Gland"

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Although primary melanoma of the adrenal gland is a recognized entity, these lesions are exceptionally rare with only 23 cases having been described, and the underlying genetic changes have yet to be documented. The involvement of the adrenal gland by metastatic melanomas of cutaneous or visceral origin is far more common. In cases with a single gland involvement and unknown site of origin, the histologic and clinical distinction between a visceral primary and a metastatic disease can be challenging. This distinction is particularly important to determine appropriate therapy for localized versus advanced metastatic disease. Recent advances in our understanding of the genetic alterations in different subtypes of melanoma and specific drug targetable mutations have changed the way in which we approach patient management. We describe a case of a single mass in the adrenal gland, diagnosed as melanoma by histologic and immunohistochemical examination, without an identifiable visceral or cutaneous primary confirmed by PET-CT scan. We performed targeted sequence analysis of a panel of 200 genes, including many with clinically actionable mutations, as well as others frequently present in cancers. Four pathogenic mutations were identified: BRAF c.1799T>A (p.Val600Glu; aka. V600E), RB1 c.18_19delinsTT (p.Arg7Ter), RB1 c.234G>A (p.Trp78Ter), and PTEN c.491dupA (p.Val166fs). One mutation of unknown significance, also in RB1 c.411A>T (p.Glu137Asp) was identified. BRAF V600E and PTEN mutations are commonly seen in melanomas derived from intermittently sun-exposed skin, and are related to UV radiation damage in cutaneous melanocytes. Concurrent mutational inactivation of the PTEN and RB1 tumor suppressors has been described as a potential mechanism for loss of BRAF/MEK dependence in melanomas harboring BRAF V600E mutations, such as this case. While this combination of mutations can be seen in metastatic melanoma of cutaneous origin, to our knowledge, this is the first genetic analysis of isolated adrenal gland melanoma. Genetic analysis of similar cases and a more extensive sequence analysis for a UV signature may further our understanding of the origin of such cases. Importantly, the identification of actionable mutations is a critical step in determining appropriate therapy for improved patient care.
Histologic Attributes of Melanoma: An Interobserver Comparative Study.
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Dermatopathologists apply histological criteria to distinguish benign melanocytic nevi from melanoma. The aim of this study was to calculate the accuracy, reproducibility sensitivity and specificity of 10 histologic attributes between five dermatopathologists. We created a study set from 100 difficult cases reviewed at an internationally recognized melanoma consultation center (study gold standard diagnosis). Study inclusion criteria included a primary biopsy and a definite benign or malignant gold standard diagnosis. Gold standard diagnoses with ambiguous features were excluded from the study. The cases were distributed to five dermatopathologists with criteria definitions and a standardized data entry sheet. Statistical analysis was used to calculate interobserver agreement, accuracy, sensitivity, specificity, positive and negative predictive values of each attribute. The average consensus Benign-Malignant Ratio (BMR) was 1.54; compared to 1.38 from the study gold standard. The observers group and the gold standard average agreement on final diagnosis was 76.8% and the intra-class observer agreement on final diagnosis was fair to moderate (K=0.32-0.64). There was higher intra-class observer agreement on broad surface diameter, pagetoid melanocytosis and lentiginous pattern (K=0.73, 0.51 and 0.48, respectively). Intra-class observer agreement was lowest for consumption of epidermis (K=0.16). Logistic regression analysis revealed that when present, pagetoid melanocytosis, lentiginous pattern, solar elastosis, and asymmetry are accurate at predicting the probability of a gold standard diagnosis of melanoma (p<0.05). Findings from this study may help design a diagnostic algorithm for difficult melanocytic lesions.

Early Versus Late Metastatic Recurrence in Melanoma: Nature Beats Nurture
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Increased tumor infiltrating lymphocytes (TIL) are associated with improved prognosis/responsiveness to immunotherapy, and are thought to reflect T-cell recognition of melanoma. During immune equilibrium, T-cells maintain cancer cells in a subclinical state. We sought to determine whether the immune contexture or inherent tumor characteristics predict time in equilibrium (time to recurrence) in a cohort of early versus late metastasizing tumors. 15 late recurring (>6 yrs, median 99, range 74-197 months) metastatic melanomas were compared to 15 metastatic cases with typical recurrence (median 23, range 1-66 months) that were matched for T stage and equally distributed by patient age/gender. Immune infiltrates were quantified by IHC (CD3, CD8, PD1) with Aperio digital image analysis algorithms, and grouped according to present or absent PD-1L expression. Primary tumor characteristics were also analyzed. Discriminating features were evaluated for statistical significance (2-tailed t-test). The cohorts did not differ significantly in the mean number/mm2 of CD3 (687 vs 405, p= 0.095), CD8(414 vs 245, p= 0.293), or PD1 (73.1 vs 124, p=0.41) positive cells, or the average of the proportion of CD8/CD3 and
PD1/CD3 cells (0.54 vs 0.51, p=0.836; and 0.38 vs 0.80, p=0.48 respectively). PD-1L expression (>1% cells) was seen in 7/15 (47%) late and 11/15 (70%) early recurrent cases (n.s.). Compared to late recurring tumors, those with early recurrence had significantly higher primary tumor mitotic rates (mean 6.23 vs 0.94/mm², median 6 vs 1/mm², range 0-20 vs 0-2/mm²; p<0.04). Breslow’s thickness and presence of ulceration did not significantly differ between the cohorts, although there was a trend toward increased ulceration in early recurring cases (40% vs 13%; p=0.1). The data suggest that tumor innate (genetic) factors may play a more important role than microenvironmental (immune) factors in early versus late recurrence in the absence of therapeutic intervention.

278
Tumor Cell Adhesion as a Risk Factor for SLN Metastasis and Predictor of Disease Recurrence in Primary Cutaneous Melanoma
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The ability to distinguish between lethal cancers that need treating and non-lethal cancers that don’t is an important challenge that – if met – could revolutionize the way we prevent, diagnose and treat cancer. Here we address this challenge in the context of cutaneous melanoma by applying our knowledge on a cancer-defining biologic system, cell adhesion, to identify high-risk melanoma at the time of diagnosis. We present data from a multi-institutional study to discover new molecular risk factors associated with SLN positivity and melanoma recurrence. Gene clusters with functional roles in melanoma metastasis were discovered by next-generation sequencing and validated by quantitative PCR. We then used PCR to quantify a targeted set of genes in >500 consecutive melanoma samples from unique patients. Outcome of interest was i) SLN biopsy metastasis within 90 days of melanoma diagnosis and ii) disease recurrence after the initial work-up phase. Logic and logistic regression analyses were used to develop a model for the likelihood of SLN metastasis and disease recurrence from molecular, clinical and histologic variables. A model to identify SLN positive melanoma that included β3 integrin, laminin B1, tissue-type plasminogen activator, and tumor protein p53 expression in combination with clinicopathologic variables (patient age, Breslow depth and tumor ulceration) performed significantly better than a model that only considered clinicopathologic variables and also performed well in a validation cohort. The aforementioned molecular model was also useful to assess relapse free survival after an initial work-up period of 90 days. We conclude that the addition of cell adhesion-linked gene expression variables to clinicopathologic variables improves the identification of patients with SLN metastases within 90 days of melanoma diagnosis and may aid in the identification of patients at risk for disease recurrence.
Lentigo Maligna Melanoma: A Unique Case Illustrating Evolution Over Many Years Eventuating into Deeply Invasive Disease Colonizing Squamous Cell Carcinoma
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Lentigo maligna was classified as benign in the past because invasive disease often did not develop for many decades. We present the case of a woman who underwent periodic evaluation for melanoma in situ of lentigo maligna type on her nose that eventuated into invasive disease. Her tumor was intimately associated with an invasive squamous cell carcinoma. Diagnostic criteria for lentigo maligna and the reports of associated “collision tumors” will be reviewed.

Histopathologic Findings of Talimogene Laherparepvec Treated Cutaneous Melanoma
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Talimogene laherparepvec (T-VEC) is an oncolytic immunotherapy utilizing a genetically engineered herpes simplex virus type 1 (HSV-1) vector designed to selectively replicate within the tumor cells and produce human granulocyte–macrophage colony-stimulating factor (GM-CSF). When injected within the tumor, it has been shown to induce regression of the injected tumor through a direct lytic effect, and of uninjected tumors through the induction of a systemic antitumor immune response, mediated primarily through the virally encoded GM-CSF. Following FDA approval in October 2015 for the treatment of unresectable melanoma, T-VEC has been increasingly utilized. However, detailed histopathologic descriptions of regressed melanoma lesions in the context of T-VEC therapy have been lacking. To understand the histopathologic characteristics of tumor regression following T-VEC therapy, we performed an analysis of regressed tumors from a 54 year old male patient with stage IIIC (T4aN3) melanoma involving left scalp. Multiple recurrent left scalp satellite tumors were treated with 12 biweekly intratumoral T-VEC injections. Three clinically regressed lesions with persistent pigment were biopsied and examined. All sections showed an intense mixed superficial and deep dermal inflammatory infiltrate, composed of neutrophils, eosinophils, lymphocytes and histiocytes. Residual tumor cells were not seen. SOX-10 and MART-1 immunostains highlighted normal melanocytes in the basal layer of epidermis but no cells in the dermis, confirming complete tumor regression. CD163 and myeloperoxidase immunostains highlighted histiocytes and neutrophils, respectively. Interestingly, the neutrophil-rich inflammatory infiltrate seen in these biopsy specimens is suggestive of an early neutrophilic dermatosis such as Sweet’s syndrome. This latter finding may be attributed to the activity of GM-CSF, which is known to induce Sweet’s syndrome when administered systemically.
Cellular Blue Nevus with Extensive Regression and Associated Granulomatous Inflammation: An Unusual Morphologic Pattern and Potential Pitfall of Malignancy

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Blue nevus is a relatively frequent, benign melanocytic lesion commonly seen in the face, buttocks, and acral locations. We report the case of a 52-year-old African American man that presented with a 1.5 cm, brown/blue patch on the right dorsal lateral foot. Histopathologically, there were two well-circumscribed dermal nodules composed of heavily pigmented dendritic spindled cells and melanophages, surrounded by fibrosis and extensive granulomatous inflammation composed of macrophages and multinucleated giant cells. Immunohistochemistry for SOX-10 highlighted few dendritic cells consistent with dermal melanocytes; these cells lack mitotic activity and display uniform nuclei, with inconspicuous nucleoli. Many of the macrophages expressed NKI/C3. Therefore, we established a final diagnosis of blue nevus with extensive regression and granulomatous reaction. Despite an extensive review of the literature, we did not find a report of overtly granulomatous inflammation occurring in regressed blue nevi and we believe that practicing dermatopathologists should be aware of this morphologic pattern.

Imaging Mass Spectrometry to Differentiate Benign Melanocytic Nevi from Melanoma

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Imaging Mass Spectrometry (IMS) is a new tool that can detect proteomic signatures. Imaging mass spectrometry (IMS) is a new tool that can provide proteomic information from specific cell types within formalin-fixed, paraffin-embedded tissues. IMS can provide proteomic information from specific cell type within formalin-fixed, paraffin-embedded tissues. We sought to identify differences in proteomic information in non-Spitzoid Melanoma as compared to conventional melanocytic nevi. IMS analysis was performed on 30 non-Spitzoid Melanoma and 30 conventional melanocytic nevi. Proteomic differences between the two groups were detected.
Melanoma is an uncommon diagnosis in children and is vanishingly rare in the first decade of life. Less than 2% of cutaneous melanomas occur before puberty, and less than 1% occur under age ten. Melanoma is a sinister diagnosis and not one to be rendered lightly at any age. In a child, especially the younger in age, the diagnosis of melanoma can be much more difficult for both pathologists and clinicians. These difficulties bring with them the risk of delaying diagnosis, and in turn, treatment. This is, unfortunately, more common in the pediatric patient, with more than half of cases having an increased mortality due to late diagnosis. We present a case of an otherwise healthy 18-month old girl who presented with a 3mm papule on her right upper arm. Treated initially with Cantharidin for presumed molluscum contagiosum, the lesion resolved but recurred in 2-months and was enlarging. Biopsy demonstrated an asymmetrical deep compound proliferation of large, fusiform and epithelioid melanocytes, which in the dermis did not mature and contained numerous deep easily identified mitotic figures. Ki-67 cell proliferation index was elevated and the tumor demonstrated significant loss of p16 immunoreexpression. Array-based comparative genomic hybridization demonstrated loss in chromosome 9 and gain in chromosome 20. These results supported the diagnosis of spitzoid melanoma in the setting of the malignant appearing histology. The rarity of childhood spitzoid melanoma coupled with its often difficult and poorly characterized classifications of tumors within its differential make it a difficult diagnosis to render. Knowledge of the histologic appearance, immunoreexpression profile and molecular findings in childhood spitzoid melanoma will aid in the accurate and timely diagnoses necessary to avoid treatment delays.

Case Report: Presentation of Phenotypic Heterogeneity in an Atypical Blue Nevus

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Background: Variants of blue nevi are defined by their cellular elements and histological appearance. Blue nevi manifest a high degree of morphological overlap amongst different variants. Herein we present an atypical blue nevus with phenotypic heterogeneity consistent with features of conventional, sclerosing, cellular and epithelioid variants. Case Report: An African-American female presented with an asymptomatic dark, domed lesion of the back, unchanged for several years. Clinically it appeared as a 1 centimeter cyst. Histology revealed a solid, fibrotic, spindle cell lesion with atrophic epidermis. It was deep-seated and focally involved the subcutaneous fat. Pigmented spindled and dendritic melanocytes were admixed with anastomosing fascicles of spindle cells. Melanophages, polygonal melanocytes and clear cells were also present in the lesion. The periphery appeared comparatively hypocellular. There were no mitoses or necrosis. Melan-A was positive and a bleached stain revealed low-grade melanocyte cytologic atypia. Because of large size, phenotypic heterogeneity and cytological atypia, the lesion was concerning for more than a conventional blue nevus: however, the lesion lacked sufficient criteria for melanoma. Discussion: Blue nevi may cause diagnostic difficulty because of a phenotypically diverse
Atypical Spitzoid melanocytic lesions are diagnostically and clinically challenging. To aid in the diagnosis of these lesions, fluorescence in situ hybridization (FISH) has been employed with success, particularly when results are diagnostically certain. However in 2.3% of cases, heterozygous loss of cyclin dependent kinase 2 a (CDKN2A, chr 9p24) has been identified. Though homozygous loss of CDKN2A is a known tumor suppressor in melanoma, heterozygosity has not been clinically correlated. We report eleven cases with heterozygous loss of CDKN2A with clinicopathologic correlation. Average age at the time of diagnosis is 28.5 years (range 2-55 years) with a female predilection (3M:8F), occurring on the extremities in 90.9% of cases. Morphologically, 9 of 11 lesions are characterized by a compound atypical Spitzoid proliferation with dermally based mitoses, while the remaining two lesions are described as malignant melanomas. Ki-67 proliferation index was performed in 72.7% (8 of 11) cases, with an increased labelling. 81.8% (9 of 11) of biopsies were completely re-excised due to narrow margins, with no recurrence of disease to date. Recommendation for sentinel lymph node biopsy was made in 3 cases, which are negative with no reported metastases. The mean follow up for all cases is 2 years. Heterozygous loss of CDKN2A in atypical Spitzoid lesions with dermal mitoses, may represent a step in the progression of malignant melanoma however to date, none are associated with aggressive biologic behavior.

Melanoma is the most common tumor to metastasize to the gastrointestinal tract, commonly affecting the small intestine, colon and anorectum. Primary mucosal melanoma can arise in any gastrointestinal site, most frequently affecting anorectal mucosa. Melanoma involving gastric mucosa, specifically, is exceedingly rare and carries a poor prognosis with a median survival of five months. The presence of atypical melanocytes exclusively within gastric epithelium has not been previously described. We report a case of a 52-year-old man with widespread BRAFV600E mutant metastatic melanoma who was referred to our institution for immune checkpoint antibody blockade therapy. The patient had previously been treated with BRAF inhibitors, and despite initial response to therapy, developed
resistance leading to disease progression and multi-organ involvement including the liver, spleen, and axial skeleton. Immune checkpoint antibody blockade with ipilimumab and pembrolizumab has been shown to induce significant tumor regression in patients with melanoma by upregulating T cell activity and removing the natural check on the host immune response. After his first dose of combination therapy, the patient underwent an upper gastrointestinal tract endoscopy for severe nausea and was found to have two pigmented lesions within the gastric body, one of which was biopsied. The biopsy showed gastric oxyntic mucosa with melanophages and scattered atypical intraepithelial melanocytes within the lamina propria which were strongly positive for S100, HMB45, SOX10, and MITF. A Fontana Masson silver stain was performed for confirmation. The finding of predominantly atypical intraepithelial melanocytes associated with melanin pigment most likely represents metastatic melanoma to the stomach with some regression in response to immune-checkpoint blockade therapy.

287 RESIDENT

Combined Cutaneous Tumors: A Case of Combined, Intermingled Melanoma and Carcinoma

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Tumors with biphasic or dual differentiation, combined tumors, occur in the skin. The combination of malignant melanoma with carcinoma is relatively rare. We present a patient with combined melanoma and carcinoma. The patient developed a persistent, irregularly pigmented and eroded papule on his right forehead, which he reported had increased in size. On exam, it was ~5 mm in diameter and was violaceous to erythematous with focal pigment at the periphery. His past medical history is significant for three primary melanomas at other sites (back, arm and posterior scalp), a severely dysplastic nevus, and small lymphocytic lymphoma. A punch biopsy of the new lesion showed an upper dermal nodule of epithelioid cells with predominantly peripheral pigmentation and architectural features supporting a lesion primary to this site. A subpopulation of the lesional cells showed cytomorphic features of a malignant melanoma. These were predominantly peripherally located, with distribution as single cells through the nodule. They were immunoreactive for melanocytic markers (S100, Melan-A, HMB-45 and MiTF) and non-reactive for keratins (CK5/6, MNF-116 and CK-7). The remainder of the lesion was composed of malignant epithelioid cells with focal single cell keratinization and intercellular bridges suggesting squamous differentiation. These were immunoreactive for keratins (CK5/6, MNF-116) but not for the melanocytic markers. Mitoses were seen within both the melanocytic and squamous components. Using conventional staging parameters the lesion invaded to a depth of 2.25 mm, anatomic level IV with melanocytic mitoses detected. As combined melanoma and squamous carcinoma is rare, knowledge of its biologic behavior and prognosis is limited. However, there are some data to suggest that combined melanoma – carcinoma may have a better prognosis when compared to conventional melanomas with similar parameters.
288
Identification of a Novel OTOF-ALK Genetic Fusion in a Case of Vaginal Mucosal Melanoma
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Activating kinase fusions involving anaplastic lymphoma kinase (ALK) have been reported in 10% of
spitzoid neoplasms and mutations in ALK have been reported in 3.5% of cases of cutaneous melanoma
according to COSMIC. Herein, we report the first case of mucosal melanoma possessing a previously
undescribed, and novel OTOF-ALK t(2;2)(p23.1;p23) translocation. The patient, a 74-year-old female
presented to her primary care provider with small amounts of vaginal spotting. Examination revealed a
30.0mm, ulcerated, vaginal polyp extending from the distal anterior third of the vagina. The tumor
consisted of a nested proliferation of epithelioid cells with prominent nucleoli involving the mucosa and
submucosa to a depth of 9.0mm. Frequent mitotic figures were present (8mits/10hpf). By
immunohistochemistry, the neoplastic cells uniformly and strongly expressed S100 protein and MelanA.
The margin of the polyp stalk was negative. The patient chose to undergo additional genomic profiling
by clinical grade next-generation sequencing which revealed a fusion gene between exon 1 of Otoferlin
(OTOF) and exon 3 of ALK. Fluorescence in situ hybridization confirmed rearrangement of ALK and
expression of ALK was also identified immunohistochemically. In a 30-month follow-up period, the
patient has not developed any local recurrences or metastatic disease. In summary, with the poor
outcome often associated with vaginal mucosal melanoma (5-year survival rate <14%) and with the
potential for kinase inhibitors to suppress oncogenic signaling, the presence of this novel OTOF-ALK
fusion in mucosal melanoma may serve to offer future patients therapeutic options where their only
recourse previously has significantly limited.

289
Optimizing Detection of Lymphatic Invasion in Primary Cutaneous Melanomas with the Use of D2-40
and a Paired Melanocytic Marker (S100, SOX10, MART-1)
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Purpose: The presence of lymphatic invasion (LI) in primary cutaneous melanomas is a significant
negative prognostic factor associated with positive sentinel lymph node status and poor patient
outcomes. The use of dual D2-40/S100 immunohistochemical staining (highlighting endothelial and
melanoma cells respectively) has been shown to significantly aid in LI detection. The current study aims
to determine the optimal staining protocol for detecting LI and assess its prognostic significance.
Experimental Design: 34 cases of primary cutaneous melanomas diagnosed between 2003-2011 with a
5-year minimum of follow-up data were assessed. 13 cases were selected with known in-transit disease,
14 with positive sentinel biopsies, and 11 with neither. Dual-immunohistochemical staining was
performed for D2-40/S100, D2-40/MART-1, D2-40/SOX10. The slides were independently reviewed by
two blinded pathologists and re-reviewed for consensus. Four cases with incomplete staining were
excluded. Results: When assessing the rate of in-transit or SLN positivity, D2-40/S100 and D2-40/MART1
had a shared sensitivity of 0.57 (D2-40/SOX10: 0.34) and D2-40/SOX10 and D2-40/MART-1 had a specificity of 0.89 (D2-40/S-100: 0.67). Univariate logistic regressions show that D2-40/MART-1 LI positivity predicts higher odds of SLN positivity by a factor of 7.3 (p=0.01) and higher odds of either SLN positivity or in-transit disease by a factor of 10.7 (p=0.04). Conclusions: D2-40/MART-1 has sensitivity that is at least as great and higher specificity compared with D2-40/S100 and D2-40/SOX10 LI positivity for predicting either SLN positivity or in-transit disease status. Dual D2-40/MART-1 staining is a promising technique for LI detection in primary cutaneous melanomas.

290
Patterns of Follicular Involvement in Melanoma
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Background: Folliculotropism in melanoma is poorly characterized and standard categorization for follicular involvement by melanoma is unavailable. As the biologic behavior of melanomas with deep follicular involvement is unknown, we propose a logical categorization system. Methods: We conducted a search of our archives over a 24 year time span for cases reporting “follicle” and “melanoma”. Patterns of follicular involvement were studied and reporting practices of dermatopathologists was examined. Results: We identified 90 cases of melanomas where involvement of the hair follicle was explicitly reported in the diagnosis. Distinct histologic patterns of follicular involvement were identified. The invasive patterns were primary follicular, folliculotropic, and invasive arising from in situ. Involvement by melanoma in situ was either lentiginous, nested, or a combination of both. 61 cases were melanoma in situ or lentigo maligna. 33 involved the hair follicle in a lentiginous pattern, 10 formed nests, and 18 had both lentiginous and nested components. Involvement of the hair bulb was 3-4 times more common (17%) in invasive melanoma than in melanoma in situ (5%). 29 invasive melanomas were identified. 12 had an invasive component around the hair follicle. 2 were primary follicular melanomas, 7 demonstrated folliculotropism, and 3 were invasive melanomas arising from an in situ follicular component. 17 invasive melanomas had follicles involved by melanoma in situ (9 nested, 6 nested and lentiginous, 2 lentiginous). 2/3 of the cases (n=62) occurred on the head and neck with the next most common site being the back (n=16). The male to female ratio was 2:1. Conclusion: We propose that the three distinct patterns of follicular involvement by invasive melanoma and the three distinct patterns of melanoma in situ will be valuable for logically categorizing involvement of the hair follicle by melanoma.

291
Melanoma of the Breast: A 36-Year Retrospective Review of Demographics and Histologic Characteristics from a Single Institution
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Melanoma of the breast is uncommon. This submission characterizes a 36 year retrospective review of surgical pathology cases accessioned with a site designation of breast and a diagnosis of melanoma. A retrospective review of electronic pathology records (Cerner CoPath Plus - 01/01/1980 through
12/31/2015) was performed to identify all breast specimens (89,414) diagnosed with melanoma (64, 0.07%). Records were reviewed for demographics, specimen types, and relevant histologic characteristics. Retrospective review confirmed 64 patients with melanoma involving the breast. Of these, 37/64 (58%) had primary melanomas of the skin of the breast and 27/64 (42%) had metastatic melanoma from other body sites involving the substance of the breast. The mean age of patients was 53 years (range 19 to 84) with 46/64 (72%) being female and 18/64 (28%) being male. The majority (at least 57%) of the primary lesions showed a superficial spreading growth pattern. The average Breslow thickness of the primary melanomas was 0.61 mm. Most (42%) of the primary lesions were Clark’s level I (in situ). Additional Clark’s levels were 14%, 25% and 19% for II, III, and IV, respectively. Prognostic and predictive molecular and/or immunohistochemical studies were conducted in some cases (9/64, 14%), with such testing being first pursued in the year 2011. The skin of the breast is minimally sun exposed in comparison to many other body sites, and primary melanomas of the breast are uncommon. Although rare, melanomas involving the parenchyma of the breast are encountered by surgical pathologists and can histomorphologically mimic breast carcinoma. Our review confirms that melanomas of the breast in aggregate represent less than 0.1% of breast specimens. Previous publications have suggested that metastatic melanoma to the breast is more commonly encountered than primary melanomas of the breast; however, our data suggest the converse with the ratio of clinically recognized primary versus metastatic melanomas of the breast being 1.4:1.

292
Cryotherapy-Induced Atypical Balloon Cell Change in Spitzoid Melanocytic Lesions
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Balloon cell change in melanocytic lesions is a degenerative process well-described in the literature. However, to our knowledge the rare phenomenon of cryotherapy-induced atypical balloon cell change has never been previously discussed. Here we present the first two cases highlighting rapid growth of atypical Spitz tumors with balloon cell change and marked atypia following treatment with cryotherapy. Case 1: A 39 year old female presented with a small verrucous papule on her hand, clinically consistent with verruca vulgaris. After several treatments with cryotherapy the lesion rapidly grew into a large nodular lesion measuring approximately 1.3 cm. Sections displayed a symmetrical dermal neoplasm arranged in fascicles and syncytia, consisting of notably atypical cells with vacuolated cytoplasm and scattered mitotic activity. The cells were positive for S100 and SOX-10, but negative for HMB-45, MITF, tyrosinase, SMA, CD34, and P63. FISH studies were negative for copy number aberrations. The lesion was suggested to be consistent with an atypical Spitz tumor. Case 2: An 11 year old male presented with a small papule measuring 0.2 cm located on his malar cheek which was assumed to be Molluscum contagiosum. The lesion rapidly expanded after several attempts to treat with cryotherapy to a size of 1.0 cm. Sections displayed a fairly well-circumscribed melanocytic neoplasm with expansile nests of cells with prominent balloon cell changes with vacuolated cytoplasm. The cells were markedly pleomorphic with nuclear atypia and lack of maturation. The cells were positive for S100 and melan-A, but negative for HMB-45. Ki67 displayed a brisk proliferative index extending to the base of the lesion. FISH and CGH studies showed copy number gains at 7q34 and 11p, and therefore the lesion was classified as an intermediate grade atypical Spitzoid/balloon cell melanocytic neoplasm. Overall, these two cases highlight for the first time the rare phenomenon of rapid growth and atypical balloon cell change of melanocytic neoplasms following cryotherapy. It is important for dermatopathologists to consider the
diagnosis of a Spitzoid lesion when faced with similar clinical scenarios in order to exclude other clear cell neoplasms and also ensure appropriate molecular workup to accurately assess the biologic potential of the lesion.

293

WITHDRAWN
Neoplasia, Carcinogenesis, Tumor Biology

500

Cutaneous PEComa
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Introduction: PEComas are mesenchymal neoplasms composed of perivascular epithelioid cells with clear to eosinophilic cytoplasm which express variable melanocytic and muscle markers by immunohistochemistry. The PEComa family includes angiomyolipoma of the kidney, clear cell sugar tumor of the lung, lymphangioleiomyomatosis, and lymphangioleiomyoma. A subset of PEComas, particularly angiomyolipoma and lymphangioleiomyomatosis, are associated with tuberous sclerosis. PEComas usually arise in the retroperitoneum or a visceral site and only rarely involve the skin (superficial dermis) / soft tissue. To date, no association between cutaneous PEComa and tuberous sclerosis has been demonstrated. CASE: A 34 year old man presented with a nodule on right hand. The clinical differential included keratoacanthoma versus infection. Histopathologic sections revealed a dermal neoplasm composed of nests of epithelioid cells surrounding prominent thin-walled branching vessels. The neoplastic cells had voluminous clear to eosinophilic / granular cytoplasm and centrally placed round to oval vesicular nuclei. Occasional multinucleated giant cells were noted. There was no significant nuclear atypia or mitotic activity. The neoplastic cells were positive for HMB45, Mart1, MITF, and smooth muscle actin, and were negative for S100, SOX10, EMA, p63, keratins, CD31, and CD34. CONCLUSION: Cutaneous PEComa is an important entity to consider when one comes across a dermal neoplasm with clear cell features. The differential diagnosis for a predominantly dermal neoplasm with clear cells would include clear cell dermatofibroma, balloon cell nevus, balloon cell melanoma, clear cell sarcoma, dermal mesenchymal clear cell neoplasm, and metastatic renal cell carcinoma. Clear cell dermatofibroma demonstrates the usual epidermal changes seen in conventional dermatofibromas such as epidermal hyperplasia, basilar pigmentation, and follicular induction, and lacks expression of melanocytic markers. Balloon cell melanocytic neoplasms and clear cell sarcoma express S100 and SOX10. Additionally, clear cell sarcoma will demonstrate (12:22) (EWS-ATF1) gene fusion. Dermal mesenchymal clear cell neoplasm is histologically very similar to PEComa, but does not express melanocytic markers. Metastatic renal cell carcinoma expresses PAX8.

501

Leiomyoma with Ossification and Transepidermal Elimination of Mineralized Bone
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Introduction: Leiomyomas are benign smooth muscle tumors, with the majority occurring in the genitourinary and gastrointestinal organs in adults. Uncommonly, especially in infancy, they arise from the smooth muscles of arrector pili muscles of hair follicles. Case History: A 3-year-old previously healthy girl presented with a left chest nodule first recognized 2.5 years ago. Since it was identified, the mass had not changed in size or shape. An excisional biopsy showed a lobulated dark-tan papule measuring...
Background: Actinic keratosis (AK), like cervical dysplasia, is the first identifiable change in a continuum from normal epithelium to invasive squamous cell carcinoma (SCC). Interestingly, despite their precancerous nature, most AKs do not progress to SCC. Currently, it is not possible to clinically or histopathologically determine AKs that progress to SCC (pAK), especially on superficial, transected biopsies. Therefore, treatment is based on the clinical morphology of the residual lesion or the lesion is re-biopsied to establish a definitive diagnosis. Early detection of pAK could circumvent clinical monitoring and re-biopsy of AKs, saving patient concern and physician time and decreasing health care costs. While the role of p16 and Ki67 is established in the progression of dysplasia in the cervix, their role in determining pAK is unknown. This study examines immunohistochemical staining of p16 and Ki67 in transected AK that have progressed to SCC on subsequent biopsy. Methods: 5 cases of AK without progression, 5 cases of transected pAK, and 5 cases of SCC were analyzed for the presence of p16 and pattern of Ki67 immunohistochemical staining. Results: 20% of AK without progression, 40% of pAK, and 80% of SCC were positive for p16. 20% of AK without progression showed basal Ki67 positivity, while 100% of pAK and 100% of SCC showed suprabasilar Ki67 positivity. Conclusion: Suprabasilar Ki67 positivity may be indicative of pAK. p16 positivity does not demonstrate clear evidence of progression. Further studies are necessary to determine whether suprabasilar Ki67 positivity can aid in distinguishing AK from pAK.

RESIDENT

502
Prognostic Value of p16 and Ki67 Immunohistochemical Staining in Evaluating Progression of Actinic Keratosis to Squamous Cell Carcinoma
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Background: Nevoid basal cell carcinoma syndrome (NBCCS) is an autosomal dominant, multisystem disorder presenting with multiple basal cell carcinomas (BCC). Trichoepitheliomas (TE) have not been reported in association with NBCCS. Here, we present a patient with a history of NBCCS presenting with a TE. Case: A 10 year-old female with history of NBCCS and multiple BCCs presents with a white/yellow pearly papule measuring 0.3 cm on the right cheek that was subsequently excised. Histology demonstrated dermal nests of basaloid epithelium interspersed by a fibromyxoid stroma. There was no clefting between the tumor islands and stroma, and no obvious epidermal connection to the tumor cells. CD10 showed stromal immunoreactivity. The overall features were consistent with a trichoepithelioma. Conclusion: Trichoepitheliomas have not been reported in association with NBCCS. Although TE and BCC represent two different clinical entities, there is evidence supporting common pathogenetic features. Studies have shown that sporadic TEs are associated with loss of heterozygosity at 9q22.3, the region where PTCH1 is located. Thus a common gatekeeper mechanism for both TE and BCC is postulated.

Background: Proliferating trichilemmal tumor (PTT) is a benign tumor originating from the outer root sheath of a hair follicle, often presenting as a solitary lesion on the scalp. They are typically nodulocystic and range from 1 to 10 cm in size. When presenting in an unusual location, it can pose a diagnostic challenge and may be misdiagnosed as a squamous cell carcinoma (SCC). Case: The patient is a 48 year-old male who presented with a mass in the left scrotum that the patient reported had recently increased in size. Ultrasound showed a mass of mixed echogenicity with uncertain involvement of the testis and spermatic cord. It only became clear during surgery that the mass did not in fact involve the spermatic cord and testis. Gross examination demonstrated a cyst containing a 1.3 cm solid fleshy nodule. Histology revealed a well-circumscribed cyst filled with eosinophilic keratin and lined by keratinizing squamous cells with peripheral palisading. No high-grade atypia or infiltration into the surrounding tissue was present. While SCC was seriously considered, a diagnosis of PTT was eventually reached. Conclusion: PTTs are rare, slow-growing tumors that can pose a diagnostic dilemma due to its ability to mimic squamous cell carcinoma, especially when presenting in an unusual location. To our knowledge, this is the first case of a PTT described in the scrotum of a middle-aged male.
Squamous cell carcinoma (SCC) is the second most common form of skin cancer with many subtypes associated with a variety of clinical behavior and metastatic potential. Spindle cell/sarcomatoid SCC is an uncommon form of SCC, typically seen on sun-damaged skin of the head and neck of the elderly patients. Myxoid spindle cell squamous cell carcinoma (MSC SCC) is an uncommon variant of SCC with prominent extracellular stromal mucin deposition and a spindle cell epithelial component. Herein, we report the case of an 83 year old male who presented with a 1.2 cm rapidly growing right cheek lesion. The mass was excised and showed a well-defined, unencapsulated dermal nodule composed of typical spindle cells with hyperchromatic nuclei and embedded in a myxomatous stroma. Mitotic figures including atypical forms were readily identified. No clear connection to the overlying epidermis was noted. The histologic differential diagnoses included sarcomatoid carcinoma, various myxoïd sarcomas, spindle cell melanoma and atypical fibroxanthoma. By immunohistochemistry, the spindled cells were strongly positive for cytokeratins (CK8/18, CK5) and p63 and were negative for Melan-A, S-100 protein, smooth muscle actin and desmin. Based on the morphologic and immunohistochemical profile, a diagnosis of myxoid spindle cell squamous cell carcinoma was rendered. At one year following excision, patient is doing well with no evidence of local recurrence or distant metastasis. In summary, we describe an unusual variant of spindle cell SCC with a prominent myxoid stroma and highlight the various histologic differential diagnoses based on morphology. Use of immunohistochemistry is critical in excluding the mimics and confirming the diagnosis of MSC SCC. It is likely that the prognosis of this rare variant is similar to the spindle cell SCC with less than 2% potential for metastasis.

