2014 Slide Library

Case Summary Questions
&
Answers with Discussions

51st Annual Meeting
November 6-9, 2014
Chicago Hilton & Towers
Chicago, Illinois
November 2014

Dear Fellows of the American Society of Dermatopathology,

The American Society of Dermatopathology would like to invite you to submit slides to the Reference Slide Library. At this time there are over 9300 slides in the library. The collection grew 2% over the past year. This collection continues to grow from member’s generous contributions over the years. The slides are appreciated and are here for you to view at the Sally Balin Medical Center. Below are the directions for submission.

Submission requirements for the American Society of Dermatopathology Reference Slide Library:

1. One H & E slide for each case (if available)
2. Site of biopsy
3. Pathologic diagnosis

Not required, but additional information to include:

1. Microscopic description of the slide illustrating the salient diagnostic points
2. Clinical history and pertinent laboratory data, if known
3. Specific stain, if helpful
4. Clinical photograph
5. Additional note, reference or comment of teaching value

Teaching sets or collections of conditions are especially useful. In addition, infrequently seen conditions are continually desired. Even a single case is helpful. Usually, the written submission requirement can be fulfilled by enclosing a copy of the pathology report prepared for diagnosis of the submitted case. As a guideline, please contribute conditions seen with a frequency of less than 1 in 100 specimens. Contributions should be sent to our facility at:

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ASDP Reference Slide Library Collection
The Sally Balin Medical Center
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Media, PA 19063
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COURSE OBJECTIVES

Upon completion of this course, participants should be able to:

- Explain the histologic diagnosis of various skin conditions, including the use of ancillary studies, where appropriate.
- Interpret the histologic diagnosis of uncommon skin diseases.
- Critique cases that highlight diagnostic challenges.
- Apply morphological criteria to the differential diagnosis of cutaneous lesions.
- Describe soft tissue tumors.
- Identify scenarios presented for diagnosis.

View the 2014 and 2013 Slide Library online at www.asdp.org.
CASE SUMMARIES
CASE #1 -- SLIDE #1
A 26 year-old woman presents with a painless nodule of the lateral abdomen. Clinically, a lipoma or Fibrolipoma was suspected. An excisional biopsy was performed. The best diagnosis is:

A. Dermatofibroma
B. Dermatofibrosarcoma protuberans
C. Leiomyoma
D. Solitary fibrous tumor
E. Schwannoma

CASE #2 -- SLIDE #2
A 25 year-old woman presents with a periumbilical painful nodule. The best diagnosis is:

A. Metastatic Melanoma
B. Epithelioid sarcoma
C. Metastatic adenocarcinoma (Sister Joseph’s Nodule)
D. Endometriosis
E. Adenosarcoma

CASE #3 -- SLIDE #3
An otherwise healthy appearing 56 year-old man presents with a painless nodule of the left neck. The best diagnosis is:

A. Cylindroma
B. Adenoid basal cell carcinoma
C. Metastatic salivary gland carcinoma (adenoid cystic type)
D. Primary cutaneous adenoid cystic carcinoma
E. Primary cutaneous cribriform carcinoma

CASE #4 -- SLIDE #4
A 25 year-old HIV-positive man presents with a painless nodule in his right nasolabial fold. The best diagnosis is:

A. Keratin granuloma
B. Foreign body giant cell reaction to Artecoll
C. Foreign body giant cell reaction to Dermalive
D. Foreign body giant cell reaction to Sculptra
E. Foreign body giant cell reaction to silica
CASE #5 -- SLIDE #5
59 year-old woman with yellow-brown plaques on the neck, chest and arms. The best diagnosis is:

A. Annular elastolytic granuloma
B. Granuloma annulare
C. Necrobiotic xanthogranuloma
D. Rheumatoid nodule
E. Sarcoidosis

CASE #6 -- SLIDE #6
40 year-old woman with arthralgias and a pruritic rash of 6 months duration involving the back. The clinical impression of her primary care physician was chronic urticaria. The best histopathologic diagnosis is

A. Erythema annulare centrifugum
B. Erythema chronicum migrans
C. Granuloma annulare
D. Lupus erythematosus
E. Secondary syphilis

CASE #7 -- SLIDE #7
71 year-old woman with a pink well-demarcated plaque on the buttock. She experienced an identical rash on precisely the same anatomic site 6 times over the past 3 years. Naproxen sodium had been taken several hours before the onset of eruption. The best diagnosis is:

A. Alpha-1 antitrypsin deficiency
B. Henoch-Schonlein purpura
C. Linear IgA dermatosis, drug-induced
D. Neutrophilic fixed drug eruption
E. Pressure urticaria

CASE #8 -- SLIDE #8
80 year-old man purplish-re macules and papules on the chest and abdomen. The best diagnosis is:

A. Epithelioid hemangioma
B. Hobnail hemangioma
C. Inflammatory breast carcinoma
D. Microvenular hemangioma
E. Reactive angioendotheliomatosis
CASE #9 -- SLIDE #9
A 65 year-old woman with a 3 month history of a single lesion on the thigh. The clinician described a central black papule surrounded by a 2cm purpuric patch. The best diagnosis is:

A. Acquired progressive lymphangioma
B. Angiosarcoma
C. Kaposi’s sarcoma
D. Retiform hemangioendothelioma
E. Targetoid hemosiderotic hemangioma

CASE #10 -- SLIDE #10
This nodule was removed from the flank of a 54 year-old male. The best diagnosis is:

A. Spindle cell lipoma
B. Metaplastic synovial cyst
C. Solitary fibrous tumor
D. Rudimentary meningocele
E. Fibrous hamartoma

CASE #11 -- SLIDE #11
Submitted as a mass from the chest of a 70 year-old male. The best diagnosis is:

A. Spindle cell lipoma
B. Solitary fibrous tumor
C. Fibrous hamartoma
D. Elastofibroma dorsi
E. Metaplastic synovial cyst

CASE #12 -- SLIDE #12
A 39 year-old pregnant female presented with a 6-week history of erosive papules and plaques on the perineum and oral mucosa. The best diagnosis is:

A. Papular acantholytic dyskeratosis of the vulva
B. Pemphigus vegetans
C. Pemphigoid gestationis
D. Paraneoplastic pemphigus
E. Contact dermatitis with superimposed herpes simplex infection
CASE #13 -- SLIDE #13
“Hives that resolve with purpura.” The best diagnosis is:

A. Dermatitis herpetiformis  
B. Erythema marginatum  
C. Urticaria  
D. Drug eruption  
E. Purpuric gloves and socks syndrome

CASE #14 -- SLIDE #14
Nodule from the scalp. The best diagnosis is:

A. Metaplastic synovial cyst  
B. Solitary fibrous tumor  
C. Fibrous hamartoma  
D. Spindle cell lipoma  
E. Rudimentary Meningocele

CASE #15 -- SLIDE #15
52 year-old female with nodule of the flank. R/O DF. The best diagnosis is:

A. Dermatofibroma  
B. Xanthoma  
C. Dermatomyofibroma  
D. Metastatic carcinoma  
E. Lymphoma

CASE #16 -- SLIDE #16
54 year-old male with nodule of the cheek. R/O BCC. The best diagnosis is:

A. Fibrous papule  
B. Dermatomyofibroma  
C. Trichilemmoma  
D. Metastatic carcinoma  
E. Malignant clear cell acanthoma

CASE #17 -- SLIDE #17
The best diagnosis is:

A. Malignant melanoma  
B. Melanocytic nevus  
C. Paget’s disease  
D. Bowen’s disease  
E. Pagetoid dykeratosis
CASE #18 -- SLIDE #18
Nodule on flank. The best diagnosis is:

A. Neurofibroma
B. Dermatomyofibroma
C. Dermatofibroma
D. Dermatofibrosarcoma protuberans
E. Desmoplastic Melanoma

CASE #19 -- SLIDE #19
A 28 year-old male with a nodular mass of the elbow, and a clinical diagnosis of keloid, rheumatoid nodule, or granuloma annulare. The best diagnosis is:

A. Rheumatoid nodule
B. Tuberous xanthoma
C. Deep Granuloma annulare
D. Eruptive xanthoma
E. Cutaneous Rosai-Dorfman disease

CASE #20 -- SLIDE #20
A 19 year-old female with a linear plaque on the right posterior lower let, present since childhood. The best diagnosis is:

A. Lichen psoriasis
B. Lichen simplex chronicus
C. Epidermal nevus
D. Inflammatory linear verrucous epidermal nevus (ILVEN)
E. Lichen striatus

CASE #21 -- SLIDE #21
A 17 year-old female Peace Corps volunteer, recently back from a trip to Ethiopia, presents with a pruritic black papule on the lateral plantar foot. She is otherwise healthy. The best diagnosis is:

A. Tick bite granuloma
B. Scabies
C. African Trpanosomiasis
D. Tungiasis
E. Toxoplasmosis
CASE #22 -- SLIDE #22
An 82 year-old female with complaints of headaches. On physical exam, there are palpable nodules on the scalp, and laboratory exam shows an elevated ESR. The best diagnosis for this biopsy from one of the scalp nodule is:

A. Atrophie blanche
B. Kawasaki’s disease
C. Temporal arteritis
D. Leukocytoclastic vasculitis
E. Thromboangiitis obliterans (Buerger’s disease)

CASE #23 -- SLIDE #23
A 41 year-old female presents with a nodular mass of the inner thigh, which is diffusely CD34 positive. The best diagnosis is:

A. Angiosarcoma
B. Neurofibroma
C. Giant cell fibroblastoma
D. Myxoid malignant fibrous histiocytoma (MFH)
E. Pleomorphic lipoma

CASE #24 -- SLIDE #24
This biopsy is from the thigh of a 69 year-old man with small red scaly keratotic papules on upper and lower extremities: rule out Darier’s or Grover’s disease. The best diagnosis is:

A. Lichenoid actinic keratosis
B. Hyperkeratotic mycosis fungoides
C. Hyperkeratosis lenticularis perstans
D. Acrokeratosis paraneoplastica
E. Lupus erythematosus

CASE #25 -- SLIDE #25
The biopsy is from the arm of a 37 year-old man with a differential diagnosis of sarcoidosis. Scattered large cells are CD30 positive. The best diagnosis is:

A. Lymphomatoid papulosis
B. Cutaneous B cell lymphoma
C. Lymphoid allergic reaction
D. Halo nevus with reactive CD30 cells
E. Syphilis
CASE #26 -- SLIDE #26
A 60-year-old man presented with a 6 mm “unusual” tumor on the base of his left thumb, reportedly present for a month. The best diagnosis is:

A. Fibrosarcoma
B. Cellular dermatofibroma
C. Leiomyosarcoma
D. Cellular hypertrophic scar
E. Cellular fibromatosis

CASE #27 -- SLIDE #27
There are papular lesions of the hands. The best diagnosis is:

A. Dystrophic calcinosis
B. Dermatoheliosis
C. Acrokeratoelastoidosis
D. Fibroblastic rheumatism
E. Colloid milium

CASE #28 -- SLIDE #28
An 84-year-old man presents with a swollen ear. The best diagnosis is:

A. Chondrodermatitis nodularis helicis
B. Elastotic nodule of the ear
C. Amyloidosis of the auricular concha
D. Relapsing polychondritis
E. Endochondral pseudocyst

CASE #29 -- SLIDE #29
A 32-year-old woman presents with multiple dermal nodules, fever and arthralgia. The best diagnosis is:

A. Leishmaniasis
B. Tuberculoid leprosy
C. Lepromatous leprosy
D. Erythema nodosum
E. Erythema nodosum leprosum
F. None of the above
CASE #30 -- SLIDE #30
A 4-year-old girl presents with disseminated, hypopigmented plaques. Biopsy has been done to rule out parapsoriasis vs. lymphoma vs. pityriasis alba vs. psoriasis. As the pathologist, which would you recommend?

A. Repeat biopsy
B. Lymphocyte marker studies
C. T-cell gene rearrangement studies
D. All of the above
E. None of the above

CASE #31 -- SLIDE #31
A 41 year-old man presented with pruritic erythematous papules and nodules at different stages of development, predominantly on the trunk and extremities. Some of these lesions have spontaneously regressed. The patient is otherwise healthy. The best diagnosis based on the clinical and histopathologic findings is:

A. Pagetoid reticulosis
B. Mycosis fungoides
C. Lymphomatoid papulosis (LyP)
D. Epidermotropic CD8+ T-cell lymphoma
E. Pityriasis lichenoides

CASE #32 -- SLIDE #32
A 33-year-old woman presents with firm plaques on both buttocks and thighs. The clinical differential diagnosis is panniculitis vs. lupus vs. alpha-1-antitrypsin deficiency vs. scleroderma vs. cutaneous T-cell lymphoma vs. eosinophilic fasciitis. The best diagnosis is:

A. Paraffinoma
B. Lepromatous leprosy
C. Leishmaniasis
D. Calcinosi cutis
E. Morphea

CASE #33 -- SLIDE #33
A 48 year-old female presents with a 1.09 cm violaceous nodule on the wrist. The best diagnosis is:

A. Aggressive digital papillary adenoma (adenocarcinoma)
B. Metastatic adenocarcinoma
C. Papillary eccrine adenoma
D. Hidradenoma papilliferum
E. Microcystic adnexal carcinoma.
CASE #34 -- SLIDE #34
What is your diagnosis for this 2 cm scalp lesion in an 82 year-old male?

A. Malignant cylindroma  
B. Eccrine spiradenoma  
C. Trabecular carcinoma (Merkel cell carcinoma)  
D. Metastatic follicular thyroid carcinoma  
E. Trichoblastoma.

CASE #35 -- SLIDE #35
This 41 year-old male presented with a tender one centimeter subcutaneous nodule on the thigh. What is this lesion called?

A. Schwannoma  
B. Dermatofibrosarcoma protuberans  
C. Leiomyoma  
D. Leiomyosarcoma  
E. Nodular Kaposi’s sarcoma.

CASE #36 -- SLIDE #36
A 71 year-old Asian female had multiple subcutaneous tender nodules on the abdomen and chest. Your diagnosis is:

A. Eccrine carcinoma  
B. Metastatic adenocarcinoma, GI primary  
C. Metastatic lobular carcinoma of the breast  
D. Metastatic renal cell carcinoma  
E. Metastatic ovarian carcinoma

CASE #37 -- SLIDE #37
This 60 year-old male with fever, anemia and thrombocytopenia complains of a three-week history of a boggy, violaceous nodule on his right forearm. What does this lesion represent?

A. Kaposi’s sarcoma  
B. Cellulitis  
C. Angioinvasive fungal infection  
D. Thrombotic thrombocytopenic purpura  
E. Pigmented purpuric dermatosis
CASE #38 -- SLIDE #38
A 28 year-old woman presented with an erythematous lesion on her vulva. What does this lesion represent?

A. Squamous cell carcinoma
B. Hobnail hemangioma
C. Kaposi’s sarcoma
D. Angiosarcoma
E. Angiomyxoma

CASE #39 -- SLIDE #39
A two year-old male presented with a history of blisters on the face, groin and legs. The lesions have been present for about one month. What do they represent?

A. Bullous pemphigoid
B. Bullous lupus erythematosus
C. Dermatitis herpetiformis
D. Chronic bullous disease of childhood
E. Epidermolysis bullosa

CASE #40 -- SLIDE #40
A 72 year-old male presented with fatigue, jaundice and a three week history of numerous pruritic papules around the neck and waistline. The best diagnosis is:

A. Mycosis fungoides
B. Lymphomatoid papulosis type A
C. Diffuse large B-cell lymphoma
D. Mastocytosis
E. Langerhans cell histiocytosis

CASE #41 -- SLIDE #41
What is the diagnosis for this large lesion on the right thigh of a 29 year-old male?

A. Synovial sarcoma
B. Angiosarcoma
C. Myositis ossificans
D. Epithelioid sarcoma
E. Dermatofibrosarcoma protuberans
CASE #42 -- SLIDE #42
A 58 year-old woman presented with an expanding erythematous plaque on the upper lateral thigh. This proliferation is commonly seen in the setting of:

- A. Celiac disease
- B. Hepatitis C
- C. Renal cell carcinoma
- D. Renal transplantation
- E. Rheumatoid arthritis

CASE #43 -- SLIDE #43
The patient was a 71 year-old man who presented with a skin rash and fatigue. Subsequent investigations revealed a striking peripheral blood Lymphocytosis at 299000; flow cytometry detected an aberrant peripheral blood lymphocyte population that manifested CD4 and CD7 positivity. Peripheral blood cytogenetic studies revealed an inverted chromosome 14. The best diagnosis is:

- A. Adult T-cell leukemia lymphoma
- B. Large granular lymphocytic leukemia
- C. Sézary syndrome
- D. Acute T-cell lymphoblastic lymphoma
- E. T prolymphocytic leukemia.

CASE #44 -- SLIDE #44
A six year-old male presented with multiple scalp nodules. The tumor cells were CD10, TdT and CD20, CD99 and CD43 positive. What is your diagnosis?

- A. Ewing’s sarcoma/primitive neuroectodermal tumor
- B. T-cell lymphoblastic lymphoma
- C. Small cell malignant melanoma
- D. B-cell lymphoblastic lymphoma
- E. Diffuse large cell B-cell lymphoma of probable follicular cell origin.

CASE #45 -- SLIDE #45
The patient is a 60 year-old with a recent diagnosis of multiple myeloma. The patient now presents with purple red painful toes. What is the best diagnosis?

- A. Monoclonal cryoglobulinemia
- B. Monoclonal cryofibrinogenemia
- C. Antiphospholipid antibody syndrome
- D. Cholesterol embolism
- E. Thrombocythemia.
CASE #46 -- SLIDE #46
The patient was a 50 year-old female with a past history of thymoma who presented with Myositis in 2000 followed by the development of a Photodistributed skin rash and progressive dyspnea. An open lung biopsy showed severe pulmonary fibrosis. She developed deep vein thrombosis. Serologic studies revealed antibodies to OJ, and, as well, her aldolase levels were high. She had moderate to high levels of three different antiphospholipid antibodies including Anticardiolipin, antiphosphatidyserine and antiphosphatidylcholine. The best diagnosis is:

A. Sclerodermatomyositis  
B. Scleroderma  
C. Anti-synthetase syndrome  
D. Mixed connective tissue disease  
E. Antiphospholipid antibody syndrome.