Granular cell tumors (GCT) are rare mesenchymal soft tissue neoplasms of Schwann cell/neural origin. They can be solitary or multiple and more frequent in women between the age of 40 and 69. Malignant granular cell tumors (MGCT) represent <1-2% of all GCT. GCT is considered malignant when regional or distant metastasis occurs regardless of the histopathologic features. Other clinical parameters suggestive of malignancy include rapid growth, size greater than 4 cm and necrosis. Fanburg-Smith et al assessed six histologic criteria: necrosis, spindling, vesicular nuclei with large nucleoli, increased mitotic activity (>2 mitoses/10 high-power fields at 200x magnification), high nuclear to cytoplasmic (N:C) ratio, and pleomorphism. Neoplasms were classified as histologically malignant if they met three or more of these criteria; atypical if they met one or two criteria; and benign if they displayed only focal pleomorphism but fulfilled none of the other criteria.

We report a case of a 58-year-old African- American woman with a history of invasive ductal carcinoma of left breast who presented with a rapidly enlarging left groin mass (9.5 cm) that was excised. Histological examination revealed a subcutaneous nodule of composed of cells with abundant, eosinophilic granular cytoplasm and forming clusters gland-like structures. The nuclei are variably sized,
pleomorphic and hyperchromatic with prominent nucleoli. Mitotic count was >2/10 Hpf and areas of focal necrosis were also present. Neoplastic cells were immunoreactive for S-100 and vimentin and negative for cytokeratin. According to the criteria proposed by Fanburg-Smith et al, the histologic pattern was consistent with a MGCT. Three years later, the patient was found to have a metastasis to the lung as well as a local recurrence. Eight years from the primary diagnosis, the patient developed metastases to the right breast, confirmed by fine needle aspiration and subsequently expired from metastatic MGCT.

Although the histologic parameters of a GCT are not always predictive of biologic behavior, the presence of atypical features may be indicative of an aggressive clinical behavior including recurrence and metastases. Metastasis to the breast from a MGCT is uncommon and may histologically mimic a primary apocrine carcinoma of the breast.

507

Multiple Eccrine Poromas in a Patient Treated with Chemotherapy and Bone Marrow Transplant
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Poroma is a benign tumor of the sweat glands which derives from cells of the terminal ducts and it is usually connected to the epidermis. It can be either of eccrine or apocrine lineage. They present as solitary papules, plaques, or nodules usually over the palms and soles and occasionally on the nose, eyelids, neck, and chest. Rarely, multiple poromas can occur throughout the body. In such case, the condition is termed as Poromatosis. Poromatosis in a background of prior immune suppression/bone marrow transplant is pretty rare. Our case is a 68 year-old male diagnosed 2 years earlier with mantle cell lymphoma and underwent chemotherapy with bone marrow transplant. A few months after his transplantation and chemotherapy he started to develop several small papulo nodular lesions on the feet as well as the trunk and scalp. Biopsy of one of the lesions demonstrated a well-circumscribed tumor extending from the upper epidermis to the dermis in broad columns with central cystic degeneration. It was composed of a proliferation of small uniform basaloid cells, with regular nuclei some of them with a clear cytoplasm. Occasional mitosis, small areas of necrosis and ductal structures surrounded by eosinophilic cuticular cells were seen. The stroma surrounding the tumor was richly vascular. The tumor was tested for human papillomavirus (HPV) DNA by nested polymerase chain reaction (PCR), and results were negative for HPV. In our patient chemotherapy with bone marrow transplant, may played a role in the pathogenesis of development of multiple poromas.

508

Atypical Fibroxanthoma Metastasis: A Mystery for One Thousand and One Nights
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Atypical fibroxanthoma (AFX) is a spindle cell tumor classified as a low-grade sarcoma associated with chronic sun exposure particularly in the head and neck area. Less than 40 examples of metastatic AFX have been published. A 75-year-old man presented with a 2 year history of a lesion on the left temple. A shave excision was performed on a 1.1 cm well-demarcated, ulcerated, brown pigmented plaque.
Microscopically, sections showed a dermal proliferation of atypical spindle cells without infiltrative growth or subcutaneous involvement. The tumor cells were negative for S100, Melan A, AE1/AE3, and CD34. The tumor was strongly immunopositive for CD10 with focal expression of smooth muscle actin (SMA), consistent with AFX. Two and a half years later, he presented with a left neck mass. Tumor cells from a fine needle aspiration biopsy showed the same morphology and immunophenotype as the skin tumor (in addition, 34BE12, MNF116 and p63 were all negative), consistent with metastatic AFX. In conclusion, although AFX is not considered an aggressive tumor, metastasis can occur rarely. Immunohistochemical stains play an important role in diagnosing AFX and metastatic lesions and differentiating these tumors from other spindle cell lesions such as melanoma, spindle cell squamous cell carcinoma, angiosarcoma, and rarely dermatofibrosarcoma protuberans, among others.

509
Detection of Merkel Cell Polyoma Virus and Beta Human Papillomavirus in Multiple Eccrine Poromas in a Patient with Acute leukemia Treated with Stem Cell Transplant
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Poroma is a benign adnexal neoplasm composed of cells with glandular/ductal differentiation of either apocrine or eccrine origin. Poromas usually occur as asymptomatic, solitary, slow-growing, skin-colored, papules or nodules. Fewer than ten cases of multiple poromas have been previously reported. We describe a 45-year-old man who developed multiple poromas following allogeneic stem cell transplant for acute myeloid leukemia (AML). The tumors were tested for human papillomavirus (HPV) DNA by nested polymerase chain reaction (PCR), and Merkel cell carcinoma associated virus (MCPyV) using a detection primer set within the small T viral DNA region. The lesions were positive for beta-HPVs (type 9, FAIMV.S15.1/FAIMVS 15.3 and FA14) and MCPyV. To our knowledge, this is the first case of positive MCPyV and the second report of beta-HPV identified in multiple poromas.

510
Primary Cutaneous Calcifying Fibrous Pseudotumor
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Calcifying fibrous pseudotumor is a rare soft tissue lesion of unclear origin that usually occurs in children and young adults. Typically, these lesions appear in the subcutaneous or deep soft tissue as opposed to superficially within the skin (1,2). We herein present a rare case of a superficial primary cutaneous calcifying fibrous pseudotumor in a 6-year-old female presenting as a subcutaneous left groin mass. Histologically the lesion presented as a well circumscribed, non-encapsulated, somewhat lobulated dermal to subcutaneous tumor composed of focally hyalinized fibrosclerotic tissue with a mild lymphoplasmacytic inflammatory infiltrate. Rare lymphoid follicles were identified. The lesion appeared hypocellular with scattered cytologically bland, fibroblastic to myofibroblastic spindled cells. Focal psammomatous calcifications were also identified. Overall this case represents a rare
presentation of a superficial calcifying fibrous pseudotumor. The diagnosis should be considered in the histologic differential diagnosis of fibromatosis, nodular fasciitis, fibroma of the tendon sheath and calcifying aponeurotic fibroma.

511

Pleomorphic Dermal Sarcoma: A Rare Cutaneous Entity

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Pleomorphic dermal sarcoma is a rare neoplasm with histopathological and immunohistochemical features similar to those of atypical fibroxanthoma but with deep infiltration, necrosis and/or vascular/perineural invasion. They appear restricted to the head and neck regions and present as tumors and plaques with no gender predilection. We present a case of pleomorphic dermal sarcoma in a 79 year old female who presented with a rapidly growing lesion on the right forehead of two months duration. On exam, there was a 4.0 x 3.5 cm ulcerated exophytic red nodule. Previous shave biopsies revealed a spindle cell neoplasm of unclear etiology and an excision was recommended, following which a Moh’s procedure was performed. Multiple sections reviewed demonstrate a dermal based spindle cell neoplasm extending to the resection margins. The spindle cells are arranged in a fascicular pattern with numerous mitotic figures. The spindle cells have pleomorphic nuclei with prominent nucleoli and pale eosinophilic cytoplasm. The lesional cells are strongly positive for Vimentin, CD10 with moderate staining for CD99, CD68 and SMA. The cells are negative for pancytokeratin, desmin, HMB-45, Mart -1, S100 and CD34. Pleomorphic dermal sarcoma have a more aggressive clinical behavior. They lack immunoreactivity to cytokeratins, S100 protein, desmin and CD34. The differential diagnosis includes other spindle cell neoplasms, including melanoma, spindle cell squamous carcinoma and sarcomatoid carcinoma. For now it remains a diagnosis of exclusion and dermatopathologists should be aware of this rare entity.

512

A Case of a Malignant Trichilemmal Cyst

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Trichilemmal cysts (pilar cysts) are common benign cysts that are derived from the outer root sheath of the hair follicle. Although rare cases of trichilemmal cysts with carcinoma in situ have been described, no case of invasive carcinoma arising in a trichilemmal cyst has been reported. A 28-year-old white female presented with a nodule on her scalp. The excision specimen revealed a grossly circumscribed 1.2 x 1 x 0.7 cm unilocular cystic lesion. Microscopically, the lesion consisted of a cystic space lined by trichilemmal-type epithelium and filled with amorphous eosinophilic material. On higher power, the epithelial cells were moderately to markedly atypical, with anisonucleosis and prominent red nucleoli. Mitotic figures were frequent. The amorphous material within the lumen had features of tumor necrosis, including a granular texture and fading and smudged nuclei. Pushing tongues of atypical epithelium and frankly invasive cells were identified within the connective tissue surrounding the cyst, and the presence of invasion was confirmed by stains for cytokeratins and p63. The benign trichilemmal cyst is a common entity in dermatopathology. The related but less common proliferating trichilemmal
Eyelid Cutaneous Angiomyolipoma in A Young Child with the Tuberous Sclerosis Complex: A Case Report

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Angiomyolipoma is a mesenchymal neoplasm in the PEComas (the neoplasms with perivascular epithelioid-cell differentiation) family. Most PEComas are sporadic, but a small subset is associated with the tuberous sclerosis complex (TSC). Angiomyolipoma associated with TSC usually presents in the kidney and extrarenal cases are uncommonly seen in the liver, nasal cavity, oral cavity, heart, colon, lung, and skin. Cutaneous angiomyolipoma is extremely rare and most reported cases are not TSC-related. We present a TSC associated cutaneous angiomyolipoma in a child. A 2 year old boy with a cyst can rarely undergo malignant transformation; these malignant proliferating trichilemmal tumors are associated with local recurrence and nodal metastases. Carcinoma in situ within the epithelium of a simple (non-proliferative) trichilemmal cyst, while surpassingly rare, has been reported; but not, to our knowledge, has a case of invasive carcinoma. Here we present a unique case of a malignant trichilemmal cyst, by which we hope to raise awareness of this previously unknown and easily missed entity.
diagnosis of TSC2-related TSC presented a 1.0 x 0.7 x 0.5 cm, yellow-tan lobulated lesion on his left eyelid which was removed by the ophthalmologist. He also has cortical tubers, renal cysts, cardiac rhabdomyomas, and hypomelanotic macules. Molecular test showed a heterozygous for a reported TSC2 missense mutation. Microscopically, dermis shows mild fibrosis with scattered dilated venues. A few thick-walled artery-like vessels and adjacent mature adipose tissue are seen between dermis and orbicular muscles. Those thick wall vessels are composed of smooth muscle-like cells and lack of elastic lamina which show immunoreactivity to smooth muscle actin and HMB45 antibodies (patch) antibodies. Adjacent adipose tissue is immunoreactive to S-100 protein. Morphology and immunophenotypes are consistent with the diagnosis of cutaneous angiomyolipoma, TSC associated. Cutaneous angiomyolipoma is an extremely rare entity in children which has not been reported by PUBMED search. Sharing this case will expand the differential diagnosis on the eyelid and skin disorders in young TSC patients.

515

Cutaneous Metastatic Papillary Renal Cell Carcinoma: A Case Report

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Renal cell carcinoma accounts for 3% of all adult malignancies and has four major histologic subtypes: clear cell (75%), papillary (15%), chromophobic (5%), and collecting duct (2%). Cutaneous metastases of renal cell carcinoma represent about 6% of all skin metastases. Most of the reported cases are clear cell type, with the papillary type being very rare, possibly a function of the different degrees of incidence. We present a case of metastatic papillary renal cell carcinoma presenting as cutaneous lesions. A 72 year-old male with a past medical history of papillary renal cell carcinoma, for which he underwent left total nephrectomy ten years ago, presented with a clinical history of multiple firm nodules on his face and chest. A lesion was biopsied and revealed dermal neoplastic nodules with central necrosis and tightly packed tubulopapillary structures. The neoplastic cells are positive for cytokeratin 7, pan-keratin, and RCC immunoperoxidase stains, and negative for cytokeratin 20 and synaptophysin. The morphologic and immunohistochemical features are consistent with the diagnosis of metastatic papillary renal cell carcinoma. Cutaneous metastases of renal cell carcinoma represent a bad prognosis with an average life expectancy ranging from 3 to 21 months. Detection of these lesions in previously-diagnosed patients may help to restage the disease. This case illustrates that papillary renal cell carcinoma can rarely metastasize to the skin and reinforces the need of periodic complete dermatologic examination in patients with a previous history of malignant tumors with metastatic potential such as renal cell carcinoma.

516

Invasive Paget’s Disease of the Breast

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An 83 year old woman with biopsy-proven Paget’s disease underwent simple mastectomy. Gross examination revealed a 0.5 x 0.2 cm erythematous region adjacent to the nipple, a nodular, tan-white
cut nipple surface and subjacent nodular fibrosis. No definitive tumor or lesion was grossly appreciated. Histologic exam demonstrated predominantly epidermal, large, epithelial neoplastic cells extensively involving the nipple and breast skin, with a 5mm focus of direct dermal invasion. The neoplastic cells were positive for CK-7, E-cadherin and GCDFP. A small focus of apocrine ductal carcinoma in-situ was also identified in the underlying breast parenchyma. Paget’s disease of the breast is often associated with underlying invasive or in-situ carcinoma. Direct invasion of Paget’s disease from the epidermis into the dermis, however, is exceedingly rare. The staging and thus prognosis of mastectomy specimens demonstrating Paget’s disease is based on the size and type of parenchymal disease. Mastectomies demonstrating Paget’s disease only are staged as Tis, or T4 if an underlying invasive carcinoma extends to involve the skin. No staging system currently exists for invasive Paget’s disease. Although current literature suggests a similar prognosis for Paget’s disease with or without direct dermal invasion, our case demonstrates that it may represent the only focus of invasion identified, and thus represents a diagnostic pitfall for dermatopathologists.

517
Case Report of Vulvar Porocarcinoma
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We present a 49 year-old female with a two year history of a persistent pruritic papule on her right labia majora that had never been treated medically. The papule was grossly described as an 8 mm smooth, flesh-colored, and hard lesion. Upon shave biopsy, the histopathology examination of the tissue was diagnostic for porocarcinoma. On histology, there are malignant epithelial cells emanating from the epidermal surface and infiltrating into the dermis as cords and variably-sized nests. There is squamoid (eosinophilic cytoplasm and intercellular bridging) and ductal (luminal duct formation) differentiation present with cellular pleomorphism. Apoptotic bodies and atypical mitoses are scattered throughout the lesion. On immunohistochemistry, there is a strong and diffuse staining with p63, CK5/6, and EMA. mCEA, MOC-31, and Ber-EP4 are focally positive, predominantly in the superficial portion of the specimen. These staining patterns further support the diagnosis of a primary adnexal carcinoma. Porocarcinoma (malignant eccrine poroma) is defined as a high grade carcinoma of the eccrine sweat glands.1,4 Although this is a rare tumor, it is the most frequent malignant sweat gland tumor and is found more commonly in elderly females. The tumor originates from the intraepidermal portion of the eccrine sweat duct, most often on the lower extremities, trunk, head, and upper extremities, in descending frequency, but can be found in the genitalia and nail beds.4 Porocarcinomas are indolent but can metastasize to regional lymph nodes in up to 20% of reported cases leading to increased morbidity and mortality.2 Six prior cases of vulvar porocarcinoma have been reported.3 Despite its rarity, it is important to keep this entity on the differential when evaluating regions with sweat gland formation, to include genital lesions.
518

Hidradenitis Suppurativa Complicated by Squamous Cell Carcinoma in a Background of Human Papillomavirus within the Anal Canal: Literature Review and Case Report

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We are reporting a long-standing case of chronic Hidradenitis Suppurativa recently complicated by Invasive Squamous Cell Carcinoma in a background of Human Papillomavirus within the anal canal of a male patient with HIV. To the best of our knowledge there are no cases illustrating the association of Squamous Cell Carcinoma (SCC) with Hidradenitis Suppurativa (HS) and Human Papillomavirus (HPV) in the anal canal. We describe a case to discuss the carcinogenesis of HS and HPV to question synergistic effects leading to the development of Squamous Cell Carcinoma through the Notch signaling pathway. This is a retrospective review of a 15-year course of treatment involving chronic Hidradenitis Suppurativa. A block of the specimen stained with p16 was consistent with HPV cellular changes. We are currently confirming the presence of HPV by polymerase chain reaction (PCR). A systematic literature review was conducted pertaining to Hidradenitis Suppurativa, Human Papillomavirus, and or without key terms Squamous Cell Carcinoma and anal canal throughout PubMed, Medline, Google Scholar, ClinicalKey and OMIM. It was found that chronic HS and a HPV oncogene independently influences the Notch signaling pathway. Squamous Cell Carcinoma in the anogenital region, especially the anal canal is rare. SCC has been well documented as arising in the setting of chronic Hidradenitis Suppurativa (HS) as well as being associated with Human Papillomavirus (HPV). However, there are no reports detailing the presence of SCC arising in the background of both HS and HPV in the anal canal. There may be a link to chronic inflammation produced by HS and HPV E6 oncogenesis synergistically inducing SCC in the anal canal through their combined effects on the Notch signaling pathway. Further studies are required to investigate the association of HS, HPV and SCC, which may influence the management of recurrent perianal nodules or mucopurulent lesions.

519

Apocrine Gland Cyst with Hemosiderotic Dermatofibroma-like Stroma

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Apocrine gland cyst with (hemosiderotic) dermatofibroma-like stroma (AGCDS), also known as adenodermatofibroma, is an extremely rare and only recently recognized entity. Only five cases have been reported to date. AGCDS is described in the literature as a benign, indolent dermal nodule with apocrine gland cysts surrounded by dermatofibroma-like proliferating stroma with or without hemosiderotic features. It presents as a cystic mass present for several years with areas of brown coloration. AGCDS occurs in both male and female patients with an average age of 48-years-old. It has no apparent predilection for any particular anatomic locations. It is categorized in the family of benign fibrous histiocytomas with a non-malignant clinical course and no recurrence. Histologically, AGCDS appears as a non-circumscribed, non-encapsulated, biphasic dermal nodule. The two components consist of ductal cystic spaces lined by bilayered epithelial with apocrine differentiation and squamous epithelium focally, and a surrounding compact stroma with fibroblasts, histiocytes, and giant cells. The stroma also contains areas of hemorrhage, abundant intra and extracellular hemosiderin, and thickened capillaries and veins. Mitoses, necrosis, pleomorphism, and atypia have not been observed. Here, we
present a new case of AGCDS on the calf of a 46-year-old male that conforms to the clinical and histologic features presented in prior cases.

**520**

**RESIDENT**

**Cutaneous Malignancies Simulating Seborrheic Keratoses: An Underappreciated Phenomenon?**

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**BACKGROUND:** Seborrheic keratosis (SK), a common benign skin neoplasm, is usually diagnosed clinically without the need for a biopsy. In some cases, SK may mimic cancer clinically, especially when inflamed, and a biopsy may be required. Clinicians may also perform biopsies on SK for other reasons such as cosmetic disfigurement, inconvenience to the patient and if they are located at a site where they are prone to become irritated. We have observed a number of SK biopsied and submitted to our laboratory with only the diagnosis of “SK or Irritated SK (ISK)” preferred yet when examined microscopically, proved to be malignancies. We sought to determine the frequency of this phenomenon and its clinical significance. **OBJECTIVE:** To identify cutaneous malignancies suspected to be SK with no clinical concern for malignancy. **METHODS:** Biopsy specimens from 2015 obtained from private and university locations were retrospectively assessed. Cases included in the study were those submitted with the diagnosis of “SK” or “ISK” with no other diagnosis given. Cases with modifiers potentially suggestive of malignancy such as “SK rule out other,” changing, growing, etc. were excluded. A total of 4361 eligible cases were identified and used for analysis. **RESULTS:** Of the 4361 cases identified as only “SK” or “ISK” in the clinical data, 3759 (86.2%) proved to be SK or ISK. 466 of the cases (10.7%) were an assortment of various non-malignant entities such as dermatofibroma, nevus, and benign lichenoid keratosis. There were 136 (3.1%) cases histologically diagnosed as malignancies. The majority (91 of 136 cases; 67%) of these were in situ or invasive squamous cell carcinoma; 24.3% (33/136) were basal cell carcinoma, and 8.8% (12/136) were melanoma. **LIMITATIONS:** Detailed clinical history from the patients was unavailable. The extracted data were based solely on the clinical data written on the pathology requisition form. Whether clinicians may have simply written SK or ISK yet truly considered other entities could not be assessed using these methods. **CONCLUSIONS:** Lesions clinically thought to be SK or ISK may prove to be malignancies in a significant number of cases. Clinicians should be aware of this phenomenon and evaluate any SK or ISK from the standpoint that it could possibly be malignant and consider biopsy, especially if there are any changes over time.

**521**

**RESIDENT**

**Metastatic Endocrine Mucin-Producing Sweat Gland Carcinoma**

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Endocrine mucin-producing sweat-gland carcinoma (EMPSGC) is an extremely rare indolent sweat gland carcinoma with neuroendocrine differentiation. Only 29 cases have been described in the literature to date. EMPSGC typically presents as an indolent, skin-colored, ill-defined plaque or cystic nodule on the eyelid or cheek of elderly patients (median age 70) and has a strong predilection for women. EMPSGC is considered a low-grade carcinoma due to the infrequency of recurrence; no metastasis has ever been reported. Histologically, EMPSGC commonly appears as a nodular dermal tumor with solid, papillary,
and cystic areas. The neoplasm is composed of small to medium sized cells with salt-and-pepper chromatin and inconspicuous nucleoli; intracytoplasmic and occasional extracellular mucin are often observed. EMPSGC stains positively on immunohistochemistry for neuroendocrine markers chromogranin and synaptophysin, mucucarmine, estrogen receptor, progesterone receptor, and CK7, and negative for S-100 and p53. Here, we present a new case of EMPSGC in a 39-year-old man with evidence of lymphovascular invasion in multiple lymph nodes. The lesion was diagnosed as endocrine mucin-producing sweat gland carcinoma based on immunohistochemistry. This novel case of EMPSGC has a more malignant histology and lymphovascular invasion that has never been reported in literature, suggesting that long-term follow-up and total body workup may be necessary in addition to excisional treatment.

522

Syringoid Eccrine Carcinoma of the Foot
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Syringoid eccrine carcinoma (SEC) is a rare malignant adnexal tumor characterized by proliferation of atypical basaloid cells forming glandular or tubular structures with syringoma-like morphology. It usually presents as a plaque or nodule on the scalp, and less commonly, the trunk or extremities. Involvement of the lower extremity in SEC is exceedingly rare with only one case reported in the literature. Here, we report a unique case of CD117- and S100-positive SEC in a 47-year-old female presenting with a slow-growing nodule on the lateral aspect of the right plantar foot. On physical examination, a 3.9 x 3.1 cm hyperpigmented lesion with an irregular border was noted, clinically suspicious for melanoma. Excisional biopsy revealed numerous infiltrative branching tubular to cystic structures lined with atypical basaloid cells with mitoses within the dermis. The tumor focally assumed a syringoid morphology along with occasional cribriform growth pattern. Perineural invasion was focally present; no epidermal involvement was noted. No follicular differentiation or keratinous cysts were identified. The tumor was diffusely positive for CK7, EMA, p63 (weakly), CD117, and S100, and negative for CK20, CDX2, ER, PR, mammaglobin, and melanoma cocktail stain. A thorough clinical examination with imaging was performed to rule out skin metastasis from visceral adenocarcinoma. The differential diagnosis also included microcystic adnexal carcinoma, adenoid basal cell carcinoma and primary cutaneous adenoid cystic carcinoma. Re-excisions of the lesion showed residual tumor with more prominent syringoid features. By morphology and immunophenotype, the findings were most consistent with SEC. To the best of our knowledge, this is the first reported case of SEC of the foot.

523

Basaloid Squamous Cell Carcinoma: A Rare Case of Cutaneous Metastasis
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A 62yo man presented to dermatology for a rapidly growing nodule on his chin for 1 month. Aside from a history of acid reflux and a recent history of dysphagia, he was otherwise healthy and took only antacids as needed. He was a former smoker without a history of cancer. On exam, he had a 2 cm
eroded nodule on his chin. The clinical differential was infection versus neoplasm. Tissue cultures for fungus, atypical mycobacteria, and bacteria were negative. A punch biopsy showed a basaloid tumor expanding the dermis and eroding thru the epidermis. The tumor showed peripheral palisading and multiple foci of comedonecrosis. The cells were atypical appearing with many atypical mitoses. Additionally, several tumor nodules were identified within the lymphatics. A p16 stain was negative. The histology was thought to be most consistent with a basaloid squamous cell carcinoma, although basosquamous cell carcinoma, a type of basal cell carcinoma, was also considered. Additional immunohistochemical stains were not needed in this case, but these two tumors can be differentiated based on differences in staining patterns with 34βE12, UEA-1, Ber-EP4, Bcl-2, and MOC-31. The tumor was excised via Mohs. On post-op day 1, the patient complained of worsening dysphagia and inability to tolerate liquids. A CT scan of the neck and chest showed 2 large esophageal masses with obstruction of the esophageal lumen and invasion of the IVC as well as widely metastatic disease involving the subcutaneous skin, lymph nodes, lungs, and liver. An EGD was performed with biopsy of the mid-distal esophageal mass and stent placement for dysphagia. The esophageal mass was histologically identical to the chin lesion, and it was concluded that he had a cutaneous metastasis of an esophageal basaloid squamous cell carcinoma. Basaloid squamous cell carcinomas are highly aggressive tumors that are typically of aerodigestive primary and often metastatic at presentation. There is a high rate of HPV positivity, which correlates with tumor response to treatment. It is typically not found in the skin, with only a few cases reported of metastatic as well as primary skin lesions. Our patient was treated with palliative carboplatin/paclitaxel chemotherapy with good response. It is important to recognize this tumor in the skin so that an appropriate metastatic work-up can be performed.

**RESIDENT**

**A Rare Case of Oncocytic Hidradenoma**

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A 70 yo man with past medical history significant for multiple basal cell carcinomas presented to dermatology for routine skin screening. On examination, he was noted to have a 5 mm erythematous papule on his left scalp. The clinical impression was basal cell carcinoma. A shave biopsy showed a nodular, dermal-based adnexal tumor with prominent ductal differentiation, composed of multiple small, well-formed lumina surrounded by enlarged, bland-appearing epithelioid cells. The cells showed abundant pale to eosinophilic, somewhat granular-appearing cytoplasm, consistent with apocrine differentiation. Although the nuclei were mildly enlarged and hyperchromatic-staining, there was no definite high grade atypia, infiltrative features, or increased mitotic activity to suggest malignancy. Additionally, the tumor was relatively symmetric and well-circumscribed-appearing peripherally. EMA and CEA stains highlighted the ductal lumina, and a CK7 stain was diffusely and strongly positive, consistent with adnexal differentiation. GCDFP-15 highlighted the ductal lumina and the cytoplasm of some cells, and an androgen receptor stain showed scattered nuclei staining, both of which were consistent with apocrine differentiation. CD68 and lysozyme stains were negative, but PTAH highlighted the cytoplasmic granules, consistent with mitochondria. The overall findings were consistent with oncocytic nodular hidradenoma. Oncocytes are epithelial cells characterized by their abundant eosinophilic and finely granular cytoplasm. The histologic appearance is due to excessive amounts of cytoplasmic mitochondria. Oncocytes are considered benign and generally occur in the setting of benign neoplasms. Oncocytomas, or tumors composed primarily of oncocyes, are typically found in the
Adenoid cystic carcinoma is a rare and slowly growing tumor. It usually occurs in the salivary glands but less frequent primary sites include bronchus, breast and lachrymal glands. Very rarely, it arises in the skin. Primary cutaneous adenoid cystic carcinoma (PCACC) was first described in 1975, and there are now ~70 cases reported in the English literature. We present a case of a PCACC occurring on the thigh. A middle-aged woman presented with a 5-year history of a slowly enlarging painful growth on her distal anterior thigh. The lesion was thought to be a dermatofibroma or a cyst but continued to expand slowly. An incisional biopsy was performed. This showed a partially cystic partially solid lesion spanning the dermis and superficial subcutaneous fat. Histology suggested a low-grade sweat gland carcinoma. The patient underwent a wide local excision and sentinel lymph node biopsy. The tumor showed varying morphology with cystic and solid areas with glandular differentiation. Infiltrative basaloid nests (some solid, some cribriform, and some with focal cystic change and central debris) with surrounding mucinous stroma and true tubular and ductal structures surrounded a central cyst. Cytologic atypia was minimal with low mitotic activity and no necrosis. Tumor cells were variably immunoreactive for cytokeratin-7 and cytokeratin 5/6. CEA and EMA highlighted intra-lesional ductular differentiation. Cells at the periphery of the tumor nests stain for smooth muscle actin and p63. All components stained strongly with CD117 (C-kit). Mucinous areas stained strongly with Alcian blue. No lymphovascular space or perineural invasion was identified. The duration of the lesion combined with the immunohistochemical and morphologic findings of a cribriform pattern, true ducts and mucin deposition are consistent with a PCACC. Perineural invasion, although characteristic of adenoid cystic carcinoma, may be absent in PCACC. Sentinel lymph nodes were negative.

Basaloid squamous cell carcinoma (BSCC) is a rare variant of squamous cell carcinoma which is often associated with an aggressive clinical course. It typically presents in the upper aerodigestive tract but can also involve the anal canal, lung, esophagus, uterine cervix, vulva, thymus and nasopharynx. Historically, it has been reported to be most prevalent in men in their 6th-7th decade of life and associated with excessive tobacco and alcohol use. However, more recently it is recognized that most cases which arise in the oropharynx and anogenital regions are associated with high-risk human papillomavirus (HPV) integration. We describe two cases of HPV-related BSCC originally misinterpreted with only 1 previously reported case in the literature.
by referring institutions as primary cutaneous adnexal neoplasia. The first case presented as a 1.2 cm vulvar nodule in a 51-year-old woman. Histopathology revealed multiple fragmented tumor lobules composed of closely packed hyperchromatic basaloid cells intermixed with hyaline basement membrane-like material. These features were remarkably reminiscent of spiradenoma. However nuclear atypia, mitotic activity, and prominent comedo-type necrosis were evidence of a malignant phenotype. In our second case, a 50-year-old woman presented with a 3.0 cm cystic nodule on the posterior scalp. Histopathology showed an attenuated subcutaneous cyst lined by malignant epithelial cells with squamous and basaloid features. Some areas of the cyst wall were proliferative and reminiscent of a malignant proliferating trichilemmal tumor. Like the previous case, central comedo-like necrosis was present. In both cases, tumors were strongly immunoreactive for p16 (a surrogate marker for high-risk HPV integration), and RNA in-situ hybridization (ISH) detected high-risk HPV within neoplastic cells. These two cases illustrate that HPV-related BSCC may mimic cutaneous adnexal neoplasia. Key histologic clues to the diagnosis of HPV-related BSCC include basaloid cytology, comedo-type necrosis, and cystic architecture. Diagnosis can be confirmed with immunostain for p16 in conjunction with ISH for high-risk HPV. As illustrated in these cases, differentiating between BSCC and primary adnexal neoplasia has important implications with regards to additional clinical work-up, screening, and therapeutic intervention.

527
Superficially Sampled "Benign" Adnexal Neoplasms: Proceed with Caution!
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Hidradenocarcinoma, a rare skin tumor, arises from the intradermal duct of eccrine sweat glands. This tumor may arise from a benign hidradenoma, however, it more commonly arises de novo. Contrary to its benign counterpart, hidradenocarcinomas are aggressive malignant tumors with local recurrence, metastasis, and poor outcome frequently observed. These tumors often arise in the head and neck region, with regional or distant metastases common. The clinical presentation is generally that of a “benign” solitary skin lesion that follows an indolent course with local and multiple recurrences. Eventually, however, the lesion transforms to overt malignancy through mechanisms currently unknown. Further study is required to isolate molecular markers of pathogenesis and efficacy of adjuvant chemotherapy. We present a case of an 83 year old male who presented with a superficially sampled benign nodular-cystic hidradenoma, which revealed hidradenocarcinoma upon subsequent excision. As diagnostic features of malignancy were only present on re-excision, this case highlights the diagnostic difficulty of a rare entity and demonstrates the necessity for re-excision when a "benign" adnexal neoplasm is superficially sampled.
Indeterminate cell histiocytosis (ICH) is a cutaneous proliferation of histiocytes that are morphologically and immunophenotypically similar to Langerhans cells. Indeterminate cells lack Birbeck granules (the ultrastructural pathognomonic feature of Langerhans cells) and are non-reactive with antibodies to langerin (a useful immunohistochemical surrogate for Birbeck granules). Wood et al. first described ICH as a distinct pathologic entity in 1985. Since that time, approximately 45 to 50 cases have been reported in the literature. Reported cases have exhibited varied clinical, histomorphologic, immunohistochemical, and molecular features. Very few cases of ICH have been reported in children. We report the case of a 6-year-old girl who presented with a five-year history of progressively enlarging polypoid and verrucous vulvar nodules. A biopsy showed a largely dermal-based proliferation of cytologically bland histiocytes. Some of the histocytes demonstrated reniform nuclei and a spindled morphology. A small component of the proliferation involved the epidermis. The tumor cells expressed CD1a and S100 diffusely within the epidermis and partially within the dermis by immunohistochemistry. A majority of the cells were positive for CD163, and a subset were positive for CD68. The neoplastic cells were negative for langerin. Immunohistochemical staining for the BRAFV600E mutation was equivocal, and subsequent molecular analysis of the tumor showed no BRAFV600E mutation. Imaging studies (bone scan, CT, and brain MRI) were negative, and the process was classified as isolated cutaneous ICH. We present a new case of ICH in a 6-year-old child and a review of the literature with an emphasis on the characteristics of the disease in pediatric patients. Due to the varied clinical and pathologic features of ICH in previously reported cases, our intention is to organize and summarize the available data regarding this rare entity.

Dermatofibrosarcoma protuberans (DFSP) is a rare low-grade cutaneous sarcoma that often recurs locally but rarely metastasizes. The rarity of this tumor and varied clinical presentation can cause initial misdiagnosis and delayed treatment. One of the authors has been involved in DFSP patient support groups on Facebook. Patient members of these groups partnered with us to design a survey; 218 DFSP Facebook group members (n=203 patients, n=15 family members) worldwide responded to the survey in the three weeks it was open. This is the largest survey of DFSP patients to date. Results were purely obtained from survey responses; medical charts or pathology materials were not reviewed. Mean time from patient first noticing the tumor to visiting a medical provider for evaluation was 3.5 yrs (range: 0-31; median 1 year). Mean time from initial medical visit to diagnosis of DFSP was 3.6 yrs (range: 0-41;
Eccrine adenocarcinoma is a rare primary cutaneous malignancy which histomorphologically and immunophenotypically mimics mammary carcinoma. Distinguishing between a primary cutaneous adenocarcinoma and metastatic malignancy is often difficult, requiring careful clinical and radiologic correlation. Although the increased risk of multiple malignancies including breast and ovarian is well documented in patients with BRCA-1 and BRCA-2 mutations, no known association with eccrine malignancies has been reported to date. We report a case of primary eccrine adenocarcinoma occurring on the scalp of a 67 year old Caucasian woman with no known prior history of malignancy. The biopsy revealed a well-differentiated adenocarcinoma in the dermis with focal Pagetoid involvement of the overlying epidermis and associated adnexa and background fibrosis. Immunohistochemical labeling studies returned positive for CK5/6 and GCDFP15, and negative for TTF-1, mammaglobin, p63, CK14 and CK17. The histomorphologic findings were consistent with both eccrine adenocarcinoma as well as cutaneous metastasis, specifically of mammary adenocarcinoma; and clinical correlation with exclusion of a primary site was recommended prior to definitive treatment. The patient underwent consultation with oncology during which a significant family history of breast and gynecologic malignancies was identified. The patient was referred to genetic counseling wherein a pathogenic mutation c5410_5411delGT in the BRCA 2 gene was identified. Imaging studies including mammogram and PET-CT were negative for additional lesions. Definitive treatment for the scalp lesion included wide local excision with 1 cm margins. Additionally, the patient elected for a prophylactic hysterectomy with bilateral salpingo-oophorectomy and close clinical follow up including annual mammography, clinical breast examinations every 6 months and total body skin examinations with Dermatology every 6 months. She remains free from cancer recurrence or new malignancy with 20 months of follow-up.
Multicentric reticulohistiocytosis with Dermatomyositis-like Features
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Multicentric reticulohistiocytosis often presents with arthritis and skin lesions. Although papules and nodules are typical, erythematous plaques in a photodistribution are sometimes encountered. The presence of weakness, fever, and weight loss can raise a differential diagnosis that includes dermatomyositis or other types of connective tissue disease. Biopsy is essential for diagnosis and reveals multinucleated giant cells with ample eosinophilic cytoplasm. Although a paraneoplastic etiology has been suggested, this remains controversial. A case of multicentric reticulohistiocytosis associated with dermatomyositis-like features is presented and the features and associations of this uncommon disorder are reviewed.

Punctate Follicular Porokeratosis: Report of a New Case and Review of the Literature
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Porokeratosis is a disorder of keratinization characterized histologically by coronoid lamella formation. Punctate follicular porokeratosis is a rarely encountered variant that relies on the recognition of the characteristic histologic features for diagnosis. A 51yr old woman presented to her physician with hyperkeratotic papules and few verrucous plaques on the face, neck, upper chest and back. These had been present for several years and were variably pruritic. She denied photosensitivity or systemic symptoms. She had no relevant past medical or family history. On close examination, there was a peculiar papular eruption with associated apparent follicular hyperkeratosis. She additionally presented with admixed verrucous plaques. Multiple initial biopsies demonstrated an interface to lichenoid dermatitis with some degree of hyperkeratosis and follicular plugging, raising largely an initial differential of a connective tissue disorder including chronic cutaneous or discoid lupus. Due to clinical persistence and only partial response to therapy with topical steroids, additional biopsies were performed that demonstrated prominent cornoid lamella formation that was largely associated with the follicular infundibulae with associated dyskeratotic infundibular keratinocytes. In view of this histologic finding as well as the presence of impressive hyperkeratotic follicular spiny projections and verrucous plaques, a clinical-pathologic diagnosis of punctate follicular porokeratosis was made. This case illustrates the challenging nature of the diagnosis of this unusual porokeratosis variant, as well as the potential clinical overlap with chronic cutaneous lupus, and the importance of repeat skin biopsies to examine for the presence of follicular cornoid lamella formation. Awareness of this disorder as a distinct clinical entity and recognition of the characteristic histologic features, with a low threshold for further sampling, is necessary to prevent diagnostic delay.
Symmetric Multifocal Atypical Granular Cell Tumors Presenting as Long-standing Right and Left Wrist Masses in a 15 Year-Old African American Female

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Granular cell tumor (GrCT) is a benign nerve sheath tumor. These features are considered atypical in GrCT: necrosis, spindling, vesicular nuclei with large nucleoli, > 2 mitoses/10 HPF, high nuclear to cytoplasmic (N:C) ratio, pleomorphism. A GrCT with 3 or more of these features is considered malignant; these may be aggressive. If only 1-2 atypical features are seen, it is classified as atypical GrCT; these are indolent. Atypical GrCT may rarely be multifocal. We report a case of multifocal atypical GrCT that was also symmetric. A 15 year old African American girl presented with right and left wrist masses of 8 years duration but with recent growth. On physical examination, both masses were favored to be ganglion cysts. Ultrasound showed hypoechoic soft tissue lesions with some internal echogenicity. On excision, both masses were histologically similar: circumscribed, lobulated, and attached to tendon. Large epithelioid cells with abundant granular eosinophilic cytoplasm arranged in syncytial cords and trabeculae percolated through background collagen. Many cells displayed nuclear pleomorphism and/or prominent nucleoli. Mitotic figures, spindling, high N:C ratio, and necrosis were absent. Both masses showed diffuse S100 protein but negative desmin and pancytokeratin expression. Ki-67 proliferative index was 1-2%. p53 was positive in 5-10% of nuclei. Both masses met criteria for atypical (but not malignant) GrCT. Margins were positive in both; taking additional tissue would compromise hand function. Our case shows that atypical GrCT may be not only multifocal but also symmetric. We speculate that migration of defective neural crest stem cells along both upper limb buds during embryogenesis may have allowed these essentially identical rare tumors to arise in mirror image on bilateral wrists simultaneously.

Papillary Eccrine Adenoma Presenting Clinically as a Keloid

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We present a case of a 47-year-old African American female who presented for removal of an enlarging, painful and pruritic hypertrophic nodule in the left lower abdomen. The patient had a significant past surgical history of laparoscopic cholecystectomy, cesarean section, and hysterectomy. All abdominal incisions healed appropriately, but she subsequently formed a large, pedunculated lesion (~3-4 cm) on the left abdomen. The clinical impression was that of a keloid. Surgical excision was performed. Histologic sections demonstrated a well circumscribed/unencapsulated nodular expansion of the reticular dermis by a proliferation of innumerable cystic spaces lined by flattened to cuboidal epithelium that formed intraluminal micropapillary projections. Many of the dilated cystic spaces contained eosinophilic amorphous material as well as neutrophils. The epithelium lining the microcystic spaces exhibited positive immunoreactivity for p63, calponin, and SMA, highlighting an intact myoepithelial layer. There were no areas of infiltrative growth. There was no evidence of keloid. Papillary eccrine adenoma is a rare neoplasm of eccrine sweat glands that occurs most frequently in African American woman in the distal extremities and present clinically as firm nodules. Histologically, the appearance is
“syringoma-like” with numerous dilated ducts of varying size with the addition of papillary projections into the lumen. The ducts have a myoepithelial layer present in accordance with the benign natural history of the lesion. Some consider papillary eccrine adenoma to be a variant of “adenocarcinoma in situ,” however this concept is not widely accepted in the scientific literature. We submit this case for the benefit of training and practicing dermatopathologists who may not yet have encountered this entity in their practice.

535

Metastatic Large Cell Neuroendocrine Carcinoma of the Larynx: A Rare Case of Presentation and Extreme Tumor Burden
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Laryngeal large cell neuroendocrine carcinoma (LCNEC) is an aggressive form of neuroendocrine carcinoma that typically affects smokers at an average age of 60 years. LCNEC is characterized by large cells with round to ovoid nuclei distributed in a trabecular or nested growth pattern. Mitotic activity is increased at >10/10 high power fields (HPFs), and the tumor cells show neuroendocrine phenotype on immunohistochemistry (synaptophysin, chromogranin). Previous classification considers LCNEC to be grouped with the atypical carcinoid tumor due to much histologic overlap. However, LCNEC has been found to have a higher mitotic rate and worse prognosis, which has led to proposed classification as a variant of poorly differentiated neuroendocrine carcinoma. A 56-year-old Caucasian female with a past medical history of smoking presented with painful subcutaneous skin lesion on her right upper extremity. Initial biopsy suggested a metastatic adenocarcinoma, and subsequent workup revealed an epiglottic lesion on PET imaging, which was biopsied and diagnosed as metastatic adenocarcinoma of unknown primary. Work up was negative for metastatic disease to bone, liver, or lungs. At the outside institution, the patient received radiotherapy followed by chemotherapy for her metastatic skin lesion. The patient continued over the course of four years to develop over 100 subcutaneous nodules ranging in size from 5 to 10 mm. She was referred to our institution, where review of her biopsies were consistent with metastatic large cell neuroendocrine carcinoma, with the epiglottic lesion favored to represent the primary. She received two rounds of chemotherapy but then was lost to follow up at our institution. Review of literature has only revealed one reported case of LCNEC with skin metastasis. This is the first reported case of both skin metastasis as the initial presentation as well as such a heavy metastatic burden to the skin.

536

WITHDRAWN
Extensive Sectioning Protocol of Merkel Cell Carcinoma Sentinel Lymph Nodes Supports Improved Survival with Non-solid Involvement in Immunocompetent Patients

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We recently reported clinical implications for solid (pattern 1, poor survival) versus non-solid (patterns 2-5, improved survival) Stage IIIA Merkel cell carcinoma (MCC), suggesting AJCC sentinel lymph node (SLN) staging may need to be altered. Minimal tumor burden (similar to patterns 2-5) is weighted in other cancer types based on the propensity for more tumor to be discovered upon extensive sampling. Extensive deeper sections (at 250 µm intervals x 5) were performed in 11 patterns 2-5 positive SLN biopsy cases and 8 negative (pattern 0) SLN biopsy cases to evaluate for the presence of pattern 1 disease. No case showed pattern 1 disease in deeper sections. Of 11 SLN-positive cases, 4 showed the same pattern in all deeper sections, 2 had no tumor seen after two or four deeper sections, and 5 showed gains of additional non-solid patterns. Of 8 pattern 0 cases, 6 showed no additional disease, while 2 showed isolated tumor cells (pattern 5) on deeper sections. No significant difference was identified in overall survival from diagnosis of pattern 0 (1 of 8 died of disease (DOD)) and patterns 2-5 (1 of 11 DOD, 1 of 11 died of unknown cause) cases (p=0.62, exact logrank test). In pattern 0, DOD was not correlated with tumor in deeper sections (not seen in 1 patient who DOD at 51 months), but the patient was immunosuppressed. In patterns 2-5, the two deaths (15 and 29 months; median follow-up for all positive cases 38 months, range 15-142) that occurred were in patients with additional non-solid tumor cells on deeper sections (1 DOD and was immunosuppressed; 1 cause of death unknown) (p=0.18 vs cases without additional patterns on deeper levels, exact logrank test). The data support unique MCC tumor biology in cases with solid versus non-solid SLN involvement. Solid versus non-solid categorization stability on extensive sampling facilitates our interpretation of this biology. Our results continue to support the prognostic role of immune status in MCC.
Primary Cutaneous Solitary Fibrous Tumor (SFT) – A Report of 5 Cases
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SFT occur in a variety of anatomic locations, especially deep soft tissue. While cutaneous SFT have been described, definitive diagnosis has been historically difficult, due to overlapping features with other dermal spindle cell lesions. In particular, cutaneous SFT is often mistaken for fat-free/low-fat variants of spindle cell lipoma, as both are composed of bland CD34+ spindled cells arranged in a variety of patterns with intermingled thickened collagen bundles. Herein, we describe 5 cases of cutaneous SFT confirmed by immunohistochemical (IHC) staining for nuclear STAT6, a sensitive and specific surrogate for SFT-defining NAB2-STAT6 translocation (4 of 4 tested). 3/5 cases occurred in women (ages 46, 54, and 55 yrs) on the thigh, eyelid, and scalp respectively. 2/5 cases occurred in men on the upper lip and great toe (ages 41 and 47 yrs, respectively). Histopathologically, all tumors were relatively well-circumscribed, involved the dermis/subcutis, and showed classic SFT features: short, ill-defined fascicles of ovoid to spindled cells with admixed collagen and a hemangiopericytomatosus to ectatic vasculature. Of note, the thigh lesion (F) demonstrated features consistent with malignant SFT: striking hypercellularity, mitotic rate of 5/10 HPF, and necrosis. The eyelid lesion (F) showed a vague storiform pattern and pseudovascular spaces lined by multinucleated giant cells, consistent with the giant-cell rich form of SFT. The scalp lesion (F) was sparsely cellular with abundant collagen. The right great toe lesion (M) showed little fibrosis and the upper lip lesion (M) entrapped salivary gland tissue. By IHC, all cases were positive for CD34 (4 of 4 tested). Cutaneous SFT pose a diagnostic challenge and raise the differential diagnosis of spindle cell lipoma, benign and malignant nerve sheath tumors, and cellular fibrous histiocytoma. STAT6 IHC can resolve this differential and should be used when cutaneous SFT is considered.
540

A Rare Case of Cutaneous Metastasis of Jejunal Adenocarcinoma presenting as a Sister Joseph Nodule

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Sister Mary Joseph’s nodule (SMJN) is the moniker given to a metastatic lesion involving the umbilicus and originating from intra-abdominal or pelvic malignancy. Its incidence is 1%–3% of all abdominopelvic malignancies. SMJN presents either as the first clinical manifestation of an undiagnosed primary malignancy or as metastasis from a previously-diagnosed cancer, representing an ominous prognostic finding. Recent reports have suggested that prognosis is better with aggressive management; the mean survival being 17.6–21 months with surgery and adjuvant chemotherapy. Surgery is usually recommended only in patients with a solitary umbilical metastasis and it should be avoided in cases with widespread disseminated disease; in such cases, effective palliation can be achieved with chemoradiotherapy. The mechanism of umbilical seeding from primary tumors is not clearly understood; however, authors worldwide have proposed several hypotheses. A seeding process can occur through several routes including: contiguous spread of peritoneal infiltration (the most common route) or through arteries, veins, or lymphatic channels, or spread along remnants of embryonic structures. We report a case of umbilical metastasis (SMJN) as the component of a patient’s initial presentation with underlying an underlying adenocarcinoma of the jejunum. To the best of our knowledge, this is the first report of a jejunal adenocarcinoma metastasis presenting as Sister Mary Joseph’s nodule. Metastatic adenocarcinoma cells are present in the deep dermis and subcutis while also involving the underlying tissues, ultimately extending to undermine the peritoneal surface.

541

Cutaneous Epithelioid Angiomatous Nodules: A Rare but Important Mimicker of Malignant Vascular Tumors

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Epithelioid vascular proliferations are a heterogeneous group of lesions that range from benign to frankly malignant. Cutaneous epithelioid angiomatous nodule (CEAN) is a rare, benign vascular lesion originally described by Brenn and Fletcher in 2004. Clinically, CEAN presents as small, single to multiple, erythematous to violaceous papules or nodules on the extremities or trunk. Histologically one sees a well-circumscribed, solid proliferation of large, epithelioid cells within the dermis. The cells show abundant eosinophilic cytoplasm, often with intracytoplasmic vacuoles, and contain vesicular nuclei with prominent nucleoli. Mitotic figures may be present but are never atypical. Immunostains will
highlight the vascular nature of the lesion. Once excised, CEAN does not recur and is clinically benign. We present a case of a 31-year-old male with a one year history of erythematous to violaceous papules and nodules on the right arm and chest. The lesions were occasionally pruritic and would bleed with trauma. These lesions had been increasing in size and number, leading to clinical suspicion for a vascular malignancy. Histology shows a circumscribed nodular proliferation of plump epithelioid cells with abundant cytoplasm with focal vacuolation and prominent vesicular nuclei. Immunostains for CD31 and Factor VIII highlight a prominent vascular network associated with red blood cell extravasation. The Ki-67 proliferative marker uptake was also increased. The combined clinical presentation and histological findings initially raised Kaposi sarcoma in the differential diagnosis. However, the patient was negative for HIV and had no significant past medical history. Repeated staining for HHV8 was negative. Since the entity of CEAN is rare, an outside expert opinion was sought, confirming the diagnosis of CEAN. CEAN is believed to be a reactive condition with an unknown etiology that must be differentiated from other more common vascular lesions, such as Kaposi sarcoma. This case demonstrates the importance of considering the rare entity of CEAN when evaluating a patient with multiple cutaneous vascular lesions, as CEAN can mimic malignant vascular tumors.

542
Sebaceous Mantleoma (Mantle Adenoma): Reappraisal of the Problematic Benign Neoplasm with Sebaceous Mantle Differentiation
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Few cases of a true benign neoplasm with sebaceous mantle differentiation have been reported, and little is known about this tumor. Herein, we present an example of the rare neoplasm called sebaceous mantleoma, with a comparison to the histology and immunoprofile of normal sebaceous mantles. A pedunculated polyp occurred on the scalp of a 51-year-old woman. Histologically, the tumor showed lobulated epithelial-mesenchymal units, which were separated from normal dermis by clefts. The lesion was composed of cords and columns of basaloid cells containing a few mature sebocytes, with a focal connection to infundibulocystic structures as well as dense fibrotic or fibromyxoid stroma. Immunohistochemically, androgen receptor, estrogen receptor, and CD117 were partially positive for the tumor, and CD8 (clone: C8/144B) and epithelial membrane antigen were focally positive. Additionally, cytokeratin 20–positive Merkel cells were individually admixed in the tumor nests as well as in normal sebaceous mantles. This case report could reveal the characteristic histology and immunoprofile of the problematic benign neoplasm and would help us to establish this entity.
543
Low-grade Neuroendocrine Carcinoma of the Skin (Primary Cutaneous Carcinoid Tumor) as a Distinctive Entity: A Clinicopathologic Study of 3 Cases with Literature Review
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Background: There is a scarcity of information on primary cutaneous low-grade neoplasms commonly known as carcinoid tumors, owing to their rarity. Herein, we describe the characteristics of tumors in cases we experienced as well as in the literature. Methods: We present three cases of what we named ‘low-grade neuroendocrine carcinoma of the skin’ (LGNECS); these occurred in the dermis and subcutis of the anterior chest or the inguinal. Results: Histologically, the tumors showed infiltrating proliferation of various sized nests, with low-grade neuroendocrine cytologic features but without mucin production. All cases exhibited varying degrees of intraductal tumor components. On immunohistochemical examination, these tumors expressed estrogen receptor alpha, progesterone receptor, androgen receptor, gross cystic disease fluid protein 15, mammaglobin, and GATA3 as well as neuroendocrine markers. Although a literature review revealed eight additional possible cases with no evidence of other diseases, it was difficult to determine if these were true cases of LGNECS because of the limited information available. Conclusions: Based on its characteristic histologic features and immunoprofile, we propose designating LGNECS as a distinct entity among cutaneous neuroendocrine tumors. Otherwise, such tumors could be misdiagnosed as mammary carcinomas (particularly when involving the skin of the breast) or as metastatic visceral neuroendocrine tumors of the skin.

544
Merkel Cell Distribution in Sebaceous Lesions
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Background: Trichoblastomas contain various numbers of Merkel cells within tumor nests, whereas basal cell carcinomas contain no Merkel cells. However, the Merkel cell distribution in sebaceous tumors has never been established. This study aimed to evaluate the Merkel cell distribution in various sebaceous tumors by using cytokeratin 20 immunohistochemistry. Methods: Cytokeratin 20 (mouse monoclonal, clone Ks20.8, dilution 1:4) immunostaining was evaluated in 3 seatoctomomas, 2 sebaceous gland hyperplasias, 4 fibrofolliculomas, 1 sebaceous mantleoma, 5 usual sebaceomas, 4 rippled pattern sebaceomas, 2 labyrinth pattern sebaceomas, 3 carcinoid-like pattern sebaceomas, 4 sebaceous adenomas, 5 sebaceous carcinomas, and perilesional normal tissues of these samples. Results: Cytokeratin 20–positive Merkel cells were observed in seatoctomomas (2/3), fibrofolliculomas (3/4), sebaceous mantleoma (1/1), carcinoid-like pattern sebaceomas (2/3), and labyrinth pattern sebaceoma (1/2) with varying proportions. Both the seatoctomoma and fibrofolliculoma, which did not include any
Merkel cells, were small-sized lesions (1–2 mm diameter). The labyrinth pattern sebaceoma with mixed Merkel cells had only 3 Merkel cells, 2 of which were distributed in a tumor area with a carcinoid-like pattern. Normal sebaceous mantles also contain a few Merkel cells within the epithelial components. Conclusions: In sebaceous lesions, Merkel cell distribution was observed in normal sebaceous mantles and mantle-associated lesions, and it could be supporting evidence of mantle differentiation. In addition, this study demonstrates that the carcinoid-like pattern in sebaceomas might show a phenotype of sebaceous mantle differentiation.

545
Metastatic Pilomatrix Carcinoma: Case Report and Review of Literature
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Pilomatrix or pilomatrixal carcinoma, a malignant counterpart of pilomatrixoma (also known as pilomatrixxoma), is a hair follicle neoplasm. Pilomatrix carcinomas are locally aggressive tumors which tend to recur locally, but rarely metastasize. Pilomatrixoma was first described in 1880 by Malherbe, hence the name “calcified epithelioma of Malherbe”. It was not until a century later that a malignant transformation was reported, suggesting a new entity, pilomatrix carcinoma or calcified epitheliocarcinoma of Malherbe. We present a case of a 69 year-old male who presented with multiple liver metastases three years following surgical excision of pilomatrix carcinoma of the right upper back. The original tumor was resected with negative margins, and axillary lymph nodes were negative for carcinoma. The diagnosis of metastatic pilomatrix carcinoma was made on a fine needle aspiration and a biopsy specimen from the liver, although initially it was thought to represent possible metastatic urothelial carcinoma given the GATA-3 positivity on immunostain. Further clarification of the patient’s history, evaluation of GATA-3 immunostain positivity on the original skin tumor, and the lack of any urothelial lesions on cystoscopy/ureteroscopy confirmed the diagnosis of metastatic pilomatrix carcinoma. Histologically, pilomatrix carcinoma resembles pilomatrixoma with the addition of high mitotic activity, marked cytologic atypia, infiltrative borders, and occasional lymphovascular invasion. Since this tumor is exceedingly rare and only the basaloïd portion of the tumor metastasizes, the diagnosis becomes a challenge if the history is unknown or unclear, and differential diagnosis can include basaloïd squamous cell carcinoma or urothelial carcinoma. In addition, the GATA-3 expression in skin adnexal tumors, such as pilomatrix carcinoma, urothelial carcinomas and breast carcinomas can pose additional diagnostic challenge. On recent follow-up of 3 months after the diagnosis of metastasis, the patient has responded well to cisplatin and gemcitabine.

546
Extramammary Paget’s Disease with Squamous Differentiation in a 75 Year-Old Man
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Extramammary Paget’s disease (EMPD) is a rare form of adenocarcinoma that usually presents in postmenopausal women and is characterized by atypical glandular epithelium, often with signet ring cell morphology, within the epidermis. Here, we present the unique case of a 75-year-old man who
presented with a tan 2cm mass lesion involving the scrotum. Excisional biopsy was performed and was significant for an ulcerated, moderate to poorly-differentiated invasive tumor with squamous morphology and positive lateral margins. However, the subsequent re-excision specimen revealed atypical epithelioid cells exhibiting a pagetoid growth pattern which spared the basal layer and focally invaded into the dermis. Immunohistochemical (IHC) stains were performed for CK7, EMA, p63, and MART-1. IHC showed strong positivity for EMA and CK7 in the tumor cells. The stains for p63 and MART-1 were negative. Subsequent re-review of the original biopsy focally demonstrated the atypical epithelioid cells adjacent to the squamous cell carcinoma component. The differential diagnosis in this case includes a so-called collision tumor versus squamous differentiation in EMPD. The latter is favored due to the relationship between the two tumors, the absence of a history of genital wart, and the absence of p16 expression in the squamous cell carcinoma component. Squamous differentiation in EMPD has been reported in the literature and should be considered when confronted with this combination of histologic findings.

547 Histologic Comparison of Angiolymphoid Hyperplasia with Eosinophilia (ALHE), Cutaneous Follicular Lymphoma, and Arthropod Bite Reactions
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Background: The classic histology of angiolymphoid hyperplasia with eosinophilia (ALHE) consists of proliferating blood vessels lined by plump cells with numerous eosinophils, vacuolated endothelial cells, and a surrounding lymphocytic infiltrate that may form follicles. Follicle formation may lead to the consideration of follicular lymphoma (FL). In addition, both of these entities can share clinical and histologic features with arthropod bite reactions (AR). In our study, we aim to determine the key differentiating histologic features between these entities. Design: 4 ALHE, 3 cutaneous FL, and 5 AR (concerning for lymphoma) were retrieved from the archives of Loyola University Medical Center Department of Pathology. The following features were evaluated: 1. vessel proliferation, 2. thick walled vessels, 3. histiocytoid endothelial cells, 4. vacuolated endothelial cells, 5. presence of eosinophils, 6. follicle formation, 7. overlying epidermal changes. Results: Vessel proliferation, histiocytoid endothelial cells, and eosinophils were seen in all ALHE. These features were seen in 60%, 40%, and in 100% of AR respectively. None of these features were seen in FL. 75% of ALHE and 20% of AR had numerous eosinophils, and no eosinophils were seen in FL. Follicle formation was seen in 50% of ALHE, 67% of FL, and in none of the AR. Thick walled vessels were seen in the majority of ALHE (75%), in 33.3% of FL and none of the AR. Vacuolated endothelial cells were seen in 75% of ALHE, 20% of AR, and were not seen in FL. Overlying epidermal changes were seen in 60% of AR (mainly interface changes) and no significant changes were seen in ALHE and FL cases. Conclusions: Overlapping clinical and histologic features between these entities can lead to diagnostic confusion. Key features to distinguish ALHE and FL included vessel proliferation, presence of eosinophils, and the presence of histiocytoid and/or vacuolated endothelial cells. Key features to distinguish ALHE and AR included thick walled blood vessels, follicle formation, and vacuolated endothelial cells (only rarely seen in AR). Overlying epidermal changes were seen only in AR, and not in ALHE or FL. No histologic features overlapped between FL and AR.
Panfolliculoma is a neoplasm composed all components of the hair follicle including infundibular, isthmic, stem, and bulbar differentiation. The cystic variant of panfolliculoma (CPF) is uncommon and may be difficult to differentiate from other cystic follicular lesions as all of the elements of a panfolliculoma may not be apparent in a given plane of section. Here we describe 10 examples of the cystic variant of this neoplasm. The age range was 23 to 75 years with an equal M:F ratio; five were from the head and neck and five from the trunk or extremities. All included a large central cyst lined by predominantly infundibular epithelium and containing orthokeratin. Eight of ten had hair shafts within the cyst contents. The cyst contents of two tumors also included foci of blue-grey inner root sheath keratin and in one tumor foci of isthmic-type keratin. The epithelial component emanating from the cyst wall was composed predominantly of reticulated basaloid germinative epithelium. Follicular bulbs and papillae were easily found in 7/10 tumors. Matrical epithelium or ghost cells were present in all cases but required careful search to identify in three of the tumors. Inner root sheath differentiation including trichohyalin granules was the most difficult epithelium to locate and in most was present in only small foci. One tumor had foci with prominent sebaceous epithelium. Nine of ten tumors were surrounded by fibrous stroma and one tumor was surrounded by myxoid stroma. Prominent calcification was present in two tumors. As matrical and inner root sheath epithelium may be inconspicuous in CPF the presence of hair shafts in the cyst contents will help in identifying these uncommon tumors.

Cutaneous Multiple Myeloma

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Cutaneous involvement of multiple myeloma (MM) is uncommon, typically occurs in late stage disease, and is a dismal prognostic indicator with an approximate 8 month median survival. We present a 51-year-old man with relapsed lambda light chain MM who developed abrupt asymptomatic skin metastases. Biopsy revealed a dermis replete of atypical plasma cells, positive for CD138 and CD45. In situ hybridization confirmed lambda light chain restriction. Despite rescue antmyeloma therapy with the anti-CD38 drug daratumumab, he rapidly declined clinically and succumbed to the disease 4 weeks after presentation. A standard treatment approach for cutaneous MM does not currently exist; however, various techniques to detect cytogenetic abnormalities are emerging and will provide additional prognostic value and direct individualized therapy.
Primary cutaneous ganglioneuroma is a rare benign neoplasm first described in 1972. Including our case, only 19 cases have been reported in the literature. Ganglioneuromas are comprised of mature ganglion cells interspersed with Schwann cells. The pathogenesis of these benign tumors is thought to be from aberrant migration, differentiation and proliferation of neural crest-derived cells in the skin. The staining pattern is consistent with neural cell tumors: positive for S-100 and glial fibrillary acidic protein (GFAP). We report a 77-year-old female who presented to a dermatology clinic with a flesh-colored, cerebriform sessile nodule on her left breast. The lesion had been present for as long as the patient could remember, but had recently grown in size. The patient had no history of neurofibromatosis, neuroblastoma, or multiple endocrine neoplasia. A shave biopsy showed a pedunculated dermal proliferation with overlying epidermal hyperplasia. The dermis contained a banal, spindled neural proliferation with myxoid change. Individual nerve bundles were seen in some areas. Other areas vaguely resembled myxoid neurofibroma. Scattered mature ganglion cells were seen throughout the dermis and focally entrapped within the epidermis. No neuroblastoma or melanocytic components were identified. Our case represents one additional cutaneous ganglioneuroma, a benign, but exceedingly rare neoplasm of the skin.

Polarizable crystals have been well documented in breast core biopsies, generally associated with benign apocrine glands. In contrast, polarizable crystals are only rarely reported in skin adnexal neoplasms. We report three different cases of sweat gland tumors with polarizable crystals morphologically suggestive of CaOx: one apocrine hidrocystoma and two tubular apocrine adenomas. Clinical presentation summary included two males and one female, ages 53 to 74, with lesions located on the left cheek, inferior vertex scalp and the left eyebrow. In case #1, the biopsy was bisected by the dermatologist; half was frozen for a rapid tissue diagnosis and stained with toluidine blue, and the remainder was processed in a glyoxyl-based, formalin free fixative. The other two cases were formalin fixed. All three cases were then paraffin embedded (FFPE) for permanent sectioning. All three cases showed polarizable, geometric, plate-like and fractured, colorless crystals within the lumens of the neoplasm. Of note, these crystals were seen only on the toluidine blue-stained section of Case #1, but were not present on the corresponding permanent section. We hypothesize that polarizable crystals may be present in sweat gland neoplasms more often than previously documented, but that they may often dissolve with routine processing, accounting for their rare visibility. We highlight rare finding, and suggest that it may be underreported. This finding was seen exclusively in benign apocrine tumors; further investigation would be necessary to determine whether crystals are seen exclusively in this subgroup of cutaneous adnexal neoplasms.
552
Angiomatoid Fibrous Histiocytoma of the Scalp with a Reticular Pattern Mimicking Cutaneous Angiosarcoma: A Potential Histopathological Pitfall
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A 29-year-old Japanese male presented with a 5-year-history of a mass in the scalp. The biopsy was examined at a local hospital and he was referred to our department. Cutaneous angiosarcoma (AS) was suspected as the initial diagnosis. A wide local resection revealed the nodular lesion located in subcutaneous fat. The lesion was relatively well-circumscribed with encircled fibrous pseudocapsule and lymphoid cuff. It was composed of histiocytic and/or spindle cells with palely eosinophilic cytoplasm. In a large area of the lesion, a reticular arrangement of the neoplastic cells and hyalinized stromal change were present. This reticular pattern seemed to correspond with pseudovascular reticular space in the initial small biopsy. Most of the lesional cells had mild nuclear atypia, although moderately pleomorphic cells were scattered. The neoplastic cells were immunoreactive for desmin, calponin and EMA. Although the presence of numerous intervening CD31-positive histiocytes mimicked vascular neoplasm, desmin-positive neoplastic cells were negative for CD31. FISH technique for the probe of EWSR1 displayed break-apart signals. The final diagnosis of Angiomatoid fibrous histiocytoma (AFH) was rendered. It has not been emphasized that AFH shows mimicking features for AS histologically and immunohistochemically in the literatures. However, it is conceivable that the misdiagnosis of AFH as AS occurs in medical practice and is potentially a diagnostic pitfall, especially in small biopsy specimens of head lesions. The combination of the following three histopathological features were misleading: the presence of a nuclear pleomorphism, pseudovascular reticular space, and CD31 immunoreactivity of numerous intervening histiocytes.

553
Sebaceous Adenoma with Numerous Lipidized Histiocytes: Potential Pitfall in Mismatch Repair Protein Immunohistochemistry
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Muir-Torre syndrome (MTS) is an autosomal dominant disorder that predisposes individuals to sebaceous neoplasms and a variety of visceral malignancies, most commonly colorectal cancer. It is regarded as a variant of hereditary nonpolyposis colorectal cancer (HNPCC), comprising about 28% of HNPCC families. Close clinical follow-up and annual cancer surveillance studies are recommended for MTS patients. The majority of MTS patients have mutations in DNA mismatch repair (MMR) genes resulting in loss of MMR protein expression and microsatellite instability. A large percentage (66%) of newly diagnosed sebaceous neoplasms demonstrate MMR protein deficiency by immunohistochemical (IHC) staining. A panel of IHC stains for MMR proteins (MLH1, MSH2, MSH6, and PMS2) is routinely performed on newly diagnosed sebaceous neoplasms as a screening test for MTS. Patients with loss of MMR protein immunoreactivity should undergo further diagnostic evaluation for MTS such as detailed family medical history, genetic counseling and germline molecular studies. We recently encountered a sebaceous adenoma partly surrounded by dense sheets of lipidized cells, confirmed to be histiocytes by
CD68 immunoreactivity and absence of cytokeratin staining. Expression of mismatch repair proteins was retained in the lipidized histiocytes, but MSH2 and MSH6 expression were lost in the lesional sebocytes. If the histiocytic population is not correctly recognized, the IHC stains could easily be misinterpreted as preserved or heterogeneous MMR protein expression. Awareness of this phenomenon will facilitate correct interpretation of IHC stains and proper identification of patients who should undergo further diagnostic evaluation for MTS.