CASE #47 -- SLIDE #47
A 34 year-old African American woman presented with numerous, yellow-brown papules distributed over the face. The best diagnosis is:

A. Sarcoidosis  
B. Lupus miliaris disseminatus faciei  
C. Interstitial granulomatous dermatitis  
D. Granuloma annulare  
E. Granuloma faciale

CASE #48 -- SLIDE #48
This 28 year-old African-American female developed a diffuse itchy, burning, papulosquamous and pustular eruption starting on her wrist in late January 2005 and spreading over her whole body and face by mid-February. She reported fevers, constipation and pelvic discomfort. Immediately prior to the eruption, she had had an upper respiratory tract infection, was wearing an estrogen patch and taking weight loss and vitamin pills. What is your diagnosis?

A. Erythema multiforme  
B. Erosive lichen planus  
C. Paraneoplastic pemphigus  
D. PLEVA variant  
E. Other
CASE #49 -- SLIDE #49
A 54 year-old female presented with a dorsal foot mass. The best diagnosis is:

A. Kaposi sarcoma  
B. Kaposiform hemangioendothelioma  
C. Epithelioid hemangioendothelioma  
D. Spindle cell hemangioma  
E. Spindled angiosarcoma

CASE #50 -- SLIDE #50
A 25 year-old Indian male presents to the clinic with a 1.5 cm bluish-black firm nodule on the dorsum of the right foot. The patient states that the lesion appeared within the last year. What’s your diagnosis?

A. Nodular melanosis  
B. Cellular blue nevus  
C. Monsel’s solution artifact  
D. Pigmented epithelioid melanocytoma  
E. Tattoo

CASE #51 -- SLIDE #51
A 45 year-old healthy patient presented with a solitary, asymptomatic nodule. What is your diagnosis for this lesion?

A. Chondroid syringoma  
B. Hemangiopericytoma  
C. Intravascular papillary endothelial hyperplasia  
D. Cutaneous myofibroma  
E. Cutaneous cartilaginous tumor

CASE #52 -- SLIDE #52
An 87 year-old woman presented with a lesion of the face. What is it?

A. Squamous cell carcinoma  
B. Merkel cell carcinoma with squamous differentiation  
C. Squamous cell carcinoma with chronic lymphocytic leukemia  
D. Anaplastic large cell lymphoma  
E. Metastatic oat cell carcinoma
CASE #53 -- SLIDE #53
A 44 year-old woman with a history of myxoid mammary fibroadenomas, pituitary adenoma, psammomatous melanotic schwannoma and atrial myxoma had multiple skin nodules. The best diagnosis is:

A. Mucinous Fibrofolliculoma
B. Chondroid syringoma
C. Syringofibroadenoma
D. Cutaneous myxoma with epithelial elements
E. Cutaneous focal mucinosis with fibroadenomas.

CASE #54 -- SLIDE #54
A 14 year-old girl presented with a three-year history of a flesh-colored papule on the forearm that had increased in size. The clinical impression was “juvenile xanthogranuloma vs. dermatofibroma.” What is your diagnosis?

A. Involuting Spitz nevus
B. Epithelioid histiocytoma
C. Involuting hemangioma
D. Angiofibroma
E. Epithelioid hemangioma.

CASE #55 -- SLIDE #55
This is an excision biopsy of an ill-defined mass (2 X 3 cm) from the lower leg of a 71 year-old male. The patient states that it has been present and slowly growing for about one to two years. What is the best diagnosis for this lesion?

A. Nodular fasciitis
B. Myxoid desmoplastic malignant melanoma
C. Adult fibrosarcoma
D. Dermatofibrosarcoma protuberans
E. Myxofibrosarcoma

CASE #56 -- SLIDE #56
This is an excision biopsy from the upper lip of a 68 year-old man. Your histologic diagnosis is:

A. Sebaceoma
B. Sebaceous adenoma
C. Basal cell carcinoma with sebaceous differentiation
D. Sebaceous epithelioma
E. Sebaceous gland carcinoma
CASE #57 -- SLIDE #57
This is an excision biopsy from the back of a 32 year-old Asian male. Another laboratory has reported that the tumor cells are S100 positive. What is your histologic diagnosis?

A. Metastatic malignant melanoma  
B. Subcutaneous Rosai-Dorfman disease  
C. Subcutaneous Reticulohistiocytoma  
D. Subcutaneous juvenile xanthogranuloma  
E. Malignant fibrous histiocytoma

CASE #58 -- SLIDE #58
This is an excision biopsy from the foot of a four year-old girl who had recently returned with her parents from a Caribbean vacation. This lesion represents:

A. Sparganosis  
B. Tungiasis  
C. Myiasis  
D. Embedded tick  
E. Dracunculiasis (dracontiasis)

CASE #59 -- SLIDE #59
A 46 year-old man presented with a lesion (thought to be a wart) on the nose. The best diagnosis is:

A. Balloon cell nevus  
B. Metastatic renal cell carcinoma  
C. Clear cell hidradenoma  
D. Sebaceous carcinoma  
E. Clear cell fibrous papule.

CASE #60 -- SLIDE #60
A 77 year-old woman complained of an ulcerated nodule on the lower leg. This lesion represents:

A. Amyloidosis  
B. Calcinosis cutis due to dermatomyositis  
C. Lupus panniculitis  
D. Ischemic ulceration  
E. Nodular vasculitis
CASE #61 -- SLIDE #61
What is your diagnosis for these multiple papules in a 45 year-old woman?

A. Lupus erythematosus
B. Focal cutaneous mucinosis
C. Metastatic spindle cell carcinoma
D. Papular mucinosis
E. Myxedema

CASE #62 -- SLIDE #62
A 58 year-old man with a history of chronic sun damage presented to the office of a dermatologist for a baseline skin examination at the urging of his wife. A 0.9 x 0.7 cm indurated, erythematous macule with a halo is noted on the left upper back. A biopsy was performed. An initial immunohistochemical profile was as follows: actin negative, desmin negative, HMB45 negative and CD68 negative. Immunoreactivity with which additional immunostain would be most supportive and most likely to be positive in desmoplastic melanoma?

A. A. CD99
B. B. CD163
C. C. MART-1
D. D. MITF
E. E. Sox-10

CASE #63 -- SLIDE #63
What is your diagnosis for this lesion on the thigh of a 34 year-old woman?

A. Leukocytoclastic vasculitis
B. Cryoglobulinemia
C. Anticardiolipin-antibody syndrome
D. Spider bite
E. Tick bite

CASE #64 -- SLIDE #64
A previously healthy 40 year-old woman presented with tender indurated plaques and nodules on the thighs and elbows after falling down a flight of stairs. The most likely diagnosis is:

A. Erythema nodosum
B. Neutrophilic lobular panniculitis (subcutaneous Sweet’s syndrome)
C. Subcutaneous leukocytoclastic vasculitis
D. Alpha-1 antitrypsin deficiency panniculitis
E. Pancreatic Panniculitis
CASE #65 -- SLIDE #65
A 26 year-old woman presented with a slowly-growing asymptomatic 2 cm firm subcutaneous nodule on the left upper arm. The most likely diagnosis is:

A. Low-grade fibromyxoid sarcoma
B. Nodular fasciitis
C. Myxoid neurofibroma
D. Collagenous fibroma (desmoplastic fibroblastomas)
E. Fibromatosis

CASE #66 -- SLIDE #66
A 36 year-old woman presented with a 5 cm pedunculated nodule in the anal area. The clinical impression was “hemorrhoid.” This lesion represents:

A. Metastatic adenocarcinoma
B. Hidradenoma papilliferum
C. Tubular apocrine adenoma
D. Syringocystadenoma papilliferum
E. Adenoma of anogenital mammary-like glands

CASE #67 -- SLIDE #67
A 39 year-old woman with obesity, diabetes mellitus and recent onset end stage renal disease presented with rapidly progressive painful, symmetric indurated plaques on the bilateral thighs. The overlying skin demonstrated a peau d’orange texture. Your diagnosis for these lesions is:

A. Nephrogenic fibrosing dermopathy
B. Morphea
C. Scleromyxedema
D. Generalized granuloma annulare
E. Dermatofibrosarcoma protuberans

CASE #68 -- SLIDE #68
A 25 year-old woman presented with red brown plaques in the axilla. The lesions waxed and wanted and were mildly pruritic. The best diagnosis is:

A. Candidiasis
B. Confluent and reticulated papillomatosis of Gougerot and Carteaud
C. Granular parakeratosis
D. Porokeratosis
E. Psoriasis
CASE #69 -- SLIDE #69
This biopsy was obtained from a 50 year-old woman with hyperpigmented patches over her trunk. What is the most likely diagnosis for these lesions?

A. Atrophoderma of Pasini and Pierini
B. Becker’s nevus
C. Lichen sclerosus et atrophicus
D. Radiation dermatitis
E. Superficial morphea

CASE #70 -- SLIDE #70
This biopsy was obtained from a nodular area within a giant congenital nevus. What is the most likely diagnosis?

A. Clonal nevus
B. Combined nevus
C. Deep penetrating nevus
D. Melanoma arising within congenital nevus
E. Proliferative nodule arising within congenital nevus

CASE #71 -- SLIDE #71
The best diagnosis for this slide is:

A. Bacillary angiomatosis
B. Epithelioid angiosarcoma
C. Hidradenocarcinoma
D. Metastatic renal cell carcinoma
E. Pyogenic granuloma

CASE #72 -- SLIDE #72
This patient presented with multiple hyperpigmented flat-topped papules over the arms, noted after sun exposure. The most likely diagnosis is:

A. Lichen nitidus
B. Lichenoid drug eruption
C. Lupus erythematosus
D. Photo allergic eruption
E. Polymorphous light eruption
CASE #73 -- SLIDE #73
A 4 mm punch biopsy specimen was taken from an inflamed bald spot on the scalp of a healthy 45 year-old woman. What is the most appropriate diagnosis?

A. Tinea capitis
B. Follicular degeneration syndrome/central, centrifugal scarring alopecia
C. Folliculitis decalvans
D. Lichen planopilaris
E. Chronic cutaneous lupus erythematosus (discoid LE)

CASE #74 -- SLIDE #74
A 4 mm punch biopsy specimen was taken from a patch of inflamed, partially bald scalp skin. This 40 year-old white man was otherwise healthy. What is your diagnosis for this lesion?

A. Tinea capitis
B. Follicular degeneration syndrome/central, centrifugal scarring alopecia
C. Folliculitis decalvans
D. Lichen planopilaris
E. Chronic, cutaneous lupus erythematosus (discoid LE)

CASE #75 -- SLIDE #75
A 4 mm punch biopsy specimen was taken from the normal appearing occipital scalp of a 14 year-old girl. What is the best diagnosis?

A. Normal scalp
B. Telogen effluvium
C. Trichotillomania
D. Alopecia areata
E. Traction alopecia

CASE #76 -- SLIDE #76
A 4 mm punch biopsy specimen was taken from the crown of the scalp of a 45 year-old African-American woman. The most appropriate diagnosis is:

A. Tinea capitis
B. Central, centrifugal cicatrical alopecia
C. Folliculitis decalvans
D. Lichen planopilaris
E. Chronic, cutaneous lupus erythematosus (discoid LE)
CASE #77 -- SLIDE #77
A 4 mm punch biopsy specimen was taken from an otherwise healthy 42 year-old man who is complaining of severe longstanding (years) hair loss. The best diagnosis for this lesion is:

A. Normal scalp  
B. Telogen effluvium  
C. Androgenetic alopecia  
D. Alopecia areata  
E. Traction alopecia

CASE #78 -- SLIDE #78
A 65 year-old female physician noted several asymptomatic pustules. The best diagnosis is:

A. Bowel bypass syndrome  
B. Acute generalized exanthematous pustulosis (AGEP)  
C. Majocchi’s granuloma  
D. Fire ant bite  
E. Anthrax

CASE #79 -- SLIDE #79
A 27 year-old soldier had several lesions on his right wrist for two or three months. What is your diagnosis?

A. Anthrax  
B. Tularemia  
C. Leishmaniasis  
D. Sporotrichosis  
E. Histoplasmosis

CASE #80 -- SLIDE #80
A 46 year-old woman had noted a Multinodular plaque on her right thigh for three months. What is your diagnosis for this lesion?

A. Lymphoma  
B. Pseudolymphoma  
C. Leishmaniasis  
D. Sarcoid  
E. Rosai-Dorfman disease
CASE #81 -- SLIDE #81
Give the best diagnosis to this biopsied lesion from the trunk of a 47 year-old male. The clinical impression was “urticarial vs. drug eruption.”

A. Mycosis fungoides  
B. Lichenoid photoeruption  
C. Lupus erythematosus  
D. Secondary syphilis  
E. Mucha-Habermann disease

CASE #82 -- SLIDE #82
What is your diagnosis for this large lesion excised from a patient’s abdomen?

A. Targetoid hemosiderotic hemangioma  
B. Tufted angioma  
C. Kaposi’s sarcoma  
D. Congenital melanocytic nevus  
E. Cellular blue nevus

CASE #83 -- SLIDE #83
A 71 year-old woman presented with an ill-defined nodule in the right breast. What is it?

A. Infectious panniculitis  
B. Liposarcoma  
C. Lupus panniculitis  
D. Silicone implant reaction  
E. Traumatic fat necrosis

CASE #84 -- SLIDE #84
A 46 year-old woman presented with a six-month history of a painful and dystrophic left fourth fingernail. The most likely diagnosis is:

A. Acral hemangioma  
B. Fibrokeratoma  
C. Onychomatricoma  
D. Subungual neurofibroma  
E. Unguioblastoma
CASE #85 -- SLIDE #85
A 34 year-old man recently noticed a nodule on his back. What is your diagnosis for this lesion?

A. Dermatofibroma  
B. Dermatofibrosarcoma protuberans  
C. Malignant fibrous histiocytoma  
D. Pleomorphic fibroma  
E. Xanthogranuloma

CASE #86 -- SLIDE #86
A 38 year-old woman had had two recurrences of this lesion on her forehead. What does the lesion represent?

A. Epithelioid sarcoma  
B. Extraskeletal osteosarcoma  
C. Giant cell rich malignant fibrous histiocytoma  
D. Proliferating tricholemmal cyst  
E. Soft tissue giant cell tumor

CASE #87 -- SLIDE #87
A 55 year-old man was evaluated for a “boil” on his buttock. What is the most likely diagnosis for this lesion?

A. Aggressive angiomyxoma  
B. Atypical lobular capillary hemangioma (pyogenic granuloma)  
C. Cutaneous myxoma  
D. Hemangioendothelioma  
E. Myxoid neurofibroma

CASE #88 -- SLIDE #88
A 33-year-old female presented with a long standing nodule on her upper arm. The tumor is strongly positive for MITF-1. What is your diagnosis?

A. Melanoma  
B. Spitz nevus  
C. Neurothekeoma  
D. Metastatic sarcoma  
E. Melanocytic nevus
CASE #89 -- SLIDE #89
A 31 year-old HIV-positive febrile man from Burma presented with about 15 papules averaging 3 mm in diameter on the face and arms. The most likely diagnosis is:

A. Leishmaniasis  
B. Toxoplasmosis  
C. Cryptococcosis  
D. Penicilliosis  
E. Protothecosis

CASE #90 -- SLIDE #90
The substance that was implanted was:

A. Zyderm (collagen)  
B. Restylane (hyaluronic acid)  
C. Gelfoam (gelatin sponge)  
D. Silicone  
E. Bioplastique (biphasic copolymer)

CASE #91 -- SLIDE #91
This unfortunate immunosuppressed patient has co-infection in this skin biopsy with fungus and also:

A. Amebiasis  
B. Cytomegalovirus  
C. Onchocerciasis  
D. Trypanosomiasis  
E. Schistosomiasis

CASE #92 -- SLIDE #92
This 49 year-old man had a nonhealing nodule on his right bicep for ten years. Key areas with organisms have been circled on each slide. The diagnosis on these PAS-stained sections is:

A. North American blastomycosis  
B. Cryptococcosis  
C. Coccidioidomycosis  
D. Actinomycosis  
E. Sporotrichosis
CASE #93 -- SLIDE #93
A 25 year-old man presented with a lesion on the upper ear. What does this lesion represent?

A. Minocycline pigmentation  
B. Localized argyria  
C. Pseudo-ochronosis  
D. Blue nevus  
E. Nevus of Ota

CASE #94 -- SLIDE #94
A 78 year-old man developed a rapidly enlarging lesion on his forehead. The most likely diagnosis is:

A. Tumor stage Kaposi’s sarcoma  
B. Atypical fibroxanthoma  
C. Desmoplastic malignant melanoma  
D. Cutaneous leiomyosarcoma  
E. Cutaneous angiosarcoma

CASE #95 -- SLIDE #95
Give the correct diagnosis for this papule on the hand of a 42 year-old female.

A. Myxoid pleomorphic fibroma  
B. Myxofibrosarcoma  
C. Superficial angiomyxoma  
D. Cutaneous leiomyosarcoma  
E. Pleomorphic malignant fibrous histiocytoma

CASE #96 -- SLIDE #96
A rash developed in a 36 year-old man after taking a cephalosporin antibiotic. The lesions were concentrated in skin folds and on the face. The best diagnosis is:

A. Scabies presenting with pustular lesions  
B. Pustular psoriasis precipitated by medication  
C. Tinea corporis with Majocchi’s granuloma  
D. Acute generalized exanthematous pustulosis  
E. Subcorneal pustular dermatosis (Sneddon-Wilkinson)
CASE #97 -- SLIDE #97
A 27 year-old man with no significant past medical history presented with a vascular appearing nodule on the penile base. The best diagnosis is:

A. Epithelioid hemangioma, penile type
B. Epithelioid hemangioendothelioma
C. Epithelioid sarcoma-like hemangioendothelioma
D. Kaposi sarcoma
E. Epithelioid angiosarcoma, sporadic soft tissue type

CASE #98 -- SLIDE #98
A 12 year-old girl presented with a deep 10 cm mass of the buttock. The best diagnosis is:

A. Fibromatosis (desmoid tumor)
B. Myxoid neurofibroma
C. Perineurioma
D. Low grade fibromyxoid sarcoma
E. Low grade myxofibrosarcoma

CASE #99 -- SLIDE #99
A one year-old boy presented with a firm nontender nodule on the third digit. The best diagnosis is:

A. Myofibroma
B. Angiofibroma
C. Acquired digital fibrokeratoma
D. Infantile digital fibroma
E. Palmar fibromatosis

CASE #100 -- SLIDE #100
A one year-old girl presented with a firm plaque on her abdomen, with a clinical impression of dermatofibrosarcoma protuberans. What is your diagnosis?

A. Fibrous hamartoma of infancy
B. Myofibroma
C. Dermatofibrosarcoma protuberans
D. Giant cell fibroblastomas
E. Dermatofibroma
CASE ANSWERS
CASE #1 - SLIDE #1

DIAGNOSIS: SOLITARY FIBROUS TUMOR (ANSWER D)

Clinical Features:
Solitary fibrous tumor (SFT) is an uncommon mesenchymal neoplasm that was initially described in the pleura. Subsequently, it has been reported to arise at almost any site. With cutaneous involvement, the neoplasm typically occurs as a painless nodule in the head and neck region of adults.

Histologic (and Immunophenotypic) Features:
Solitary fibrous tumors are well-circumscribed and composed of bland-appearing spindle cells arranged in a "patternless" growth pattern, foci of hyalinized collagen, and a prominent hemangiopericytoma-like vascular pattern. SFTs are typically reactive for vimentin, CD34 and bcl-2, but not for EMA, cytokeratins, melanocytic and neural markers (S-100, GFAP, Melan-A, Mart-1 and HMB-45), SMA, MSA, histiocytic markers (CD68, AAT and AACT), factor-XIIIa, and vascular markers (CD31 and F-VIII).

Differential Diagnosis:
- Dermatofibroma
- Dermatofibrosarcoma protuberans (DFSP)
- Spindle cell lipoma (adipocyte poor)
- Leiomyoma
- Leiomyosarcoma
- Cutaneous myofibroma
- Spindle cell carcinoma
- Melanoma
- Peripheral nerve sheath tumor

Discussion:
Although the cells in most SFTs are bland and uniform, like their counterparts in the pleura, a small number of soft tissue SFTs demonstrate histologic evidence suggestive of malignancy including pleomorphism, high cellularity, numerous mitotic figures (>4 mitoses/ten high-power fields), both normal and abnormal, and tumor cell necrosis. Such cases are more likely to recur and/or metastasize. A complete excision is the treatment of choice and usually eventuates in cure. Because the clinical behavior of SFT is unpredictable, if there are histologic features suggestive of malignancy, more aggressive therapy may be warranted. In the very least, such cases require closer clinical follow-up. Recurrence is unlikely following excision.

References

CONTRIBUTED BY SHANE A. MEEHAN, M.D
CASE #2 - SLIDE #2

DIAGNOSIS: DECIDUALIZED ENDOMETRIOSIS

Clinical Features:
Cutaneous endometriosis usually occurs in a periumbilical location or in abdominal surgical scars but has been described in almost every organ. Concurrent pelvic disease is often not present. Decidualized endometriosis has also been reported in numerous ectopic locations but is most often seen within the cervix or ovary.

Histologic (and Immunophenotypic) Features:
The lesion is usually comprised of nodules of enlarged polygonal to rounded stellate or fusiform cells with a stroma that may be slightly edematous or myxoid. The cells have abundant eosinophilic or pale-staining, slightly granular cytoplasm, vesicular nuclei, small but conspicuous nucleoli and express CD30 and vimentin. Dilated or compressed glands may also be present and are lined by plump cuboidal epithelium. Mitoses are rare or absent. The relative proportion of glands to stroma is variable.

Differential Diagnosis:
Adenosarcoma
Epitheliod sarcoma
Adenocarcinoma
Melanoma

Discussion:
Decidualization refers to the morphologic and physiologic alteration of endometrial glands and stroma during pregnancy or in other states when there is sufficient progesterone. There are competing theories regarding the origin of endometriosis. Some think it arises following physiologic migration of endometrial glands through the fallopian tubes followed by access to the angiolymphatic vasculature or mechanical transfer during a surgical procedure. Others think it results from metaplasia of pluripotential celomic remnants of the embryonic wall. Decidualized endometriosis is important to recognize because of its pseudomalignant appearance.

References

CONTRIBUTED BY SHANE A. MEEHAN, M.D
CASE #3 - SLIDE #3

DIAGNOSIS: ADENOID CYSTIC CARCINOMA

Clinical Features:
Cutaneous adenoid cystic carcinoma is a rare sweat gland carcinoma that has been reported at a variety of sites but has been most frequently reported on the scalp. It is slowly growing but can be locally aggressive. Metastases have been reported.

Histologic (and Immunophenotypic) Features:
The neoplasm exhibits a characteristic cribriform architecture being comprised of islands of cells with basaloid nuclei in which are uniform round spaces containing predominantly myxoid and foci of basement membrane material. Perineural invasion may be present. Adenoid cystic carcinoma expresses EMA and can react for S100.

Differential Diagnosis:
Adenoid basal cell carcinoma
Metastatic adenocarcinoma
Primary cutaneous cribiform carcinoma

Discussion:
Adenoid cystic carcinoma also occurs in the salivary gland, lung, prostate and breast, and may metastasize to the skin. However, metastatic involvement from such primary sites occurs late in the disease course when the patient has overt and disseminated disease. Direct extension from an underlying salivary gland, for example, must also be excluded. Primary cutaneous cribiform carcinoma is a variant of apocrine carcinoma that some consider a variant of adenoid cystic carcinoma.

References:
CASE #4 - SLIDE #4

DIAGNOSIS: FOREIGN BODY GIANT CELL REACTION TO POLY-L-LACTIC ACID (SCULPTRA, NEW-FILL)

Clinical Features:
Sculptra was initially FDA approved and used specifically to restore volume in HIV patients with facial lipoatrophy.

Histologic Features:
There are irregularly, sharply-shaped polarizeable particles within the dermis associated with numerous multinucleated foreign body giant cells, some of which may contain asteroid bodies, in addition to dermal fibrosis.

Differential Diagnosis:
Keratin granuloma
Dermalive (hyaluronic acid plus acrylic hydrogel particles) foreign body giant cell reaction
Artecoll (polymethylmethacrylate microspheres) foreign body giant cell reaction

Discussion:
Sculptra, or New-Fill, is a biodegradable filler comprised of synthetic poly-L-lactic acid (PLLA) microspheres (2-50um) suspended in mannitol and carbomethoxycellulose solution. The size and degradation kinetics of the PLLA microparticles are intended to stimulate collagen production to provide lasting results from 18-24 months. Foreign body giant cell reactions to Sculptra are considered rare by the manufacturer who considers it nonimmunogenic but other groups have reported incidence rates of late complications from 5 to 10 percent. One must exclude the possibility of infection in such reactions with use of special stains and/cultures, especially in light of the fact that the patient may be immunocompromised. Foreign body giant cell reactions to Dermalive, Restylane (hyaluronic acid) and Artecoll have also been reported.

References

CONTRIBUTED BY SHANE A. MEEHAN, M.D
Clinical Features:
Necrobiotic xanthogranuloma (NXG) is a rare, chronic disorder associated with paraproteinemia. Patients typically present with red-orange, yellow, or violaceous nodules and plaques, often with ulceration. The face, especially the periorbital area, is most commonly involved. Extracutaneous involvement has occasionally been reported.

Histologic Features:
• Dense palisading granulomas filling the dermis and subcutaneous adipose tissue
• Foam cells
• Multinucleate giant cells (Langhans, Teuton, and bizarre variants)
• Broad zones of degenerated collagen ("necrobiosis")
• Cholesterol clefts
• Lymphoid follicles

Differential Diagnosis:
• Necrobiosis lipoidica
• Granulomatous infection
• "Churg-Strauss" granuloma
• Granuloma annulare
• Rheumatoid nodule

Discussion:
Necrobiotic xanthogranuloma (NXG) can usually be differentiated from other palisading granulomas by the greater degree of necrobiosis and by the more massive nature of the inflammatory infiltrate. Among entities in the differential diagnosis, necrobiosis lipoidica is the closest histologic simulator of NXG. Necrobiosis lipoidica may uncommonly show lymphoid follicles and cholesterol clefts, although those features are more frequently encountered in NXG. Clinical features, especially anatomic distribution, may also be helpful in distinguishing the two entities.

References:

CONTRIBUTED BY DAVID J. DICAUDO, M.D
CASE #6 - SLIDE #6
DIAGNOSIS: SECONDARY SYPHILLIS

Clinical Features:
Secondary syphilis is a "great imitator" with diverse clinical presentations. Macular, maculopapular, papular, and annular eruptions are most common. Associated findings may include condylomata lata, oral mucous patches, and patchy alopecia. Copper-colored patches on the palms and soles are characteristic, as seen in this patient.

Histologic Features:
• Superficial and deep perivascular infiltrate of lymphocytes and plasma cells
• Epithelioid granulomas with multinucleate giant cells
• Lichenoid and/or psoriasiform reaction patterns
• Papillary dermal edema
• Endothelial cell swelling
• Neutrophilic exocytosis into epidermis; neutrophils within foci of parakeratosis
• Scattered necrotic keratinocytes within epidermis
• Plasma cells infiltrating the perineurium and arrector pili muscles

Differential Diagnosis:
• Granuloma annulare
• Erythema chronicum migrans
• Viral exanthem
• Leprosy
• Drug eruption
• Pityriasis lichenoides

Discussion:
In this case, the combination of numerous plasma cells and focal epithelioid granulomas led to suspicion for syphilis, which was confirmed by serologic testing. Numerous plasma cells would be an uncommon finding in the other choices listed. The histologic patterns of secondary syphilis are strikingly diverse. Silver stain confirms the diagnosis when spirochetes are identifiable, but the stain is frequently negative. Both clinically and histologically, secondary syphilis needs to be kept in mind as a "great imitator".

References:

CONTRIBUTED BY DAVID J. DICAUDO, M.D
CASE #7 - SLIDE #7

DIAGNOSIS: NEUTROPHILIC FIXED DRUG ERUPTION

Clinical Features:
A 71-year-old woman suddenly developed a mildly tender, well-demarcated pink plaque on the buttock and thigh. She had experienced a similar plaque at precisely the same anatomic location 6 times over the past 3 years. Naproxen sodium had been taken several hours prior to the onset of the eruption. Following the diagnosis of neutrophilic fixed drug eruption, the patient avoided naproxen for 5 months, and experienced no recurrences during that time period. When she subsequently took naproxen for a sprained ankle, she rapidly developed her seventh recurrence of the eruption.

Histologic Features:
- Diffuse dermal infiltrate composed mostly of neutrophils
- Leukocytoclasis
- Marked subepidermal edema
- Exocytosis of neutrophils into epidermis

Differential Diagnosis:
- Sweet's syndrome - histologically similar, but clinically not site-specific
- Erysipelas - histologically similar; Gram stain and culture sometimes helpful

Discussion:
Neutrophilic fixed drug is a recently described entity with only two prior case reports in the literature. Patients present with recurrent plaques at fixed anatomic locations. The eruption arises within hours of taking a specific medication. In contrast to regular fixed drug eruption, the dermal infiltrate is composed almost entirely of neutrophils. Prior case reports have described neutrophilic fixed drug eruption in association with amoxicillin-clavulanic acid and naproxen. Neutrophilic fixed drug eruption should be considered in the differential diagnosis of neutrophilic dermatitis, if the clinical history is supportive.

References:

CONTRIBUTED BY DAVID J. DICAUDO, M.D
CASE #8 - SLIDE #8

DIAGNOSIS: REACTIVE ANGIOENDOTHELIOMATOSIS

Clinical Features:
Reactive angioendotheliomatosis (RAE) is a rare disorder which usually arises in the setting of an underlying systemic disease. Patients present with erythematous or violaceous patches and plaques, clinically mimicking Kaposi's sarcoma or angiosarcoma. Ulceration is sometimes present. RAE is associated with a number of systemic disorders, especially subacute bacterial endocarditis, other heart valve disorders, antiphospholipid antibody syndrome, other autoimmune diseases, chronic lymphocytic leukemia, monoclonal gammopathy, renal failure, or prior renal transplantation.

Histologic Features:
• Proliferation of endothelial cells within dermal vessels
• Intravascular thrombi frequently present
• Mild perivascular lymphocytic or lymphoplasmacytic inflammation

Differential Diagnosis:
• Intravascular large B-cell lymphoma - CD20-positive atypical cells within vessels
• Intravascular histiocytosis - CD68-positive cells within vessels
• Epithelioid hemangioma - plump, vacuolated endothelial cells; infiltrate of lymphocytes and eosinophils
• Inflammatory breast carcinoma - clusters of cytokeratin-positive atypical epithelioid cells within dermal vessels

Discussion:
Early descriptions of an angioendotheliomatosis designated two variants: benign and malignant. Subsequently the malignant variant was recognized as an intravascular B-cell lymphoma. The benign variant, as demonstrated in this case, represents "true" angioendotheliomatosis, in which endothelial cells proliferate within vascular lumina. As described above, numerous systemic disorders have been associated with angioendotheliomatosis. Intravascular occlusion appears to be a common underlying mechanism.

References:

CONTRIBUTED BY DAVID J. DICAUDO, M.D
CASE #9 - SLIDE #9

DIAGNOSIS: TARGETOID HEMOISIDEROTIC HEMANGIOMA

Clinical Features:
Targetoid hemosiderotic hemangiomas are small solitary lesions (typically 0.5 -2 cm) most often located on the trunk or extremities in young or middle-aged adults. The center of the target is a violaceous papule, which is surrounded by a paler zone and a peripheral brown or purple ring. A history of trauma may be present.

Histologic Features:
• Biphasic pattern
• Ectatic vessels with plump (hobnail) endothelial cells in superficial dermis
• Vascular channels dissecting collagen bundles in deep dermis
• Intraluminal thrombi in superficial vessels
• Perivascular lymphocytic inflammation
• Hemosiderin deposition

Differential Diagnosis:
• Kaposi's sarcoma - plasma cells, eosinophilic inclusions, nuclear hyperchromasia
• Well-differentiated angiosarcoma - cytologic atypia and multi-layering of cells
• Retiform hemangioendothelioma - deeper infiltration; less circumscribed
• Progressive lymphangioma - lacks biphasic growth pattern; less "hobnailing"

Discussion:
The term "hobnail hemangioma" has been proposed to include both targetoid hemosiderotic hemangioma (THH), as well as other histologically similar vascular tumors which lack the distinctive clinical features of THH. In addition to the points listed above, the biphasic growth pattern is particularly important in distinguishing these lesions from other more worrisome diagnoses. The clinical behavior is benign, but the infiltrative histologic pattern may mimic a malignancy.

References:

CONTRIBUTED BY DAVID J. DICAUDO, M.D
CASE #10 - SLIDE #10

DIAGNOSIS: METAPLASTIC SYNOVIAL CYST

Clinical Features:
- Tender nodule
- History of prior surgery or trauma

Histologic (and Immunophenotypic) Features:
- Cystic/solid structure with villous projections resembling hyperplastic synovium
- Vimentin and CD68 positive lining cells variably present
- Often only fibrin present

Differential Diagnosis:
- Villonodular tenosynovitis
- Spindle cell lipoma
- Fibrous hamartoma
- Organizing cyst or abscess cavity
- Solitary fibrous tumor

Discussion:
Metaplastic synovial cyst of the skin is characterized by a tender intradermal nodule that usually occurs at a site of previous trauma. Most reported cases have a history of antecedent cutaneous injury. Histologically, the lesion demonstrates a cystic structure with villous-like projections and a lining resembling hyperplastic synovium. The presence of vimentin and CD 68 positivity of the cells lining the cyst walls supports the similarities between normal and metaplastic synovium.

References:

CONTRIBUTED BY DIRK ELSTON, M.D
CASE #11 - SLIDE #11

DIAGNOSIS: ELASTOFIBROMA DORSI

**Clinical Features:**
- Large soft tissue mass, usually on the back of an older male

**Histologic (and Immunophenotypic) Features:**
- Collagen and amorphous elastin
- Elastic tissue stain demonstrates dystrophic elastic fibers

**Differential Diagnosis:**
- Spindle cell lipoma
- Keloid
- Scar
- Solitary fibrous tumor

**Discussion:**
Elastofibroma is a rare fibrous tumor that most commonly occurs as a solitary tumor in periscapular soft tissues. Rarely, tumors occur on the thighs or other sites such as the oral mucosa. Multiple tumors rarely occur. Histologically, the tumors are composed of spindled and stellate cells that are often CD34-positive. Large masses of collagen form over time with interspersed amorphous elastin. Elastic tissue stains demonstrate abnormal elastic fibers. Nonrandom inactivation of the androgen receptor gene in two tumors in women suggests the possibility of clonality. In one study, 9 of 27 cases exhibited DNA copy number changes involving one or more chromosomes. The most common change was a gain at chromosomal locations Xq12-q22. PET scans, CT scans, ultrasound, and magnetic resonance imaging have all been used to delineate these tumors. In CT scans, the masses are of soft tissue density, similar to adjacent musculature, and may contain linear areas of low density corresponding to fat. On MRI, variable enhancement is noted. A characteristic layered pattern of fatty tissue is noted in CT and MRI scans (low-density by CT, high-signal on T1 images and intermediate signal on T2 MRI images) and fibrous tissue (similar to muscle by CT and by MRI). Low-grade diffuse F-18 FDG uptake is noted with PET scans.