554  
**RESIDENT**  
**CDX2 Expression in Pilomatrical Carcinoma: A Novel Diagnostic Role for a Gastrointestinal Transcription Factor**  
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Pilomatrical carcinomas are rare neoplasms of the skin and the malignant counterpart of pilomatricomas. Unlike pilomatricomas, pilomatrical carcinomas can be diagnostically challenging. Previous studies have reported β-catenin expression and gene mutations in both benign and malignant pilomatrical tumors, and in both sporadic tumors and tumors associated with familial adenomatous polyposis. CDX2 is a transcription factor essential for gastrointestinal (GI) development during embryogenesis, and both its over- and under-expression have been described in colorectal neoplasms. Studies have identified CDX2 as an upstream regulator on Wnt signaling and β-catenin activity. To further study CDX2, we compared its expression along with two other GI markers (CDH17, SATB2), β-catenin, androgen receptor, CK5, and CK19 in 13 pilomatrical carcinomas and other common non-pilomatrical cutaneous basaloid malignancies. Cases and controls were compared using Chi-square analysis. Statistically significant differences were observed in CDX2 expression (13/13 cases; 0/6 controls; \(p=1.3\times10^{-5}\)) and β-catenin expression (nuclear and membranous pattern in 13/13 cases; 1/6 controls; \(p=1.3\times10^{-4}\)). The expression profiles of pilomatricomas and pilomatrical carcinomas were the same. Interestingly, CDX2 expression was most consistent within a histologic subgroup of pilomatrical cells. Our data support CDX2 as an effective diagnostic marker for pilomatrical carcinoma. Although CDX2 is of great importance with respect to GI differentiation and has been implicated in GI neoplasia, other GI immunostains did not achieve statistical significance for expression in pilomatrical tumors in our study. Additional research is needed to elucidate the precise role of CDX2 and its relationship with the Wnt signaling pathway in gastrointestinal and pilomatrical neoplasms.

555  
**RESIDENT**  
**Melanocytic Neuroectodermal Tumor of Infancy: A Wolf in Sheep’s Clothing: A Case Report and Review of Literature**  
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Melanocytic neuroectodermal tumor of infancy (MNTI) is a rare soft tissue tumor of primitive neural crest origin, usually diagnosed within the first year of life. The predilection site of MNTI is anterior maxilla. Although the tumor is usually benign, its rapidly growing nature, ability to cause major deformities in surrounding structures, possibilities of malignant transformation and metastasis, necessitates early diagnosis and aggressive surgical resection, however extent of surgical resection and optimal amount of
margin clearance has not been delineated. Up to 15% of cases develop recurrence despite surgical resection. Herein, we present a case of aggressive MNTI and discuss clinico-pathologic features, treatment alternatives and prognosis. A 4-month female infant was referred to our department presenting a rapidly growing 2.5 cm mass of the anterior right maxilla. CT scan of right maxilla revealed low-density lesion with unclear boundaries. Microscopically, tumor displayed a biphasic cell population in a background of fibrous connective tissue stroma. One cell type displayed large polygonal epithelioid appearance with tubular and clustering pattern containing melanosomes, positive for Pancytokeratin, melanin and HMB-45. The other cell type was neuroblast-like, positive for synaptophysin, CD99 and NSE. The Ki-67 index was 60% consistent with high-grade MNTI. Recently it has been shown that some of the MNTI are prone to harbor the oncogenic BRAFV600E mutation. We hypothesize that use of BRAF-targeted therapies represent potential alternative treatments for aggressive MNTI, especially to treat cases not amenable to surgical management or to minimize facial mutilation.

556
A Case of Squamous Cell Carcinoma of the Lower Lip: Rapid Growth Triggered by Punch Biopsy
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Squamous cell carcinoma (SCC) is one of the common malignant tumors of oral mucosa. SCC of the lips accounts for approximately 30% of oral cavity malignancies. SCC of the lower lip often invades the deep muscle and mandible and also, metastases to regional lymph nodes. In this report, we present a case of a rapidly enlarging mass on the lower lip diagnosed as SCC. A 64-year-old female presented with 1cm-sized, hyperkeratotic plaque on her lower lip for several months. Histopathologic examination by punch biopsy revealed pseudoepitheliomatous epidermal hyperplasia. After 3 weeks of punch biopsy, the lesion had rapidly grown to about 2.5cm-sized mass. On the additional biopsy, the specimen was suggestive of keratoacanthoma (KA). For total excision and exact diagnosis, she was referred to plastic surgery department and underwent total excision and local flap coverage. The specimen showed features of moderately differentiated squamous cell carcinoma. Distant metastases were found in submental, submandibular lymph node and right upper internal jugular chain on PET-CT and neck CT scan. She is undergoing concurrent chemoradiotherapy. There have been no report of rapidly engaging SCC triggered by trauma. We suggest that trauma from punch biopsy would trigger rapid growth of SCC and herein report this case as a rare one.

557

WITHDRAWN
differentiate bullous morphea, bullous pilomatricoma, lymphangioma, insect bite etc. On microscopic examination, sections showed normal epidermis with underlying dilated lymphatic channels. The well-circumscribed tumor showed both basophilic and shadow (ghost) cells appearing as collections of pale staining cells with no cellular or nuclear details. Bullous pilomatricoma is a rare disorder characterized by semitransparent, erythematous, bluish, or skin colored, heavily folded or striae-like flaccid blisters overlying a solitary firm to hard nodule. Bullous pilomatricoma is seen mainly on the shoulder and upper limbs in contrast to head and neck for non-bullous pilomatricoma. Theories have been proposed to explain the bullous appearance seen on pilomatricomas. The main role in bullous appearance is attributed to lymphatic obstruction, and it has been postulated that the pressure on the area around the hard core of the pilomatricoma induces the obstruction of lymphatic vessels and congestion of lymphatic fluid. This results in dilation of lymphatic vessels, the leakage of lymphatic fluid, and edema in the dermis surrounding the tumor, producing a bullous appearance. Like classical pilomatricoma, since this form does not regress spontaneously, surgical excision is the treatment of choice because recurrence is rare. Although malignant transformation has been described, it is exceedingly rare.

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558
Myopericytoma of Distal Extremity: A Case Report
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Myopericytoma is a rare soft tissue tumor exhibiting a hemangiopericytoma-like vascular architecture and perivascular myoid differentiation. These neoplasms often present as benign painless, well-circumscribed subcutaneous masses localized to distal extremities. We report on a 46-year-old female who presented with a 1.0 cm firm, crateriform pink nodule with peripheral scale on the right proximal arm that clinically resembled a keratoacanthoma or excoriated prurigo nodule. Histology showed an ulcerated lesion with numerous dermal endothelial-lined vessels in the background of round to ovoid cells with well-defined cell boundaries. Immunohistochemistry for CD34 and smooth muscle actin showed reactivity in the endothelial-lined vessels and background cells. Additionally, endothelial-lined vessel cells showed reactivity for CD31, whereas desmin, cytokeratin, Mart 1 and S-100 protein were uniformly nonreactive. The final diagnosis was myopericytoma. Treatment involved local and complete excision. Myopericytoma shares many characteristics with other more common perivascular neoplasms, particularly glomus tumors, hemangiopericytomas, angioleiomyoma, and myofibromas, and mimic them not only in clinical presentation, but also microscopically. In this report, we aim to describe the clinical and histopathologic features of this rare tumor.
Isolated Cutaneous Meningioma of the Scalp: Another Mimicker of Primary Adnexal Tumor

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Cutaneous meningiomas are rare tumors most commonly located in the skin and soft tissue of the scalp. They may be congenital (type I), acquired and derived from ectopic arachnoid tissue in the skin (type II), or arise through direct extension from an intracranial meningioma (type III). Despite their well-established documentation in the literature they may escape recognition when classic features are not present. Herein, we present a case of a cutaneous atypical meningioma (≥4 mitotic figures/10 HPF) on the posterior scalp of a 31-year-old male with histologic features mimicking a malignant adnexal tumor. The biopsy showed diffuse sheets of epithelioid cells with a syncytial growth pattern interspersed among variably sized, thin-walled vessels and small lymphocytes. The tumor nuclei were focally hyperchromatic with irregular nuclear membranes, occasional pseudoinclusions, and obvious mitotic figures (11/10 HPF). The cells had a moderate amount of eosinophilic cytoplasm. Given the location and histologic features, hidradenoma/hidradenocarcinoma was favored in the diagnosis. When the case was referred in consultation, immunohistochemical studies showed the majority of cells labeling for EMA with focal PR positivity. Wide-range anti-keratins were negative. Neuroimaging excluded cutaneous extension of an intracranial meningioma. To our knowledge, this is the first case of isolated cutaneous meningioma mimicking an adnexal neoplasm. Thus, cutaneous meningiomas should be considered in the differential diagnosis of dermal and subcutaneous epithelioid neoplasms of the scalp.

An Unusual Presentation of a Cutaneous Leiomyosarcoma Originating from a Pilar Leiomyoma

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Cutaneous leiomyosarcoma may arise from the arrector pili muscle or from the smooth muscle of cutaneous vessels. It is most unusual to detect the transformation of leiomyosarcoma from leiomyoma, as the majority of cutaneous leiomyosarcomas are believed to arise de novo rather than as a malignant transformation of a pre-existent leiomyoma. We present a case of a leiomyosarcoma in association with a pilar leiomyoma in the right proximal thigh of an 83 year-old male. The clinical presentation was that of a nodule with a differential diagnosis of pilomatrixoma versus “epidermal inclusion” cyst. Histologic examination showed a dermal-based spindle cell lesion arranged in fascicles and extending into the subcutaneous tissue. The cells exhibited focal nuclear pleomorphism and hyperchromasia with 17 mitotic figure per 10 HPF. Immunohistochemistry showed diffuse positivity for SMA and desmin. The cells were negative for SOX-10, Mart-1, and CK 5/6. At the periphery of the tumor, a distinctly less cellular region contained cells with minimal cytologic atypia, consistent with a pilar leiomyoma. To our
knowledge, there is only one other report of a cutaneous leiomyosarcoma occurring concomitantly with a leiomyoma. Since leiomyosarcoma is the most common sarcoma metastasizing to the skin, the detection of a benign component helps establish a diagnosis of a primary lesion.

561
Merkel Cell Carcinoma within Sebaceous Carcinoma Lesion in the Palpebral Conjunctiva
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Merkel cell carcinoma (MCC) of the skin is a rare, aggressive cutaneous malignancy originating from Merkel cells and predominantly affects older adults or immunocompromised individuals. It has a propensity for local recurrence and regional lymph node metastasis. There are several reports on MCC concomitant with benign tumors, such as seborrheic keratosis, or other malignant neoplasms, such as squamous cell and basal cell carcinomas. There has been only one reported case of MCC concomitant with sebaceous carcinoma to date; here we report the second. Case report: A 68-year-old Japanese man presented with a 2-month history of papillomatous nodule in the palpebral conjunctiva of the right lower eyelid. He was diagnosed with sebaceous carcinoma through punch biopsy and underwent wide local excision by 5-mm margins concurrently with sentinel node biopsy. Histopathologically, the lesion was an exophytic tumor that contained sebocyte-like cells with vacuolated, foamy cytoplasm, significant nuclear atypia, and mitoses. In addition, there was a basophilic submucosal cluster within the lesion of sebaceous carcinoma. The submucosal tumor was composed of monotonously uniform, round, blue cells without sebaceous differentiation. On immunohistochemical analysis, the cells were to be positive for neuroendocrine markers and perinuclear dot-like pattern for cytokeratin 20. Based on these findings, the patient was diagnosed with combined MCC and sebaceous carcinoma. Sentinel nodes were negative for MCC and sebaceous carcinoma. Afterward, the patient had multiple metastases to lymph nodes and skin and required additional surgery and radiotherapy.

562
Dermatofibrosarcoma Protuberans with S100 protein-positive Sarcomatous Tumor Nodule
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Background: Dermatofibrosarcoma protuberans (DFSP) is a low grade sarcoma, but some tumors are associated with high-grade transformation, which usually has the appearance of a fibrosarcoma. It may or may not express CD34, but is usually negative for other markers. We present a case that aberrantly expressed S100 protein. Clinical Presentation: 42 year old woman with a slow growing mass on her scalp with recent rapid growth. Methods: Immunohistochemistry for CD34, S100 protein and Sox10 and fluorescence in situ hybridization (FISH) for PDGFB(22q13). Results: The tumor involved dermis and subcutis, measuring 19 mm. A nodule with a mitotic rate of 16 mitoses/10 HPF was surrounded by a storiform spindle cell proliferation. All tumor cells were positive for CD34. The spindle cell nodule was
positive for S100 protein, but negative for SOX10. FISH analysis revealed PDGFB gene rearrangement in nearly all cells. Discussion: In the differential diagnosis of DFSP from other malignant spindle cell tumors, positive labeling for S100 protein usually argues against DFSP. However, as illustrated in our case, there are rare exceptions. In our case the diagnosis of DFSP with a high grade nodule aberrantly expressing S100 protein is supported by FISH documenting that nearly all tumor cells were associated with PDGFB gene rearrangement. The case illustrates a potential diagnostic pitfall, but also highlights the value of cytogenetic methods when immunohistochemistry yields an unexpected result.

Clear Cell Acanthoma of the Vulva
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Clear cell acanthoma (CCA) is a benign proliferation of keratinocytes. Its clinical presentation is relatively nonspecific and elicits a wide differential diagnosis including inflammatory processes and benign and malignant neoplasms. Biopsy is necessary for diagnosis as unique histopathologic features differentiate these entities and impact clinical management. Herein, we describe a case of clear cell acanthoma on the vulva, the first to our knowledge reported at this anatomic location. A white female in her 70’s presented with a several year history of an asymptomatic, firm, smooth, skin-colored, approximately 0.3 cm papule on the labia majorum. Shave biopsy was performed. Microscopic examination revealed a well delineated region of epidermal hyperplasia composed of cleared keratinocytes. Numerous neutrophils were scattered throughout the epidermis and within the parakeratotic stratum corneum. The histologic features of hyperplastic epithelium, glycogen-containing keratinocytes infiltrated by neutrophils, and overlying parakeratosis with neutrophils supported the diagnosis of clear cell acanthoma. Clear cell acanthoma most often presents as a solitary, painless plaque or nodule on the leg, thigh, or trunk which can bleed with trauma. CCA is most common in middle aged to elderly patients and has no gender predilection. The lesions do not regress spontaneously and incomplete excision can result in recurrence. While most often found on the trunk and extremities, CCAs have been reported in several uncommon locations including the nipple, vermilion lip, hallux, palm and scrotum. The only other report of a clear cell acanthoma in the female genitalia describes the giant variant on the perineum of a 14 year old girl. The pathogenesis of CCA is not completely understood. Although classically thought of as a benign epidermal tumor, hypotheses have emerged about CCA representing a localized, inflammatory reaction. Multiple reports have described CCAs associated with inflammatory dermatoses including hidradenitis suppurativa, folliculitis, stasis dermatitis, and scars. Regardless of underlying etiology, this case highlights the importance of considering CCA as a possible genital entity because management is conservative, in contrast to the infectious processes and malignancies it may mimic.
Malignant Pilomatricoma: A Potential Diagnostic Pitfall
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Malignant pilomatricoma is a rare neoplasm of hair matrical differentiation. Similar to its more common benign counterpart, pilomatricoma, activating mutations in the CTNNB1 gene encoding b-catenin have been reported in malignant pilomatricoma. These rare tumors generally present in adult males as solitary lesions in the head and neck region with or without documentation of a benign precursor. In contrast to benign pilomatricomas, malignant pilomatricomas show infiltrative growth, necrosis, and nuclear pleomorphism in the basaloid cell component. We report here a case of a 24-year-old female who presented with a 1.5 cm nodule on the right cheek that on biopsy showed classic features of pilomatricoma with an associated focus of architecturally atypical matrical cells infiltrating the dermis in small nests and cords. There was no evidence of perineural or angiolymphatic spread. Re-excision of the lesion reportedly achieved clear margins. Three months later necrotic pulpal tissue was noticed during a dental procedure prompting a CT scan that showed an osteolytic mass that extended from the medial portion of the right maxilla to the associated buccal soft tissue that was separate and distinct from the previous right cheek lesion. Histological sections confirmed an atypical pilomatrical tumor in soft tissue that also infiltrated maxillary bony trabeculae. There was no evidence of previous scar tissue associated with this new focus. Taken together, the clinical, radiological, and histological data supported local metastasis of the right cheek malignant pilomatricoma. We conclude that biologically aggressive malignant pilomatricomas can have only subtle cytological atypia, and thus may be difficult to diagnose by histopathology. The presence of infiltrative growth pattern alone should inform pathologists of this possibility.

A Rare Case of Perineural Invasion in Cutaneous Metastatic Diffuse Large B-Cell Lymphoma
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Diffuse large B cell lymphoma (DLBCL), the most common type of Non-Hodgkin lymphoma (NHL), accounts for 30% of all lymphomas. Although it is commonly aggressive in nature, it rarely metastasizes along the nerves. Perineural invasion (PNI) is the process of neoplastic invasion of the nerves. PNI is frequently observed in solid malignant tumors, including those of the colon and prostate. PNI is a prognostic factor for poor outcomes and potential resistance to therapy. Herein, we report a 63-year-old man with chemotherapy-refractory diffuse large B cell lymphoma who developed multiple cutaneous nodules along the cutaneous superficial nerves. A series of skin biopsies revealed that the superficial nerve endings were intensively surrounded by large atypical cells with nuclei that were twice the size of lymphocytes. Immunohistochemical analysis revealed that the tumor strongly expressed CD20 and CD79a, while staining negatively for terminal deoxynucleotidyl transferase (TDT). Upon treatment with advanced chemotherapy, the metastatic nodules flared up quickly. Our case might support the hypothesis that endogenous neurotrophin secreted by the nerves promote tumor cell survival. PNI of DLBCL is rare, but it may occur with resistance to both chemotherapy and rituximab,
which warrants the use of other advanced treatment strategies. This case supports the need for further investigation of chemotherapy-refractory DLBCL.

566  
Spindle Cell Lipoma on the Finger  
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A 56-year-old man presented with a 9-year history of solitary papule on the pulp of the middle finger of her left hand. The papule was about 0.5 cm in diameter and was firm on palpation. Histological examination of the excised lesion revealed well-circumscribed but unencapsulated proliferation of bland spindle cells admixed with mature adipocytes in a collagenous and myxoid stroma involving deep dermis and subcutaneous tissue. The spindle cells were uniform, and exhibited elongated nuclei and narrow cytoplasm without atypia. No lipoblastic cell was observed. Immunohistochemically, the spindle cells were positive for CD34 and negative for S100. The histopathology and immunohistochemistry analysis suggested the diagnosis of spindle cell lipoma. Spindle cell lipoma usually occurs in the posterior neck, the shoulder or the upper back of elderly males. In our case, the lesion occurred in the finger, which is a rare location of this tumor.

567  
Isolated Cutaneous Epithelioid Hemangioendothelioma in a 14 Year-Old Female  
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A 14 year old female presented with a four month history of an ulcerated 1.6 cm lesion on the top of her scalp. A punch biopsy and subsequent excision revealed dermal clusters of plump epithelioid cells with vesicular chromatin and eosinophilic cytoplasm embedded in a fibromyxoid stroma. Many of the tumor cells contained cytoplasmic vacuoles some of which displaced the nucleus forming signet ring-like cells. Significant atypia, mitotic activity, or necrosis was not identified. Immunohistochemical reactions showed that the lesional cells were strongly positive for CD31 and D2-40 supporting the diagnosis of an epithelioid hemangioendothelioma. Additional work-up failed to identify other lesions and the patient remains tumor free after six months of follow-up. First described by Enzinger and Weiss in 1982, epithelioid hemangioendothelioma is a rare low grade malignant neoplasm arising from vascular endothelium. Mainly occurring in adults, the tumor usually arises in the soft tissues of the extremities, but can originate in the liver, lungs, bones, other internal organs and skin. Most of the skin tumors are associated with an underlying bone tumor and patients may develop multiple lesions in the same general anatomic region. Childhood onset of an isolated cutaneous epithelioid hemangioendothelioma is extremely rare with only six published cases. Although the sample size is very small, half of these pediatric patients have lymph node metastases suggesting that this neoplasm is more aggressive than previously thought. Therefore, it is important to recognize these painful primary cutaneous tumors to ensure that the patients receive a complete surgical excision, systemic workup to exclude metastases, and close clinical follow-up.
Merkel Cell Carcinoma Associated with Basal Cell Carcinoma: A Matter of Collision or Collusion?
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The majority of Merkel cell carcinomas display pure neuroendocrine differentiation but there exists a subset with combined neuroendocrine and non-neuroendocrine elements. With regard to the latter, co-existent squamous neoplasia or intratumoral squamous differentiation is the most common finding. Merkel cell carcinoma associated with basal cell carcinoma, however, is exceedingly rare with only a few reported cases in the literature. Herein, we describe two additional cases, include a review of the literature and explore whether this occurrence represents a collision or collusion of entities. Furthermore, in one case, the close resemblance of Merkel cell carcinoma to the associated basal cell carcinoma serves as a reminder that these two tumors can be easily mistaken for one another in some instances.

Intrinsic PD-1 Expression in Merkel Cell Carcinoma Tumor Cells
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Merkel cell carcinoma (MCC) is an aggressive cutaneous neuroendocrine neoplasm that carries a poor prognosis with limited treatment options. The inflammatory microenvironment has been proven to correlated with improved patient outcomes. Targeting the pathway of programmed cell death protein 1 (PD-1) in tumor infiltrating lymphocytes (TILs) and its ligand (PD-L1) on tumor cells has been successful in many refractory neoplasms. However, expression of PD-1 in TILs and PD-L1 in MCC is patchy and not clearly associated with outcomes. In this study, immunohistochemistry for PD-1, PD-L1, CD3, FOXP3, CD168, CD33, Granzyme B, and S100A9 were performed on eleven paraffin-embedded cases of primary and metastatic MCC. PD-1 expression is categorized as no, patchy or strong expression. Additional tumor infiltrating cells are also identified. Of the eleven MCC cases, seven are primary tumors, three distant metastases and one lymph node metastasis. All MCC tumors have strong peritumoral and less intratumoral TILs, but not correlative with PD-1 expression in lymphocytes. PD-1 expression within tumor cells was also identified in 80% of MCC cases. Additional tumor infiltrating inflammatory cells are also identified. The majority of the MCC cases contained tumor cells with albeit weaker expression of PD-1, as described previously in melanoma cell lines. If tumor cell intrinsic PD-1 expression is possible, they may potentially be a predictor of tumors that could respond to monoclonal antibody against PD-1 and re-evaluate our understanding of the pathway. Additional studies are needed to evaluate the clinical significance of PD-1 expression on MCC cells.
**570**  
**A Classic Case of Squamous Cell Carcinoma Arising in Epidermolysis Bullosa**  
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Epidermolysis bullosa (EB) is a clinically and genetically heterogeneous group of rare inherited disorders characterized by trauma-induced blistering of the skin. The disease is usually inherited in an autosomal dominant or autosomal recessive fashion and, with the aid of immunomapping, is best classified on the basis of the level at which the skin separates. Dystrophic EB is a subtype in which the separation occurs sub-lamina densa. The most significant complication in patients with EB is cutaneous squamous cell carcinoma (SCC). A recent study reported the prevalence of SCC in EB to be as high as 80% or 90% by the ages of 45 and 55, respectively. The SCC that arises is extremely aggressive, and death frequently results. Given the rarity of EB and its clear association with aggressive SCC, it is important to increase awareness among pathologists. It can be very difficult to diagnose early SCC in skin undergoing constant ulceration and repair. For this reason, we report the case of a 45-year-old female with a history of recessive dystrophic EB. Over the past five years, she has developed several invasive and subtle in-situ SCCs in areas of EB bullae, with some in-situ lesions closely mimicking reparative epidermis. Excisions have thus far been curative, but the need for frequent skin self-exams and regular full skin checks at dermatology clinic has been stressed going forward.
Hyalinized Neurofibromas: Not Just Rare Variants in the Skin of the Breast

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Although classical neurofibromas are commonly encountered skin lesions, histologic variants are seen less frequently. We herein report a greater than 15 year retrospective review of a single institution’s experience with the histopathologic diagnosis of neurofibroma of the breast with a focus on hyalinized variants. An electronic record review of histopathology files (CoPathPlus; Cerner Corp.) was conducted for the 15 year 10 month interval 01/01/2000 to 10/16/2015. The search catalogued all specimens in which the anatomic site was "breast" and the diagnosis was "neurofibroma". All cases were microscopically revisited and subclassified into one of seven histopathologic categories. Immunohistochemical (IHC) stains for S100, tryptase, and CD117 were performed on 19 hyalinized and 19 age-matched classical neurofibromas. Number of tryptase-positive and CD117-positive mast cells per high-power field (hpf) was recorded (average of 5 hpfs) for each case. During the study period, 62,021 breast specimens were reviewed at our institution. Of these, 86 samples (0.14%) were diagnosed as neurofibromas. Patient ages ranged from 17 to 94 years, with nearly equal occurrence on right (57%) versus left (52%) breast. Amongst the 86 cases, there were 50 classical (58.1%), 19 hyalinized (22.1%), 6 diffuse (7%), 5 cellular (5.8%), 3 myxoid (3.5%), 2 epithelioid (2.3%), and 1 plexiform (1.2%) neurofibromas. All hyalinized and age-matched classical neurofibromas were S100 positive. For the hyalinized subset, the average number of IHC-positive mast cells per hpf was 34.5 by tryptase and 26.8 by CD117. For the age-matched classical cohort, mast cells were enumerated at 22.5 by tryptase and 19.3 by CD117. The hyalinized variant of neurofibroma comprises a sizeable proportion of neurofibromas of breast. Published literature reports a 2.6% incidence of hyalinized neurofibromas at non-special cutaneous sites. Our series details a 22.1% incidence of hyalinized neurofibromas in the anatomic location of the breast. Regarding pathophysiology, there is a statistically significant increase in the average number of IHC-positive mast cell per hpf in hyalinized variants when compared to classical neurofibromas of the breast when measured by both tryptase (p=0.00157) and CD117 (p = 0.00901) (GraphPad; La Jolla, CA).

Proliferating Pilomatricoma of the Leg: A Case Report

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Proliferating pilomatricoma is a rare type of pilomatricoma which was described by Kaddu et. al in 1997. To date there are less than twenty-five cases reported in the literature. It is a benign tumor, characterized by hair matrix differentiation. It usually presents as a large, painless, solitary cutaneous lesion ranging in size between 1.5 and 6 cm, most commonly on the head and neck region, upper extremities and back of older individuals in their 5th to 7th decade. It has a higher potential for local recurrence after incomplete excision as compared to classic pilomatricoma. We herein report a case of a 56-year-old man who presented with a 6 cm exophytic cutaneous mass of the leg, an unusual location. The tumor was present for two years with recent growth over the past several weeks, clinically simulating a keratoacanthoma. Histologically, the lesion demonstrated a relatively large, lobulated, fairly...
well circumscribed appearance with involvement of the dermis and the subcutis. It was composed of basaloid matrical cells with variable atypia and many mitotic figures (15/10HPF), as well as sheets of anucleated squamous cells. Calcification and ossification were not present. Tumor cell necrosis, lymph-vascular/perineural invasion and infiltrative boarders were not observed. The overlying epidermis was ulcerated but there was no evidence of origination from the epidermal surface. There was surrounding inflamed granulation tissue with a giant cell reaction. The tumor was excised with clear margins. This report of a large proliferating pilomatrixoma contributes to the limited existing literature of this rare entity. It is also the second report of such a tumor occurring on the lower extremities. In addition, it highlights the histologic features which may help distinguish it from classic pilomatrixoma, matricoma, basal cell carcinoma with matrical differentiation, and pilomatrix carcinoma.

574
Metastatic Urothelial Carcinoma masquerading as Cutaneous Digital Papillary Adenocarcinoma: The Importance of Clinicopathological Correlation
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Accurate dermatologic diagnosis requires integrating clinical findings with histopathologic findings seen in a biopsy, also known as clinicopathologic correlation. Erroneous diagnoses resulting from lack of adequate clinicopathologic correlation confer an increased risk of inappropriate prognostication and therapeutic intervention. We present the case of a 76-year-old man who presented with an ulcerated papule on his dorsal left thumb, present for 4 months. Histology showed an atypical epithelial proliferation in the dermis with glandular and focal squamous differentiation, mitotic figures without atypia, and lymphovascular invasion. A diagnosis of cutaneous digital papillary adenocarcinoma (CDPA) was made, and imaging studies to screen for metastasis were recommended. Unbeknownst to dermatology at the time, the patient had muscle –invasive urothelial carcinoma for which he was being evaluated for surgical resection. Imaging showed numerous pulmonary mets and lytic lesions of the ribs and spine, and the question arose: were the metastases from the bladder cancer or the thumb lesion? Review of the original bladder tumor biopsy slides showed a glandular variant of urothelial carcinoma, with histology identical to that in the thumb lesion. Originally called Aggressive Digital Papillary Adenocarcinoma, CDPA occurs in distal hands and feet with metastasizes to lymph nodes or lung in up to 26% of cases. Metastases are significantly reduced with amputation or complete excision. Minimal treatment options exist for metastatic disease. Urothelial carcinoma (UC) comprises 90% of bladder malignancies with histologic variants including sarcomatoid, squamous, and glandular. Non-metastatic UC with invasion to the bladder muscularis propria is treated with cystectomy. Metastasis to bone, lymph nodes, lungs, and liver are present in up to 25% of muscle invasive UC and are treated with a combination chemotherapy regimen. This exceedingly rare case of metastatic urothelial carcinoma masquerading as cutaneous digital papillary adenocarcinoma emphasizes the importance of relevant clinical information to avoid errors in histopathologic diagnosis that carry potential consequences for treatment options and prognosis.
Cutaneous squamous cell carcinoma with osteoclast-like giant cell proliferation is an exceedingly rare entity that was first described in 2007. Since that time, only 13 cases have been described in the literature. Histopathologically, these poorly differentiated lesions are often difficult to distinguish from carcinosarcoma and atypical fibroxanthoma. While cytokeratin positivity on immunohistochemistry distinguishes these tumors from atypical fibroxanthoma, discriminating from carcinosarcoma is more difficult and must be made histologically. We present 3 cases of cutaneous squamous cell carcinoma with osteoclast-like giant cell proliferation. Within all tumors, the osteoclast-like giant cell population stained positive for CD68 with variable positivity for antipancytokeratin (AE1/AE3). Histomorphology as well as immunohistochemical staining patterns of our cases will be further described and compared to prior cases. These 3 cases were identified during a 5 year period at one dermatopathology laboratory. This suggests that this entity may be more common than previously recognized.

Seborrheic keratoses are generally considered benign tumors. However, they have been reported to occur in association with secondary skin tumors, such as keratoacanthomas, squamous cell carcinomas (in situ and invasive), basal cell carcinomas, and melanomas. To date, there have been five reported cases of trichilemmal tumors arising in seborrheic keratoses, all in Japanese patients. Trichilemmal carcinoma is a very rare malignant tumor thought to be derived from the outer root sheath epithelium of hair follicles. Some authors believe most diagnosed cases are really squamous cell carcinomas with clear cell differentiation. We herein report a rare case of trichilemmal carcinoma arising within a seborrheic keratosis, in a 77-year-old non-Japanese man. The patient, who was a heavy smoker for over 50 years but otherwise healthy, presented with a lesion on his right temple of 3-year duration. Clinically, the lesion was a seborrheic keratosis, which was confirmed histologically on two occasions. A lesion remained which measured 3 x 1.4 cm and was brown, irregular, variegated, ulcerated and firm. Due to the disfiguring nature of the lesion, re-excision with cheek advancement flap closure was performed. Microscopic examination showed areas with variable hyperkeratosis and papillomatosis, acanthosis, horn pseudocysts and squamous eddies, diagnostic of a seborrheic keratosis. Within this lesion there was a morphologically different neoplasm showing prominent epidermal expansion by generally uniform lightly eosinophilic to clear epithelial cells with distinct cellular borders. The lesional cells were shown to contain cytoplasmic glycogen with special stains. There were areas showing nuclear atypia more towards the peripheral layers of the proliferating epithelium, with increased mitotic activity. The neoplasm had an irregular papillary surface topped by a scale crust and a base that formed expansile irregular tongues, without a definite infiltrating growth pattern. The features favored a low-grade
trichilemmal carcinoma arising in association with an irritated seborrheic keratosis. Margins were not involved and there has been no clinical recurrence at the site during a 7-month follow-up period.

577
A Case of Primary Signet-ring Cell/Histiocytoid Carcinoma on the Scrotum.
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Primary signet-ring cell/histiocytoid carcinoma (PSRCHC) is a rare neoplasm that typically occurs on the eyelid and axilla. The origin of this tumor, either eccrine or apocrine, remains controversial; however, recent studies have indicated an apocrine origin. We herein report a case of a 91-year-old Japanese man who underwent surgery for colon cancer 3 years ago. He was histologically diagnosed with welldifferentiated adenocarcinoma and subsequently remained free of recurrence. He presented to our Department with a slowly growing induration on his scrotum. No urological abnormalities were detected. An examination of a biopsy sample from the scrotum revealed the diffuse and scattered proliferation of neoplastic cells in the dermis to the subcutis without epidermal involvement. Neoplastic cells were round to polygonal in shape and had oval nuclei with an eosinophilic cytoplasm, which are the characteristic histopathological features of a histiocytoid appearance. Some neoplastic cells had a rich pale cytoplasm and large eccentrically located nuclei, and resembled signet-ring cells. Immunohistochemically, proliferating cells were positive for CK7, GCDFP-15, EMA, androgen receptor (AR), and E-cadherin, and negative for CD68, CK20, estrogen receptor (ER), progesterone receptor (PgR), HER-2, CDX2, PSA, TTF-1, and calretinin. Metastases from internal malignancies, such as gastrointestinal tract carcinoma, prostate cancer, pulmonary carcinoma, and breast cancer were ruled out by a clinicopathological correlation with systemic surveillance. The occurrence of PSRCHC has been limited to the axilla and eyelid, which normally contain apocrine glands. Genital lesions also contain apocrine glands, and thus, we herein described the first case of PSRCHC on the scrotum.

578
Cutaneous Well-differentiated Neuroendocrine Tumors (WDNET): Series of Six Cases and Diagnostic Utility of Cytokeratin 5/6 and p63
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Cutaneous WDNETs (carcinoid / atypical carcinoid) are rare and can be mistaken for primary cutaneous adnexal neoplasms. WDNETs in skin may be either be primary cutaneous or metastatic. While cytokeratin 5/6 and p63 can be helpful to differentiate metastatic adenocarcinomas from primary cutaneous adnexal neoplasms in the majority of cases, it is unclear if these immunohistochemical stains can help identify cutaneous WDNETs. Herein, we present a series of six cutaneous WDNETs which were evaluated for CK5/6 and p63 with a review of pertinent histopathologic features and the relevant differential diagnoses. Skin biopsies (4 scalp, 1 post-auricular and 1 back) from six patients (age range 53 to 84 years) with the diagnosis of WDNET were reviewed. The histopathologic features included an organoid pattern with nests, islands and rosettes of round/polygonal cells with finely stippled nuclear chromatin and no significant cytologic atypia. 5/6 cases had a mitotic count of <2 /10 high power fields
(hpfs) while one case had 17 mitoses / 10 hpfs. Focal necrosis was present in two cases. Features of melanocytic or sebaceous differentiation were not identified. All tumors were positive for at least one keratin and neuroendocrine marker. 6/6 cases were negative for cytokeratin 5/6 and p63. In conclusion, negative staining for cytokeratin 5/6 and p63 can be useful to distinguish WDNETs from cutaneous adnexal neoplasms.