**References:**
Clinical Features
Pemphigus vegetans is a rare variant of pemphigus that presents with vegetative plaques involving the flexural areas and oral cavity. Two clinical subtypes are described: the Neumann variant (more extensive erosive lesions) and the Hallopeau variant (pustular lesions that evolve into vegetative plaques and may result in spontaneous remission).

Histopathologic Features
- Suprabasilar acantholysis (often subtle.)
- Extensive epidermal hyperplasia and papillomatosis.
- Intraepidermal microabscesses with numerous eosinophils.
- Eosinophilic spongiosis.

Immunopathologic Features
- Similar to pemphigus vulgaris.
- DIF – Epithelial cell surface staining with IgG and C3.
- ELISA testing positive for desmogleins (Dsg3>Dsg1).

References

CONTRIBUTED BY CARILYN N. WIELAND, M.D.
DIAGNOSIS: URTICARIAL DERMATITIS HERPETIFORMIS

Clinical Features:
- Urticarial lesions with variable pruritus
- May resolve with purpura
- Generalized pruritus may be present
- May also have pruritus and excoriations over extensors, posterior scalp and buttocks

Histologic (and Immunophenotypic) Features:
- Neutrophils at dermal epidermal junction
- Neutrophils in dermal papillae
- Fibrin at tips of dermal papillae
- Eosinophils may sometimes be numerous

Differential Diagnosis:
- Urticarial pemphigoid
- Epidermolysis bullosa acquisita
- Bullous lupus erythematosus
- Urticaria
- Arthropod reaction

Discussion:
Dermatitis herpetiformis generally presents with pruritus and excoriations on the posterior scalp, extensors and buttocks. Occasionally, linear hemorrhagic lesions are seen on the distal digits. Urticarial lesions may occur, similar to those seen in bullous pemphigoid. Neutrophils are present at the dermal epidermal junction, sometimes clustering in dermal papillae. Fibrin may be noted at tips of dermal papillae. Direct immunofluorescence demonstrates continuous granular IgA at the dermal epidermal junction, typically denser in the papillae. A picket fence pattern of deposits may be noted.

References:
CASE #14 - SLIDE #14

DIAGNOSIS: RUDIMENTARY MENINGOCOELE

Clinical Features:
- Nodule on scalp
- May simulate dermoid cyst, lipoma, or nevus sebaceous

Histologic (and Immunophenotypic) Features:
- Dense, hyalinized collagen bundles intermingled with cuboidal, epithelioid cells
- Pseudovascular spaces
- Cuboidal cells are often gathered in clusters
- Wrap around collagenous fibers, producing "collagen bodies"
- Positive for vimentin and may be positive for an epithelial membrane antigen and desmin.
- Fail to stain for keratin, S100, CD43, Ulex europeus or CD31.

Differential Diagnosis:
- Meningioma
- Spindle cell lipoma

Discussion:
Rudimentary meningocele is a malformation in which meningotheelial elements are noted in the skin and subcutaneous tissue. In the past, some lesions have been described under the designation cutaneous meningioma. Classic meningocele and rudimentary meningocele appear to represent a continuous spectrum. In the majority of cases, no underlying bony defect can be detected. However, imaging studies to exclude any communication to the central nervous system should precede any surgical intervention. Histologically, the dermis and subcutis demonstrate dense, hyalinized collagen bundles intermingled with cuboidal, epithelioid cells that may surround pseudovascular spaces. The cuboidal cells are often gathered in clusters. Meningocytes wrap around collagenous fibers, producing "collagen bodies". They also dissect between collagenous fibers, creating anastomosing spaces that mimic a vascular tumor. Psammoma bodies may be seen. The lesions lack the nodular and sheet-like growth patterns typical of meningiomas of most primary ectopic meningiomas. The flattened or cuboidal cells are positive for vimentin and may be positive for an epithelial membrane antigen and desmin. They fail to stain for keratin, S100, CD43, Ulex europeus or CD31. Ultrastructurally, they had elongated cytoplasmic processes, intermediate filaments in the cytoplasm, and desmosomal junctions.

References:

CONTRIBUTED BY DIRK ELSTON, M.D
CASE #15 - SLIDE #15

DIAGNOSIS: METASTATIC BREAST CARCINOMA

Clinical Features:
52 yo female with nodule of the flank. R/O DF.

Histologic Features:
• Sparsely cellular lesion.
• Cells dispersed interstitially amongst reticular dermal collagen bundles.
• High N/C ration, vesicular chromatin, and prominent nucleus

Differential Diagnosis:
• Dermatofibroma

Discussion:
Most texts state that the common metastases are from lung, breast and colon. Helwig et al found that 69% of metastases in women are breast carcinoma. In our laboratory (and probably many others) the incidence is even much higher than that. Most examples of breast carcinoma are easily recognized as malignant lesions, even if the primary site is in question. Some show an Indian filing pattern typical of breast carcinoma, and most patients have a known history of breast CA. Occasional examples of breast CA are difficult to recognize. This occurs when cellularity is sparse. Such lesions can mimic dermatofibroma and even xanthoma. Metastatic breast CA can show stromal desmoplasia, further mimicking DF. A close inspection of cytologic features usually demonstrates feature typical of adenocarcinoma, including high N/C ration, vesicular chromatin, and prominent nucleus. Such features are not indicative of a DF and should be an impetus for keratin staining.

References:

CONTRIBUTED BY EARL J. GLUSAC, M.D
CASE #16 - SLIDE #16

DIAGNOSIS: METASTATIC RENAL CELL CARCINOMA

Clinical Features:
54 yo male with nodule of the cheek. R/O BCC.

Histologic Features:
• Clear cells
• Minimal pleomorphism
• Unimpressive vasculature

Differential Diagnosis:
• Dermatofibroma

Discussion:
Metastatic renal cell carcinoma is said to account for approximately 6% of cutaneous metastases. In our laboratory, it is the most common metastasis after breast carcinoma and melanoma. Most cases of RCC are easily recognized by the presence of large clear tumor cells with pleomorphic vesicular nuclei. Most exhibit prominent vasculature that is relied upon to make a diagnosis of metastatic RCC. Some have even been reported to mimic pyogenic granuloma and Kaposi's sarcoma. Occasional examples exhibit none of these findings.

References:
CASE #17 - SLIDE #17

DIAGNOSIS: “SPARKS NEVUS”
(NEVUS WITH FEATURES OF SPITZ AND CLARK’S DYSPLASTIC NEVUS)

Clinical Features:
37 yo. male, thigh, atypical nevus vs. melanoma

Histologic Features:
• Broad, symmetric lesion
• Large monomorphic melanocytes
• Nest predominate
• Confluence of nests, with fibroplasia
• Relatively well circumscribed
• Dull pink epidermal globules
• Cells above dermal-epidermal junction in foci

Differential Diagnosis:
• Malignant melanoma

Discussion:
While neither rare nor newly recognized, little has been written about Spark's nevus. It predominantly an oral teaching, attributed to A.B. Ackerman. In 1999, Toussaint and Kamino reported that approximately 3% of "dysplastic" nevi show Spitzoid features. The combination of Spitzoid cytologic changes with Clarks/dysplastic architectural features may lead to misdiagnosis of this lesion as malignant melanoma. (It should be noted that the pigmented spindle cell nevus often exhibits a Clark's/dysplastic-like growth pattern. Lesions with Spitzoid cells of the epithelioid type are less common, and, in my experience, less easily recognized.) While not well studied, Sparks nevi appear to be most commonly encountered on the thighs of women.

References:


CONTRIBUTED BY EARL J. GLUSAC, M.D
CASE #18 - SLIDE #18

DIAGNOSIS: DERMATOFIBROSARCOMA PROTUBERANS

Clinical Features:
34 yo. female with "lesion" of shoulder.

Histologic Features:
• Monomorphous spindled cells, in parallel array (few in number in this biopsy)
• Cells entrap lipocytes (again, few in number in this biopsy)

Differential Diagnosis:
• Dermatofibroma
• Neurofibroma, diffuse type
• Dermatomyofibroma

Discussion:
Dermatofibrosarcoma protuberans (DFSP) is well known to dermatopathologists. While most examples are readily diagnosed, small superficial biopsies (such as this one) can lead to misdiagnosis and to some of the poorest outcomes in dermatology. It is a lesion of low-grade malignancy with a propensity for frequent local recurrence. It typically presents on the trunk or proximal extremities, but may present on the head and neck. Young adults are most commonly affected. DFSP is a lesion of the deep dermis and subcutis. It is composed of monomorphous spindled cells. Paradoxically, they are more uniform and less "atypical" appearing than the cells of many dermatofibromas. DFSP typically exhibits wavy bundles of these cells in parallel array (in plaques) or in a storiform pattern (in nodules). The most characteristic feature of DFSP is that it tends to entrap lipocytes and form a tiered pattern in the subcutis (honeycombing). Some lesions exhibit prominent mucin, which is a helpful feature in the differential diagnosis between DFSP and other sclerotic tumors. Plaques of DFSP are typically CD34 positive, while nodules are CD34 negative. Diffuse type neurofibroma can be excluded by negativity for neural markers, such as S100, myelin basic protein, Leu 7 and neuron specific enolase. Some studies have shown up to a 60% recurrence rate with DFSP, including a recurrence rate of up to 23% with 4 cm margins. Several articles have been written regarding Moh's surgery in the setting of DFSP. In interpreting a Moh's specimen for DFSP, it is prudent to inform the surgeon that the margins show completely normal skin (i.e. no scar, as it can be extraordinarily difficult to differentiate scar from tumor).

References:

CONTRIBUTED BY EARL J. GLUSAC, M.D
Clinical Features:
This biopsy is from a 28-year old male with a nodular mass of the elbow. The clinical differential diagnosis was keloid versus rheumatoid nodule versus granuloma annulare. Upon further questioning, the patient disclosed a history of serum lipid abnormalities since the age of 15, which have been controlled with diet.

Histologic Features:
• A fairly well circumscribed nodular aggregate of histiocytes within the dermis
• Most histiocytes exhibit foamy (lipidized) cytoplasm
• Histiocytes are dispersed as small clusters, aggregates, or cords between coarse collagen bundles
• Touton type giant cells with accompanying neutrophils and/or eosinophils (features of xanthogranuloma) are absent

Differential Diagnosis:
• Xanthelasma and other types of xanthomata
• Xanthogranuloma and other types of non-Langerhans cell histiocytoses
• Lipidized (ankle-type) fibrous histiocytoma

Discussion:
Tuberosus xanthoma is most often seen in association with familial dysbetalipoproteinemia Type III, but can also be associated with other types of hyperlipidemia, including homozygous Type HA hypercholesterolemia, Type IV hyperlipoproteinemia, cerebrotendinous xanthomatosis, and 3- sitosterolemia. Clinically, tuberous xanthoma presents as yellow-red nodules on the elbows or knees. The histologic appearances of xanthelasma, tendinous xanthoma, and tuberous xanthoma are nearly identical, and clinical locale is used to accurately diagnose these xanthoma subtypes. Tuberous xanthoma lacks the Touton type giant cells and accompanying neutrophils, and eosinophils that characterizes xanthogranuloma, and other types of non-Langerhans cell histiocytoses. Lipidized fibrous histiocytoma is a distinctive type of histiocytoma that characteristically occurs around the ankle and is usually not associated with errors of lipid metabolism.

References:
Clinical Features:
This biopsy is from a 19 year old female with a linear plaque of the right posterior lower leg, which has been present since early childhood.

Histologic Features:
- Epidermal hyperplasia (psoriasiform) with mild papillomatosis and broad rete ridges
- Hyperkeratosis with sharply demarcated alternating zones of orthokeratosis and parakeratosis
- Beneath zones of orthokeratosis, there are cup-shaped dells with hypergranulosis
- Mild perivascular lymphocytic inflammation with epidermal spongiosis and exocytosis of lymphocytes

Differential Diagnosis:
- Epidermal nevus
- Linear psoriasis
- Lichen striatus

Discussion:
Inflammatory linear verrucous epidermal nevus (ILVEN) is a rare form of epidermal nevus, which has its onset at birth or in early childhood. Sites of predilection include the legs and thighs. Clinically, the lesion presents as itchy, erythematous papules that coalesce into plaques with a linear distribution, often along the lines of Blaschko. Females are affected more often than males (4:1 female: male ratio), and the left side of the body is affected more often than the right. Rare cases can be bilateral or generalized. ILVEN can be associated with psoriasis, the epidermal nevus syndrome, and arthritis. Histologically, a characteristic feature is the sharply demarcated alternating pattern of parakeratosis and orthokeratosis. The latter distinguishes ILVEN from other forms of epidermal nevus. As in the current case, the zones of orthokeratosis usually occur above shallow dells within the epidermis.

References:
CASE #21 - SLIDE #21

DIAGNOSIS: TUNGIASIS

Clinical Features:
This biopsy is from a 17 year old female Peace Corps volunteer, who recently returned from a trip to Ethiopia. Clinically, there was a black papule on the lateral plantar foot, which the patient described as pruritic. A shave biopsy was performed.

Histologic Features:
- Immediately beneath a hyperplastic epidermis, there is a truncated ectoparasite (the hind parts of the burrowing sand flea, Tunga penetrans), with a chitinous exoskeleton
- A narrow ostium through the hyperplastic epidermis allows the flea to breathe, defecate, and shed its eggs
- Within the body cavity, there are cross sections of numerous round to oval eggs

Differential Diagnosis:
- Tick bite
- Myiasis
- Other parasites, including cutaneous larva migrans and dracunculiasis
- Foreign body

Discussion:
Tungiasis is a parasitic infection, due to the burrowing sand flea, Tunga penetrans. The flea is endemic to South America, the Caribbean, and parts of sub-Saharan Africa, including Ethiopia. In addition to humans, reservoir hosts include cattle, horses, dogs, pigs and rats. The gravid female burrows head first into the skin of the host, with its hind parts exposed to the outside world via a narrow orifice. In humans, the site of penetration is usually the foot, in particular the plantar, interdigital or periungual areas. Over the course of 2-3 weeks, the female increases in size due to accumulation of hundreds of eggs within her body cavity. Clinically, this produces a papule or nodule with a central black punctum. The eggs are eventually shed and fall to the soil, where they hatch and become adults. The imbedded mother flea subsequently dies and is eventually sloughed. The majority of cases resolve spontaneously, without sequelae, but rare cases can lead to secondary bacterial infection including cellulitis, gangrene, and tetanus. Treatment options include manual extraction, surgical excision, cryotherapy, topical ivermectin, niridazole (not available in the U.S.), and suffocation with petrolatum.

References:

CONTRIBUTED BY JEFF D. HARVELL, M.D
CASE #22 - SLIDE #22

DIAGNOSIS: TEMPORAL (GIANT CELL) ARTERITIS

Clinical Features:
An 82 year old female presented with a chief complaint of headache. On physical exam, there were palpable nodules within the scalp, distributed along the temporal artery. Laboratory exam disclosed an elevated ESR and an elevated C-reactive protein.

Histologic Features:
• A medium caliber arteriole exhibits a mononuclear cell vasculitis
• The vasculitis is characterized by fibrinoid necrosis of the vascular wall, along with infiltration by an inflammatory infiltrate composed of lymphocytes and histiocytes
• In this case, significant numbers of multinucleated macrophages are absent

Differential Diagnosis:
• Polyarteritis nodosa
• Takayasu's arteritis
• Systemic vasculitides, including Wegener's granulomatosis

Discussion:
Temporal (giant cell) arteritis is a form of vasculitis which chiefly affects the elderly, with a marked female predominance. It is often associated with polymyalgia rheumatica, and blindness is a potential complication. Histologically, temporal arteritis is a mononuclear vasculitis, the principal inflammatory cells being histiocytes and lymphocytes. Multinucleated macrophages are characteristic and are seen in association with destruction of the elastic lamina. However, some cases (like the current one), may lack multinucleated macrophages, and the latter are not requisite for the diagnosis. Takayasu's arteritis can show virtually identical histopathologic features, but Takayasu's arteritis typically affects patients younger than 40, and principally involves the aorta and its major branches.

References:

CASE CONTRIBUTED BY JEFF D. HARVELL, M.D
Clinical Features:
A 41 year old female presented with a nodular mass of the inner thigh.

Histologic Features:
- A hypocellular proliferation within the dermis, composed of spindle cells with wavy nuclei that are set within a variably collagenous, sclerotic, or myxoid background stroma
- Scattered multinucleated giant cells, many of which line compressed, irregularly branching angiectoid spaces. Giant cells have hyperchromatic, angulated nuclei, which are either conglomerated toward the center of the cell or arranged at the periphery in a characteristic "floret-like" pattern
- Spindle cells and multinucleate giant cells are CD34 positive

Differential Diagnosis:
- Neurofibroma
- Lymphangioma
- Myxoid malignant fibrous histiocytoma (MFH)

Discussion:
First recognized in 1982 as a juvenile form of DFSP, giant cell fibroblastoma (GCF) is a histologic variant of DFSP, which primarily affects children, predominantly males. Occasional cases have also been reported in adults. Supporting evidence that GCF and DFSP are related tumors includes a common t(17;22) in both, CD34 positivity in both, cases of GCF which recur as DFSP (or Bednar tumor), cases of DFSP which recur as GCF, and hybrid lesions which show components of both GCF and DFSP (or Bednar tumor) within the same primary or recurrent lesion. Like DFSP, GCF is a locally aggressive tumor of intermediate malignancy, with a substantial 50% or greater chance for local recurrence if incompletely excised. The t(17;22) (q22;q13) translocation, results in a chimeric COL1A1-PDGFB gene that encodes for a transforming protein with growth factor effects similar to normal PDGFB.

References:
Clinical Features:
This biopsy is one of two from a 69-year-old man with a biopsy from his thigh, r/o Darier's disease or Grover's disease. There are numerous crusted red scaly papules on his arms and legs.

Histologic Features:
• Epidermal atrophy with hypogranulosis, surmounted by discrete area of compact hyperkeratosis
• Band-like lymphocytic infiltrate in the papillary dermis.
• These changes are flanked by elongated rete

Differential Diagnosis:
• Lichenoid keratosis
• Lichenoid actinic keratosis
• Mycosis fungoides
• Acrokeratosis paraneoplastica (Basex Syndrome)
• Lupus erythematosus

Discussion:
Hyperkeratosis lenticularis perstans, also known as Flegel's Disease, is a rare condition described by Flegel in 1958. It is characterized clinically by numerous 1-5mm hyperkeratotic papules that typically arise on the extremities, especially the dorsal feet and lower legs. It was initially considered to be autosomal dominant, but numerous sporadic cases, arising in late adulthood have been reported. Clinically, the lesions simulate stucco keratoses, actinic keratoses, porokeratosis, Kyrle's disease, and Darier's disease. The lesions may involve the trunk and oral mucosa. Histologically, the lesions are characterized by discrete foci of compact hyperkeratosis, overlying an area of epidermal atrophy, with hypogranulosis. The underlying papillary dermis usually shows a dense band-like T lymphocytic infiltrate, with cerebriform atypia, and a predominance of helper T cells. Adjacent to this is rete hyperplasia. Only rarely have cases of Flegel's without the lymphocytic infiltrate been reported. Ando, Hattori, and Yamauchi reported histopathological features of both early and late lesions, and demonstrated lesions with hyperkeratosis without an associated lymphocytic infiltrate. Ultrastructural studies have shown absent, diminished or malformed membrane-coating granules (lamellar granules and Odland bodies) within the lesional keratinocytes, however, these findings have not been confirmed by other authors. Abnormalities of the cornified envelope have also been reported, suggesting that Flegel's disease may be a complex disorder of epidermal differentiation, leading to retention hyperkeratosis.

References:
CASE #25 - SLIDE #25

DIAGNOSIS: TATTOO DERMAL ALERGIC REACTION ASSOCIATED WITH CD30 (+) CUTANEOUS LYMPHOID HYPERPLACIA

Clinical Features:
The biopsy is from a 37 year old man from the left upper arm, submitted with the differential diagnosis of sarcoid and allergic reaction. This biopsy is actually taken from within a tattoo.

Histologic Features:
• There is an intense lymphocytic infiltrate in the superficial and deep dermis
• There is exocytosis into a mildly hyperplastic epidermis with early scale-crust
• The infiltrate is composed predominantly of small to medium-sized lymphocytes with scattered larger atypical lymphocytes
• Immunohistochemical stains demonstrated a CD3 predominant infiltrate with minimal B cell staining
• Many large lymphocytes stained positive for CD30, but these cells did not predominate
• Amidst the infiltrate are macrophages containing red pigment

Differential Diagnosis:
• Insect bite reaction
• Idiopathic cutaneous lymphoid hyperplasia
• Lymphomatoid papulosis
• Halo reaction to a melanocytic proliferation
• Syphilis
• Lupus erythematosus

Discussion:
Tattoo reactions present most often with a lichenoid allergic reaction, but cutaneous lymphoid hyperplasia (CLH) may be seen. Tattoo reactions are often seen with red pigment, but reactions to multiple colors have been reported. The immunogenic potential of mercury compounds that are often present in red tattoo dye may explain this common reaction. There may be a dense nodular superficial and deep infiltrate, simulating B cell lymphoma. In this case, a mixture of B and T lymphocytes admixed with histiocytes, eosinophils, and plasma cells and a predominance of the T cells, favor cutaneous lymphoid hyperplasia. The biopsy from this patient showed features of cutaneous lymphoid hyperplasia, but was unusual, in that there were numerous CD30 positive cells, simulating lymphomatoid papulosis.

References:

CONTRIBUTED BY JACQUELINE M. JUNKINS-HOPKINS, M.D
CASE #26 - SLIDE #26

DIAGNOSIS: CELLULAR PHASE OF PALMAR FIBROMATOSIS

CLINICAL FEATURES:
A 60 year old man presents with a 6 mm “unusual” tumor at the base of his left thumb, reportedly present for one month.

HISTOLOGIC FEATURES:
• Cellular, vaguely fascicular array of fibrocytes and myofibrocytes that form a larger cellular nodule
• Relatively high cellularity with only modest nuclear variation
• Mitotic figures identifiable in modest numbers
• Background of “conventional” fibromatosis, sometimes

DIFFERENTIAL DIAGNOSIS:
• Fibrosarcoma—differs from fibromatosis in that it typically shows greater cellularity, a greater degree of nuclear variation and greater numbers of mitoses, and in most instances, a stereotypical “herring-bone” configuration with cross-hatched fascicles.
• Hypertrophic scar—there is considerable overlap between the findings of a cellular scar and cellular fibromatosis; greater cellularity favors the latter, while an accentuated vascular pattern and an accentuated degree of collagenization favors the former

DISCUSSION:
The findings in palmar-plantar fibromatosis are relatively well characterized. Histopathologically, one expects a tendon-like, vaguely fascicular fibrous proliferation that is generally restricted to the reticular dermis. Overall cellularity is usually relatively low, and there is little risk of misinterpretation as a soft tissue neoplasm or sarcoma. In some patients, cellular nodules develop within a background of fibromatosis. This phenomenon has not been well characterized; the term “cellular phase” of fibromatosis was coined by Chris Fletcher. Such lesions present in nodular, tumor-like fashion. Although formal study to date has been only anecdotal, experience to date suggests that such nodules are completely harmless.

REFERENCES:

CONTRIBUTED BY: TIMOTHY MCCALMONT, MD
CASE #27 - SLIDE #27

DIAGNOSIS:  ACROKERATOELASTOIDES MARGINALIS
(WEATHERING NODULES)

CLINICAL FEATURES:
There are papular lesions of the hands, especially along the sides of digits.

HISTOLOGIC FEATURES:
- Marked elastosis of the upper dermis, with both amorphous elastotic collections and smaller fragmented fibers, the latter calcified
- Superficial hyperkeratosis, typically orthokeratotic
- Scattered strikingly thickened collagen fibers in the upper reticular dermis
- Associated telangiectasia, often

DIFFERENTIAL DIAGNOSIS:
- Colloid milium—linked to acrokeratoelastoidosis through its elastotic background, but differs in that refractile, glassy deposits are evident in the upper dermis
- Nodular solar elastosis—consists of amorphous, globular elastotic deposits, in contrast to the filamentous and vaguely fascicular pattern of acrokeratoelastoidosis

DISCUSSION:
Acrokeratoelastoidosis is more common than recognized but remains a poorly understood entity with poor and inconsistent nomenclature. Some authorities consider it a disorder of connective tissue, while others (notably Weedon) view reported cases as representing a type of keratoderma. It may be that several distinct disorders with overlapping clinical findings have been aggregated in existing reports, contributing to confusion.

The designation “weathering nodules” has also been inconsistently applied in the literature and in textbook presentations of the subject. Some authorities utilize the term synonymously with acrokeratoelastoidosis, while to others a weathering nodule is restricted to the ear.

REFERENCES:

CONTRIBUTED BY: TIMOTHY MCCALMONT, MD
DIAGNOSIS: ENDOCHONDRAL PSEUDOCYST OF THE EAR

CLINICAL FEATURES:
Endochondral pseudocyst (EP) presents as non-inflammatory, fluctuant swelling of the upper ear. It is typically unilateral, but bilateral cases have been reported. It is usually asymptomatic, and often there is no history of trauma. Aspiration reveals yellow, viscous fluid. Recurrence following aspiration is common, and surgical intervention is often necessary.

HISTOLOGIC FEATURES:
Histologic findings vary somewhat on when the sample is taken. Early, there is central replacement of involved cartilage by an unlined space. Residual cartilage, if present, may exhibit eosinophilic degeneration and replacement by fibrosis. Longstanding lesions have more fibrosis, and can exhibit granulation tissue. A mild perivascular lymphocytic and plasmacytic infiltrate, telangiectasia and dermal edema may be present.

DIFFERENTIAL DIAGNOSIS:
Subperichondrial hematoma (othematoma) – contains blood; not intracartilaginous
Relapsing polychondritis - more perichondrial, more inflammation
Chondrodermatitis nodularis helicis
Cellulitis

DISCUSSION:
EP was first described in 1886, and the first histologic description was reported by Engel in 1966. A synonym is benign idiopathic cystic chondromalacia. Seroma of the auricle is likely the same entity. It is more common in men, and most patients are between 20 and 45. The cause of EP is unknown. Theories include an embryologic malformation resulting in a potential space, a lysosomal disorder, or repeated, low level trauma to the ear, causing either ischemic necrosis of the cartilage or overproduction on glycosaminoglycans. This later finding may be secondary, not causative, and the finding of increased LDH in EP fluid suggests that degenerated cartilage is likely the fluid source.

There is little written in the literature on EP. A retrospective study by Heffner and Hyams identified 23 cases. These authors point out that the importance of the intracartilaginous rather than pericartilaginous findings on biopsy, which may not be obvious in a small specimen. Occasional cases demonstrated proliferation of cartilage, which could have a few atypical cells. Prominent granulation tissue could suggest a vascular neoplasm. However, the histopathologic diagnosis is usually straightforward if one is aware of the entity and the specimen is adequate. The only known association of EP with other disorders is a report of four children with EP and atopic dermatitis. Treatment is surgical, and resultant deformity is common. The age of this patient and presence of calcification are unusual features, although calcification has been reported in two patients.
REFERENCES:

CONTRIBUTED BY: LYNNE J. GOLDBERG, MD
CLINICAL FEATURES:
Erythema nodosum leprosum (ENL) is an inflammatory reaction which occurs in patients with lepromatous or borderline lepromatous leprosy. Patients present with bilaterally symmetric, tender crops of tender dermal and/or subcutaneous nodules that arise on normal skin of the face and extensor extremities, at times associated with fever, chills, arthritis, and malaise. Lesions can rarely be vesiculobullous, ulcerative, hemorrhagic and erythema-multiforme like. The reaction can be spontaneous, at times leading to the initial diagnosis of leprosy, or precipitated by things such as treatment, concurrent bacterial or viral infections, or pregnancy.

HISTOLOGIC FEATURES:
Histologic findings are quite variable. The typical findings are a superficial and deep perivascular infiltrate of lymphocytes and foamy histiocytes, at times involving the subcutis. Neutrophils are present in most, but not all, cases. They range in density from mild and perivascular to marked with abscess formation. Some, but not all, biopsies exhibit leukocytoclastic vasculitis. More neutrophils and vascular changes are present in early lesions. Aggregates of foamy histiocytes with organisms on Fite stain is a universal finding.

DIFFERENTIAL DIAGNOSIS:
Lepromatous leprosy (not in reaction)
Infections with parasitized histiocytes

DISCUSSION:
Leprosy is a chronic, slowly progressive infection with Mycobacterium leprae that primarily affects the skin and peripheral nervous system. It is classified based on the morphology of the lesions clinically, and the mycobacterial load. Reactional states in leprosy are acute exacerbations which are serious and need to be promptly diagnosed and treated to avoid permanent disability. With the successful use of multi-drug therapy for leprosy, reactions are now one of the most significant leprosy patient management issues.

ENL is a reactional state that occurs in patients with multibacillary leprosy. It is proposed that ENL is a manifestation of immune-complex mediated vascular injury, based on direct immunofluorescent findings of perivascular immunoglobulins and complement deposition in lesional skin, circulating C1q precipitants in serum, and immune-complex mediated glomerulonephritis in some patients. It is estimated that nearly 25% of patients will develop this complication, and half of these will have nerve involvement as well as skin lesions.

The incidence of ENL appears to have decreased with the introduction of multidrug therapy. Interestingly, it is often the reaction that prompts a clinician visit, despite the presence on longstanding symptoms of leprosy. The presence of neutrophils in a biopsy with changes of lepromatous leprosy is a clue to the diagnosis. In a study of 28 ENL patients by Rea and Levan, neutrophils were present in 86%, and leukocytoclastic vasculitis in 25%. Hussain, et al. found neutrophils on 65% of their 45 ENL patients, and found that neutrophil positive patients were more likely to have recurrent episodes of ENL. In a study on cutaneous microvascular alterations in ENL, vascular findings other than LCV included perivascular mononuclear infiltrates, endothelial swelling, luminal obliteration, distortion of vascular architecture, and fibrin deposition, all found in vessels of varying caliber. EM revealed electron dense deposits in
the perivascular basement membrane zone, similar to changes described in the kidney, evidence the authors felt favored an immune complex etiology. The take home message is that neither vasculitis nor neutrophils are necessarily always present in ENL, and the diagnosis can not be excluded based on their absence.

REFERENCES:
DIAGNOSIS: HYPOPIGMENTED MYCOSIS FUNGOIDES

CLINICAL FEATURES:
Hypopigmented mycosis fungoides (HMF) is a variant of cutaneous T-cell lymphoma that, as the name implies, presents with hypopigmented macules. Some, but not all, patients have other more typical lesions of mycosis fungoides (MF). It is seen mostly in dark skinned individuals, tends to occur in a younger age group than standard MF, and can be seen in children. The diagnosis is often delayed, especially because frequently MF is not initially suspected. Patients are usually stage I, and prognosis is similar to that of normally pigmented patients.

HISTOLOGIC FEATURES:
The histologic and immunophenotypic findings in HMF can be indistinguishable from non-hypopigmented MF. Many early reports describe both individual atypical lymphocytes within the epidermis, as well as small collections of atypical lymphocytes and Pautrier’s microabscesses. The epidermis is not atrophic. The dermal infiltrate can be sparse. It soon became apparent that the neoplastic lymphocytes could either be CD4 predominate or CD8 predominate, and one large retrospective series has found that the majority of cases were CD8+ (El Shabrawi-Caelen et al). Individual case reports of negative T-cell gene rearrangements were followed in 2000 by a series by Qari et al. in which 3 of 4 patients tested had a positive T-cell gene rearrangement.

DIFFERENTIAL DIAGNOSIS:
Vitiligo
Pityriasis alba
Pityriasis lichenoides chronica
Clinically hypopigmented entities – leprosy, tinea versicolor, atopic dermatitis, lichen sclerosis, sarcoidosis, syphilis

DISCUSSION:
Hypopigmented mycosis fungoides was first reported by Ryan et al. in 1973. The mechanism of hypopigmentation remains uncertain. Early reports documented degenerative changes in melanocytes on electron microscopy, however, these changes are not specific for mycosis fungoides. Others feel that faulty melanosome transfer leads to hypopigmentation. Possibly multiple factors are at work. While most reported patients have been dark skinned, scattered patients with light skin have been reported, including a recent series in Caucasians (Ardigo et al.).

The increased incidence of HMF in children in comparison to non-hypopigmented MF is disconcerting, especially because it is this age group in which the disease is most unsuspected. In studies of MF in childhood, the percentage of patients with HMF ranged from 20% to 89%. Variables that could affect these figures include the age range chosen, and whether patients who also had non-hypopigmented lesions were included. Most patients respond well to treatment, although the disease is often recurrent.
REFERENCES:

CONTRIBUTED BY: LYNNIE J. GOLDBERG, MD
Clinical and Histopathologic Findings
The diagnosis of LyP can be challenging to the dermatopathologist due to the protean histologic features of the disease. Rare histologic variants may pose a diagnostic problem, especially if not all the relevant clinical information is provided. LyP is well-recognized as an entity with characteristically discrepant clinical and histologic features, with an indolent clinical course despite a frequently worrisome histologic picture. LyP type D, is a recently described histologic variant that mimics an aggressive epidermotropic cytotoxic lymphoma, highlighting the importance of close clinicopathologic correlation to establish a correct diagnosis. Awareness of this variant is important for the correct management of these patients. The histology of LyP type D shows marked epidermotropism of atypical lymphoid cells, with almost complete replacement of the epidermis, in a pagetoid reticulosis-like pattern, and associated spongiosis, ulceration, and overlying scale crust. In the dermis, there is usually a population of small- to medium-sized lymphocytes with many admixed large cells containing large nuclei. By immunohistochemistry, the atypical lymphoid infiltrate in LyP type D has a cytotoxic profile (CD8+) along with co-expression of CD30.

References
CLINICAL FEATURES:
Paraffinoma, sometimes referred to as sclerosing lipogranuloma, is a granulomatous foreign body reaction typically resulting from injection of paraffin or mineral oil into the skin. Paraffin and mineral oil, its liquid counterpart, consist of straight-chain saturated hydrocarbons. Injections have been done for medicinal or cosmetic indications, including male pattern hair loss and penile enhancement. Cases without a history of injection have been reported, including one from a retained nasal packing impregnated with an antibiotic in a paraffin base. Patients present with variable swelling, nodularity and tenderness. The onset can be delayed, and occurs weeks to years after injection. Extracutaneous involvement of lymph nodes and lungs has been described, presumably from lymphatic or hematogenous dissemination.

HISTOLOGIC FEATURES:
The diagnostic histologic changes occur in the deep dermis and subcutis. There are multiple round to oval spaces likened to Swiss cheese. A variable inflammatory infiltrate of histiocytes and lymphocytes may be present. Hyalinization of collagen has been described, and fibrosis occurs over time. Lipid can be found on staining of fresh frozen tissue for Oil Red O. The presence of lipid can be confirmed by infrared-absorption spectrophotometry and thin layer chromatography.

DIFFERENTIAL DIAGNOSIS:
The histologic picture is fairly typical. One could consider an infectious process.

DISCUSSION:
Substances containing paraffin were used in intramuscular injections and for cosmetic purposes in the early 1900’s, but their use was short lived due to reports of disabling and deforming tissue reactions. While most medical professionals have abandoned their use, cases still occur due to use by non-medical personnel and patients themselves. Most recently reported cases have been due to self-injection of the penis for purposes of enhancement. Our patient had injections to her buttocks in South America, presumably for cosmetic enhancement.