579
Unexpected Malignancies in Sentinel Lymph Node Biopsies for Melanoma
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Objective: To report incidental findings encountered in sentinel lymph node (SLN) biopsies for melanoma. Background: SLN biopsies are recommended for patients with intermediate-thickness melanomas. The use of SLN biopsy in this population provides a highly accurate and low morbidity staging procedure that can be used to guide treatment options as well as entry into clinical trials. SLN biopsies have been the standard of care at our institution since 1998. An average of 50 (range 39-73) SLN biopsies is performed annually. Method: Electronic records were searched for incidental malignancies encountered in sentinel lymph node biopsies performed for melanoma from January 2009 to April 2016. Results: Out of 370 SLN biopsy procedures, three cases with incidental malignancies were indentified: one case of angioimmunoblastic T-cell lymphoma, one case of breast carcinoma and one case of a papillary serous tumor. Conclusion: SLN biopsies are routinely performed as a staging procedure in the treatment of melanoma. Rarely, these nodes may reveal unexpected pathology. In addition to low grade B-cell lymphomas, breast adenocarcinoma in axillary nodes, prostate adenocarcinoma in pelvic nodes, papillary thyroid carcinoma in cervical nodes; other malignancies can be identified. Careful histopathological examination of SLN may lead to identification of important pathology with significant impact for the patients.

580
A Case of Plaque-like Myofibroblastic Tumor of Infancy
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Spindle cell tumors of fibroblastic and myofibroblastic origin represent 12% of pediatric soft tissue tumors in the first two decades of life. These tumors have subtle histological differences with varied clinical morphologies, making distinction challenging. Many of these lesions are benign, but some tumors do have the possibility of metastasis and a propensity for local invasion and recurrence. Thus, accurate distinction is important for definitive treatment. Our patient is a 5-year-old female with with a history of pink papules and nodules on the lower back first noted in the first year of life. The lesions have grown larger over time and have been associated with tenderness and irritation. An outside biopsy report was read as a dermatofibroma. On exam, the patient had three pink, grouped, and sclerotic nodules on the mid-lower back. Given the inconsistency between the clinical exam and previous histology, an incisional biopsy was performed. Histopathology showed a spindle cell proliferation
involving the entire dermis with peripheral collagen trapping. Immunohistochemistry showed positivity for FXIIIa and smooth muscle actin, while CD34 was negative. Given the clinical morphology and histopathology, a diagnosis of plaque-like myofibroblastic tumor of infancy was rendered. Plaque-like myofibroblastic tumor of infancy is a rarely reported entity with histologic features similar to a dermatofibroma. Dermatofibromas are not typically seen in the first months of life and typically involves the extremities as discrete papules. Our patient had a distinct morphology with large sclerotic nodules coalescing into a plaque-like lesion. This morphology as well as the histology is similar to what has been described in previous reports. Complete excision has been described as an effective treatment, however, long term follow-up is recommended given the paucity of clinical experience. Our patient was referred to plastic surgery for complete surgical excision.
Aggressive Digital Papillary Adenocarcinoma (ADPA) is a rare aggressive malignant neoplasm of the sweat glands. Often mimicking benign adnexal neoplasms, studies now suggest that these lesions are underdiagnosed. Our case is that of a 32-year old homeless male who presented to the emergency room with left mid-foot pain. The patient reported a history of a healed left foot fracture several years prior. He experienced a recent return of pain in the foot over the preceding 10 months. On physical examination a firm fixed tender soft tissue mass was identified. Subsequent cross sectional imaging revealed a large necrotic mass in the mid-foot, invading adjacent soft tissue, musculature, and bone. The clinical differential diagnosis included synovial sarcoma, osteosarcoma, and lymphoma. A biopsy revealed a dermal-based, infiltrative tumor consisting of hyperchromatic epithelial cells exhibiting glandular differentiation and displaying solid, cystic, and focally canalicular growth patterns. The tumor invaded the subcutis, adjacent bone, and muscle. The neoplastic cells stained positive for cytokeratin (AE1/AE3) and were negative for carinoembryonic antigen, S-100 protein, and thyroid transcription factor-1. Fluorescence in-situ hybridization (FISH) was negative for t(X,18). Given foot location and glandular morphologic features, a diagnosis of ADPA was made. The patient subsequently underwent a below-knee amputation. Outcome studies, specific to ADPAs of the foot, are needed to characterize the natural behavior of ADPAs of the foot, particularly in younger patient populations.

Merkel cell carcinoma (MCC), or primary neuroendocrine carcinoma of the skin, is a rare, highly aggressive malignancy. MCC typically presents as a rapidly growing, solitary, pink-red to violaceous dome-shaped papule in sun-exposed areas in older Caucasian individuals. MCC is primarily situated in the dermis. Fewer than 10% of cases have an intraepidermal component, and when present, is often associated with a more common cutaneous neoplasm, such as a squamous cell carcinoma. Here, we describe a 61 year-old immunosuppressed man who presented with an asymptomatic lesion on the scalp that had been present and enlarging for a few months. Clinical examination revealed a non-tender, asymptomatic 8 mm hyperkeratotic papule on the vertex scalp. A hypertrophic actinic keratosis or squamous cell carcinoma was suspected. Histopathologic examination demonstrated a cutaneous horn with compact parakeratosis overlying an acanthotic epidermis with basilar keratinocyte atypia most consistent with a hypertrophic actinic keratosis. However, multiple discrete nests of small blue cells with characteristic hyperchromatic nuclei, scant cytoplasm, nuclear molding, and frequent mitotic figures were scattered along the dermal-epidermal junction. Immunohistochemical studies demonstrated these cells to be strongly positive for CK20 (membranous), synaptophysin, and Ber-Ep4, but negative for S-100.
and TTF-1, consistent with intraepidermal Merkel cell carcinoma, or Merkel cell carcinoma in-situ. Merkel Cell Polyomavirus (MCPyV) antibodies were negative. To our knowledge, this is the 11th case of Merkel cell carcinoma in-situ. We report this case to add to the limited literature available, and further describe the biologic behavior and histopathologic features of an intraepidermal variant of an aggressive tumor.

584
Immunohistochemical Evaluation of Infiltrative Basal Cell Carcinomas
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Cutaneous basal cell carcinoma is the most common malignant neoplasm of the skin. Though it has a variety of forms, the more aggressive forms can be difficult to evaluate due to an infiltrative growth pattern. It was recently shown that up to 80% of infiltrative or morpheaform basal cell carcinomas can show single cell growth beyond the primary mass, and that evaluation of the extent of the tumor and margins may be improved with immunohistochemistry. Ten excisions of basal cell carcinoma with an infiltrative growth pattern were evaluated with four immunohistochemical stains: Ber-EP4, Pan-cytokeratin (AE1/AE3), p63, and p40. Each immunostain was evaluated for the quantity of tumor cells stained as well as intensity of staining. Ber-EP4, while known to be more specific, was commonly lost in poorly differentiated regions. It was found that pan-cytokeratin and p40/p63 have similar efficacy. Pan-cytokeratin showed intense cytoplasmic staining and was therefore easiest to evaluate, with the caveat that it showed occasional, weak non-specific single cell staining, likely tumor associated fibroblasts. This could lead to confusion with single cell invasion of tumor cells. Additionally, the pan-cytokeratin was focally lost in one case in an area of squamous differentiation. The p40 and p63 were the most sensitive for all areas of tumor cells. The intensity of nuclear staining was higher in p40 as compared to p63 in our laboratory. In conclusion, when evaluating a highly infiltrative basal cell carcinoma for extent of tumor or margins, immunohistochemistry for either p40 or pan-cytokeratin is a useful adjunct whenever single cell invasion is suspected. Both stains in combination may have the best overall profile for accuracy and efficiency.

585
Pediatric Lumps and Bumps: Cutaneous Metastases at Birth
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Cutaneous metastases from non-hematopoietic malignancies in the pediatric population are a rare occurrence. In many of these cases, cutaneous metastases can be the presenting sign of disease and can be multifocal. Neuroblastoma and rhabdomyosarcoma are the most common non-hematopoietic pediatric malignancies to metastasize to the skin. Neuroblastoma accounts for 8% of pediatric malignancies and is the most common extracranial solid tumor of infancy. A less common presentation seen in infants less than 6 months old is metastases to the skin, liver and bone marrow from a small primary tumor. We present a case of an otherwise healthy 32 day old term female infant with a history of a 2.6cm firm, fixed subcutaneous nodule on the right cheek since birth. A few additional small, firm, mobile nodules appeared on the trunk after birth. Histopathologic examination of one of these nodules
was remarkable for a proliferation of small blue round cells with hyperchromatic angulated nuclei and scant cytoplasm infiltrating the deep dermis. Immunohistochemical staining for synaptophysin and chromogranin were strongly and diffusely positive. Given the pathological findings, this infant was diagnosed with poorly differentiated neuroblastoma, with low mitosis-karyorrhexis index and favorable histology. In addition to the subcutaneous nodules, MRI revealed a 6x6cm right adrenal mass and liver metastases. We present this case of an infant with multiple subcutaneous nodules to add cutaneous metastases, specifically, metastatic neuroblastoma to this differential diagnosis which also includes vascular anomalies, cysts, and soft tissue tumors.

586
Malignant Circumscribed Acral Hypokeratosis
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Circumscribed acral hypokeratosis is a recently described acquired dermatosis with distinct clinical and histopathologic features. Given the novelty and rarity of the condition, it is not well recognized by dermatologists despite its unique characteristics. Circumscribed acral hypokeratosis typically presents as a solitary, sharply circumscribed, depressed erythematous patch with ridged borders that is persistent for years. It most commonly occurs on the palmar aspect of the hands and less commonly on the soles of adult to elderly women. On microscopy, an abrupt step-down in the height of the stratum corneum is observed in the transition from non-involved to involved skin. There is typically hypogranulosis underlying the diminished cornified layer, and parakeratosis and cornoid lamellation are absent. Potential causes of circumscribed acral hypokeratosis include trauma, HPV infection, and keratinization defects; however, these theories remain speculative. Various treatments have been reported in the literature, but optimal treatment of this disorder is yet to be determined. The benign nature of this entity has recently been brought into question following the report of its occurrence in association with an actinic keratosis. We present a case that clinically presented as circumscribed acral hypokeratosis on the sole of an adult woman. However, the histologic findings demonstrated Bowen’s disease with aberrant keratinization resulting in the depressed area seen clinically. The presentation of Bowen’s disease presenting clinically as circumscribed acral hypokeratosis has not been previously reported.

587
An Unusual Presentation of Cutaneous Myopericytoma: A Report of Four Cases
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Myopericytoma belongs to the group of perivascular neoplasms with myoid differentiation. Its incidence is difficult to establish, since the after the first descriptions by Requena (1996) and Granter (1998), only a few case reports and one large series described by Mentzel have been published. It is a rare lesion, which presents either as single or multiple skin and soft tissue nodules, affecting mainly the extremities of adults and males. The majority of the cases are benign and it is produced by the activation of the GLI
oncogene. The myopericyte is believed to be a transitional cell, between pericytes and vascular smooth muscle cells. It affects the dermis, composed of thin walled vessels and concentric perivascular arrangement of plump spindle to round cells, SMA and H-Caldesmon positive, but Desmin negative. Architectural histologic variants include: classical-solid, hemangiopericytoma-like, angioleiomyoma-like, myofibroma-like, intravascular, and malignant. It needs to be differentiated from other entities in the hemangiopericytoma spectrum. We report four cases that were gathered from our hospital archive files in 10 years duration, the first one was multiple and affected a 81 years old male, located on the dorsal and medial region of the left foot, with focal areas of resembling glomangioma and myofibroma; the other cases affected women in the fourth decade of life, the lesions were located in left palm, left temple and right dorsal wrist, demonstrating classical-solid, hemangiopericytoma-like vessels and intravascular patterns, respectively. In sum, we report 4 additional cases of myopericytoma, emphasizing its benign clinical behavior and atypical presentation.

588

RESIDENT

An Unusual Presentation of Bilateral Gluteal Giant Condyloma Acuminatum of Buschke-Lowenstein with Verrucous Carcinoma Transformation

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Buschke-Lowenstein tumor (BLT) is a rare form of condyloma acuminatum known to be associated with a sexually transmitted infection of human papilloma virus in the ano-genital region. BLT is a histologically benign, slow growing tumor that is locally aggressive and can cause extensive tissue damage. We, herein, present a 58 year old Hispanic female with enlarging, bilateral, gluteal, exophytic, confluent, cauliflower-like lesions. The patient’s past medical history is significant for poorly controlled psoriasis with non-healing ulcerations masking an infiltrative squamous cell carcinoma in the right buttock. She underwent a surgical resection of the carcinoma with negative margins. However, in the following two years, the patient continued to have poorly controlled psoriasis and developed giant, diffuse, bilateral, gluteal masses. She subsequently underwent another surgery with wide surgical resections of the pan-gluteal masses with local flap placement. Microscopic examination shows invasive, well differentiated verrucous carcinoma arising in a giant condyloma acuminatum with coexistent lichen simplex chronicus. The immunohistochemical stain p16 shows tumor positivity. With prolonged years (>5 years) of neglect, the malignant potential of BLT is 40-60%. Verrucous carcinoma is a subtype of squamous cell carcinoma that presents as a well-defined, cauliflower-like, exophytic growth. This extraordinary case of a patient with BLT, is a lesson to be learned that underlying skin conditions such as psoriasis, inadequate tissue sampling and loss to follow-up can lead to the development of invasive verrucous carcinoma. We present this unusual case to raise awareness of the locally aggressive nature of BLT that was initially masked by psoriasis on a clinical basis.
589  
**Cutaneous Metastasis from Hürthle Cell Thyroid Carcinoma**

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Cutaneous metastasis from Hürthle cell thyroid carcinoma (HCTC) is very rare. To date, there have been only two other cases documented. Our patient is a 45-year-old man with an eleven-year history of HCTC who was diagnosed with indolent HCTC lung metastases six years ago. He presented with a papule on his posterior scalp that had been slowly growing over the past two years. Upon examination, there was a 7mm, skin-colored, mobile papule that resembled a pilar cyst. Histologic examination of the lesion revealed circumscribed nodules of tumor cells. At high power, the individual tumor cells contained abundant eosinophilic cytoplasm and irregular nuclei. Immunohistochemical studies revealed that the tumor cells stained positively for thyroglobulin, thyroid transcription factor-1 (TTF-1), and CK7, and they were negative for antibodies to CK5/6. These findings were consistent with the diagnosis of metastatic Hürthle cell carcinoma of the thyroid. This is only the second reported case of cutaneous scalp metastasis from HCTC. Cutaneous metastasis from an internal malignancy is uncommon. However, when distant metastasis to the scalp occurs, it is most commonly in association with either renal, breast, or lung carcinoma. Cutaneous metastasis of thyroid cancer, especially to the scalp, is very rare. Hence, diagnosing cutaneous metastasis of HCTC is challenging and necessitates integrating the clinical presentation with the histopathological and immunohistochemical examinations. This case emphasizes the rarity of this presentation and the importance of being vigilant when a patient with cancer develops a new cutaneous lesion.

590  
**Eruptive Dermatofibromas in Autoimmune Disease: An Unusual Presentation Mimicking Malignancy**

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Multiple eruptive dermatofibromas (MEDF) is a rare clinical occurrence thought to be associated with underlying diseases involving immune dysregulation (e.g. autoimmune disease, HIV) and the immunomodulatory treatments thereof. MEDF is generally accepted as the presence of fifteen dermatofibromas and the development of five to eight dermatofibromas within a four-month period. The diagnosis is also invoked in the context of dynamic changes in dermatofibroma lesions over a short period of time, regardless of the number of lesions. We present an unusual case of eruptive dermatofibromas arising from the lower extremity of a patient with psoriatic arthritis treated with etanercept and methotrexate. A 55-year-old woman presented with the recent development of a nodular, enlarging mass of the right medial thigh, at the site of a remote debridement for a skin and soft tissue infection. On physical examination, there was a 4 cm polypoid, nodular mass and adjacent papule arising from a scar as well as palpable subcutaneous nodules located several centimeters superior to the index lesion, in the inguinal region. An inguinal ultrasound revealed two adjacent hypoechoic solid nodular masses in the subcutaneous fat with internal vascularity, each measuring 2 cm. The clinicoradiologic impression was suspicious for a malignant process with satellite metastasis, such as melanoma or dermatofibrosarcoma protuberans. The patient underwent a right thigh radical resection with inguinal resection of the subcutaneous nodules. Histopathologic evaluation of the three masses
and papule showed hypercellular mixtures of bland spindle cells and xanthomatous cells dissociating thickened collagen bundles. Hemosiderin deposition was noted in each lesion. Immunohistochemical stains were positive for factor XIIIa and negative for CD34, S-100, Melan-A, and pan-cytokeratin. A diagnosis of dermatofibromas (benign fibrous histiocytomas) was rendered. Pure subcutaneous dermatofibromas are rare; they are exceedingly rare in the context of eruptive dermatofibromas. Because eruptive dermatofibromas can precede the usual manifestations of the underlying immunologic process, the diagnosis should prompt clinical exclusion of the disease states known to be in association.

591
Two Cases of Variant Histology in Dermatofibroma: Revisiting Granular Cell Change and a First Report of Osteoma Cutis
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Dermatofibroma (benign fibrous histiocytoma) is a common cutaneous neoplasm for which numerous histologic variants have been reported. We report two cases of dermatofibroma with variant histology. Case one is a 34 year old man with a 3 year history of a painless, non-pigmented raised mass on the right shoulder. The excision specimen demonstrated a 2.5 cm well-circumscribed, homogenous, solid, firm, tan-white nodule. Histologic sections showed classic features of dermatofibroma with a predominant second cell population of polygonal cells with abundant eosinophilic, granular cytoplasm associated with prominent myxoid change and interspersed amorphous pink material, suggestive of a soft tissue neoplasm or cutaneous amyloidosis, respectively. The spindle cells showed strong, diffuse Factor XIIIa expression, while stains for Congo red, S100, cytokeratin AE1/AE3 and Fite were negative throughout the specimen. Case two is a 67 year old man with a history of Crohn’s Disease, managed with adalimumab and azathioprine, who presented with a 2 year history of a raised, stable, painless lesion on the left anterior shin. Physical examination identified a 0.9 cm, violaceous firm papule with a sclerotic center, but fully intact overlying skin. Histologic sections of the punch biopsy specimen demonstrated characteristic histologic features of dermatofibroma with intermixed dermal deposits of lamellated bone of varying sizes, consistent with osteoma cutis. Neither patient endorsed inciting factors. Dermatopathologists should be aware that these variants may be encountered in longstanding dermatofibromas and may show co-existing, overlapping histologic patterns mimicking other neoplastic and non-neoplastic processes; therefore, underscoring the importance of clinical correlation and application of immunohistochemical and special stains.

592
Cytokeratin 7 Negative Metastatic Invasive Breast Carcinoma: A Diagnostic Pitfall
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Cytokeratin 7 is considered to be a reliable marker of adenocarcinomas, an attribute exploited in the workup of metastatic carcinoma of unknown primary. The histopathological diagnosis of primary or metastatic breast carcinoma is often aided by its characteristic CK7 expression, but rare cases of CK7-negative breast carcinoma have been described. We report a 76-year-old woman with history of high-grade invasive lobular carcinoma of the right breast, metastatic to 1 of 24 regional lymph nodes, treated
with adjuvant radiation and tamoxifen. Eight years later, she was diagnosed with ipsilateral ER-positive, PR-positive, Her-2/neu-negative grade I invasive ductal carcinoma, and she underwent simple mastectomy without lymph node dissection or adjuvant therapy. Nineteen years after the diagnosis of lobular carcinoma of the right breast, the patient developed right chest wall pruritus and a 7.5 cm x 5.0 cm aggregate of erythematous nodules along the right mastectomy scar, as well as a palpable subcutaneous nodule with overlying peau d’orange features of the left breast. Skin biopsy of a right breast nodule confirmed metastatic carcinoma, positive for ER, PR, mammaglobin (focal) and GATA3, but negative for CK7 and Her-2/neu. Skin biopsy of the left breast nodule also revealed CK7-negative metastatic breast carcinoma. PET-CT scan showed FDG-avid uptake in both breasts, axillae and multiple skeletal sites. She received palliative therapy with palbociclib, letrozole and denosumab. This case demonstrates the diagnostic pitfall of relying on a single “screening” immunostain, and highlights the importance of integrating clinical, histopathological and immunohistochemical attributes into a final pathologic diagnosis.

593
Primary Cutaneous Mucoepidermoid Carcinoma: A Case Report
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Mucoepidermoid carcinoma is the most common malignant salivary gland neoplasm. However, it has also been reported as a primary tumor in the lungs, breast and skin. As a primary cutaneous tumor, mucoepidermoid carcinoma is exceedingly rare, with only a few case reports in the literature. The tumor classically presents in older adults and has a predilection for the head and neck. We report a case in a 72 year old woman, presenting as a solitary upper eyelid nodule. Histologic sections showed a well circumscribed but unencapsulated tumor, composed of solid nests along with glands, admixed with both epidermoid and goblet cells. The tumor cells were cytologically bland, however mitoses were easily identified. Immunohistochemical stains for EMA and CEA were positive, helping to confirm the diagnosis. Historically, primary cutaneous mucoepidermoid carcinoma and adenosquamous carcinoma had been considered synonymous. However, more recent literature has elucidated adenosquamous carcinoma as a distinct entity, representing a high grade tumor with both glandular and squamous differentiation. Primary cutaneous mucoepidermoid carcinoma is classically a low-grade tumor composed of squamoid or epidermoid cells, together with basal cells and mucigenic/goblet cells (similar to its namesake in the salivary gland). Follow up data is limited in patients with primary mucoepidermoid carcinoma, as there are so few cases reported in the literature. Before rendering a diagnosis of primary cutaneous mucoepidermoid carcinoma it is important to rule out secondary or metastatic involvement of the skin by a salivary or lacrimal gland neoplasm.
Cutaneous Ewing sarcoma is a rare primary cutaneous tumor with an overall favorable prognosis and survival rate of approximately 91%. It differs from primary bone Ewing sarcoma in its later median age of onset of 17 and its 2:1 female predominance. Treatment is varied and includes surgical resection with or without chemotherapy or radiation. We present the case of a 27 year-old female with a complicated medical history including relapsed acute myelogenous leukemia currently undergoing consolidation therapy, pulmonary and lymphatic sarcoidosis, and Mycobacteria chelonae infection of a tattoo on antimicrobials. She presents with a two-year history of a bump on the plantar foot that rapidly grew and became painful over four months. Exam showed a 4 mm hyperkeratotic, firm papule with interrupted dermatoglyphics and a surrounding violaceous rim. Histopathology demonstrated a tumor composed of sheets of primitive-appearing cells that stained positive for CD99, vimentin, and focally for pan-keratin. Negative stains included CD45, CD43, CD34, KIT, MPO, PU.1, CD68, S-100, SOX10, CK7, CK20, chromogranin, synaptophysin, CD31, ERG, SMSA, desmin, myogenin, TLE1, and INI1. The staining pattern was concerning for Ewing Sarcoma or PNET and subsequent fluorescent in situ hybridization revealed 91% of cells with EWSR1 rearrangement, consistent with Ewing Sarcoma. MRI and PET/CT were negative for systemic involvement, and the patient was diagnosed with with primary cutaneous Ewing Sarcoma. She had wide local excision. The histopathologic differential diagnosis for a small, round blue cell tumor is broad and includes primary tumors such as Merkel cell, lymphoma, poorly differentiated adnexal tumors, leukemia, and cutaneous metastases from primary bone Ewing, small cell lung carcinoma, neuroblastoma, and others. Unfortunately, treatment in previously reported case series has been varied with no comparative data. Given the overall good prognosis of primary cutaneous Ewing sarcoma, less aggressive treatment, such as surgery without systemic chemotherapy is increasingly being considered. This case highlights characteristic histopathologic features and the use of FISH to help with the diagnosis.

Introduction Proliferating Pilar Tumor is a rare tumor with just few cases well documented in the literature. There is a disparity of interpretation about the nature and behavior of this entity. PPT may be locally aggressive or/and report malignant transformation. With this study we want to correlate the IHC patterns of Calretinin, berEP4 and CD34 as hair follicle markers in PPTs with one of its main also rare differential diagnosis trichoblastoma, a benign hair follicle tumor originating from follicular germinative cells. Material and Methods Descriptive study of 28 cases, 4 solid PPTs, 2 malignant PPTs and 22 trichoblastomas, in a period of 27 years. The diagnosis was confirmed in H&E-stained slides. The tissues were deparaffinized and rehydrated and heat-induced epitope retrieval was performed. The IHC results were analyzed semi-quantitatively and scored positive - mild +, moderate ++ and severe +++ or negative. Results 4/ 22 trichoblastomas were positive for CD34, 1/6 for all PPTs; corresponding to 1/2 in the
malignant PPT group. Calretinin was positive in 1/22 trichoblastomas (<10% tumor mass) and 4/6 cases of PPT. Ber-EP4 was positive in 16/22 cases of TB and 1/6 cases of PPT. The differences of intensity are shown in Tables. P53 and Ki67 staining confirmed the nature of both groups. Conclusion: It is essential to differentiate PTT and TB since the recommended treatments are so different. The PTT recommendations are complete excision with margin control while its malignant counterpart, is complete excision with 1 cm margins and if lymph node involvement adjuvant chemotherapy and radiation. TB is considered a benign follicular tumor. Here again it needs to be differentiated from its rare malignant counterpart for which complete excision and/or Mohs micrographic surgery is recommended. The diagnosis of both the benign and malignant follicular tumors can be difficult. For this reason, our study and IHC profiles of these tumors should assist in the diagnosis. Based on our findings, we propose the use of Calretinin, P53, and berEp4 antibodies as diagnostic aids to differentiate between TB and PPTs. CD34 showed significant affinity for the outer root sheath cells of malignant PPT but still show a weaker affinity for the germinative follicular cells of TB, making it a reliable marker in the differentiation of these two tumors.

596
Anetodermic Pilomatricoma: A Rare Variant with Distinct Clinical and Histologic Findings
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Pilomatricomas are relatively common, benign dermal adnexal neoplasms, which in their classical form do not usually pose diagnostic difficulties. They are well circumscribed tumors of the lower dermis consisting of a cellular stromal matrix supporting basaloid nests of cells with admixed eosinophilic shadow cells; occasionally they exhibit pigmentation and calcification. We are presenting two cases of the so-called anetodermic pilomatricoma which have also been reported as a “bullous” or “lymphangiectatic” pilomatricomas. This variant is rare with only 24 cases reported in the English literature. These neoplasms differ from conventional pilomatricomas because they present as a bullous process and most commonly occur around the shoulder or upper arms. They exhibit the classic morphologic findings of a pilomatricoma but in addition there is prominent edema with widely dilated lymphatic vessels, a mixed inflammatory cell infiltrate and a reduction in elastic fibers in the overlying dermis, which results in a bullous clinical appearance. These findings are thought to be the consequence of trauma or obstructed lymphatic channels. Clinicians and pathologists alike should be aware of this variant due to its distinct clinical and histologic findings. Anetodermic pilomatricoma should be considered in the differential of solitary nodulocystic and bullous lesions, particularly in the shoulder region.

597

WITHDRAWN
A Painful, Rare Lesion on the Arm: Epithelial Sheath Neuroma

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A 46-year-old immunosuppressed, renal transplant patient was seen for excruciating, radiating pain in her right forearm three months after Mohs micrographic surgery for squamous cell carcinoma. Apart from a well-healed surgical scar, there was no cutaneous lesion appreciated. MRI demonstrated a plaque like dermal lesion with reactive changes related to the prior procedure. The original biopsy was reviewed and revealed superficial and deep dermal squamous epithelial aggregates surrounding markedly hypertrophied nerves. No scar, regression, or atypia was appreciated. These findings were most consistent with epithelial sheath neuroma, a recently described, rare entity seen thus far only on the backs of older adults. Less than ten cases have been reported. The patient underwent re-excision of the lesion with subsequent resolution of her symptoms. Recognition and appropriate management of this entity are of utmost importance to limit morbidity associated with therapies used to treat perineural extension of cutaneous malignancy. To the best of our knowledge, this is the first description of epithelial sheath neuroma on an extremity and with this depth of involvement.
599

A Case of Clear Cell Nodular Hidradenoma Involving the Lymphatic System
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Clear cell nodular hidradenoma (CCNH) is a benign sweat gland neoplasm. As previously reported by Stefanato et al. (2012), rarely CCNH can show local/regional or even distant spread, and are termed “CCNH-like tumor of uncertain malignant potential.” We report another very rare case of CCNH involving the lymphatic system in a 36-year-old woman, who presented with a subcutaneous mass in her left groin. She had been treated 8 years prior for a CCNH in the same region. Histopathologically, the tumor was nodular and well-circumscribed, and located within the subcutaneous tissue involving a lymph node. The tumor was composed of sheets of epithelial cells with ductal differentiation and cystic change surrounded by lymphoid tissue. The tumor cells demonstrated abundant pale to clear cytoplasm and focal squamoid features, and ductal cells had eosinophilic cytoplasm. Nuclei were round to oval and monomorphic with no atypia. An infiltrative growth pattern, necrosis or significant mitoses were not identified. Immunohistochemically, the epithelial cells were positive for p63, CK7 and CK903. EMA and CEA highlighted areas of ductal differentiation. Clinical follow-up since has not demonstrated any recurrence. This case further demonstrates that lymphatic spread of CCNH can carry an excellent prognosis in the absence of other histopathologic features of malignancy and as described previously, these lesions should best be labeled routinely as “CCNH-like tumors of uncertain malignant potential” until long-term follow-up data is available.

600

Primary Cutaneous Adenomyoepithelioma: A Case Report
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Adenomyoepithelioma (AME) is a rare neoplasm with only a few reported cases in the literature. AME is a biphasic adnexal tumor composed of both epithelial and myoepithelial components, and is regarded as a low grade tumor with borderline malignant potential. We present a case of primary cutaneous AME in a 72-year-old man presenting as a solid mass in the left upper arm. The differential diagnosis included a metastatic adenocarcinoma as the patient had a known history of renal, prostate and pancreatic cancers. Histopathologically, the tumor was located within the mid-dermis, was well circumscribed, with lobulated architecture. The tumor demonstrated closely packed small ductules forming glandular structures, some with sparse secretions in the lumens, surrounded and separated by polygonal and spindled myoepithelial cells. The tumor cells contained clear cytoplasm. Infiltration or necrosis was not identified. Immunohistochemically, glandular cells were CK7, CK5/6 and Cam5.2 positive; and
myoepithelial cells were p63, S-100, SMA and calponin positive. Clinical long follow-up and imaging demonstrated no evidence of recurrence or metastasis to date.

601
Bilateral Endocrine Mucin-Producing Sweat Gland Carcinomas
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Endocrine mucin-producing sweat gland carcinoma (EMPSGC) is a rare cutaneous adnexal tumor with a predilection for the eyelid. Here, we describe a case of bilateral EMPSGCs presenting 7 years apart on the right upper eyelid and subsequently left lower lid, in a 60-year-old female. In both instances, the tumor clinically presented as a slow growing swelling. Histology was similar in both cases, with both tumors demonstrating well-circumscribed solid and cystic nodules with papillary architecture, multiple lumina and the presence of mucin. Tumor cells were composed of small to medium-sized oval to polygonal epithelial cells with bland nuclei and inconspicuous nucleoli, and pale to pink cytoplasm. Apocrine differentiation was also focally noted and rare mitotic activity was identified. Immunohistochemical analysis showed that tumor cells of the surface epithelium were positive for cytokeratin (CK) 7, synaptophysin, EMA, CEA, estrogen receptor and progesterone receptor, and negative for CK20. Immunohistochemical staining with p63 demonstrated myoepithelial cells partially lining tumor nodules. Clinical follow-up demonstrated no evidence of recurrence or metastasis to date.

602
Iatrogenic Kaposi’s Sarcoma in the Setting of Thrombotic Thrombocytopenic Purpura
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Kaposi’s sarcoma (KS) is a low grade vascular neoplasm with four recognized clinical variants: classic, endemic (African), AIDS-related and iatrogenic. Despite the epidemiologic differences in these clinical variants, human herpes virus 8 (HHV-8) is the etiologic agent for all types of KS. We present a case of a 51-year-old male with history of thrombotic thrombocytopenic purpura (TTP) who presented with “purpuric” lesions involving bilateral upper and lower extremities, which were considered to be related to his TTP. Physical exam revealed violaceous non-blanching sharply demarcated firm papules and plaques. Punch biopsy demonstrated an irregular dermal vascular proliferation positive for CD31. The relatively bland endothelial cells of the vascular proliferation were positive for HHV-8. Additionally, a phosphotungstic acid-hematoxylin stain highlighted intravascular fibrin thrombi consistent with TTP related thrombotic microangiopathy. The morphologic and immunohistochemical features were consistent with KS. Of note, 5 months prior to presentation, our patient received plasmapheresis, rituximab and prednisone for treatment for his TTP. Laboratory testing for human immunodeficiency virus (HIV) was negative. Iatrogenic KS is associated with immunosuppressive therapy and is mainly seen in renal transplant recipients. However, this is a rare complication in patients receiving
immunosuppressive therapy for autoimmune conditions and to our knowledge, this is a unique case of iatrogenic KS occurring in a HIV negative patient with TTP. Our case illustrates the importance of considering alternative etiologies for purpuric lesions in a patient with TTP and recognizing iatrogenic KS as a rare complication of immunosuppressive therapy.

603
PD-L1 Expression in Metastatic Cutaneous Squamous Cell Carcinomas
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Programmed cell death ligand 1 (PD-L1), which can temper host anti-tumor immune responses, is co-opted by multiple cancer types. We have previously surveyed expression of PD-L1 in 40 primary and 5 metastatic cutaneous squamous cell carcinomas, and documented correlation of PD-L1 expression with high-risk histologic features. The current study expands on this prior report with investigation of PD-L1 expression in ten additional metastatic cases of cutaneous squamous cell carcinoma. Archived cases were collated, and immunohistochemical staining with antibody to PD-L1 was performed as previously described. Cases were reviewed by all authors, and PD-L1 expression was categorized by the tumor proportion score method as negative, low, or high, accordingly to previously published methodology. Our pilot series found that PD-L1 expression is more likely to be found in primary cutaneous squamous cell carcinomas with aggressive histologic features, and demonstrated low or high PD-L1 expression in 5 out of 5 metastatic cases. In the additional 10 metastatic cases studied here, low expression was detected in 6 out of 10 cases, while the remaining cases were not found to express PD-L1. Therefore we now describe PD-L1 expression in 11 out of 15 total cases of metastatic cutaneous squamous cell carcinoma. Although a remarkably high degree of expression occasionally may be found in advanced primary and metastatic cases, PD-L1 expression, when present, was more commonly categorized as low expression. Tumor PD-L1 expression has been demonstrated in two case reports of cutaneous squamous cell carcinomas that responded to treatment targeting the PD1 / PD-L1 axis. However, it is unknown whether the presence or degree of PD-L1 expression is predictive of response to treatment in this tumor type. Future studies are needed to correlate expression of PD-L1 with clinical outcomes and to determine potential therapeutic implications.