As opposed to vegetable oils, which are sometimes used in the administration of certain hormones for injection, the body lacks enzymes to metabolize petroleum derived oils such as paraffin and mineral oil. Most patients in contact with these oils will not have any reaction, but a small percentage will develop paraffinoma due to a non-specific inflammatory response to the deposited oil. It is not known whether dose, structure of the oil, impurities present, or host factors play a role.

Paraffinoma is important to recognize histologically, as patients will often deny self-injection at first, and are at times incorrect about the nature of the substance injected. A patient with a right upper quadrant mass underwent surgery for a diagnosis of atypical lipomatous tumor made on frozen section. Only when it was discovered that she had paraffinoma did she admit to injections to both breasts several years before. Death has been reported from pulmonary edema and pulmonary paraffinoma following penile paraffinoma from self injection.
REFERENCES:

CONTRIBUTED BY: LYNNE J. GOLDBERG, MD
CASE #33 - SLIDE #33

DIAGNOSIS: PAPILLARY ECCRINE ADENOMA

CLINICAL FEATURES:
---Rare tumor, usually found on extremities
---Predilection for black females
---Slow growing, asymptomatic
---Benign, recurrences rare.

HISTOPATHOLOGY:
---Located in mid to lower dermis
---Well circumscribed but unencapsulated
---Dilated branching ducts and cysts
---Lined by banal eosinophilic cells with papillary projections and cribriform pattern
---Foci of clear cell change may be present, but decapitation secretion should not be present
---Necrosis, atypia and mitotic figures are NOT typical findings.

DIFFERENTIAL DIAGNOSIS:
---Aggressive digital papillary adenocarcinoma
   ---more infiltrative with nuclear atypia and mitotic activity
---Metastatic adenocarcinoma
   ---more infiltrative with nuclear atypia and mitotic activity
---Hidradenoma papilliferum
   ---usually in groin, prominent decapitation secretion
---Tubular apocrine adenoma
   ---rare, found in axilla or scalp
   ---prominent decapitation secretion.

REFERENCES:

CONTRIBUTED BY J. MARGARET MORESI, M.D.
DIAGNOSIS: MALIGNANT CYLINDROMA

CLINICAL FEATURES:
--- Extremely rare
--- May arise from pre-existent solitary tumor or from the autosomal dominant multiple tumor variant (Turban tumor)
--- Most common on scalp
--- Most patients aged 70-90 years.
--- Some cases have developed following therapeutic radiation.

HISTOPATHOLOGY:
--- Prominent basement membrane structure surrounding lobules
--- No connection to the overlying epidermis
--- Some retention of jigsaw or mosaic pattern, but also exhibit a sheet-like growth pattern
--- Infiltrating growth pattern, necrosis and nuclear pleomorphism.

DIFFERENTIAL DIAGNOSIS:
--- Cylindroma: lack necrosis, well-circumscribed, retain the jigsaw pattern
--- Eccrine spiradenoma: biphasic cell population, ductular differentiation
--- Trabecular carcinoma (a/k/a Merkel cell carcinoma): nuclear molding, neuroendocrine features
--- Trichoblastoma: condensation of stroma, primitive hair germ formations.

REFERENCES:
CASE #35 - SLIDE #35

DIAGNOSIS: LEIOMYOSARCOMA

CLINICAL FEATURES:
---Superficial tumors can be further subdivided into two groups:
   ---Cutaneous (predilection for lower limbs)
      ---usually derived from arrector pili
      ---can recur if incompletely excised
      ---metastasis rare.
   ---Subcutaneous
      ---may arise from vascular structures
      ---recurrence common
      ---metastasis in 50%.

HISTOPATHOLOGY:
---Cutaneous leiomyosarcoma tends to present as a non-circumscribed, diffuse lesion
---Subcutaneous typically a well-circumscribed nodule
---Interlacing bundles of spindle cells with blunt-ended nuclei and perinuclear clearing
---Significant pleomorphism
---Mitotic figures, including atypical forms
---Immunohistochemistry: positive for desmin, actin and other smooth muscle markers; no staining with S100, keratin or CD34.

DIFFERENTIAL DIAGNOSIS:
---Schwannoma: tapered nuclei, S100 positive, Antoni A/B areas with Verocay bodies
---Dermatofibrosarcoma protuberans: storiform pattern, CD34+, actin-
---Nodular Kaposi’s sarcoma:
    ---Spindle cells forming slit-like vascular channels, CD34+
    ---Hemorrhage, plasma cells, promontory sign.

REFERENCES:

CONTRIBUTED BY J. MARGARET MORESI, M.D.
CASE #36 - SLIDE #36

DIAGNOSIS: METASTATIC ADENOCARCINOMA CONSISTENT WITH GI (BILIARY) PRIMARY

CLINICAL FEATURES:
This patient had a history of gallbladder carcinoma two years prior to the development of these subcutaneous nodules.
---Metastatic adenocarcinomas are the most common variant of cutaneous metastasis.
---Breast is the most frequent source, with lung and large intestine as other possible primary sites.
---Well-differentiated glandular architecture favors an intestinal primary.
---The presence of cutaneous metastasis is associated with an average survival of six months following diagnosis.
---Complete knowledge of the patient’s history is vital in definitive diagnosis.

HISTOPATHOLOGY:
---Infiltration of the dermis and subcutaneous tissue by ductular structures as well as single pleomorphic cells
---Surrounding desmoplastic stroma
---Marked nuclear atypia and mitotic activity.

DIFFERENTIAL DIAGNOSIS:
---Primary adnexal carcinoma, such as eccrine carcinoma, is difficult to distinguish histologically, but metastatic disease tends to exhibit more marked atypia and desmoplasia.
---Positive p63 immunostaining was recently reported as an indicator of primary cutaneous adnexal neoplasms.

REFERENCES:

CONTRIBUTED BY J. MARGARET MORESI, M.D.
CASE #37 - SLIDE #37

DIAGNOSIS: ANGIOINVASIVE FUNGAL INFECTION

CLINICAL FEATURES:
This patient had a history of hairy cell leukemia and was neutropenic. Cultures of the skin biopsy subsequently grew out Fusarium moniliforme.
---Angioinvasive fungal infections are more common in immunosuppressed patients
---Zygomycetes, Aspergillus, Fusarium and Pseudallescheria are all genera that have been responsible pathogens.
---Neutropenic patients are particularly at risk for systemic dissemination and may develop widespread pulmonary infiltrates.
---Lesions start as red papules which may become pustular or noduloulcerative.

HISTOPATHOLOGY:
---Vascular injury and purpura
---Brisk mixed dermal inflammatory infiltrate
---Infiltration of vessel walls by hyaline, branching septate hyphae: fungal forms also present in the interstitium.

DIFFERENTIAL DIAGNOSIS:
---Zygomycetes: fungal forms of variable width, broad and ribbon-like with right-angle branching; cultures provide definitive distinction.
---Cellulitis: neuts in dermis; lacks hemorrhage; need cultures
---Thrombotic thrombocytopenic purpura: non-inflammatory fibrin thrombi
---Pigmented purpuric dermatosis: hemorrhage; no vasculitis
---Kaposi’s sarcoma: atypical spindle cell proliferation with hemorrhage.

REFERENCES:

CONTRIBUTED BY J. MARGARET MORESI, M.D.
DIAGNOSIS: ANGIOSARCOMA

DISCUSSION:
Angiosarcomas are highly aggressive neoplasms that can affect many areas of the skin, but they are most frequent on the face and scalp. In some cases angiosarcomas are associated with chronic lymphedema, usually after mastectomy while other cases develop after radiation. Regardless of the clinical variant, angiosarcomas are histopathologically similar.

KEY HISTOLOGIC FEATURES:
---Poorly circumscribed neoplasm which infiltrates the entire dermis and extends into the subcutaneous tissue, destroying all pre-existing structures.
---Irregular vascular spaces which dissect collagen bundles, these spaces are lined by atypical endothelial cells with large pleomorphic nuclei. Numerous mitosis both typical and atypical are easily identified.
---Other areas may show solid cellular aggregates, which sometimes have areas of necrosis.
---In some cases there is an intense inflammatory reaction, mainly composed of lymphocytes and histiocytes. Sometime the reaction is so intense that the lesion may be confined with an inflammatory lesion or lymphoma.

DIFFERENTIAL DIAGNOSIS:
---Kaposi’s sarcoma
---Hobnail hemangioma
---Carcinomas in cases of epithelioid type of angiosarcoma.

REFERENCES:
DISCUSSION:
The term linear IgA dermatosis designates a group of diseases which are mediated by IgA antibodies against different components of the epidermal basement membrane. These diseases can affect adults and children, and it is felt that they are indistinguishable by either histology or immunofluorescence. Both show linear deposition of IgA along the basement membranes. Reports on the association of linear IgA disease with various medications as well as with autoimmune, gastrointestinal and infectious diseases have been made. Additionally, linear IgA disease has been reported in association with multiple malignancies.

KEY HISTOLOGIC FEATURES:
--- Early lesions show collections of neutrophils along the dermal-epidermal junction forming microabscesses.
--- Late lesions have subepidermal vesicles filled with neutrophils and lymphocytes.
--- Direct immunofluorescence studies: linear deposits of IgA along the dermal-epidermal junction.

DIFFERENTIAL DIAGNOSIS:
--- Epidermolysis bullosa
--- Dermatitis herpetiformis
--- Bullous pemphigoid
--- Bullous lupus erythematosus.

REFERENCES:
Clinical Features
Langerhans cell histiocytosis (LCH) incorporates a wide variety of clinical presentations ranging from single or localized cutaneous lesions to widespread multisystem involvement with organ failure. Generalized involvement is most often seen in young children less than 2 years of age with reddish-brown papules around the scalp, groin, axillae and torso. Involvement in adults and elderly patients is rare, and can follow a chronic course or be similar to acute generalized LCH in children with organ dysfunction and high mortality. The spleen, lymph nodes, bone marrow, liver (as in our patient), and lungs can all be involved. LCH is also reported in association with other, especially hematologic, malignancies.

Histopathologic Features
- Cells with reniform nuclei.
- Abundant pale, eosinophilic cytoplasm.
- Epidermotropism with Pautrier-like microabscesses.
- Adult form may show periadnexal or follicular distribution.
- Numerous eosinophils may be present.

References
DISCUSSION:
Epithelioid sarcoma is a malignant neoplasm which usually involves the deep dermis and underlying soft tissues. It usually affects the extremities of young adults. Clinically, it presents as one or more slow growing, painless nodules with an infiltrating margin which may ulcerate. It is fairly common for these lesions to recur and metastasize. Adverse prognostic features include: proximal or axial locations, tumor size greater than 5 cm, deep extension, vascular invasion and numerous mitotic figures.

KEY HISTIOLOGIC FEATURES:
---Nodular aggregate with prominent central areas of necrosis surrounded by large cells
---In some cases the neoplastic cells dissect the collagen bundles.
---The neoplastic cells are oval to polygonal with eosinophilic cytoplasm with pleomorphic nuclei.
---Mitotic figures are easily identified.
---Immunohistochemically, the neoplastic cells are positive for cytokeratin, EMA and vimentin.

DIFFERENTIAL DIAGNOSIS:
---Granuloma annulare
---Synovial sarcoma
---Infectious diseases
---Ulcerated squamous cell carcinoma.

REFERENCES:

CONTRIBUTED BY OMAR P. SANGÜEZA, M.D.
**Clinical Features**
Intravascular histiocytosis (IH; also known as intravascular lymphangitis) is a rare condition first reported in 1994 by O’Grady et al. This indolent lesion has a predilection for the lower extremity overlying or near a joint and often presents as ill-defined, livedoid patches with mild erythema or hyperpigmentation. Fewer than 40 cases have been reported, but the majority of cases have occurred in association with rheumatoid arthritis, hence the term “RA-associated intravascular histiocytopathy.” Other associations include diabetes mellitus, lupus anticoagulant, antiphospholipid antibodies, tonsillitis, Merkel cell carcinoma, and breast cancer. There have also been reports of IH in association with metal implants. This process is thought to be reactive. Histologic similarities to reactive angioendotheliomatosis (RAE), a reactive proliferation of intravascular endothelial cells, have also motivated theories that IH represents an early stage of RAE; however, RAE is a proliferation of endothelial cells rather than histiocytes.

**Histopathologic Features**
- Intraluminal proliferation of mononuclear cells that stain for histiocytic markers within dilated reticular dermal vascular structures.
- Histiocytes are normal-appearing, epithelioid and without atypia.
- Immunohistochemistry:
  - Endothelial cells: CD31+, CD34+, D2-40+, Lyve-1+, Prox-1+
  - Intravascular histiocytes: CD68+

**References**

**CONTRIBUTED BY VALENCIA D. THOMAS, MD**
DISCUSSION:
T-cell prolymphocytic leukemia is an aggressive form of leukemia characterized by a proliferation of small and intermediate sized t-lymphocytes involving the blood, bone marrow, lymph nodes, liver, spleen and skin. This rare form of leukemia accounts for 2% of all forms of small lymphocytic leukemia in adults over the age of 30. The patients present with peripheral blood involvement along with skin lesions, generalized lymphadenopathy and hepatosplenomegaly. There is a slight male preponderance. Anemia and thrombocytopenia are common, and, as well, the peripheral blood lymphocyte count is very high. The most common clinical presentation is one of infiltrative erythema with prominent facial involvement including striking edema. Other characteristic features include a symmetrical linear and petechial eruption. The introduction of purine analogues such as fludarabine, deoxycoformycin and 2-chlorodeoxyadenosine has brought new therapeutic expectations with some patients at least in the initial phase of follow-up showing an apparent involvement.

PATHOLOGIC ABNORMALITIES:
Dense dermal infiltrate comprising lymphocytes, characteristically in an angiocentric array. May assume a band like disposition superficially; there is minimal epidermotropism. Hemorrhage can be extensive.

CYTOMORPHOLOGY:
Intermediate in size manifesting a small single nucleolus and a finely dispersed heterochromatin, eosinophilic cytoplasm with protrusions or blebs.

PHENOTYPIC PROFILE:
---Mature post-thymic T-cell lymphoma, primarily of the CD4 phenotype
---Rare cases of the CD8 subset and/or express both CD4 and CD8
---Striking reservation of CD7; weak membrane expression of CD3
---Presumptive cell of origin: intermediate stage of differentiation between a cortical thymocyte and a peripheral blood T-lymphocyte.

DIFFERENTIAL DIAGNOSIS:
---Acute T-cell lymphoblastic lymphoma (mediastinal disease): TdT+, CD10+, co-expression of CD4 and CD8
---Sézary syndrome (chronic course, erythroderma, cerebriform lymphocytes, CD7 negative)
---Large granular cell leukemia (chronic, no skin involvement, granzyme positive, CD8 positive)
---Adult T-cell leukemia lymphoma (chronic course, HTLV1 positive, floret cells, CD7 negative, CD62L positive)
---Cytogenetic abnormalities: the most frequently detected cytogenetic abnormality is one involving chromosome 14 with breakpoints at bands q11 and q12 as demonstrated by case 4.

CONTRIBUTED BY CYNTHIA M. MAGRO, M.D.
CASE #44 - SLIDE #44

DIAGNOSIS: CUTANEOUS PRECURSOR B-LYMPHOBLASTIC LYMPHOMA

DISCUSSION:
B-cell lymphoblastic neoplasms are defined by either lymphoblastic lymphoma and lymphoblastic leukemia, representing malignancies derived from pre-B cell lymphoblasts. The distinction is based on extent of peripheral blood and bone marrow involvement; in lymphoblastic lymphoma there is less than 25% of the marrow cellularity and as well there must be less than 10% blasts in the peripheral blood. Seventy-five percent of all children are less than six years of age (M:F=2.5:1). Multiple cutaneous nodules is the classic presentation typically involving the head and neck area. Patients with B-cell lymphoblastic lymphoma are frequently found to have generalized lymphoma during the general workup. Long term remission can be achieved with multidrug chemotherapy.

PATHOLOGY:
---Extensive pandermal infiltrate with marked involvement of the panniculus
---Intermediate in size (9 to 11 micron size range) with round to oval nuclei with inconspicuous nucleoli and scant cytoplasm finely dispersed heterochromatin; the nuclear membranes are thin and indistinct.
---Mitoses are frequent.

IMMUNOPHENOTYPE:
TdT positive, CD19+, CD79+, CD10+; variable expression of CD22 and CD20. Myeloid associated antigens of CD13 and CD33 may be present. While the blasts express cytoplasmic immunoglobulin there is usually no expression of surface immunoglobulin. The most immature demonstrate CD34 positivity and lacking mature B-cell antigens such as CD20. The more mature are CD34 and TdT negative and express mature B-cell markers, including surface immunoglobulin, defining transitional pre-B cell. CD99, a marker for Ewing’s sarcoma, is seen in almost half of all cases and when accompanied by CD45 negativity, may be confused with Ewing’s sarcoma.

DIFFERENTIAL DIAGNOSIS:
---T cell acute lymphoblastic lymphoma: Mediastinal disease, CD3+, co-express CD4 and CD8
---Large cell B cell lymphoma: TdT negative, CD10 negative, surface Ig expression
---Myeloid sarcoma: TdT negative, CD20 and CD79 negative, CD34+, CD43+, CD68+
---Ewing’s sarcoma: CD99 positive/MIC 2 positive/11:12 translocation.

GENETICS:
The cytogenetic abnormalities associated with a good prognosis are hyperdiploidy between 51 and 65 chromosomes and secondary a translocation defined by (12:21)(p12;q22) while those associated with a poor prognosis are the t(9:22) the t(4:11) and hypodiploidy.
REFERENCES:

CONTRIBUTED BY CYNTHIA M. MAGRO, M.D.
CASE #45 - SLIDE #45

DIAGNOSIS: CRYOFIBRINOGENEMIA AS A CLASSIC FORM OF PAUCI-INFLAMMATORY THROMBOGENIC VASCULOPATHY

DISCUSSION:
Cryofibrinogenemia has been reported in association with underlying low grade B-cell lymphoproliferative disease. Infections may also be complicated by cryofibrinogenemia. In patients where no associated disease can be identified, the term essential cryofibrinogenemia is used. Cutaneous manifestations include cold sensitivity, acral purpura, hemorrhagic necrosis and gangrene.