604
Merkel Cell Carcinoma with Myofibroblastic Stroma Mimicking Heterologous Elements
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Merkel cell carcinoma (MCC) is a rare, aggressive cutaneous primary neuroendocrine tumor that typically lacks distinctive stroma. Here, we present the case of an 89-year-old male who presented with a 2 cm firm violaceous nodule on the right tragus. Biopsy revealed MCC. He underwent excision of the residual tumor and sentinel lymph node biopsy which revealed metastatic MCC in the draining nodal basin. Prior to additional treatment, the patient transitioned to hospice and died one month later.
Histology of the primary tumor revealed a malignant small round blue cell neoplasm consistent with primary cutaneous MCC. Immunostaining was confirmatory, with tumor cells positive for CK20 (perinuclear dot-like) and synaptophysin, and negative for TTF1. The tumor stroma displayed areas of prominent bland-appearing spindled cells with a bundled growth pattern resembling smooth muscle. Other areas resembled chondromyxoid stroma. Stromal cells displayed diffuse membranous smooth muscle actin staining, and were negative for desmin and cytokeratin. This pattern is most consistent with an unusual tumor-associated myofibroblastic proliferation, rather than true smooth muscle differentiation. This case of MCC demonstrates an unusual prominent myofibroblastic stromal proliferation mimicking smooth muscle, a finding that to our knowledge has not been previously described in MCC. This finding should not be confused with collision tumor or sarcomatoid change with heterologous differentiation in MCC. Our observation suggests that myofibroblasts may comprise the tumor stroma in MCC and raises the question of whether stromal myofibroblasts are associated with poor prognosis in MCC, as has been reported in other carcinoma types.

605
Dermatofibroma after Apple Cider Vinegar Injections: A Case Report
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A 23 year-old female presented to clinic with a 15-month history of a painful raised lesion on her right arm. The lesion first appeared 7 years ago as a hyperpigmented macule. In an attempt to resolve the macule, the patient applied apple cider vinegar and garlic to the lesion and manipulated it with a needle, at times injecting the lesion with small amounts of apple cider vinegar. She reports having been told this would resolve the macule. Instead, this resulted in a raised growth resembling a scar. Physical exam revealed a hyperpigmented nodule measuring 1.2 cm in diameter with a surrounding area of firm subcutaneous plaque on her right upper arm. Histopathology from an excisional biopsy demonstrated spindled fibrohistiocytic cells in tight fascicles with extensive intra- and extracellular deposition of hemosiderin, consistent with a hemosiderotic dermatofibroma. Although a significant number of dermatofibromas are associated with minor local trauma, particularly insect bites, to our knowledge this is the first case of a dermatofibroma developing as the result of repeated injections with apple cider vinegar. In a society with an increasing interest in alternative and homeopathic medicine, apple cider vinegar is a popular home remedy for a number of conditions. This case speaks to the potential for adverse effects associated with injecting apple cider vinegar.

606
Undifferentiated Sarcoma Arising within a Pleomorphic Fibroma
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Pleomorphic fibromas were initially described by Kamino et al in 1989. These tumors typically present in adulthood as asymptomatic, solitary, skin-colored dome shaped or polypoid papules measuring up to 2cm in size. They are benign lesions which do not recur after excision, and no previous examples of malignant transformation of a pleomorphic fibroma have been reported. On microscopic evaluation they are well-circumscribed, dome-shaped, and characterized by low cellularity with a predominance of
thick collagen bundles in a haphazard array. In addition, there are scattered spindled to stellate cells and irregularly shaped multinucleated cells which contain large pleomorphic and hyperchromatic nuclei. We present the first reported case of malignant transformation of a pleomorphic fibroma. A 76yo male patient presented with a 1.5cm erythematous papule on the temple. The histologic findings were those of a pleomorphic fibroma, with a well-circumscribed dermal proliferation of enlarged stellate cells set in a defining sclerotic stroma. Within the precursor pleomorphic fibroma, a distinct second population of epithelioid cells was identified. These cells exhibited prominent nucleoli, frequent mitotic figures, and a dense sheet-like growth pattern. A broad panel of immunohistochemical stains was performed, with the atypical focus exhibiting positivity only for vimentin. Given the lack of evidence of differentiation towards a more specific cell lineage, a diagnosis of undifferentiated sarcoma arising in a precursor pleomorphic fibroma was rendered. The patient was treated with local excision, with no clinical evidence of recurrence or metastasis three months following initial diagnosis.

607
Multiple Hybrid Cysts Arising in a Patient with Gardner Syndrome
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Gardner syndrome results from an autosomal dominant mutation in the adenomatous polyposis coli (APC) gene. This condition is allelic with familial adenomatous polyposis and considered to represent a phenotypic variant of the disease with prominent extraintestinal involvement. Clinical findings in Gardner syndrome include multiple osteomas, premalignant colorectal polyps, desmoid tumors, congenital hypertrophy of the retinal pigment epithelium, epidermoid cysts, and hybrid cysts. In this case, we report at 16 year old boy with known Gardner syndrome who presented with multiple hybrid cysts exhibiting both infundibular and pilomatrical differentiation. These two components are the most commonly encountered lines of differentiation within hybrid cysts in patients with this syndrome. Other combinations of infundibular, pilomatrical, and tricholemmal differentiation have been less commonly reported in these patients. We present this case of a patient with Gardner syndrome exhibiting multiple hybrid cysts with the goal of informing and educating physicians. The association between Garner syndrome and hybrid cysts is important to make both clinically and pathologically since hybrid cysts are often the first clue to recognizing patients with this syndrome and intervening before serious malignancies arise.

608
Vulvar “Bowen’s Disease”, a Rare Presentation of Superficial Spread of Intraepithelial Vaginal/Cervical Carcinoma: Report of 2 Cases
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Case 1: A 91year-old Japanese woman presented to our clinic with erythematous erosive plaque on her vulvar skin. Biopsy specimens revealed atypical epithelial cells at the whole epidermis, which led to the diagnosis of Bowen’s disease. Gynecological examination and radiological test, however, revealed the cervical carcinoma distributed continuously from uterus to the vulvar skin. Case 2: A 68year-old Japanese woman presented with erythematous plaque on her vulva. She had a history of surgery for
cervical cancer, and gynecological examination showed its marginal recurrence. Re-excision was performed, and locally recurrent intraepithelial carcinoma was proved to spread to the vulvar skin in the surgical specimen. Anal canal cancers or bladder cancers can spread laterally within the epithelium, and present as a perianal/vulvar Paget’s disease, which is referred as the secondary Paget’s disease. However, there are few reports about vulvar Bowen’s disease having continuity with underlying vaginal/cervical cancer. It should be noted that the vulvar “Bowen’s disease” may represent a secondary involvement of intraepithelial carcinoma from cervical/vaginal regions.

609
Mammary Adenoid Cystic Carcinoma: A Mimicker of Skin Adnexal Tumors
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A 77-year-old woman presented with pain and bruising on the left breast following a recent trauma. An ultrasound showed skin thickening associated with a 2.1 x 1.7 x 0.8 cm lobulated area of increased density. A punch biopsy of the skin revealed a nodular infiltrate in the deep dermis and subcutaneous tissue composed of solid and cribriform islands of neoplastic cells growing in a jigsaw-like pattern in a fibrous desmoplastic background. Lumens containing bluish mucinous material as well as balls of eosinophilic substance were present. The tumor was composed mostly of epithelial cells with hyperchromatic nuclei and scant cytoplasm and few cells with myoepithelial morphology. The epithelial cells were diffusely and strongly positive for CK7. CK5/6 and c-Kit were partially positive while neuroendocrine markers, ER, PR, calponin, and smooth muscle myosin were negative. No p63 positive myoepithelial cell was seen around the tumor nests. Ki-67 showed a proliferative index of 20 to 30%. Histopathologic and immunophenotypic findings were consistent with a diagnosis of adenoid cystic carcinoma (AdCC). AdCC is a rare neoplasm that represents approximately 0.1% of all breast carcinomas. A variety of microscopic growth patterns are present in AdCC and because of heterogeneity, this tumor may be difficult to recognize in small biopsies. It may create cribriform architecture resembling invasive ductal or in situ breast carcinoma. At low power magnification, AdCC may occasionally mimic a cylindroma or spiradenoma of the skin. Primary cutaneous AdCC is extremely rare and most commonly involves the head and neck region; however, for the lesions located on the breast, distinction from mammary AdCC is not readily feasible and correlation of clinical, radiologic, and pathologic findings is recommended for the management of patients. This report highlights the importance of recognizing rare subtypes of breast cancer and considering them in the differential diagnosis of adnexal tumors.
Lymphoepithelioma-like Carcinoma Arising from a Previously Treated Unknown Lesion
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Lymphoepithelioma-like carcinoma is a rare neoplasm that was first described in 1988. It may present as a skin primary or from internal sites including nasopharynx or gastric. Frequently, it occurs as a neoplasm on the head and neck of patients over the age of 50. There is controversy as to if this poorly differentiated lesion is related to squamous cell carcinoma or adnexal origin. Several case reports have discussed metastasis to cervical lymph nodes and one metastasis to the parotid gland. In this case, a 77-year-old female presents with a raised dark-red glassy nodule 1.8 x 1.2 cm on the right forehead. The patient reports that the lesion was previously treated with curettage 20 years ago and now reappeared within the last four months. Pathology was not performed on the original specimen, and clinical records from two decades ago had been destroyed. This dermal lesion consisted of cohesive non-pigmented cells with large vesicular hyperchromatic nuclei engulfed and encompassed by a dense lymphohistiocytic infiltrate. Epithelial cells are strongly positive for CK5/6 and focally positive for pankeratin. This lesion is negative for Epstein-Barr Virus, therefore it is most likely not a metastasis from nasopharyngeal carcinoma. The dense reactive lymphocytes show an appropriate admixture of CD3 and CD20 positivity. No neural or vascular invasion was identified. While, the neoplasm was 0.1 mm from the resection margin, an additional 1 cm wide re-excision was performed. The patient is being closely followed with no new lesions reported in the last six months.

Post-Radiation Histiocytic Sarcoma in the Setting of Muir-Torre Syndrome
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A 62 year old male with a past medical history of Muir–Torre syndrome, metastatic colorectal adenocarcinoma, bilateral papillary renal cell carcinoma, and also squamous cell carcinoma (SCC) of the scalp which was treated with resection and adjuvant radiation therapy presented with a non-healing skin defect of the scalp. Initial clinical impression of the skin defect was a probable recurrent squamous cell carcinoma. A biopsy was performed and the microscopic examination revealed unremarkable surgical site changes with adjacent actinic keratosis. The scalp defect was treated with excision and reconstructive surgery (bilateral fasciocutaneous flaps and full thickness skin grafts). Approximately two years post reconstructive surgery, the patient developed two small superficial ulcerated areas with
raised edges on the scalp. Punch biopsies of these lesions revealed sheets of atypical cells that were polygonal and pleomorphic with focal storiform architecture. Abundant necrosis and increased mitotic activity were also seen. The neoplastic cells were reactive only for CD163, CD14, and CD4. A myeloid sarcoma was ruled out based on negative CD43 and CD34 and other spindle cell tumors were excluded using IHC. A diagnosis of histiocytic sarcoma was rendered. The patient underwent excision of this lesion with negative margins and experienced no recurrence to date. The current case demonstrates the first case of histiocytic sarcoma and second case of post-radiation sarcoma in Muir-Torre syndrome to our knowledge.

613
RESIDENT
Primary Cutaneous Carcinosarcoma with Mucinous Stroma and Chronic Lymphocytic Lymphoma
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Primary carcinosarcomas of the skin are rare malignant neoplasms with biphasic carcinomatous and sarcomatous components and has a significant potential to recur locally and to metastasize. Reported epithelial components include squamous, adnexal and basaloid while mesenchymal malignant components described include osteoid, chondroid, spindle cell, among others. We report a case of primary cutaneous carcinosarcoma in an 85 year-old man presenting with a 2.0 cm rapidly enlarging lesion of the left cheek. Microscopic examination revealed a malignant biphasic tumor consisting of squamous carcinoma mostly in situ and dermal sarcomatous component showing epitheliod and psuedoglandular morphology with mucinous stroma in a background of chronic B-lymphocytic lymphoma. The sarcomatous component was confirmed by immunohistochemistry studies. The patient developed metastatic disease of the sarcomatous component to the regional lymph node. This is a very unusual tumor with multiple malignant components and complex growth pattern that generated a diagnostic challenge. We herein report such an interesting case with review of the literature.

614
RESIDENT
Utility of Immunohistochemistry in Distinguishing Primary Adnexal Carcinoma from Metastatic Breast Carcinoma to Skin and Squamous Cell Carcinoma
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Background: The distinction between primary adnexal carcinoma (PAC) from metastatic breast carcinoma (BrCa) to skin and squamous cell carcinoma (SCC), particularly those with ductal differentiation (SCCDD) can be quite challenging, despite adequate history. An accurate diagnosis is essential, as the treatment and overall prognosis for these different types of tumors differ tremendously. A variety of immunohistochemical stains have been previously employed to differentiate these entities, some of which we review here to confirm their diagnostic utility. In addition, we determine whether these markers may favor a diagnosis in ambiguous tumors in which no specific diagnosis was favored but given a differential which included SCCDD, PAC and a metastatic BrCa to skin.

Methods: Twenty-four cases of PAC, 7 cases of metastatic BrCa to skin, 30 cases of SCC and 18 cases of ambiguous cases (15 cases of SCCDD vs PAC; 3 cases of metastatic BrCa vs PAC) were analyzed using
CD23, PAX5, D240 and CD117. P values were calculated using Fisher's Exact test. Results: A total of 11 (46%) PACs were CD117 positive while all BrCas and SCCs were negative (0%; p=<0.0001). D240 was expressed in 14 (58%) PACs and 20 (67%) SCCs, but none of the metastatic BrCa cases (0%; p=0.0024). None of the PAC, BrCa and SCC cases expressed CD23 or PAX5. Of the 15 ambiguous tumors in which the differential included SCCDD and PAC, 10 were positive for D240 and 2 were positive for CD117. Of the 3 ambiguous tumors in which the differential included metastatic BrCa and PAC, 1 case was positive for D240 and CD117, respectively. Conclusion: Our study indicates that positive staining for CD117 favors a PAC and the sensitivity and specificity are 46% and 100%, respectively. In the ambiguous cases in which the differential includes a SCCDD and PAC, the addition of this immunohistochemical marker, favors a PAC in 2 cases. D240 expression highlighted both PACs and SCCs and was negative in all metastatic BrCas (0%) and appears to be useful in excluding the latter. Therefore, of the 3 ambiguous tumors in which the differential included a PAC and metastatic BrCa, 2 cases are favored to be PACs based on the CD117 and D240 immunopositivity. Despite prior reports, CD23 and PAX5 do not appear to be useful immunomarkers in this setting.

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**RESIDENT**

**Primary Cutaneous CIC-Rearranged High Grade Undifferentiated Small Round Cell Sarcoma**

**John Van Arnam, MD, MS**

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A 32 year old woman with an enlarging, ulcerated mass of the right foot underwent excisional biopsy. Histologic exam demonstrated an infiltrative dermal-based mass comprised of small round blue cells with occasional cored architecture, foci of rhabdoid features, and a brisk mitotic rate. Positive immunohistochemical stains for CD33, CD117, CD56, and CD99 suggested myeloid sarcoma, while Pax-5 positivity suggested lymphoma, the neoplastic cells were negative for CD43, CD45, and lysozyme. EWSR1 gene rearrangements were not detected. However, a CIC gene inversion was identified, consistent with a high grade undifferentiated small round cell sarcoma with CIC gene abnormality. Months later, a lymph node metastasis was identified with the same morphological and immunohistochemical features. Although small round blue cell “Ewing-like” sarcomas with wild-type EWSR1 have been described in the literature, recurrent genetic CIC and BCOR rearrangements have permitted more definitive classification of these tumors. Their typical presentation is in the extremity in a young adult, with the CIC-mutant tumors usually located in the subcutaneous or deep tissue. Although the presentation and histologic appearance are often consistent with Ewing sarcoma, EWSR1 rearrangements are absent, and notably, there is a worse prognosis with a median survival of less than two years. Co-expression of traditionally hematopoietic markers as seen in this case represents another important diagnostic pitfall.
616
An Umbilical Polyp with an Uncommon Finding
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Umbilical polyps are firm, bright red nodules that represent embryological remnants of either the vitelline duct (VD) or urachus. They appear early in life, and are distinguished from the more common umbilical granuloma by persistent leakage of fluid and recalcitrance to silver nitrate treatment. In addition to the formation of polyps, lack of obliteration of either the VD or urachus can lead to a variety of anomalies depending on the remaining degree of patency of each structure. For example, if only the distal portion of the VD lumen fails to close, then it leads to an umbilical polyp containing gastrointestinal mucosa. We present a rare case of a pruritic, draining, red umbilical polyp in a 7-year-old Caucasian male. The lesion was noticed after the detachment of the umbilical cord stump. The clinical pre-operative diagnosis was granulation tissue and the lesion was excised. Microscopic examination revealed a polyp comprised of colonic mucosa without overlying skin consistent with an umbilical polyp. This is unusual as most umbilical lesions contain gastric or small bowel mucosa. We present this case to describe colonic mucosa in an umbilical polyp and as a reminder of the importance of including this entity in the differential diagnosis of umbilical lesions.

617
Mammary-type Myofibroblastoma in a Male with Colon Adenocarcinoma
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Mammary-type myofibroblastoma is a rare benign soft tissue tumor that presents as a painless, slow-growing mass in the breast. An extra-mammary location is extremely rare and typically occurs along the milk line. Recurrence of the tumor after marginal excision has not been documented. We present a 62-year-old male who was recently diagnosed with colon cancer and undergoing chemotherapy. An 1.8 cm soft tissue density was incidentally found during his CT scan. Soft tissue masses in the chest wall mass raise a fairly broad differential diagnosis. Although unusual, a metastasis was also considered and the lesion was biopsied. Microscopically, the tumor showed short fascicles of uniform spindle cells and haphazardly arranged thick, hyalinized collagen bundles. The spindle cells were immunoreactive for CD34 and desmin and were negative for pankeratin, SOX10 and STAT6. The findings supported the diagnosis. As mammary-type myofibroblastoma is a rare tumor, the correct diagnosis and prompt management is imperative, and requires careful clinical and pathological workup to rule out the possibility of a malignant neoplasm.
Prostate carcinoma is the most common non-cutaneous cancer in men. When it metastasizes, prostate cancer typically goes to bone, and is indicative of severely advanced disease. Cutaneous metastases of prostate carcinoma are exceedingly rare, representing less than one percent of all cutaneous visceral metastases. Here we report a case received in consultation of a 93 year-old man with a 1.5 x 1.5 cm red upper lip nodule of uncertain duration. The patient was previously healthy without history of malignancy. Hematoxylin and eosin-stained sections showed fragments of squamous mucosa with an underlying infiltrative proliferation of epithelioid cells forming irregular glandular structures within a desmoplastic stroma. Focal micropapillary projections were seen within glandular lumens. The tumor cells had round to oval nuclei with prominent nucleoli and nuclear overlap with loss of polarity. Lesional cells were positive for CK7 (diffuse, strong) and NKX3.1 (nuclear), with patchy CK20 positivity by immunohistochemical staining analysis. TTF1 and CDX2 stains were negative. While NKX3.1 is highly sensitive and specific for prostate origin, CK7 positivity is rare, as is the lack of a clinical history. Prostate-specific membrane antigen (PSMA) staining was performed to confirm prostate origin, and showed patchy positivity. The patient was found to have an elevated serum prostate specific antigen (PSA) level. Our case adds to the list of known cutaneous sites of prostate carcinoma metastases, highlights the need for distinction between a visceral or adnexal origin of glandular tumors, and emphasizes that CK7 expression, which may be relatively increased in this setting, should not be a deterrent to the diagnosis of cutaneous metastatic prostate carcinoma.

Atypical fibroxanthoma (AFX) occurs in sun-exposed skin, and is considered by many to be a superficial form of malignant fibrous histiocytoma. A rare clear cell variant of AFX has been reported in less than 20 cases in the literature. Its clinical presentation and prognosis is similar to conventional AFX. The diagnosis usually relies on distinguishing it from other cutaneous clear cell tumors. Here we report a case of a 68 year old male presenting with 1.3 cm raised lesion on his left arm. Excisional biopsy of the lesion revealed a well-circumscribed dermal tumor with surface ulceration, epidermal collarette and rich anastomosing vasculature. The tumor was composed of tight sheets of ovoid to spindle cells with clear to foamy cytoplasm, central-located small-sized nuclei and conspicuous nucleoli. Frequent mitosis were noted, up to 10 per HPF. Occasional Touton-like cells were present and also had clear to foamy cytoplasm. The uninvolved dermis showed solar elastosis. Immunohistochemical stains showed positive CD10 and CD68 staining. Sox-10, Mart-1, HMB-45, S-100, Pax8, RCC, CD/56 and LCA are all negative. Based on the morphology and immunohistochemistry, a diagnosis of clear cell atypical fibroxanthoma was rendered.
Clitoral Basal Cell Carcinoma: A Common Cancer in an Uncommon Location
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Basal cell carcinoma (BCC) is a common neoplasm, mostly occurring in sun-exposed areas such as the head and neck. It may also occur in the non-sun exposed genital areas. Vulvar BCC accounts for about 2-3% of vulvar neoplasms. Clitoral BCC is even rarer in the literature. While ultraviolet radiation is felt to be the most important risk factor for BCC in sun-exposed area, the etiology of BCC in sun-protected sites is less well understood. The predisposing factors may include chronic irritation and inflammation, trauma, radiation, immune deficiency, and genetic conditions such as nevoid basal cell carcinoma syndrome. HPV infection has also been suggested to contribute to the development of BCC. BCC in genital areas are more often locally aggressive, with recurrence and rare metastasis. However, local excision is usually curative. Here we report a case from a 52 year old female with superficial biopsy of a clitoral lesion. Microscopic examination revealed a nested basaloid cell proliferation with peripheral palisading and peri-tumoral clefting, a stromal desmoplastic reaction, and occasional mucin production between tumor cells. Scattered mitoses and apoptosis were noted. The morphology of the lesion was typical of common basal cell carcinoma diagnosed in sun-exposed area. Interestingly, additional perineal biopsy from the patient showed a viral papilloma with high grade squamous dysplasia. This association raises the possibility of an HPV etiology in the tumor development.

External Auditory Canal Ceruminous Adenoma
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Ceruminous adenoma is a rare neoplasm of the modified ceruminous sweat glands of the external auditory canal. They have been variably referred to as ceruminous adenoma, ceruminous pleomorphic adenoma, ceruminous papillary cystadenoma and various other adnexal tumor designations. The etiology of ceruminous adenoma still remains unknown. Although generally considered a benign tumor, ceruminous adenoma may have relatively “infiltrative” growth pattern, and require complete surgical excision to prevent recurrence. Here we report a case of a 34 year old female presenting with a right ear lesion. Excisional biopsy revealed tumor consisting of a dual cell epithelial-basal/myoepithelial proliferation with well differentiated tubular, ductal and papillary structures. The tumor cells were monotonous in shape and size with minimal cytological atypia. No necrosis, perineural invasion, or atypical mitoses were noted. Superficial squamous hyperplasia and a papillary architecture with plasma cell infiltrates were present, suggesting focal ceruminous syringocystadenoma papilliferum morphology. Immunohistochemical stains showed strong CK5/6 and p63 reactivity in basal cells and CK7 reactivity stains in luminal cells. S100 showed scattered basal/myoepithelial positivity. The staining pattern supported the diagnosis of ceruminous adenoma.
Metastatic Basal Cell Carcinoma with Diffuse Ki-67 Expression
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Basal cell carcinoma (BCC) is the most common cutaneous malignancy, usually displaying slow local progression but metastasizing in only 0.0028-0.55% of cases. Metastatic BCC is thus extremely rare, and few studies have characterized it histopathologically. We describe the case of a 65 year old male with past medical history significant only for previous facial BCC treated via Mohs surgery who presented with a 2-3 year history of a progressively enlarging ulcer of the right shoulder. The patient stated the lesion had been previously diagnosed as BCC on outside biopsy when initially noticed 2-3 years prior. Since that time he had developed several other ulcerated lesions as well as several nodular lesions. Examination revealed an impressive 15 centimeter ulcer of the posterior neck and right shoulder with rolled borders, as well as two other ulcers of the left neck and lower back. Anterior to the border of the largest ulcer were several smooth, firm subcutaneous nodules. Additionally, induration was found in the right parotid region, raising suspicion for metastasis. Biopsy of the edge of the largest ulcer revealed small angulated nests of basaloid cells in a morpheaform stroma. Biopsy of a bordering nodule revealed identical histology. A diagnosis of aggressive BCC with likely in-transit and lymph node metastases was made. In-transit metastasis of BCC is exceedingly rare, with few reports to date in the literature. When metastatic, BCC normally presents in the regional lymph nodes or lungs. Stains of the biopsy specimens revealed diffuse bcl-2, BerEp4, and CK 5/6 positivity, as well as negative staining for CK 20, consistent with BCC. A Ki-67 demonstrated positivity throughout the tumor islands. Control nodular and morpheaform BCC specimens, however, displayed positivity of Ki-67 only at the periphery of most nests. Aggressive and metastatic BCCs may have higher Ki-67 positivity than their more indolent counterparts.

Syringocystadenocarcinoma Papilliferum in Situ of the Scalp: An Unusual Presentation
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Syringocystadenocarcinoma papilliferum (SCACP) in situ is an exceptionally rare malignant cutaneous glandular neoplasm. To date, only nine SCACP in situ cases have been reported in the literature since first described in 1980. We present the case of a 63-year-old Hispanic female with a 3-month history of a painless, nodule on the scalp. The nodule initially appeared large and fluctuant but progressively decreased in size until she presented to the clinic. Physical examination revealed a 33 mm tan, verrucoid papule with crusting and erosions on the posterior vertex of the scalp. A shave biopsy was performed and histological sections showed an endophytic, glandular tumor with multiple points of epidermal attachment. The deep border of the tumor was lobulated and extended to the deep edge of the biopsy. Areas of papillary, solid, and cribriform growth were present. Papillae were lined by a variably thick epithelium consisting of flattened myoepithelial cells beneath larger cuboidal to columnar cells with eosinophilic to clear cytoplasm. Papillary cores contained abundant plasma cells. A subpopulation of cytologically malignant epithelial cells was noted with hyperchromatic nuclei, loss of
polarity and frequent mitotic figures. Absence of invasion was confirmed with p63 IHC, highlighting a continuous layer of myoepithelial cells, confirming the diagnosis of SCACP in situ. The lesion was successfully excised using Mohs Micrographic Surgery. This case demonstrates an unusual presentation of a SCACP. Previous cases have reported nodules of variable duration that slowly increase in size; however, the progressive shrinkage of the tumor, as reported by the patient, is a unique course for this tumor.

624
RESIDENT
Basaloid Neoplasm with Extensive Matrical Differentiation; Basal Cell Carcinoma Versus Pilomatrical Carcinoma, Diagnostic Challenge
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Basal cell carcinoma is the most common type of skin cancer. Many variants have been described, but the presence of extensive matrical differentiation is exceedingly rare. Less than 20 cases have been previously reported in the literature. Clinically, they present as slowly growing nodules or plaques with occasional ulceration. Reported sizes range from 0.5 to 10 cm in diameter. The tumor has features of typical basal cell carcinoma with areas of matrical (follicular germinative) basaloid nests containing shadow cells. The differential diagnosis includes benign and malignant pilomatrixoma. This distinction can be challenging but is critical as pilomatrix carcinoma can metastasize and cause considerable morbidity and mortality while basal cell carcinoma with matrical differentiation behaves similar to other types of basal cell carcinoma. Several studies have demonstrated that β-catenin, a 92-kDa protein involved in both cellular adhesion and the Wnt-signaling pathway, plays a critical role in the hair cycle and the development of basal cell carcinoma and tumors with matrical differentiation. We report a challenging case of basal cell carcinoma with extensive matrical differentiation in the ear canal of a 54-year-old female. The purpose of reporting this case is to increase awareness of this entity and highlight the importance of β-catenin to confirm the diagnosis.

625
RESIDENT
Unilesional Mycosis Fungoides of 50 Years’ Duration
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Mycosis fungoides is the most common form of cutaneous T-Cell lymphoma. Classically, mycosis fungoides presents as multiple patches and plaques that can evolve to tumors. Our case is a 57 year old woman who at age 5 developed an erythematous patch of the right buttock which since that time has been persistent and slightly enlarging. It had been largely asymptomatic. Physical examination revealed a 12cm x 19cm erythematous plaque with superficial scale involving the central, medial, and lateral right buttock. She initially underwent biopsy of the lesion in 2012, which revealed atypical epidermotropic lymphoid infiltrates suggesting mycosis fungoides. T-cell gene rearrangement was negative at that time. Repeat biopsy of the lesion revealed a band-like infiltrate of lymphocytes extending between wiry collagen bundles in the papillary dermis. Small haloed lymphocytes lined up along the dermal-epidermal junction and extended as single cells into the epidermis. CD3 immunostain highlighted marked
Epidermotropism of the T-cells. Intradermal and dermal T-cells expressed CD4. There was markedly diminished expression of CD7. T-cell receptor gene rearrangement was positive by PCR. Treatment was recommended with either electron beam therapy to the area or topical nitrogen mustard. Unilesional mycosis fungoides is a rare variant of cutaneous T-cell lymphoma. It is histopathologically indistinguishable from the multilesional form, as both exhibit atypical lymphoid cells at the dermoepidermal junction, epidermotropism, and Pautrier microabscesses. Like typical multilesional mycosis fungoides, unilesional mycosis fungoides may initially present with nondiagnostic histopathologic features and may require multiple biopsies over time for confirmation of the diagnosis. The prognosis of unilesional mycosis fungoides is excellent. In the case of our patient, very slow progression occurred over a period of more than five decades. Treatment options include topical preparations, radiation, and photodynamic therapy.

Other

626

**Histologic Features of Ablative Fractional Laser Treatment**

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Ablative fractional lasers have gained widespread attention in Dermatology and Plastic Surgery. These lasers utilize very short pulses of energy to ablate microscopic portions in skin with the goal of tissue remodeling. They have widespread use in cosmetic procedures and have gained particular attention as an important tool in scar remodeling. We have been examining the histologic changes that occur when ablative fractional CO2 and Erbium:YAG laser treatment is applied to the skin at various energy settings in preclinical porcine models. We have also examined the histologic effects of ablative fractional CO2 and Erbium:YAG laser treatment on third degree burn scars. Lower energy settings appear to be stimulatory to epithelial tissue while higher energies may be associated with more of a debridement like effect. We have also noted induction of fetal like dermal cells with laser treatment in both normal and burned skin. These findings will help to better direct the use of ablative fractional lasers to remodel skin as well as guide how they may best be used in combination with other treatments.

627

**Radiation-induced Morphea: A Rare Complication of External Radiation**

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Background: Radiation induced morphea (RIM) is a rare complication of external radiation that is commonly misdiagnosed as other disorders, such as psoriasis. It has an incidence of approximately 2 out of 1000 patients receiving radiotherapy, with early changes characterized by dryness, epilation, changes in pigmentation, and erythema and late changes characterized by localized fibrosis of the skin leading to
progressive thickening of the dermis. Main observations: We report on a 70-year-old Caucasian male who presented with history of chemotherapy and external radiation in 2013 for lung carcinoma and a prior history of cutaneous squamous cell carcinoma of the left lower cutaneous lip, excised in 2002. He had no complaints of itching, burning, or soreness, but a well-demarcated, bound-down, erythematous-to-violaceous patch was noted on his left middle back during routine full skin examination. He had not pursued any medical treatment or prior biopsy of the area and denied any history of trauma to the site. Biopsy revealed thickening and hyalinization of the dermis, loss of periadnexal fat, and compression and atrophy of adnexal structures. Conclusions: The pathogenesis of RIM is not completely understood, however, it has been hypothesized that stimulation of dermal growth factors may lead to atypical myofibroblast proliferation causing progressive thickening of the dermis. Another theory is that radiation-induced neoantigen formation stimulates secretion of TGF-β, which subsequently induces fibroblast proliferation, collagen secretion, and fibrosis. Treatment of RIM typically includes systemic and topical antibiotics and corticosteroids. However, there have been multiple studies which have recently shown UVA1 irradiation to be beneficial, providing reduction in sclerotic plaques, an increase in elasticity, and reduction in skin thickness.

628

**Cutaneous Refractile Foreign Body Microemboli in Intravascular Injection of Oral Medication**

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Intravenous drug abuse (IVDA) is known to cause a spectrum of systemic and cutaneous complications. Despite the increasing incidence of IVDA around the world, there is a paucity of literature discussing cutaneous complications from a dermatopathologic perspective. We present a case of a 35 year old male with a complex medical history of Von Willebrand disease, Behcet’s disease and diverticular disease. Following a sigmoidectomy/colostomy for diverticular perforation, he presented with fever and an indurated right arm displaying livedoid purpura. The right distal fingertips showed purpura with focal ulceration. The patient was treated with antibiotics and prednisone for suspected cellulitis and Behcet’s-related vasculitis, respectively. A punch biopsy did not show evidence of vasculitis or pyogenic infection, but instead demonstrated a focus of polarizable refractile material occluding a dilated vascular lumen within the mid-dermis. Later in the hospital course, the patient, a former paramedic, admitted to injecting a suspension of crushed ondansetron tablets into the antecubital area to control post-operative nausea. It is known that direct intravascular injection can cause distal ischemia and necrosis, either by local vasoconstriction, thrombosis, or formation of microemboli. In this case, the main pathology appears to be particulate embolization of foreign body, likely an inert agent or binder contained in medications meant for oral administration. Our objective is to bring awareness to this rarely reported phenomenon and to raise clinical suspicion for IVDA when confronted with such a unique vasculopathic pattern.
We report the case of a 52-year-old morbidly obese (BMI: 54) Caucasian male with a history of alpha-1-antitrypsin deficiency (genotype PiZZ). He presented with a 34 x 21 cm erythematous, warm, tender, lower-abdominal plaque clinically suspicious for alpha-1-antitrypsin deficiency panniculitis. Histologic sections demonstrated a proliferation of dermal based, thin walled, ectatic vascular channels with extension into the subcutis. These vascular channels were positive for CD31 and CD34 immunoreactivity. Further immunohistochemical studies for HHV-8, GMS, PAS-D, AFB, FITE, and gram were negative, indicative of Diffuse Dermal Angiomatosis involving a pannus. Subsequently, he was treated and experienced significant improvement upon abdominal binding with elastic bandages. Diffuse Dermal Angiomatosis (DDA), initially identified by Krell et al. as a variant of reactive cutaneous angioendotheliomatosis, is now considered a separate entity contained under the umbrella of cutaneous reactive angiomatoses. Historically associated with heavy smoking and severe atherosclerotic disease, DDA has recently been recognized in association with obesity (i.e. within a pannus). In light of the current obesity epidemic, recognition and knowledge of this entity is important for both budding and practicing Dermatopathologists alike, as histologic mimics include low grade Angiosarcoma and Kaposi Sarcoma.