KEY HISTOLOGIC FEATURES:
---Vessels of the superficial and deep vascular plexus occluded by eosinophilic globular material; the deposits may be strongly PAS positive
---Intraluminal histiocytes containing engulfed cryoprecipitates
---Rarely a true leukocytoclastic vasculitis reflecting an immune complex comprising antifibrinogen and fibrinogen is observed (type II cryofibrinogen).

PATHOGENETIC BASIS:
Cryofibrinogenemia refers to the presence of a circulating precipitate composed of a complex of fibrinogen, fibrin, fibronectin, small amounts of albumin, immunoglobulin and factor VIII. With type II cryofibrinogenemia the precipitate is composed of anti-fibrinogen and fibrinogen. The cryofibrinogen precipitates plasma at 4°C, and redissolves at warming to 37°C. It is consumed in the clotting process and does not precipitate in cold serum. Proper collection of blood samples is imperative for correct diagnosis. In our experience a significant percentage of patients will have an underlying monoclonal gammopathy.

METHOD OF COLLECTION:
The blood is collected at 37°C, placed in a green topped heparinized tube, spun down at 37°C for ten minutes at 3000 rpm and then incubated in a refrigerator for 48 hours in a Wintrobe tube. The amount of precipitate is then read, the percentage of plasma precipitated defining the cryocrit. The same methodology is used for determining cryoglobulins, except that the blood is collected in a nonheparinized red topped tube and the incubation period is 72 hours.

DIFFERENTIAL DIAGNOSTIC APPROACH TO PAUCI-INFLAMMATORY THROMBOGENIC VASCULOPATHY:
CAUSES:
1. Defect in one or more of the three main anticoagulation systems: protein C/S thrombomodulin complex, the fibrinolytic system and the antithrombin III complex. The most common is one reflecting a reduction in the functional capacity of the protein C are: 1) hereditary protein S deficiency, 2) factor V Leiden which is a mutant factor V resistant to inactivation by protein C, and 3) elevated levels of the acute phase reactant C4b9 binding protein which binds protein C.
3. Endothelial cell dysfunction, the causes of which may be immunogenic as seen in the setting of antiphospholipid antibody syndrome and/or with select connective tissue disease syndromes associated with anti-endothelial cell antibodies (i.e., scleroderma/dermatomyositis). Nonimmunogenic causes include cholesterol embolism and homocystinuria.


REFERENCES:

CONTRIBUTED BY CYNTHIA M. MAGRO, M.D.
CASE #46 - SLIDE #46

DIAGNOSIS: ANTI-SYNTHETASE SYNDROME

DISCUSSION:
The constellation of the patient’s presentation being one of interstitial lung disease, biopsy confirmed myositis and a cutaneous skin rash in association with anti-OJ autoantibodies is diagnostic of an anti-synthetase syndrome. A simplified view of the anti-synthetase syndromes is a syndromic complex comprising dermatomyositis (DM) with interstitial lung disease in association with one or more of five antibodies to select aminoacyl-tRNA synthetases including Jo1 and OJ. There may be overlapping features with another anti-endothelial cell antibody syndrome, namely that of systemic scleroderma (SSc). The classic cutaneous scleroderma-like component of the anti-synthetase syndrome is Raynaud’s phenomenon and the Mechanic’s hand.

KEY HISTOLOGIC FEATURES:
---Cell poor interface dermatitis (+/-)
---Vasculopathic changes including endothelial cell sloughing, endothelial cell necrosis
---Vascular ectasia and vascular drop out
---Compensatory response to anoxia as mucin deposition or sclerosis, the latter resembling SSc.

PATHOGENESIS:
In both SSc and DM, a Gell and Comb’s type II immune reaction directed at endothelium is the basis of the cutaneous changes and pulmonary fibrosis. From a morphologic perspective, common to both DM and SSc is endothelial cell mummification and sloughing serologically detected by elevated factor VIII levels, vascular drop out and vascular deposits of C5b-9, the presumptive effector mechanism of microvascular injury. In the skin, lung and GI tract of patients with SSC, the response to this immune based anoxic insult is a constant one, specifically progressive fibroplasias. In contrast in the skin of patients with DM the microvascular insult characteristically leads to epithelial atrophy and mucin deposition. Extracutaneous manifestations of DM resemble those of SSc, specifically in the context of ischemic myopathy and pulmonary fibrosis. It should also be emphasized that the endothelial cell injury may lead to further epitope spreading and antibody production; this phenomenon is well exemplified in this patient by virtue of her seropositivity to three different antiphospholipid antibodies.

DIFFERENTIAL DIAGNOSIS:
---Systemic scleroderma (antibodies to centromere and Scl-70)
---Sclerodermatomyositis (antibodies to PM-Scl)
---Mixed connective tissue disease (antibodies to RNP).

All of these conditions manifest pathogenetic commonality, specifically one of immune mediated endothelial cell injury.
REFERENCES:

CONTRIBUTED BY CYNTHIA M. MAGRO, M.D.
CASE #47 - SLIDE #47

DIAGNOSIS: LUPUS MIIARIIS DISSEMINATUS FACIEI

Clinical Features
Lupus miliaris disseminatus faciei (LMDF) is an uncommon but distinct, chronic, inflammatory dermatosis characterized by reddish yellow or yellowish brown papules on the central face, particularly on and around the eyelids. They may occur singly or in crops, and often extend onto the neck and chin. Onset of the eruption is abrupt, but it usually has a self-limiting course with spontaneous resolution of the lesions occurring over 1–4 years, but often leaving disfiguring scars. Acne agminata or acnitis are synonyms. LMDF is most often seen in young adults of both sexes, although cases have been reported among children and the elderly. The clinical differential diagnosis includes granulomatous rosacea, granulomatous perioral dermatitis, facial Afro-Caribbean childhood eruption (FACE), and bacterial or fungal infections. The etiology and pathogenesis of LMDF is unknown. Originally, LMDF was thought to be a tuberculid because of the striking resemblance to the tuberculoid granuloma with caseation necrosis seen in TB. However, many studies have not supported this association. Histopathology of 17 patients in 1967 showed no tubercle bacillus. PCR analysis of active lesions of LMDF has failed to detect M. tuberculosis DNA. There is no response to antituberculous drugs, the tuberculin test is mostly negative, and mycobacteria have not been grown from the lesions. Skowron et al questioned the continued use of the term LMDF, prompting them to propose the new and less confusing name and acronym facial idiopathic granulomas with regressive evolution (FIGURE). The etiopathogenesis of this eruption is most likely a granulomatous reaction to a ruptured hair follicle including its contents such as keratins and sebum. Because cystic structures and ruptured follicular cysts have been noticed in biopsy sections of LMDF previously, this hypothesis appears well founded.

Histopathologic Features
• Characteristic superficial, perifollicular, caseating granulomas with negative stains for fungal, atypical mycobacterial, and bacterial organisms.
• Other reaction patterns seen include sarcoidal granulomas in 40%, sarcoidal granulomas with caseation necrosis in 20%, sarcoidal granulomas with abscess in 24%, and mixed sarcoidal and tuberculoid granulomas in 16% of cases.
• The histopathology of LMDF differs according to the stage of the lesion. In early lesions, there is a slight to moderately dense lymphocytic infiltrate around the hair follicle. As the lesion matures and becomes fully developed, a granulomatous reaction occurs taking a sarcoidal (with or without abscess formation), tuberculoid, or a necrotic (caseation necrosis) pattern. In older lesions, fibrosis may be more prominent.

References
DIAGNOSIS: FEBRILE ULCERONECROTIC MUCHA-HABERMAN DISEASE

DISCUSSION:
Mucha-Haberman disease or pityriasis lichenoides et varioliformis acuta (PLEVA) is generally a benign cutaneous disorder of unknown etiology characterized by successive crops of new lesions which resolve spontaneously after six to 12 months. Patients with PLEVA rarely have systemic signs. The cutaneous lesions are often asymptomatic with wide variation on the morphology of the lesions including macules, papules, vesicle, pustules and crusts.

Febrile ulceronecrotic Mucha-Habermann disease (FUMHD) is a fulminant and potentially lethal variant of pityriasis lichenoides first described by Degos in 1966. It is characterized by the abrupt onset of generalized ulceronecrotic lesions associated with high fever and systemic symptoms. Occasional deaths have been reported. The deaths have occurred in those over 40 years old. It has been postulated to represent either a hypersensitivity response to an infectious agent or a clonal lymphoproliferative disease. There is no definitive treatment, but systemic corticosteroids, tetracycline, erythromycin, methotrexate and ultraviolet light have been used with variable success. The finding of a very high tumor necrosis factor-α (TNF-α) serum concentration in one reported case suggests that treatment with a TNF-α inhibitor might be a good therapeutic option.

KEY HISTOLOGICAL FEATURES:
---Confluent epidermal necrosis with scattered single apoptotic cells
---Superficial interface infiltrate with profuse exocytosis of small round lymphocytes
---Thick parakeratotic and serous crust
---Acanthosis with prominent melanoderma in the adjacent skin
---Lack of vasculitis, plasma cells, eosinophils or neutrophils.

DIFFERENTIAL DIAGNOSIS:
---Erythema multiforme
---Erosive lichen planus
---Paraneoplastic pemphigus
---Lymphomatoid papulosis.

REFERENCES:

CONTRIBUTED BY JOAN GUITART, M.D.
CASE #49 - SLIDE #49

DIAGNOSIS: SPINDLE CELL HEMANGIOMA

Clinical Features
Spindle cell hemangioma presents typically as subcutaneous masses of the extremity. Although these are benign lesions that are more likely vascular malformations than vascular neoplasms, they are very often multifocal within the same anatomic vicinity, and, thus, local “recurrence” is quite common after excision. However, these apparent recurrences most likely represent discontinuous intravascular growth of the lesion rather than true recurrence. Although this tumor was initially considered a “spindle cell hemangioendothelioma” with intermediate malignant potential because of these clinical findings, further follow up has clarified that multifocality does not actually represent true regional metastases, and thus the tumor has been reclassified as spindle cell hemangioma.

A subset of spindle cell hemangiomas is associated with Maffucci syndrome (multiple enchondromas); an important clinical finding since Maffucci syndrome carries a risk of chondrosarcoma development within an enchondroma.

Histologic Features
• Multinodular vascular lesion.
• Often situated directly adjacent to a thick walled blood vessel.
• Bland epithelioid and spindled endothelial cells.
• Cytoplasmic vacuoles that bear a striking resemblance to miniature adipocytes.
• Solid spindled areas with slit-like vascular spaces alternating with areas composed of larger thin-walled cavernous spaces.

References

CONTRIBUTED BY JERAD M. GARDNER, MD
CASE #50 - SLIDE #50

DIAGNOSIS: PIGMENTED EPITHELIOID MELANOCYTOMA

DISCUSSION:
PEM or animal type melanoma is a borderline melanocytic tumor characterized by deep and heavily pigmented melanocytes similar to tumors seen in horses and other animals. These lesions belong to the spectrum of tumors from epithelioid blue nevus as seen in the Carney’s complex to animal-type melanoma. The tumor commonly presents in the extremities of young individuals. Regional lymph node metastases are commonly identified, but visceral metastases or tumor progression is very rare. Our patient had a positive sentinel node biopsy without further surgery or therapy.

KEY HISTOLOGICAL FEATURES:
---Deep dermal nodule (average Breslow’s thickness of over 3mm)
---Sheets of heavily pigmented epithelioid and/or spindle shaped melanocytes
---Occasional ulceration and rare cases with focal necrosis.

DIFFERENTIAL DIAGNOSIS:
---Nodular melanosis
---Cellular blue nevus
---Tattoo.

REFERENCES:

CONTRIBUTED BY JOAN GUITART, M.D.
CLINICAL FEATURES:
Cutaneous myofibroma is an uncommon benign neoplasm that histologically resembles infantile myofibromatosis. It typically presents as a solitary painless, slowly growing tumor nodule on the head and neck area, shoulder girdle or extremities. It may be found in children and adults of any age.

HISTOLOGIC FEATURES:
---Well-circumscribed, lobulated dermal or subcutaneous tumor
---Biphasic growth pattern
---Plump spindle-shaped myofibroblasts arranged in nests or whorls with variable myxoid to hyalinized stroma, occasionally chondroid; tends to be at periphery
---Cellular area with smaller, rounder cells and dilated branching vessels in a hemangiopericytoma-like pattern; less commonly glomus-like; tends to be located centrally
---Biphasic pattern NOT always present and may develop over time
---Mitotic figures rare to absent; no necrosis
---Immunohistochemistry: spindled cells and smaller cells positive for vimentin, muscle-specific actin and α-smooth muscle actin; desmin negative.

DIFFERENTIAL DIAGNOSIS:
Leiomyoma, neurothekeoma, hemangiopericytoma.

DISCUSSION:
Solitary cutaneous myofibroma has no discriminating clinical features, yet histologically it is quite distinctive. Because of the unique whorled pattern and hyalinized and/or myxoid stroma, the diagnosis should be suspected at scanning magnification. Although the plump spindled-shaped myofibroblasts seen in myofibroma are somewhat reminiscent of leiomyoma, leiomyoma has more blunt-end nuclei and lacks a biphasic growth pattern. Neurothekeoma lacks the hemangiopericytoma-like pattern and has a different immunophenotypic profile. Lastly, hemangiopericytoma lacks peripheral spindled cells arranged in a fascicular or whorled pattern.

REFERENCES:

CONTRIBUTED BY LORI LOWE, M.D.
CASE #52 - SLIDE #52

DIAGNOSIS: MERKEL CELL CARCINOMA WITH SQUAMOUS DIFFERENTIATION

CLINICAL FEATURES:
Merkel cell carcinoma (primary cutaneous neuroendocrine carcinoma) is an uncommon malignancy that typically presents as an erythematous to violaceous tumor nodule on the head and neck, upper trunk or extremities of elderly patients. The average size is 2 cm in diameter. It is a biologically aggressive neoplasm with regional lymph node involvement seen in up to 75% of cases and distant metastases in greater than 33% of cases. The five year survival rate has been estimated to be between 30-64%. Lesions with a small cell size, high mitotic rate and large tumor size are associated with a decreased survival rate.

HISTOLOGIC FEATURES:
---Sheets, nests and trabecular arrangements of tumor cells in dermis and subcutis.
---Tumor cells are small to intermediate in size (12-25 microns), round to ovoid with scant cytoplasm, inconspicuous nucleoli and uniformly distributed, delicate, “peppered” chromatin.
---Numerous mitoses and apoptotic cells
---Rare histologic patterns: epidermotropic foci, squamous, glandular, melanocytic and/or sarcomatous differentiation.

IMMUNOHISTOCHEMISTRY:
--Cytokeratin 20-positive in dot-like or button paranuclear pattern is most sensitive and specific -90% + (although can be positive rarely in small cell carcinoma of lung)
---Neuroendocrine markers variably positive: neuron specific enolase (84% +), chromogranin A (66% +), synaptophysin, neurofilaments
---Epithelial membrane antigen 84% +.

DIFFERENTIAL DIAGNOSIS:
---Basal cell carcinoma—CK20 negative, neuroendocrine markers usually negative
---Small cell carcinoma—S100 and melan-A positive, CK20 negative
---Lymphoma—LCA positive, cytokeratins negative
---Metastatic oat cell carcinoma—thyroid transcription factor-1 positive, chest x-ray.

DISCUSSION:
The differential diagnosis of small blue cell neoplasms includes Merkel cell carcinoma, metastatic small cell carcinoma of the lung, small cell melanoma, lymphoma, neuroblastoma, rhabdomyosarcoma, Lymphoepithelioma-like carcinoma of the skin and Ewing’s sarcoma. Immunohistochemistry is necessary for accurate diagnosis.

REFERENCES:

CONTRIBUTED BY LORI LOWE, M.D.
**DIAGNOSIS: CUTANEOUS MYXOMA WITH EPITHELIAL ELEMENTS**

**CLINICAL FEATURES:**
Cutaneous myxomas are seen in approximately 50% of patients with NAME or LAMB syndrome. NAME is an acronym for nevi (lentigines, blue nevi), atrial myxoma, cutaneous myxoma and endocrine abnormalities. LAMB syndrome is similar, consisting of mucocutaneous lentigines, atrial myxoma, mucocutaneous myxomas and blue nevi. Carney’s complex refers to patients with features of NAME/LAMB syndrome who also have endocrine overactivity. It is an autosomal dominant disorder with variable expressivity, mapped to chromosome 2p16. There is a female predominance. Other reported associations include myxoid mammary fibroadenomas, pituitary adenoma, thyroid disease, pigmented nodular adrenocortical disease and psammomatous melanotic schwannoma.

Cutaneous myxomas are flesh-colored papules or nodules, 1-5 cm in size. Although they can occur anywhere, there is a predilection for the perioral and postauricular regions. Solitary cutaneous myxomas may occur without any associated systemic abnormalities. Multiple cutaneous myxomas, however, may be a manifestation of Carney’s complex. Recurrence after excision may be seen.

**HISTOLOGIC FEATURES:**
--- Circumscribed, non-encapsulated lesion in dermis and/or subcutis
--- Prominent stromal mucin
--- Variably shaped fibroblasts (i.e., spindled, stellate, etc.)
--- Usually increased vascularity; if prominent, the term “angiomyxoma” can be used
--- Epithelial component may be present (epithelial strands, keratinous cysts, “Trichoblastic” epithelial strands.