A 40yo woman presented with an asymptomatic rash on her right neck, chest, and shoulder that had been present unchanged since adolescence. Trials of triamcinolone and protopic were not helpful. She had no family history of similar lesions. On exam, she had brownish-red scaly papules in a linear distribution from her right neck down her central chest. In addition, her left third fingernail showed red and white streaks but no V-nicking. The clinical differential included: epidermal nevus, inflammatory linear verrucous epidermal nevus, lichen striatus, nevus sebaceous, segmental Darier, koebnerized lichen planus or psoriasis, or blaschkitis. A biopsy showed focal suprabasilar acantholysis with dyskeratosis. The histological differential included: Grover disease, Darier disease, and epidermolytic epidermal nevus. Based on the clinical scenario and the lack of histological findings to suggest an epidermal nevus, she was diagnosed with type 1 segmental Darier. Darier disease is a rare autosomal dominant condition caused by a mutation in the ATP2A2 gene, leading to a dysfunction in intracellular calcium signaling. This results in a lower threshold for skin trauma to trigger apoptosis and is manifested histologically by acantholysis with dyskeratosis. It has a peak onset during puberty, presenting typically in a seborrhoic distribution. Other cutaneous findings include: palmoplantar keratotic papules and keratin filled depressions, flat-topped papules on the dorsal hand, whitish oral mucosal papules, and nails with V-nicking or red and white streaks. Segmental Darier is a rare variant manifesting as Darier with distribution along the lines of Blaschko. Type 1 segmental Darier is caused by a post-zygotic mutation, which leads to a mosaic pattern of skin involvement on a background of normal skin. Type 2 occurs when a heterozygous mutant has an additional segmental post-zygotic mutation in the other
631

Acquired Poikiloderma: Poikilodermatous Mycosis Fungoides or Poikilodermatous Parapsoriasis?
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Mycosis fungoides (MF) is often preceded for years by skin lesions that are neither clinically nor histopathologically diagnostic. This gradual progression of disease and variability in histopathologic features of early patch stage MF is often why it is difficult to reach a consensus on minimum criteria needed for a definitive diagnosis. We present a 64 year old white male with diabetes and hypertension with a two month history of a scaly, pruritic, erythematous rash that started on the legs and spread to the flanks and upper arms. The patient was prescribed triamcinolone 0.1% ointment and instructed to follow up in three weeks; at which time he reported an improvement of pruritus. There was also
decreased erythema and scale which revealed underlying atrophy, telangiectasia, and pigmentary changes resulting in a mottled skin appearance consistent with poikiloderma. Biopsies from different locations showed a dense band-like infiltrate of predominately CD3 and CD4 positive lymphocytes surrounding telangiectatic vessels, slight dermal fibrosis, pigmentary incontinence and exocytosis of lymphocytes with variable nuclear hyperchromasia. Scattered eosinophils were present in one of the three biopsies. Gene rearrangement studies were negative at two separate biopsy sites. Acquired poikiloderma is a challenging clinical presentation that has a broad differential diagnosis to include infection (Borrelia), connective tissue disease (dematomyositis and lupus erythematosus), radiation, medications, and neoplasia (MF). Our patient had acquired poikilodema with biopsies showing some features concerning for MF but not histopathologically diagnostic or supported by molecular studies suggesting a diagnosis of “poikilodermatous parapsoriasis”. The patient has completed 16 weeks of treatment with high-potency topical steroids and nbUVB with symptomatic relief but no significant change in the skin eruption. Continued treatment and follow-up with additional biopsies may help to determine whether or not the patient develops patch stage MF.

**633**

**Exogenous Pigmentation of the Sole Due to Exposure to Tarring Product with Melanin-like Pigment and Positive Fontana-Masson Staining: A Case Report**

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Importance: Acral lentiginous melanoma (ALM) is a type of melanoma arising on volar surfaces (soles or palms) and nail beds. ALM presents as irregular, slightly raised pigmented macules with the appearance of an “enlarging stain”. Other causes of hyperpigmentation of the soles include tinea nigra and hemorrhage. Only a few cases due to exogenous pigmentation of the sole have been reported to date in the literature. Observation: The patient is 43-year-old pregnant female who presented with a few pigmented macules on the left sole. The patient denied recent trauma. She reported that she and her husband were tarring the driveway, but that she did not think she had been exposed to the tarring material. The clinical differential diagnosis included external pigmentation, trauma, and melanocytic nevi. A shave biopsy of the largest lesion (0.5 cm x 0.3 cm) was obtained. Histopathological examination revealed melanin-like pigment in the stratum corneum without an underlying melanocytic proliferation. The pigment was positive for Fontana-Masson as seen with melanin pigment. Microscopic examination of a crack filler product used for tarring showed similar histological features as the pigment seen in the biopsied lesion as well as positive Fontana-Masson staining. Conclusion: To our knowledge, we present the first case report of melanin-like pigment and positive Fontana-Masson staining with a tarring product. This case also highlights the importance of clinical-pathologic correlation in avoiding misdiagnosis.
Two Cases with Similar Nodular Lesions and Distinct Histological Features

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Introduction: We presented two cases with similar clinical manifestation and some shared histological findings, e.g. dermal fibrosis with focal neutrophilic vasculitis. However, their distinct diagnoses were made based on thorough under microscope observation and specific staining. Case presentation: Case 1: Male, 38 year old, presented with multiple brownish nodules on leg and waist for 2 years and ulcerated spontaneously for 1 year. No predisposing factors such as trauma were reported. His general health condition was good. He denied drug addict, smoking, alcoholic, etc. Physical examination didn’t find obvious abnormality. Routine lab workup including microbiological studies, immunity assay etc. All tests were within normal limits except repeated peripheral eosinophilia. The histology of leg’s biopsy showed epidermal acanthosis and nodular pandermal mixed inflammatory infiltrations. Neutrophilic vasculitis and prominent dermal fibrosis were present. Special stains, e.g. PAS, AFB were performed to rule out infection. The overall histological findings are most consistent with Erythema elevatum diutinum.

Case 2: Male, 25 year old, presented with multiple erythematous nodules on leg for 1 year. He denied any history of drug, trauma and allergy contact. No specific medical history was recorded. Physical examination was normal except skin lesions. The routine laboratory worksups were within normal limits. The skin biopsy revealed relative intact epidermis and stromal changes with infiltrated histocytes. The focal fibrinoid necrosis of vessels were visible, however, favor secondary vascular changes. The prominent foamy cells contains a large numbers of bacilli that highlighted by AFB stain. The final diagnosis of histoid leprosy was made. Discussion: We should be aware that the variant type like histoid leprosy is easily misdiagnosed as histiocytoma due to storiform pattern features and late stage of EED appears like scar also could be resemble to histiocytoma and stumble us to make diagnosis.

A Rare Case of Cutaneous Collagenous Vasculopathy with Initial Presentation of Bilateral Forearms

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Cutaneous collagenous vasculopathy is a distinct acquired idiopathic microangiopathy involving the superficial cutaneous vasculature. It presents clinically as asymptomatic telangiectasia usually beginning on the lower legs and slowly progressing in most cases to become generalized and clinically reminiscent of generalized essential telangiectasia. A skin biopsy specimen is necessary to distinguish cutaneous collagenous vasculopathy from generalized essential telangiectasia; however, histopathologic studies are rarely performed for this condition. It is likely that cutaneous collagenous vasculopathy frequently passes unrecognized, and thus may be more common than previously thought. Microscopically, cutaneous collagenous vasculopathy resembles the superficial telangiectasias of generalized essential telangiectasia but additionally shows hyaline material in thickened vessel walls. The amorphous pink material is periodic acid-Schiff-positive and resistant to diastase. Trichrome stain and immunostaining for collagen type IV also label the concentric perivascular material. The pathophysiology is unknown although some authors suggest the possibility of intravascular obstruction resulting from local thrombosis as the primary event; however, the ultimate inciting factor remains unknown. We describe
a 64-year-old male with cutaneous collagenous vasculopathy who presented with telangiectatic vessels on both the dorsal and palmar surfaces of the forearm. Punch biopsy revealed relatively classic features of collagenous vasculopathy.

636

MUSE (Microscopy with UV Surface Excitation): A Novel Approach to Real-time Inexpensive Slide Free Histopathology
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Standard histology relies on physically sectioning either frozen or formalin-fixed, paraffin-embedded (FFPE) tissue into thin slices (typically 4-6 μ) prior to staining and viewing on a standard wide-field microscope. MUSE is a novel alternative microscopy method that works with UV excitation using oblique cis-illumination which can generate high-quality images from the cut surface of fresh or fixed tissue after a few minutes of washing and staining with no requirement of fixing, embedding and sectioning of tissue, including skin. Concordance between MUSE images and H&E slides is assessed by scoring of MUSE images (Score 0: Worse / Score 1: Equal or cannot be evaluated / Score 2: Better than H&E) on the quality of selected epidermal and dermal structures (1-stratum corneum 2-stratum granulosum 3-stratum spinosum 4-stratum basale 5-neural 6-vasculature 7-collagen and elastin 8-sweat glands 9-adipose tissue 10-inflammatory cells). MUSE is a fast, reliable and inexpensive approach for evaluating skin specimens and holds great promise as a future diagnostic modality in dermatopathology.

637

Immunohistochemistry Evaluation of IL-1beta Expression in Vitiligo Patients: A Potential Link between Vitiligo and the Inflammasome
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Vitiligo is a devastating disorder of skin pigmentation that is refractory to several lines of therapies. In recent years a better understanding of the pathophysiology underling the disease is helping in shaping a new wave of studies to find potentially effective therapeutic targets. In this study we evaluated the expression of IL-1beta, a cytokine with a central role in the immune and inflammatory response to a variety of human diseases, in biopsies of patients with vitiligo visiting our clinic. A total of 16 patients clinically and histopathologically diagnosed with vitiligo were selected from our databases and compared with five controls. In these specimens we evaluated by immunohistochemistry the expression of IL-1beta and compared his expression with non lesional skin. Our results demonstrate that IL-1beta is one of the proinflammatory cytokines that may have a potentially prominent role in the pathophysiology of the disease. Our results offer the rational for the potential use of available selective inhibitors of IL-1beta as a novel therapeutic strategy in the treatment of this neglected disease.
The American Society of Dermatopathology

638
The Role of DOG1 Immunohistochemistry in Dermatopathology
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Background: This study was designed to evaluate the immunoexpression of DOG1, a specific marker expressed in gastrointestinal stromal tumors, in normal skin tissues and cutaneous epithelial tumors. Methods: DOG1 immunostaining extent, intensity, and pattern were evaluated in 69 cutaneous apocrine/eccrine tumors, 11 sebaceous tumors, 46 follicular tumors, 52 keratinocytic tumors, and perilesional normal tissues. Results: In normal tissues, DOG1 was expressed strongly in the intercellular canaliculi of eccrine glands, moderately in the myoepithelial cells of mammary and anogenital mammary-like glands, and weakly or not at all in the periphery of sebaceous lobules and the lower layer of epidermis and follicular infundibulum. All apocrine-type cutaneous mixed tumors showed apical-luminal positivity for DOG1, and 4/9 of these tumors included intercellular canaliculi highlighted by DOG1 immunostaining. Other sweat gland tumors, including hidrocystadenoma, spiradenoma, cylindroma, and apocrine carcinoma, also expressed DOG1 focally with an apical-luminal pattern. Although slight membranous positivity for DOG1 was observed in various tumor types, hidradenoma papilliferum exhibited diffuse membranous DOG1 staining in the myoepithelial cells. Conclusions: DOG1 is a novel marker for identifying intercellular canaliculi and is a potential immunomarker of myoepithelial cells specific to mammary glands, anogenital mammary-like glands, and tumors originating therein.

639
Luteinized Thecomas with Sclerosing Peritonitis and Cutaneous Involvement: A New Extra-ovarian Manifestation of a Rare Disease
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Luteinized thecomas with sclerosing peritonitis (LTSP) is a rare entity characterized by bilateral ovarian luteinizing thecomas, acute abdominal distension, ascites, and fibrosing peritonitis often with small-bowel obstruction. Skin involvement has never been reported. We present a case of LTSP with unusual cutaneous lesions. A 53 year old female presented with a six month history of an asymptomatic scarring rash on her trunk, extremities and scalp. At around the same time she developed rapid onset of ascites, bilateral abdominal masses and peripheral edema. Biopsies were taken from three of the cutaneous lesions and bilateral salpingo-oophorectomy was performed. She subsequently developed an ileus, prompting laparotomy with ileocecectomy and peritoneal resection. Ovarian biopsies revealed bilateral luteinized thecomas, whereas ileal biopsy demonstrated a proliferation of fibroblasts expanding the subserosa. A diagnosis of LTSP was made. All skin biopsies showed similar findings of an eroded epidermis with unusual palisaded, basaloid epidermal hyperplasia and a proliferation of fibroblasts, embedded in a myxovascular stroma, abutting the epidermis. Scalp biopsy additionally demonstrated a secondary cicatricial alopecia. Immunohistochemical comparison of cutaneous and intestinal spindle cells revealed a vimentin +/smooth muscle actin (SMA) + population of fibroblasts, suggesting myofibroblastic differentiation. Based on the temporal nature of the cutaneous and systemic disease, the similar fibrosing histopathologic pattern and shared immunohistochemical profile, we conclude that this represents the first case of LTSP with cutaneous involvement as an additional manifestation of
extra-ovarian disease. Dermal and subserosal vimentin+/SMA+ fibroblasts raise the possibility of a myofibroblastic syndrome, potentially induced by an unknown ovarian-secreted factor.

640  
A Case of Insulin-derived Amyloidosis: Recognition of an Uncommon Entity and Distinction from Nodular Localized Cutaneous Amyloidosis  
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Introduction: Insulin-derived amyloidosis is an under recognized complication of insulin therapy characterized by extracellular deposition of insoluble polymeric protein fibrils in subcutaneous tissue at insulin injection sites. Patients present with firm subcutaneous masses and may have associated poor glycemic control. Diagnosis rests on histologic identification of subcutaneous amyloid deposition at sites that correlate with insulin injection. We present a case of insulin-derived amyloidosis and demonstrate insulin detection by immunohistochemistry (IHC), which may be particularly useful in the absence of clinical history. Case Description: A 33-year-old man with Diabetes mellitus type 1 on Novolog and Lantus presented with enlarging bilateral subcutaneous flank masses for 1 year. These masses measured 5 cm and 2 cm, were firm, non-tender, and were localized to sites of insulin injection. MRI of the pelvis revealed corresponding subcutaneous tissue thickening. The masses were excised and histologic examination revealed deep dermal and subcutaneous deposition of amorphous eosinophilic material in a nodular pattern with surrounding chronic inflammation and foreign body giant cells. On Congo red stain, the eosinophilic material was orange-red and showed apple green birefringence under polarized light. A subsequent immunostain for insulin was positive. Discussion: Insulin-derived amyloidosis has significant clinical and morphologic overlap with nodular localized cutaneous amyloidosis (NLCA), which is characterized by localized deep dermal deposition of AL protein that is nonreactive for insulin, and has been associated with kappa/lambda light chain restriction in local plasma cells. In contrast to insulin-derived amyloidosis, in which treatment merely involves rotation of injection sites and elective surgical excision, patients with NLCA have been reported to progress to systemic amyloidosis, warranting evaluation for monoclonal gammopathy and long-term follow-up. This case shows the utilization of insulin IHC staining in a patient with localized deep cutaneous amyloid deposition to confirm insulin-derived amyloidosis. Awareness of this entity and distinction from NLCA is important for selecting patients who may be spared extraneous evaluation.

641  
Vascular Tumors of Infancy: What it is When it's NOT an Infantile Hemangioma?  
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Background: Infantile hemangiomas (IH) are common and usually diagnosed by history and clinical examination. Unfortunately, infantile hemangiomas share many overlapping clinical and histologic features with both benign and potentially serious vascular tumors in infancy. Methods: We present five unique cases of non-Infantile Hemangioma vascular tumors in infants: Rapidly Involuting Congenital Hemangioma (RICH), Noninvoluting Congenital Hemangioma (NICH), Pyogenic Granuloma, Tufted Angioma, and Kaposiform Hemangioendothelioma. Histology and immunohistochemistry were
reviewed. Results: Clinical features and immunohistochemical characteristics of five non-IH vascular tumors in children are summarized in Table I and Table II. A summary of clinical keys, distinguishing factors, histologic findings, immunohistologic findings, and common treatments is provided. Discussion: Vascular tumors in children that are not infantile hemangiomas present a diagnostic and treatment dilemma. Pertinent history and detailed physical examination can lead to the diagnosis, histopathology aids in confirming the diagnosis. Specifically, staining for GLUT-1 is positive in IH and negative in other infantile vascular tumors. To differentiate between vascular tumors histologic findings and staining for CD34, D2-40 and LYVE1 are useful. Using 5 demonstrative cases, we present clinical keys, histologic and immunohistologic findings as well as treatment recommendations of non-infantile hemangiomas for the clinician struggling with the diagnosis, further workup and management of vascular tumors in infants.

642

Number Needed to Biopsy, a Potential Benchmark for Clinician Biopsy Guidelines

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The number of procedures to remove skin cancers has doubled in the last 15 years, paralleling the increase in the number of older adults in the population. We expect a continuing rise in biopsies to rule out skin cancer. Our goal was to study variation in the number needed to biopsy to detect one skin cancer (NNB). We calculated NNB using our large consecutive dermatopathology dataset including N=10,508 pathology reports from five general dermatologists at a single institution over a 5-year period (2011-2015). We calculated the number needed to biopsy, defined as the total number of skin biopsies divided by the sum of basal cell carcinoma (BCC), squamous cell carcinoma (SCC), and malignant melanoma (MM) cases (including SCC and MM in situ cases). We also calculated the number needed to biopsy to detect a melanoma (NNBM), defined as the total number of skin biopsies divided by the number of melanomas. We found that NNB varied by provider: dermatologist#1 NNB=7, dermatologist#2 NNB= 8, dermatologist#3 NNB=6, dermatologist#4 NNB=5, dermatologist#5 NNB=6. NNB for melanomas (NNBM) were dermatologist#1 NNBM=128, dermatologist#2 NNBM=147, dermatologist#3 NNBM=45, dermatologist#4 NNBM=83, dermatologist#5 NNBM=71. Similar studies have identified NNB for entire groups, such as a NNBM of 12 for a group of Australian dermatologists, and NNBM of 9 and 30 in specialized and non-specialized clinic settings respectively. Further research is needed to incorporate a higher number of providers and to control for variables including years of clinician experience, individual academic research interests, referrals, and patient preference. Although our data is preliminary, it is possible that the NNB may eventually serve as an important benchmark for potential future cutaneous biopsy guidelines.
Familial Cutaneous Mastocytosis: Report of the Disease in Three Siblings and Review of the Literature
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Cutaneous mastocytosis (CM) is a heterogenous group of diseases, manifesting as a variably dense proliferation of dermal mast cells. CM is considered a sporadic disease, yet more than 50 cases of familial mastocytosis have been reported with autosomal dominant pattern of inheritance in about one third of cases. In addition, mastocytosis has also been reported in more than 10 pairs of monozygotic twins and two sets of triplets, suggesting genetic factors play an important role in development of this disease. Herein we describe childhood onset cutaneous mastocytosis affecting 3 siblings. The first sibling was a 15 year old Caucasian female, who had a history of periodic scattered erythematous macules over her trunk accompanied by flushing, headache and difficulty breathing since the age of 3. The other two siblings, aged 13 and 7, had similar skin lesions developing at the ages of 2 and 4, respectively, without systemic symptoms. The youngest sibling was a half sister with a different father. Biopsy of skin lesions in all 3 siblings confirmed the diagnosis of cutaneous mastocytosis. Cutaneous mastocytosis is an uncommon disease and familial occurrence is even more rare. Although the inheritance pattern of familial mastocytosis is unknown, an autosomal dominant mode of inheritance is most commonly reported. Although absence of disease in both parents of an affected offspring usually indicates an autosomal recessive pattern of inheritance, involvement of siblings with two different fathers suggests either an autosomal dominant pattern of inheritance with incomplete penetrance or a germline mutation in the mother.

Perifollicular Lymphocytic Infiltrates in Nevus Sebaceous
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Background: Nevus sebaceous is a complex congenital hamartoma characterized by eccrine, apocrine, and sebaceous proliferation, with marked clinical and histologic plasticity reflecting the age of the lesion. Much research has focused on the constitution and rates of development of benign and malignant secondary neoplasms in nevus sebaceous. However, little is known about the prevalence and character of perifollicular inflammation in nevus sebaceous. We hypothesized that mild perifollicular lymphocytic infiltrates are a common feature of nevus sebaceous. Objectives: We sought to evaluate the frequency and character of perifollicular lymphocytic infiltrates in nevus sebaceous. Methods: The microscopic features of 52 specimens with a confirmed histologic diagnosis of nevus sebaceous without and without secondary neoplasms were reviewed by two blinded, board-certified dermatopathologists. Results: Perifollicular lymphocytic infiltrates were present in vast majority of nevus sebaceous specimens (over 90%). Approximately 2/3 were mild, 1/5 were moderate, and 1/10 were severe in character. The presence of secondary neoplasms correlated with increased density of perifollicular infiltrates. Conclusion: Perifollicular lymphocytic infiltrates are prevalent in nevus sebaceous. Further study may elucidate the relationship between such infiltrates and the development of secondary neoplasms.
Mycophenolate Mofetil-induced Ulcerative Stomatitis in a Liver Transplant Recipient
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Oral ulcerations in transplant patients can result from a number of possible etiologies, including bacterial, viral, or fungal infection, gastrointestinal disorder, systemic or localized collagen-vascular disorders, immunosuppression, and adverse drug reaction. Myophenolate mofetil (MMF) is an immunosuppressant commonly used in patients undergoing solid organ transplant. MMF-induced oral ulcers have recently been reported in liver transplant patients, with the first case described in the English literature in 2007. We report an unusual case of oral mucosal toxicity from MMF in a liver transplant patient. A 70-year-old woman with a history of hepatocellular carcinoma underwent orthopic liver transplantation and was started on an immunosuppressive regimen including prednisone, MMF, and tacrolimus. Three months later, the patient was admitted to the hospital with neutropenia and a one-week history of multiple recalcitrant oral ulcers. She denied having similar oral lesions in the past. On examination, multiple ulcerations with central necrosis were observed on the ventral tongue, upper lip, lower lip, and bilateral buccal mucosa. The ulcers ranged in size from 6 to 18 mm. No other cutaneous or mucosal lesions were identified on physical examination. Laboratory values were significant for decreased WBC (1.12) and platelet (78,000/mm3) counts and a low hemoglobin level (9.0). HSV and VZV cultures from the oral lesions were negative. EBV, CMV, parvovirus, adenovirus, and HHV6 plasma PCR were negative. Serum HIV and PRP tests were nonreactive. A biopsy from the lesion on the buccal mucosa revealed non-specific ulceration with acute and chronic inflammation. PASd was negative for fungal forms. A cytomegalovirus immunostain was negative. MMF was subsequently discontinued and dexamethasone oral rinse was started. Within one week, the oral ulcers diminished significantly in size, and the patient reported a substantial decrease in her oral discomfort. The patient reported complete resolution four weeks after discontinuation of MMF. This case highlights an unusual pattern of stomatitis in liver transplant patients and the importance of considering medication-induced oral ulcerations in the differential diagnosis.

A Case of a Giant Aneurysmal Fibrous Histiocytoma
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Aneurysmal fibrous histiocytomas are rare variants of dermatofibromas. These benign blood filled lesions can mimic malignancies due to their rapid and recurrent growth. Our patient was a 42-year-old Caucasian female with a past medical history of morbid obesity, diabetes, and hypertension, who presented with a mass on her left shoulder for 5 years’ duration. The mass oozed occasionally and would recur, replaced with progressively larger masses. Upon inspection, the patient had a large pedunculated exophytic mass with vascularity. The mass was surgically removed under general anesthesia via wide local excision. Grossly, the excised skin was purple tinged with an underlying fungating solid mass measuring 8.5 cm. Serial sections revealed a hemorrhagic, spongy, and granular cut surface. Histologically, the epidermis was hyperplastic with underlying hyaline collagen bundles. The remainder of the mass was chronically inflamed and comprised of spindled histiocytes, hemosiderin
laden macrophages, and blood-filled spaces lacking an endothelial lining. There was focal polymorphism but no significant atypia. Immunohistochemical stains were strongly positive for vimentin and negative for CD31, CD34, and desmin. The overall architecture and immunophenotype are consistent with the diagnosis of aneurysmal fibrous histiocytoma. This benign entity must be differentiated from an angiosarcoma, which is CD31 and CD34 positive. Another differential is an angiomatoid malignant fibrous histiocytoma, which has a distinctive multinodular pattern, thick pseudocapsule, and peripheral lymphoplasmacytic infiltrate. Aneurysmal fibrous histiocytomas have rarely been described in the literature, and to our knowledge, only one has been reported to be bigger than 8.5 cm.

647
Incidental Intraepidermal Acantholysis in Wound
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Incidental intraepidermal acantholysis resembling pemphigus or Hailey-Hailey disease has been reported in other diseases including basal cell carcinoma, keratocanthoma, psoriasis, tinea corporis, leukocytoclastic vasculitis, and bullous pemphigoid. However, to our knowledge, has not been described in in wounds. Here, we present two cases of wound associated with acantholysis. Case 1 71-year-old Caucasian female with past medical history of uncontrolled diabetes mellitus type 2, presented with an ulcerated erythematous indurated plaque on the right abdomen. The biopsy revealed superficial and deep perivascular and interstitial suppurative dermatitis. The epidermis revealed acantholysis. Necrosis and granulomatous inflammation were not seen. Histochemical staining with PAS, GMS ans AFB failed to demonstrate microorganisms. Tissue culture was positive for staphylococcus aureus, and streptococcus B hemolytic group A and non A. The diagnosis of ulcerated cellulitis was made. Case 2 45-year-old Caucasian female presented with chronic wounds with ragged, violaceous edge on the left thigh and left hip. The biopsy revealed ulceration and acute and chronic inflammation in the entire dermis, endothelial swelling, and extravasated red blood cells. The epidermis revealed acantholysis. Based on the clinical and pathological findings and ruling out other differential diagnoses, diagnosis of pyoderma gangrenosum was made. None of these patients had any personal or family history of recurrent blister or crusted lesions in the flexural area or any findings to suggest Hailey-Hailey disease. Knowing about this incidental finding is important and helps us not to over diagnose any acantholytic lesions as immunobullous disease or Hailey-Hailey disease

648
Sickle Cell Disease: An Uncommon Cause of Livedoid Vasculopathy
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We report a case in which a 43 year old African American male with past medical history of sickle cell disease presented with a non-healing ulcer. A biopsy revealed features of livedoid vasculopathy. Previously, livedoid vasculopathy has only been described in a patient with sickle cell trait, but not yet in a patient with sickle cell disease. The ulcer had been persistent for six months prior to biopsy. The
patient had suffered from prior vascular complications including deep vein thrombosis and multiple ulcers that have healed in the past. Labs revealed a Hgb of 8 with hypochromic microcytic indices and a hypercoaguable workup was negative. The patient had been on a short course of hydroxyurea, but the current ulcer was present before the start of the medication. Histologically, the biopsy showed an ulcer with abundant fibrous tissue, scar, prominent stasis alterations and a number of vessels were plugged with fibrin thrombi. This led to a diagnosis of stasis ulceration with features of livedo vasculitis, which is likely a manifestation of the patient’s sickle cell disease. Livedoid vasculopathy is a condition that manifests as an ulcer that histologically reveals segmental hyalinizing vessels, focal thrombosis and endothelial proliferation. When the ulcer heals, it develops into a stellite scar known as atrophia blanche. The etiology is currently unclear, but it has been shown to be related to procoagulant states. Sickle cell disease is a known hypercoagulable state, with thrombo-embolic events occurring more frequently in these patients. Livedoid vasculopathy appears to be a primarily occlusive disease, making hypercoagulable states more likely to be associated with it. Therefore, any patient with a biopsy showing livedoid vasculopathy should be worked up for various diseases associated with increased thrombosis.

649
Unusual Case of Anal Pain and Pruritus
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We present the perplexing case of a 59-year-old male with a 4-month history of perianal pain and itching. Reportedly, the symptoms began shortly following a colonoscopy and also included increased sweating from the area, drainage, and staining of the patient’s undergarments. Physical examination revealed a pink to white, firm plaque extending from the superior gluteal cleft to the perianal area. There was a central 1 cm healing erosion with ulceration that extended into the underlying subcutis. Histologic examination from the non-ulcerated area of the plaque revealed an essentially normal stratum corneum and epidermis with numerous underlying clear spaces in the papillary dermis. Surrounding the clear spaces was a sparse lymphohistiocytic inflammatory infiltrate. This combination of histologic findings favors exogenous foreign material. Similar empty spaces have been reported in both the skin and colonic mucosa, termed pseudolipomatosis cutis and pseudolipomatosis intestinalis. The former is postulated to be artifactual in nature, possibly from injection of small amounts of air during administration of local anesthetic or from the formation of gas bubbles within specimens prior to tissue fixation. Pseudolipomatosis intestinalis is proposed to be a manifestation of gas trapped in the lamina propria of the intestine after colonoscopy. In our patient, the presence of a deep ulcer in the gluteal cleft may represent a perianal fissure through which foreign material or air from the colonoscopy procedure gained entry into the skin and led to the patient’s symptoms and histologic findings.
Full Field Optical Coherence Tomography (FFOCT): A Novel Tool for the Diagnosis of Cutaneous Proliferations

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Full field optical coherence tomography (FFOCT) is a novel imaging technique based on interferometry and microscopy principles that allows micron-level imaging of fresh tissue without any stain or preparation. Several studies have shown the use of this technology for the rapid diagnosis of cancer in human tissue, including the skin. One of the issues with FFOCT is the paucity of images available to train physicians how to diagnose using this modality. The goal of our study was to image common skin neoplasms and proliferations, both malignant and benign, in order to describe their appearance on FFOCT. Over 25 skin specimens were imaged following biopsy or excision. The average imaging time
was 2-3 minutes depending on the specimen size and the number of images acquired. There were 16 different diagnoses including basal cell carcinoma, apocrine hidrocystoma, intradermal nevus, sebaceous adenoma, and squamous cell carcinoma. The FFOCT images were examined by a dermatopathologist and a FFOCT expert, and the H&E images from the permanent sections were compared. Several features of each lesion/neoplasm were noted with the corresponding findings on H&E. FFOCT is a promising new imaging modality that allows rapid histologic diagnosis of skin neoplasms in minutes without any processing or staining. Our study identified several common neoplasms/proliferations and their features on FFOCT. This information and sample images will prove to be useful in the training of future interpreters of FFOCT images.

652
Human Papilloma Virus Genotypes Associated with Conjunctival Papillomas, Dysplasia, and Carcinoma
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Human Papillomavirus (HPV) is a causative agent for intraepithelial squamous neoplasms, particularly on mucosal surfaces. It has a well-established association with squamous cell carcinoma (SCC) of the oropharynx and genital tract, which has raised the question of what role HPV has in SCC of other locations. Recently, researchers have begun to explore HPV in ocular and periocular squamous neoplasms. Although ultraviolet light is reported as an etiologic factor for ocular surface neoplasia, studies suggest HPV may play a significant role, particularly in the development of conjunctival and eyelid papillomas, dysplasia, carcinomas and pterygia. Furthermore, there are multiple HPV genotypes that can incite histologically similar squamous neoplasms, and some specific HPV genotypes that have been differentially associated with either high or low-grade lesions. Our study screens lesions with p16 immunohistochemistry, the most common marker for high risk HPV infection, to compare expression in conjunctival papillomas (n=9), versus SCC in situ and invasive SCC (n=10). Squamous papillomas show no or patchy expression of p16 (8 of 9 cases), with rare solid and diffuse p16 positivity (1 case). In comparison, in situ and invasive squamous lesions showed block positivity in 3 of 10 cases. Since p16 highlights a subset of high-risk HPV lesions and is not consistently expressed in squamous lesions of the conjunctiva, further molecular classification of these proliferations is performed using HPV PCR to test for 14 of the most common HPV genotypes. To the best of our knowledge, this is the first study to compare squamous papillomas against SCC and precursor lesions.

WITHDRAWN
Langerhans Cell Sarcoma of the Chin
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Langerhans cell sarcoma is a malignant neoplasm composed of cells differentiated into the histiocytic spectrum. Langerhans cell sarcoma (LCS) is a rare malignancy with a poor prognosis that may arise in any organ system, but most commonly presents in the skin. We report here a 41 year old man who presents with a solitary chin lesion. A punch biopsy of the lesion shows epidermal changes, including parakeratosis and acanthosis overlying a poorly circumscribed dermal lesion comprised of large, atypical epithelioid cells. These cells show no coherent architecture. They are discohesive with marked pleomorphism. The cells demonstrate variably abundant eosinophilic to amphiphilic granular cytoplasm. Nuclear atypia is marked by irregular nuclear borders, fine to coarse chromatin, and prominent nucleoli. The cells are notable for occasional nuclear clefting. Bi-nucleation and nuclear inclusions are common, as are mitoses. There is marked comedo-type necrosis with neutrophilic inflammatory infiltrate. The proliferation is confined to the dermis and shows infiltrative boarders. Immunohistochemical interrogation of the lesional cells shows reactivity to antibodies to CD1a, S100, and Langerin as well as CD68 and CD163. These cytological and molecular features are consistent with Langerhans cell sarcoma. This rare entity has a shown itself to carry a poor prognosis and as such treatment has not yet been standardized, though multi-modality therapy of surgery and chemoradiation shows promise. Prognostic factors include single site vs. local vs. disseminated, with single site lesions having the most favorable prognosis.

Primary Cutaneous Interdigitating Dendritic Cell Sarcoma of the Ear: A Case Report
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Primary cutaneous interdigitating dendritic cell sarcoma (IDCS) is an exceedingly rare neoplasm with only ten reported cases. Morphologically, cells resemble antigen presenting dendritic cells and exhibit spindled and ovoid forms. Although nodal and internal organ IDCS often exhibit aggressive behavior, primary cutaneous IDCS largely responds well to local excision. We present a 55-year-old previously healthy male who developed a mass on the ear. Excisional biopsy revealed a multinodular infiltrate within the dermis comprised of pleomorphic epithelioid and spindled cells with background population of small lymphocytes. Neoplastic cells exhibited nuclear hyperchromasia and enlargement with several bi- and multinucleated forms. Immunohistochemical studies revealed at least scattered positivity for
CD63, lysozyme, CD68, CD163, and S100. Staining for pan-cytokeratin, langerin, CD1a, CD21, CD23, CD30, melan-A, and HMB-45 was negative within neoplastic cells. Background lymphocytes were highlighted by CD3 and CD4. A diagnosis of primary cutaneous IDCs was rendered and the patient is currently alive and well without evidence of disease.

656
Going Beyond the Pallor: Rarely Described Histologic Variants Seen in Nutritional Deficiencies
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Fairly specific histologic features such as upper epidermal pallor and necrotic keratinocytes are characteristic of nutritional deficiencies. When these features are not present, it is maybe difficult to make a definitive diagnosis. We report a case series of pellagra and acquired acrodermatitis enteropathica with rare histologic features. A 17-year-old female with a history of anorexia nervosa presented with a rash for 3 weeks. The rash started on her feet, evolved to the creases of her elbows, her hands, forearms and neck. The clinical differential was pellagra and lupus. A biopsy of the ankle was performed and showed mild interface and superficial and deep perivascular dermatitis. The initial histologic impression was lupus. While serology for lupus was pending, patient was started on niacin tablets, which resolved her symptoms. The second case is of a 5-month-old male infant who presented with a crusted eruption on the thighs that spread to posterior legs, back and neck. A left back skin biopsy was performed that showed subacute spongiotic dermatitis with eosinophils. The initial histologic impression was allergic/contact and atopic dermatitis. Laboratory workup was significant for low zinc level of 17 mcg/dL and testing of mother’s breast milk showed undetectable zinc levels. Patient was prescribed zinc sulfate, and the rash resolved. Our cases demonstrate that nutritional deficiency cases can present with non-classic histology. If metabolic disorder is in the differential, it is important for pathologists to be aware of these rare histopathologic variants.

657
Pilar Cyst Contents Mimicking Gout
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Skin tophi associated with gout are the result of soft tissue accumulation of uric acid crystals in patients with long standing hyperuricemia. Tophi usually develop several years after the onset of gout and are commonly found around the elbows, hands, and feet. Small sinus tracts sometimes drain white pasty tophus material. Microscopic examination of tophi after formalin fixation and staining with hematoxylin and eosin typically demonstrates accumulation of a pink or blue amorphous matrix with feathery edges, surrounded by foreign body giant cells. The matrix sometimes contains needle shaped empty spaces. These histologic features represent crystal deposits dissolved during fixation and tissue processing and are often diagnostic of gout. The histologic differential diagnosis includes deposition of calcium pyrophosphate crystals (pseudogout) and tumoral calcinosis. We present a case with of a 73 year old patient presenting with a subcutaneous nodule over his left shoulder that intermittently drains to the surface. Histologic sections show dermal accumulation of pink amorphous material containing needle shaped clefts and surrounded by foreign body giant cells. Focal calcification was seen in the dermis.
adjacent to the amorphous material. The histologic features are identical to those seen in gout; however, the unusual location and lack of a history of elevated uric acid levels raised suspicion for an alternative process. Further microscopic evaluation revealed a small adjacent portion of pilar cyst lining. The accumulated material stained with a cytokeratin AE1/AE3 proving its derivation from cyst keratin. Calcium stains were negative ruling out pseudogout and tumoral calcinosis. To our knowledge this is the first report of a ruptured pilar cyst content mimicking a gouty tophus. We conclude that it is important to consider the possibility of a ruptured keratin containing cyst in the evaluation of a lesion resembling gout, especially if the clinical setting is not typical.

658
Dermatitis Artefacta with Multinucleated Keratinocytes
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Dermatitis artefacta is characterized by factitious self-injury. The clinical findings are typically of ulcers or plaques in unusual geometric patterns or shapes that may correlate with shape of a the injurious agent. A given patient, most commonly female, often presents with clinical lesions that are simultaneously seen in different stages of evolution and are distributed in areas manually accessible by the patient. Self-inflicted dermatological artefacts may pose a diagnostic challenge especially if they resemble a known dermatologic condition. The histologic features of dermatitis artefacta are not specific and may take the form of burn, ulcer, infection, inflammation, foreign body reaction or others. We describe a case of dermatitis artefacta in a 13 year old female who presented with oval well-demarcated slightly raised pink lesions confined to her abdomen. Some lesions appeared more recent than others. Clinically, the pattern of the lesions were highly suspicious of dermatitis artefacta; however, the patient denied self-inflicted injury, and a biopsy was obtained. The most striking histologic feature was the presence of numerous epithelial multinucleated keratinocytes. The biopsy also showed mild lichenoid inflammation, eosinophils and occasional necrotic keratinocytes. The histologic features did not fit a known clinical or pathological entity, however, herpetic infection, drug reaction and reactive/reactive keratinocytes were considered. The patient presented a month later with no improvement and a second biopsy was obtained. The second biopsy showed identical changes to those seen in the first biopsy with more prominent superficial epidermal necrosis suggesting an exogenous etiology, and prominently multinucleated keratinocytes (up to 62 nuclei per keratinocyte). A herpetic immunostain was negative. Recent reports described similar findings of multinucleated keratinocytes in patients with dermatitis artefacta. Given the compelling clinical presentation, we believe that the finding of multinucleated keratinocytes in our case further supports this being a characteristic change seen in some instances of dermatitis artefacta.

659
Calciphylaxis with Pseudoxanthoma Elasticum-like Changes: A Case Series and Proposed Pathogenesis
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Calciphylaxis and pseudoxanthoma elasticum (PXE) are rare, clinically distinct, disorders that share a common feature of cutaneous calcification that varies widely in their cutaneous presentation.
Calciphylaxis is a form of metastatic calcification resulting from systemic impairment of calcium regulatory systems. Histopathologically, it manifests as calcium deposition in small- and medium-sized blood vessels with subsequent vascular occlusion and ischemic necrosis. It occurs most commonly in patients with end stage renal disease (ESRD) or hyperparathyroidism, and often results in fatal outcomes secondary to gangrene or sepsis. PXE is a genetic, autosomal recessive, disorder causing abnormal calcification of elastic fibers in the skin, eyes, and cardiovascular system that clinically manifests as yellowish papules and redundant folds in flexural skin, angiod streaks of the retina, and cardiovascular claudication and infarctions. An intradermal PXE-like histopathologic pattern has been described in association with various autoimmune and metabolic disorders, including 3 case reports of calciphylaxis. We reviewed 10 biopsy specimens from 7 patients with known histologic evidence of calciphylaxis. Upon reexamination, we found that half of the specimens demonstrated concomitant PXE-like changes uniquely localized to the subcutaneous fat. The clinical and histological features of these patients are reviewed, and we propose a mechanism by which the pathogenesis of calciphylaxis may induce PXE-like changes in the deep reticular dermis.

660
The Itchy Monkey: Using Dermatopathology to Promote One Health
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The One Health concept, as promoted by the CDC, “recognizes that the health of humans is connected to the health of animals and the environment” and emphasizes the importance of recognizing that humans are integrated into a larger world concept. Many diseases are known to cross species boundaries, and by learning how these diseases affect both humans and animals through a multidisciplinary approach, we can provide better care for all living things. We present a case of Amigo, an adult squirrel monkey, who has a history of chronic alopecia and pruritus. Although dogs, cats, and other domesticated animals are commonly evaluated and treated by veterinary dermatologists, the approach to non-human primates often requires an integrated approach by both human and veterinary dermatologists to bridge an informational gap. Our squirrel monkey presented with extensive pruritus and subsequent alopecia, dyspigmentation, and lichenification. Histopathology demonstrated acanthosis, spongiosis, mild hyperkeratosis, a perivascular infiltrate composed predominantly of mast cells. Interestingly, the dermis was thin and also contained numerous dermal melanocytes. Also, there was a complete absence of eosinophils on non-human primate pathology with an abundance of mast cells. This case highlighted both similarities and differences that exist between human and non-human primate skin and ultimately led to the diagnosis of severe eczematous dermatitis. The unique histopathologic features in combination with knowledge of human histopathology and veterinary literature and expertise allowed for initiation of a treatment plan. We present this case of Amigo, a squirrel monkey, as an example of the One Health concept and provide additional examples of the histopathology of non-human skin as a comparison. In extending our knowledge of histopathology and pathogenesis of diseases outside of the human species, we can continue to learn and advance the healthcare of all.
Nail Lacquer: A Common Artifact That May Go Unrecognized
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Nail specimens are being submitted for histopathologic evaluation with increasing frequency to confirm a diagnosis of onychomycosis, diagnose an inflammatory dermatosis, or identify clues to an underlying neoplasm. Nail samples may be associated with a variety of decorative lacquers (i.e. polish, gel) that may vary in their appearance. Some lacquers may add challenges to maintaining an even plane of sectioning, obscure underlying findings, or separate from the nail in processing and be misinterpreted as terra firma. We review common lacquers and their histologic appearance and describe a distinct three-layer pattern associated with gel polish so that dermatopathologists can recognize these different presentations in clinical practice.

Massive Localized Lymphedema: A Pseudosarcomatous Finding in Morbidly Obese Patients
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A 61 year old morbidly obese male presented to the plastic surgery clinic with a four year history of slowly enlarging, asymptomatic, right thigh mass. CT imaging of the mass was initially read as “inflammation of the fat and skin causing enlargement, adiposis dolorosa, or liposarcoma”. The mass was excised and submitted for histologic examination. The pathology showed papillomatosis and hyperkeratosis overlying an edematous and fibrotic dermis with broad fibrous septate containing fibroblasts with hyperchromatic nuclei. These findings, in conjunction with the presence of lymphangiectasia, perivascular lymphocytes, and absence of MDM2 gene amplification by FISH was consistent with massive localized lymphedema (MLL). The etiology of MLL is not entirely clear but is most likely, at least partially due to lymphatic obstruction associated with morbid obesity. MLL presents as a progressively enlarging mass with overlying indurated peau d’orange skin, most commonly involving the thigh. Histologically there is alternating edema and fibrosis of the dermis, dilated lymphatics and small vessels surrounded by a lymphoid infiltrate, and expansion of the fibrous septae of subcutaneous fat with mildly atypical spindle cells that can mimic atypical lipomatous tumor/well-differentiated liposarcoma (ALT/WDLS). MLL, however, lacks the amplification of MDM2 seen in the later. Caution is required before diagnosing ALT/WDLS with overlying papillomatosis on the thigh of a morbidly obese patient.

Persistent Acantholytic Disorder with Lentigos: A Unique Presentation
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We present a case of a 37 year-old female with a 10-year history of pruritic skin lesions that began on her legs. The rash progressed to affect her arms, chest, and back over a period of three months with
Background: Cutaneous angiosarcoma has the propensity to arise in various clinical settings, including on the head and neck of the elderly, on the breast post-radiotherapy or lymphedema, and in the deep soft tissues of the lower extremities. The histologic findings are classically those of a highly infiltrative neoplasm forming irregular vascular channels which infiltrate through the cutaneous soft tissues (collagen, fat, etc.). A diagnostic clue that has been described in cases of post-irradiation angiosarcoma is that of free-floating or tufted pleomorphic spindle cells in the vascular lumen which have the appearance of “fish in the creek.” Our goal was to determine the frequency of this finding in cases of cutaneous angiosarcoma. Methods: 15 cases of cutaneous angiosarcoma were identified over a 20 year time period. 15 additional benign and malignant vascular tumors were also identified (Kaposi sarcoma, atypical vascular lesion, epithelioid hemangioma, etc.). Each case was examined for free-floating intraluminal spindle cells or cells which were tufting off the endothelium. Results: The histologic pattern of “fish in the creek” was identified in all 15 cases of cutaneous angiosarcoma and it was absent in all the other tumors. In our study, the finding was 100% sensitive and 100% specific for cutaneous angiosarcoma. Discussion: “Fish in the creek” is a useful and salient feature in cutaneous angiosarcoma. It goes without saying that this finding should not be the sole feature upon which a diagnosis of angiosarcoma is made as it requires corroboration with positivity of MYC, D2-40/podoplanin, and Ki-67 (>20%). However, finding “fish in the creek” should prompt a dermatopathologist to entertain the diagnosis of angiosarcoma in the appropriate clinical and histologic setting.
Case Report: Secondary Systemic Amyloidosis with Primary Cutaneous Involvement

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Background: Cutaneous amyloidoses are phenomena that represent either a localized or systemic processes causing dermal amyloid accumulation. Secondary systemic amyloidosis with cutaneous involvement is the rarest of these entities and is associated with chronic inflammatory conditions leading to the deposition of amyloid A (AA). Herein we present a case of secondary systemic amyloidosis with primary cutaneous involvement. Case Report: In February 2016, a 71 year old male presented with a painful, blistering nodule on the left fourth toe that slowly grew over the past 12 years. Past medical history was notable for a sudden onset of fatigue and arthralgias in June 2014. Laboratory studies at that time showed a weakly positive anti-nuclear antigen, at a titer of 1:320, with a homogenous pattern and an elevated erythrocyte sedimentation rate. Rheumatoid factor was negative. While these findings suggest a possible inflammatory/autoimmune process, follow-up studies were not obtained nor was a definitive diagnosis made after June 2014. The skin biopsy grossly showed a nodular, waxy lesion. On microscopy, mature adipose tissue was seen within the superficial dermis containing pale, eosinophilic deposits. These deposits were Thioflavin T immunofluorescence and Congo red positive, with apple-green birefringence. Immunohistochemical analyses were negative for κ and λ light chains and CK903. AA stain was weakly positive, suggestive of secondary systemic amyloidosis; however, systemic amyloidosis work-up was negative. Conclusion: This case represents a rare manifestation of cutaneous amyloidosis. The microscopic examination points to a secondary systemic cause, while the clinical work-up remains ambiguous.

A Giant Cell Poor Tenosynovial Giant Cell Tumor of the Tendon Sheath - A Diagnostic Pitfall

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Tenosynovial giant cell tumors are widely regarded as the prototypical tumor of the synovium. It’s location may include either intra or extra articular sites. Histologically, the broad categories include the localized (encapsulated) type or diffuse (infiltrative) type. In its most typical form, localized tenosynovial giant cell tumor of the tendon sheath consists of a somewhat circumscribed, firm lesion which is associated with a stalk adherent to the tendon sheath. Microscopic sections of classic cases demonstrate abundant osteoclast like giant cells admixed with collagen and histiocyte-like small cells. Highly cellular and recurrent lesions however, may demonstrate a lack of giant cells rendering the diagnosis of ‘Tenosynovial Giant Cell Tumor’ a challenging one. We herein present the case of a previously healthy 56 year old male who presented with a single nodule at the dorsal interphalangeal joint of the left index finger which had been present for over 10 years. Hematoxylin and eosin stained sections demonstrated an encapsulated and highly cellular lesion with extremely rare giant cells. The possibility of giant cell poor variant of tenosynovial giant cell tumor of the tendon sheath is one the pathologist must keep in mind while examining such lesions. This case is presented to raise awareness that while uncommonly encountered, tenosynovial giant cell tumors can have minimal giant cells.
Histopathology of Pemphigus Vegetans: A Case Showing Early and Late Lesions
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A 61-year-old woman reported to have a history of pemphigus vulgaris treated with cyclosporine presented for evaluation of worsening painful oral mucosa and vaginal lesions of two months duration. She had multiple crusted ulcers on the lips and oropharynx, with scattered erosions on the buccal mucosa and hard palate. She also had multiple large, violaceous, multilobular, friable nodules on her right labia majora and inguinal folds, and punctate erosions on labial mucosa and perianally. There were exudative erosions on her umbilicus with surrounding erythema and sub-millimeter blisters on the left upper groin and left axillary region. Punch biopsies of the left axilla, periumbilicus, and right groin were obtained. Histopathology of the left axilla showed an intraepidermal vesicle with minimal acantholysis, numerous eosinophils and some neutrophils, and dermal lymphocytes and eosinophils. Notably, epidermal hyperplasia was absent. Biopsy of the right inguinal fold revealed epidermal hyperplasia with focal acantholysis, intraepidermal eosinophilic pustules, neutrophils within the stratum corneum, and dermal lymphocytes with numerous eosinophils. Direct immunofluorescence of the periumbilical area demonstrated strong intercellular deposition of IgG and focal intercellular staining with C3. IgA and IgM were negative. Altogether, these findings were consistent with pemphigus. The eosinophilic microabscess formation, minimal acantholysis, and marked epidermal hyperplasia in the inguinal biopsy favored a vegetans subtype over pemphigus vulgaris. Pemphigus vegetans is a rare variant of pemphigus vulgaris characterized by vegetating plaques that primarily affect intertriginous areas. Mucosal lesions may also occur. Early lesions have less pronounced acanthosis, as observed in our patient’s axillary biopsy. This case demonstrates that eosinophilic pustules, minimal acantholysis, and limited hyperplasia are clues to early lesions of pemphigus vegetans.

A Mystery Case of Lafora Disease
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Background: Lafora is a fatal and degenerative autosomal recessive disorder with a gene locus recently mapped to chromosome 6q23-27. The disease usually presents at age 10-18 years and is characterized by the triad of seizures, myoclonus and dementia. Demonstration of the characteristic intracytoplasmic inclusions (Lafora bodies) in the presence of seizures, myoclonus and neurological disturbances reliably confirms the diagnosis. Although Lafora bodies are found in the brain, liver and muscle, the axillary skin is the most appropriate and accessible site for biopsy to observe the PAS and mucicarmine positive inclusions in the sweat gland ducts and lumens. Adjuvant to supportive measurements, efficacy for the AMPA antagonist perampanel has been shown for both myoclonus and to a lesser degree seizures. Case report: 18 years old male is presented with history of three years intractable seizures. The first seizure started with a rainbow in his left eye and evolved to a generalized epilepsy. EEG showed diffuse slowing with bifrontal bursts and brain CT/ MRI were normal. Diagnosis of Lafora disease was made by neurologist and the patient was referred to the dermatology clinic. Skin examination including both
axillae was normal. A punch biopsy from right axilla revealed typical PAS positive lafora bodies found in the cells of the ductal and luminal epithelium of apocrine/ eccrine glands. Conclusion: Lafora disease can easily be diagnosed by a simple punch biopsy of the skin such as axillae where sweat glands are numerous. The purpose of this presentation is to emphasize the usefulness of axillary skin biopsy as a convenient method for reach the specific diagnosis. Genetic counseling and DNA sequencing in patients with this rare and fatal neurologic disease is also necessary.

669

Hematoxylin and Eosin Slides versus Digital Imaging: A Cost-Benefit Analysis in the Department of Dermatopathology at UAB
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With the rapid advancement in automation, digital image processing and analysis are becoming increasingly common. In a cost-benefit breakdown, digital slide acquisition at an outside private company costs approximately $4.00 more per case than an H&E slide created in house. However, when looking at the functional life (slide fading, breaking and cover slip bubbling), the digital slide lasts a lifetime as oppose to 2-3 years for an H&E slide. At our institution, Dermatopathology averages 1000 recuts per year with close to 90% of those being repeated for diagnostic purposes. In the last 3 years, the H&E recuts for diagnostic and teaching purposes was estimated to be $18,000 for 260 new diagnoses. That is calculated to be approximately $69.23 per new diagnostic case. Additionally, we found that during teaching sessions resident requests to compare slides, when slides were not pulled, took approximately 3 minutes per case versus a virtual slide, which took approximately 5 seconds per case. This included search time, pulling time and re-filing time. Conceptually for 20 slides, that accounts for roughly 1 hour of productivity lost in a workday for both faculty and residents. These findings support the value of virtual imaging over H&E slides, for diagnostic and teaching purposes, with respect to long-term cost benefit, productivity, and teaching.

670

Penile Myointimoma Diagnosed by Skin Biopsy in an 11 Year-Old Male
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Penile Myointimoma is an extremely rare, benign, myointimal proliferation arising within the corpus spongiosum of the glans penis. These tumors often show plexiform or multinodular growth and may traverse several tissue planes simultaneously and are often associated with blood vessels of the corpus spongiosum. An 11-year-old male presented with a slightly painful, firm, indurated, papule measuring 7.6mm at the base of the glans penis. A course of antibiotics was completed with no response followed by a course of topical steroids with persistence of the lesion. An excisional biopsy was performed and examination of the histologic sections revealed a spindle cell proliferation with complex plexiform architecture involving the small vessels of the glans penis and extension to the tissue margins. The
Darier disease is an uncommon autosomal dominant genodermatosis. Mosaic forms comprise approximately 10% of cases and manifest in a linear distribution along Blaschko’s lines. A 60-year-old man presented with an intensely pruritic, red rash that was recurrent over almost 20 years. The rash was localized to the right extremities and torso. Topical clobetasol improved the pruritus. Oral prednisone resolved the rash entirely although there was recurrence upon discontinuation. On clinical examination, there were red hyperkeratotic papules in a Blaschkoid distribution along the right back, right arm, and right leg. Histopathologic evaluation of a punch biopsy revealed hyperkeratosis and acantholytic dyskeratosis with corps ronds. The clinical findings, distribution, and histopathology were most consistent with segmental Darier disease. As a trial, two different treatments were elected for the rash at the leg (tretinoin 0.1% cream topical b.i.d.) and arm (diclofenac sodium 1% gel topical b.i.d.). Both therapies were equally efficacious in resolving the lesions completely after a few weeks of treatment. Darier disease is characterized by pruritic, reddish-brown, scaly papules in a seborrheic distribution. Mutations in the ATP2A2 gene disrupt calcium signaling, resulting in loss of adhesion between keratinocytes and abnormal keratinization. Post-zygotic ATP2A2 mutations in embryogenesis account for unilateral linear/segmental Darier disease following Blaschko’s lines of cell migration. Less than 70 cases of segmental Darier disease have been described in the literature, usually in the third or fourth decades of life. Unlike in generalized disease, mucosal and nail involvement is uncommon in segmental Darier disease. The distinctive histologic pattern of acantholytic dyskeratosis with corps ronds and grains is identical between generalized and localized forms. Clinicians should consider Darier disease in evaluation of patients with recurrent scaly papules in a Blaschkoid distribution with acantholytic dyskeratosis pattern observed on histology. No cases have reported segmental Darier disease producing offspring with generalized Darier disease; however, genetic counseling may be appropriate.
Diffuse Dermal Angiomatosis with Solitary Bulla Formation in the Setting of Trauma and Lymphedema
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Diffuse dermal angiomatosis (DDA) is a variant of reactive angioendotheliomatosis that presents in patients with multiple comorbidities. Herein, we present a case of a 63-year-old female with a recent metatarsal fracture and surgical fixation, renal insufficiency, diabetes mellitus (DM), diabetic retinopathy, and hypertension (HTN) that presented to The University of Alabama at Birmingham’s immunobullous clinic for evaluation. On physical exam she had a large erythematous pink to red indurated plaque on her anterior thigh and a history of a coin shaped ruptured solitary bulla at that site a year prior. Excisional biopsy revealed a bland endothelial proliferation dissecting between collagen bundles. The endothelial cells were positive for CD31, CD34, and D2-40; and negative for HHV-8. Numerous dilated lymphatics were identified in the superficial to mid dermis with overlying extensive acanthosis. We postulate that in addition to her multiple comorbidities, her ankle fracture with surgical fixation caused vascular and/or lymphatic damage with lymphedema leading to hypoxic injury and a reactive DDA.

Efficacy of Triaging Direct Immunofluorescence in Intraepidermal Bullous Dermatoses
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Background: Direct Immunofluorescence (DIF) is considered pivotal in the diagnosis of autoimmune blistering diseases, yet biopsies frequently show negative/nonspecific findings. Our goal was to examine the efficacy of triaging cases submitted for DIF in intraepidermal bullous cases, with pemphigus vulgaris (PV) as the prototype. Methods: 62 cases from 2010-2014 submitted for DIF with an intraepidermal blistering disease listed in the differential diagnosis were reviewed by two board certified dermatopathologists to see if they would order DIF based on routine histologic findings. If either dermatopathologist requested DIF on a case it was considered “required” (94% intraobserver concordance). Results: DIF was "required" in 29% (18/62) (94% intraobserver concordance) and was positive in 17% (3/18) of those "required," leading to a diagnosis of PV (2/3) or pemphigus foliaceus (PF, 1/3). DIF was "not required" in 71% (44/62). 34/44 of these had negative/nonspecific DIF findings (77%). Of the 10 DIF+ cases, 8 were accurately diagnosed as PV based solely on the H&E findings. 3 of 44 "not required" cases were misdiagnosed. Two (2/10 DIF+) were called "spongiotic dermatitis" by H&E interpretation, yet had DIF consistent with PF. One case of acantholytic pityriasis rubra pilaris was diagnosed as pemphigus vulgaris on H&E, an error that may have been avoided with real-time clinical correlation. Conclusions: H&E diagnosis alone was 80% sensitive and 97% specific for intraepidermal blistering diseases. The positive predictive value was 89% while the negative predictive value was 94%. H&E triaging could potentially reduce DIF usage by 71%. Our data suggest that if PV is in the differential diagnosis, H&E may be sufficient to render an accurate diagnosis. In contrast, if PF is in the differential diagnosis, DIF may be necessary. Triaging by H&E can obviate the need for DIF in a significant proportion of cases, resulting in increased efficiency of work and significant cost reduction.
Myxofibrosarcoma of Unusual Sites
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Background: Myxofibrosarcoma (MFS), the most common sarcoma in elderly patients, classically presents as a subcutaneous/dermal mass in the proximal extremities (especially the thigh) or trunk. Presentation in unusual locations is a source of diagnostic difficulty. We present 5 cases of MFS that presented on the head and hands/feet. Methods: Pathology archives (2009-2015) were searched, and clinicopathologic features of MFS were recorded. Cases in unusual locations were retrieved. Results: Of 94 cases diagnosed over the time period, 5 patients (2M:3F) ranging in age from 70-92 years (median 87 y, compared to 69 y in common sites) were identified with MFS arising in the head (n=3, M:F 2:1), hand (n=1, F), and foot (n=1, F). Each had typical features of MFS: nodules of elongated, spindle- to stellate-shaped cells with eosinophilic cytoplasm in a prominent myxoid stroma associated with curvilinear blood vessels. By FNCLCC grading system, 4 were grade 2/3 (2 head, 1 foot, 1 hand) and one grade 3/3 (head). The patient with the grade 3 scalp mass had an initial superficial shave biopsy interpreted as a pleomorphic spindle cell neoplasm worrisome for atypical fibroxanthoma vs. pleomorphic dermal sarcoma. Subsequent re-excision demonstrated typical MFS histology. An attempt to get negative margins by Mohs micrographic surgery was unsuccessful due to the myxoid nature of the neoplasm. This patient was admitted to hospice care secondary to extensive dissemination of her MFS. Follow-up information was available in two other patients. The patient with MFS of the hand experienced local recurrence but subsequently died from an unrelated malignancy. The patient with MFS of the foot has been disease free since amputation. Conclusions: MFS is an aggressive sarcoma that can present outside the stereotypical location and can be confused with other myxoid lesions such as myxoid variant of atypical fibroxanthoma. Careful attention to histologic features and adequate sampling is critical for the diagnosis.

Sebaceous Carcinoma in Situ Masquerading as Paget’s Disease of the Breast
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Sebaceous carcinoma in situ (intraepithelial sebaceous carcinoma) is a poorly understood and ill-defined entity. Its' distribution is similar to its invasive counterpart in that most cases are found in a periorbital location. Review of the literature found 7 cases of extraocular sebaceous carcinoma in situ. Of those 7 cases, all but one were located in the head and neck region; the other was found on the arm. We present a unique and challenging case of sebaceous carcinoma in situ masquerading both clinically and histologically as Paget’s disease of the breast. A 61-year-old female presented to her dermatologist complaining of a 6 mm erythematous waxy papule on her medial right breast. The patient’s past medical history was significant for Muir-Torre syndrome. Clinically, the differential diagnosis included Paget’s disease of the breast, squamous cell carcinoma, and sebaceous carcinoma. A shave biopsy revealed an atypical proliferation of large single cells limited to the epidermis infiltrating in a pagetoid pattern, as well as cohesive nests of round neoplastic cells with mild nuclear atypia, prominent nucleoli, and vacuolated cytoplasm. Histologically, the differential diagnosis included Paget’s disease of the breast,
squamous cell carcinoma in situ, melanoma in situ, and sebaceous carcinoma in situ. A battery of immunohistochemical stains was performed and the lesional cells were positive for adipophilin, factor XIIIa, CK7, and EMA and were negative for CAM5.2, CK20, and MART-1 supporting a diagnosis of sebaceous carcinoma in situ. Multiple deeper sections were examined and invasion beyond the epidermis was not identified. This case adds to the paucity of information available regarding extraocular sebaceous carcinoma in situ and warns clinicians of this potential diagnostic pitfall especially in patients with Muir-Torre syndrome.

676

677
Granulomatous Reaction to Aluminum after Anthrax Vaccination
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A 27 year old African American active duty military female presented with persistent pruritic nodules on the bilateral upper extremities. Intralesional steroids failed to improve the nodules in the past. An excisional biopsy showed a patchy lymphohistiocytic inflammatory cell infiltrate with several collections of granular histiocytes within the septa of the subcutaneous fat. The granules within the macrophages
were dusty grey-brown and of distinct tinctorial quality. The granules stained positively with PAS, but did not stain with Fontana-Masson and were not removed in a melanin-bleach-stained section. Scanning electron microscopy with energy dispersive x-ray analysis of the tissue revealed the granules within the histiocytes to contain aluminum. Chart review revealed the patient had a total of nine anthrax vaccinations in the bilateral upper arms over the past 5 years. Anthrax vaccinations are well-known to contain high levels of aluminum formulated as 1.2 mg/mL aluminum, added as aluminum hydroxide in 0.85% sodium chloride. The pruritic nodules were surgically excised and had not recurred at a 6 month follow-up visit. Aluminum is widely used as an adjuvant to vaccinations to improve the immunologic response to the vaccine. However, it is well-known to cause granulomatous reactions at the site of vaccination. This has been previously well-documented, but to our knowledge, this is the first case report demonstrating the unique histopathologic findings seen specifically from anthrax vaccination.

678

Perforating Gout with Pseudoepitheliomatous Hyperplasia: A Rare Mimicker of Squamous Cell Carcinoma of the Helix of the Ear

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Gouty tophi are deposits of monosodium urate crystals in dermal and/or subcutaneous tissue and are a cutaneous manifestation of gout. They typically appear around the elbow, appendicular and acral joints and less commonly, helix of the ear, finger pads, nose, eyes and breast. Clinically gout presents as single or multiple irregular, firm, painful skin nodules containing chalky white material. The overlying skin may be skin-colored, erythematous, or ulcerated. Perforating gout as a result of transepithelial elimination of the urate crystals is rarely seen. Here we present a 71-year-old man with a history of type II diabetes, chronic kidney disease stage IIIA, basal cell carcinoma, squamous cell carcinoma, and sebaceous adenoma who presented with a rapidly growing 1.2 cm pink-tan firm nodule on the right ear. The clinical differential diagnosis included verruca vulgaris and squamous cell carcinoma. A deep shave biopsy showed dermal deposition of pale amorphous material (as a result of dissolved crystals) consistent with gout with overlying perforation and marked reactive epidermal hyperplasia. Uric acid level was found to be elevated at 8.5 mg/dL. Histopathologically, urate crystal deposits are characteristically surrounded by lymphohistiocytic or granulomatous inflammation with abundant foreign body giant cells. Fibrosis and calcification are occasionally present. Gout has been reported to be associated with pseudoepitheliomatous hyperplasia which can clinically mimic a number of other dermatologic conditions, including chronic ulcer/wound, cyst, chondrodermatitis nodularis helicis, rheumatoid nodule, verruca vulgaris, and squamous cell carcinoma. Presence of pink or white amorphous material adjacent to the epithelial proliferation is key to the correct diagnosis and superficial biopsy may not be adequate. This case demonstrates that, while rare, gout with perforation and pseudoepitheliomatous hyperplasia may occur and mimic a squamous cell carcinoma.
Dermoscopic Evaluation and its Correlation with Histopathology in Vitiligo: A Study of 60 Cases

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Vitiligo manifests clinically by the presence of depigmented macules. The diagnosis and categorization of these cases into stable and unstable vitiligo can be quite challenging as there are no standard criteria. However, this distinction is of great clinical relevance as decision regarding surgery or medical treatment is based on this. The role of dermoscopy in this area and its correlation with histopathology has not been studied in great detail as there are only a few studies. In the present study patients presenting in our institution with features of vitiligo were included. Based on clinical criteria they were divided into two groups of stable (n=30) and unstable vitiligo (n=30). Dermoscopic evaluation was done in all these cases. The findings thus obtained were then correlated with histopathology. It was observed that there is an overlap in dermoscopic findings in the two groups. However, certain features were found to be significantly more common in one group as compared to the other. Thus, sharp border, sharply defined perifollicular pigmentation and reticular pattern within vitiligo macule were significantly associated with stable vitiligo. Whereas, perilesional hypopigmentation, pseudopodia, comet tail phenomenon and nebular pattern were observed in unstable vitiligo. On correlating the dermoscopic findings with histopathological features it was seen that there was presence of spongiosis, basal cell vacuolation, epidermal and dermal lymphocytic infiltrate in the unstable group. While, these features were absent in stable vitiligo. Thus to conclude a combined dermoscopic-histopathologic approach may be employed for optimum diagnosis and management of these cases.

Integrating Facebook into Dermatopathology Education: Our Experience in a Pathology Residency Program

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The last few decades have witnessed the tremendous evolvement of information and communication technologies. Most of today’s residents are part of the Net Generation, having an earlier and more intense exposure to digital technologies, particularly social media, and use them more frequently and increasingly in daily life. Facebook (FB) is the most popular social media site; its vogue offers the opportunity for the resident to be highly engaged with educational content outside formal rotations, particularly in their fragmented time. The pathology residency program at our hospital has twelve residents totally (three residents in each academic year). The residents’ training of dermatopathology is limited and late in their training – there is only one month of required rotation in the third year of the residency. It has been found that the junior residents have more challenges in studying unknown dermatopathology conference cases. To increase residents’ exposure to dermatopathology as a supplement to the curriculum, a faculty-administrated invitation-only FB group was created including 10 out of 12 residents. A dermatopathologist posts histology images of high-yield cases with brief clinical information from his daily sign-out. Initially, the cases were posted as “spot diagnosis” challenges. The residents were enthusiastic about the novel education approach and actively participated in discussion. The average response to the posts was between 80 to 100%. The enthusiasm gradually waned over the time. An informal survey found that it was mostly because of the significant effort and time needed to
render the diagnoses of challenging cases and the concern of embarrassment for wrong questions. A change in the group was made to address this issue. The diagnoses are provided to the residents when new cases are posted. The interest level of resident has rebounded in this ongoing educational social media effort.

681

Intravascular Faciitis: A Case Report of an Unusual Variant of Nodular Fasciitis

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Nodular fasciitis is a reactive soft tissue lesion that is commonly misdiagnosed as sarcoma due to the extremely rapid growth and high mitotic activity. There are four major variants of nodular fasciitis based on the lesion location which include: ossifying fasciitis, intramuscular fasciitis, cranial fasciitis and intravascular fasciitis. Intravascular fasciitis is a relatively uncommon variant, which is typically seen in the first three decades of life and is slightly more common in male. We, herein, report a case of a 17-year-old male, who presented with a left forehead mobile mass (less than 1 cm in size) after being hit in a fight 5 months prior. Microscopic examination demonstrated a benign reactive spindle cell proliferation of undulating bundles of loosely arranged spindle cells involving the vessel wall. Immunohistochemistry stains revealed lesional cells with SMA Immunopositivity but negative for CD34, Factor XIIIa and S100. The trichrome stain highlighted the outlines of the vessel wall and the colloidal iron revealed stromal mucin deposition. In summary, this case illustrates a relative uncommon variant of nodular fasciitis, namely, intravascular fasciits.