**DIFFERENTIAL DIAGNOSIS:**
Cutaneous focal mucinosis, adnexal tumor (i.e., chondroid syringoma, Fibrofolliculoma).

**DISCUSSION:**
In the known setting of NAME/LAMB syndrome or Carney’s complex, the diagnosis of cutaneous myxoma should not pose much difficulty. Without clinical history, distinguishing cutaneous myxoma from cutaneous focal mucinosis is more difficult. The former is generally larger in size, demonstrate greater vascularity and is situated in the deep dermis or subcutis. The latter is usually less than one centimeter in size, has normal vascularity and is located in the upper dermis. If epithelial elements are present, there may be confusion with adnexal neoplasms. Clinicopathologic correlation is essential.

**REFERENCES:**

**CONTRIBUTED BY LORI LOWE, M.D.**
CASE #54 - SLIDE #54

DIAGNOSIS: INVOLUTING SPITZ NEVUS (ANGIOMATOID SPITZ NEVUS)

CLINICAL FEATURES:
Angiomatoid Spitz nevus is a variant of desmoplastic Spitz nevus in which blood vessel proliferation is conspicuous, causing possible diagnostic confusion with vascular lesions. It is presumably a phenomenon of involution or regression. I prefer the designation of involuting Spitz nevus, as the vascular component may not be constant. The typical clinical presentation is a flesh-colored to reddish-brown papule on the extremities of young adults, similar to conventional desmoplastic Spitz nevus.

HISTOLOGIC FEATURES:
--- Symmetric, circumscribed lesion
--- Expanded papillary dermis with fibrous stroma and numerous small blood vessels
--- Scattered large epithelioid cells arranged singly or in small aggregates, with vesicular nucleus and prominent nucleoli
--- Inconspicuous to absent junctional component
--- High grade atypia is lacking
--- Epithelioid cells stain with melanocytic markers (S100+, Melan A+).

DIFFERENTIAL DIAGNOSIS:
Hemangioma, epithelioid histiocytoma, regressing melanoma.

DISCUSSION:
Key to arriving at the correct diagnosis is to first identify the epithelioid cells, which may be inconspicuous and few in number, within the fibrovascular stroma. If the lesion has junctional nesting, then the melanocytic nature of the lesion is easier to recognize. If not, immunostains may be necessary to confirm a melanocytic lesion and exclude epithelioid histiocytoma (S100 negative, Fact XIIIA +).

REFERENCES:

CONTRIBUTED BY LORI LOWE, M.D.
DIAGNOSIS: SEBACEOUS GLAND CARCINOMA

CLINICAL FEATURES:
Sebaceous gland carcinomas are traditionally divided into ocular (arising from glands of Zeiss or meibomian glands) and extraocular subtypes. The majority of cases are sporadic, although some cases are associated with Muir-Torre syndrome and immunosuppressed organ transplant patients. Isolated cases have also been documented to arise in organoid nevi (nevus sebaceous of Jadassohn). Clinically they present as enlarging skin-colored to yellowish to erythematous papules or nodules with varying degrees of ulceration. Ocular lesions are often treated as ocular sebaceous gland carcinomas. They may demonstrate associated conjunctivitis-like lesions due to pagetoid extension of tumor cells. Traditionally, it has been dogma that ocular sebaceous gland carcinomas are more aggressive. Recently this has been challenged with some authors reporting high survival rates (97%) in ocular sebaceous gland carcinomas while other authors have reported small series of aggressive extraocular sebaceous gland carcinomas. The numbers are not sufficient at this time to establish whether there is a significant difference in biological behavior.

The pathogenesis is not understood. However, Muir-Torre syndrome typically demonstrates mutations in DNA mismatch repair genes, most often hMSH-2 and hMLH-1. Absence of expression in one of these two genes has been reported in about 23% of sebaceous gland carcinomas not associated with Muir-Torre syndrome.

Association with Malignancy?
The increased incidence of sebaceous gland carcinoma with Muir-Torre syndrome is clearly documented. In a recent study of 23 patients with ocular sebaceous gland carcinoma and no history of Muir-Torre syndrome, Conway and coworkers reported that 48% had an internal malignancy (colorectal cancer, liver, bronchial) suggesting a possible association.

HISTOLOGIC FEATURES:
---Low power-epithelial neoplasm that typically demonstrates connection to overlying epidermis
---Ulceration often present
---Typically larger than benign sebaceous neoplasms
---Lobular or infiltrative growth patterns
---May extend into dermis, subcutis or muscle
---Rare cases may demonstrate lymphatic invasion
---Ocular cases may demonstrate pagetoid extension in the epidermis or mucosal epithelium
---Tumor cells varying from being well-differentiated with sebocyte differentiation (rat-bite nuclei) to being basaloid and resembling the cells of basal cell carcinoma
---Cytologic atypia is most noticeable in the basaloid areas and manifests as hyperchromasia, large nuclei, pleomorphism, mitotic figures (including atypical mitotic figures)
---Sebaceous duct differentiation is absent
---Tumor cells are markedly decorated by EMA.
REFERENCES:

CONTRIBUTED BY JAMES FITZPATRICK, M.D.
CLINICAL FEATURES:
Myxofibrosarcoma is the preferred term in the World Health Organization Classification of tumors (synonym is myxoid malignant fibrous histiocytoma) for a soft tissue malignancy that most commonly affects elderly patients with the majority of cases being reported in the sixth to eighth decades. Males are more commonly affected than women. The most common location is the lower extremity followed by the upper extremity, head and neck and rarely on the trunk. Clinically they are slow growing, painless dermal or subcutaneous masses without significant epidermal change. Local recurrences are common (about 50% of cases). The propensity to develop metastases correlates with the depth of invasion and tumor grade. Low-grade tumors do not metastasize while high-grade tumors metastasize in about one-third of cases.

HISTOLOGIC FEATURES:
---Low power-superficial tumors often demonstrate a lobular pattern in the dermis and subcutis while deeper tumors often demonstrate an infiltrative growth pattern.
---Multinodular areas often demonstrate incomplete fibrous septae
---Tumor composed primarily of spindled or stellate cells with minimal ill-defined slightly eosinophilic cytoplasm and atypical hyperchromatic nuclei embedded in a matrix that may be myxoid, fibromyxoid or fibrous.
---Mitotic figures may be present but are infrequent
---In myxoid areas, the vessels may be prominent and may demonstrate a perivascular accumulation of tumor cells.
---High-grade tumors demonstrate fascicles and sheets of spindle and pleomorphic cells are often multinucleated.
---Tumor cells are decorated with vimentin. Variable staining may be seen with muscle-specific actin.

DISCUSSION:
In this case, the histological differential diagnosis is primarily between low-grade fibromyxosarcoma and low-grade myxofibrosarcoma. Low-grade fibromyxosarcomas are far less common, more commonly seen in children and young adults and more commonly affects proximal extremities. Histologically, the cells are spindle-shaped, cytologically bland, with alternating areas of fibrous and myxoid stroma. Myxoid nodules that infiltrate the surrounding tissue are commonly present. In contrast, myxofibrosarcoma is seen in elderly patients, is typically more distal and histologically more likely to demonstrate curvilinear capillaries, pleomorphism, copious myxoid stroma and absence of solid areas of tumor.

REFERENCES:

CONTRIBUTED BY JAMES FITZPATRICK, M.D
CASE #57 - SLIDE #57

DIAGNOSIS: SUBCUTANEOUS RETICULOHISTIOCYTOMA

CLINICAL FEATURES:
Reticulohistiocytoma is an uncommon neoplasm that may be solitary (Reticulohistiocytoma) or multiple (multicentric reticulohistiocytosis). Solitary lesions do not have a systemic association with multicentric reticulohistiocytosis as demonstrated by lesions of the skin, mucosa and soft tissue with frequent involvement of joints producing arthritis. Multicentric reticulohistiocytosis may also be a paraneoplastic presentation in a variety of internal malignancies (20%).

HISTOLOGIC FEATURES:
---On low power, the lesions are classically located in the papillary and superficial reticular dermis with a normal epidermis.
---Histologic variants may be pandermal or subcutaneous.
---Lesions are composed primarily of “histiocytic” cells with typically one nucleus, although scattered cells may demonstrate multiple nuclei. Nuclei may demonstrate prominent nucleoli. Occasional cases may demonstrate some spindle cells.
---Cells characteristically demonstrate eosinophilic to slight amphophilic cytoplasm that can be subtly granular or vacuolated. The cytoplasm is often described as having a “ground-glass appearance” or a “muddy-rose color.”
---Approximately 10% of cases may demonstrate focal accumulation of lipid in the cytoplasm.
---A background infiltrate of lymphocytes and scattered plasma cells typically are present.
---Some cases may also demonstrate an admixture of variable numbers of neutrophils and eosinophils.
---The histiocytic cells are PAS positive and typically decorated by lysozyme, α1-antitrypsin, factor XIIIa, vimentin, CD68 and CD45. Rare cases are S100 positive.

DISCUSSION:
Reticulohistiocytomas are usually easily diagnosed by routine H & E with the differential diagnosis usually being between this entity and juvenile xanthogranuloma. Some cases may demonstrate slightly atypical cells, and the differential diagnosis can be expanded to include atypical fibroxanthoma, malignant fibrous histiocytoma or even melanoma as happened in this case. A pitfall encountered in this case was the reliance of S100 which suggested metastatic malignant melanoma.

REFERENCES:

CONTRIBUTED BY JAMES FITZPATRICK, M.D.
CLINICAL FEATURES:
Tungiasis is an ectoparasitosis produced by the flea Tunga penetrans (chigoe, jigger, sand flea, burrowing flea), which is a parasite of man, hogs and dogs. It is found in tropical South America, the Caribbean and parts of Africa (42% of Nigerian children were infested in one study) and Asia (India). Outside the skin it is a small flea (1 mm). Human disease is produced when the female flea burrows into skin, usually feet and hands. The primary lesion is a sore with a central black spot representing the female. The number of lesions may vary from one to more than 100 in a single individual. Patients typically report severe pain, inflammation and not infrequently develop nail dystrophy. Superinfection occurs in approximately one-fourth of patients.

HISTOLOGIC FEATURES:
--- On low power there is a dermal cavity with central epidermal opening in the epidermis associated with adjacent reactive changes of the epidermis (hyperplasia, parakeratosis, compact hyperkeratosis and spongiosis)
--- Within the cavity there is a large, vaguely round to oval-shaped organism with a distinct exoskeleton. The posterior end often demonstrates a distinct pale-staining layer.
--- Variable features that may be seen include hypodermal layer, trachea, digestive tract, striated muscle, eggs and head (very small and only rarely seen).
--- The adjacent dermis demonstrates a host response of lymphocytes, macrophages and variable numbers of eosinophils.

Interesting Factoids
--- Sailors traveling with Columbus became infected with tungiasis
--- The female flea expands its volume (to the size of a pea) by a factor of 2000 after burrowing into the skin.
--- Originally limited to the New World, the flea was probably introduced more than once to Africa. The most famous is the introduction to West Africa when a ship dropped ballast sand on the beach.
--- Inspired the sailor’s oath, “I’ll be jiggered.”

DISCUSSION:
The histologic findings are diagnostic. Obviously the location (usually feet) and a history of travel to an endemic area is helpful, the finding of a large organism with an exoskeleton with a central punctum and a dermal cavity is diagnostic. Although not always present, the presence of striated muscle and eggs (absent in this biopsy since they have already been expelled are considered to be highly supportive of the diagnosis). Although there is a small diagnostic head, it is only rarely seen in sections.

REFERENCES:
CASE #59 - SLIDE #59

DIAGNOSIS: CLEAR CELL FIBROUS PAPULE

CLINICAL FEATURES:
---Most common on the nose
---May clinically resemble a wart or a fibrous papule.

HISTOLOGIC FEATURES:
---Dome-shaped dermal proliferation of epithelioid cells with small nuclei and bubbly, xanthomatous cytoplasm
---Immunoperoxidase stain positive for CD68 and sometimes Factor XIIIa
---Negative for S100 and cytokeratin, excluding a melanocytic or epithelial tumor.

DIFFERENTIAL DIAGNOSIS:
Xanthoma, balloon cell nevus or melanoma.

DISCUSSION:
This entity has been reported as either a clear cell fibrous papule or a xanthoma. The precise nature of the cells cannot be determined using typical immunhistochemical stains. Although the histology resembles a xanthoma, the characteristic location on the nose (including the lesion reported by Northcutt) favors a variant of a fibrous papule.

REFERENCES:

CONTRIBUTED BY LISA H. LERNER, M.D.
CASE #60 - SLIDE #60

DIAGNOSIS: AMYLOIDOSIS (WITH CALCIFICATION)

CLINICAL FEATURES:
---Localized cutaneous amyloid may present as one or several nodules. Approximately 15% of patients eventually develop systemic amyloidosis.
---In systemic amyloidosis, papular lesions, plaques, hemorrhagic lesions (peri-ocular hemorrhage), alopecia, macroglossia and rarely bullous lesions occur. Multi-organ systemic involvement occurs, with cardiac disease being a common cause of death. In primary systemic amyloidosis patients have a light chain paraproteinemia, most commonly a lambda light chain.

HISTOLOGIC FEATURES:
---Deposits of acellular, eosinophilic, fissured material is present in the dermis, in arrector pili muscles, around vessels and adnexa, and in the fat as “amyloid rings.”
---Amyloid stain with Congo red, crystal violet and thioflavin-T.
---Cases of localized (nodular) amyloid often have a plasma cell infiltrate, which can sometimes be shown to be clonal with stains for kappa and lambda.

DIFFERENTIAL DIAGNOSIS:
Porphyria, colloid milium, lipoid proteinosis.

DISCUSSION:
The calcification and ulceration observed in this case are unusual. Calcification has been described in the literature in cases of systemic amyloidosis affecting other organs such as the lung, liver and spleen.

REFERENCES:

CONTRIBUTED BY LISA H. LERNER, M.D.
CASE #61 - SLIDE #61

DIAGNOSIS: PAPULAR MUCINOSIS (LICHEN MYXEDEMATOSUS)

CLINICAL FEATURES:
---Firm, waxy papules, plaques and nodules, few to numerous
---Variants include an acral type and a self-healing type
---Some cases develop sclerodermoid features that overlap with scleromyxedema
---Some cases have a serum monoclonal light chain
---Can occur in association with HIV infection.

HISTOLOGICAL FEATURES:
Increased dermal mucin in association with fibrosis and increased fibroblasts.

DIFFERENTIAL DIAGNOSIS:
Myxedema, focal cutaneous mucinosis, connective tissue disease.

DISCUSSION:
Although the histology of papular mucinosis and scleromyxedema are essentially identical, the clinical presentation and clinical course are different. Overlap cases do exist. However, many cases of papular mucinosis continue without development of a light chain gammopathy or systemic disease. In contrast, the majority of cases of scleromyxedema have or eventually develop a clonal light chain. The last decade has seen multiple reports of a benign acral variant that occurs on the hands and distal forearms, as well as self-resolving cases. There have also been multiple reports of papular mucinosis in association with HIV infection.

REFERENCES:
**Clinical Features**

Desmoplastic melanomas are a spindle-cell subset of melanomas that are clinically and histologically difficult to diagnose, as they resemble fibroblastic or myofibroblastic neoplasms. Desmoplastic melanomas tend to arise on chronically sun-damaged skin and have a slight male predominance. These tumors are often amelanotic, and they present as an erythematous macule or an indurated plaque. Though recurrence is common (22-77%), nodal metastasis is observed less frequently than in other subtypes of melanoma.[1] Recent studies demonstrate a higher likelihood of nodal positivity in mixed desmoplastic melanoma subtypes than in the pure desmoplastic subtype (25% vs 14%). [3] Overall 5-year survival ranges from between 67 and 89%.

**Histopathologic Features**

- Fusiform, spindle-cell melanocytes in the background of desmoplasia.
- May be paucicellular, with individual tumor cells dispersed in dense fibrous tissue (pure desmoplastic melanoma, >90% of the invasive component) or presenting with higher cell density with solid/spindled or epithelioid melanocytes in a dense fibrous stroma (mixed desmoplastic melanoma.)
- Epidermal involvement is absent in one-third of cases.
- Nerve involvement is common.
- Immunohistochemistry: S100+ (94-100%), NSE+, Vimentin+, SOX10+ (80%-100%) HMB45- (10% + in desmoplastic melanomas, though positivity in the papillary dermis has been reported), MART-1 variable (+ in 24-60%), MITF variable (positive in 24-60%), Tyrosinase- (positive in 6% of desmoplastic melanomas.)
- SOX10 is highly specific for desmoplastic melanoma (80% - 100%) and has been suggested to be useful in the differentiation between scar and desmoplastic melanoma.

**References**


**CONTRIBUTED BY VALENCIA D. THOMAS, MD**
CASE #63 - SLIDE #63

DIAGNOSIS: TICK BITE WITH CRYOGLOBULIN-LIKE DEPOSITS

CLINICAL FEATURES:
There may be a known history of a tick bite.

HISTOLOGIC FEATURES:
---Findings depend on the stage of the bite: early on little inflammation, later on both lymphocytic and neutrophilic inflammation, surface necrosis with or without eosinophils.
---The distinctive finding is the presence of thrombi and eosinophilic cryoglobulin-like material within small upper to mid-dermal vessels.
---The material stains brightly magenta with periodic acid-Schiff, similar to the staining of cryoglobulins.
---The reports by Stefanato et al and Galaria et al differ in that the former did not observe leukocytoclastic vasculitis, whereas the latter did observe vasculitis in addition to the cryoglobulin-like deposits.

DIFFERENTIAL DIAGNOSIS:
Vasculitis, cryoglobulinemia.

DISCUSSION:
The diagnosis of a tick bite can be suspected when cryoglobulin-like intraluminal deposits and neutrophilic inflammation are present, with or without leukocytoclastic vasculitis. The clinical history should readily distinguish between a tick bite and true cryoglobulinemia, even if no tick is observed clinically or histologically.

REFERENCES:

CONTRIBUTED BY LISA H. LERNER, M.D.
CLINICAL FEATURES:
---Systemic manifestations of alpha-1-antitrypsin deficiency disease include emphysema, hepatitis, cirrhosis, acquired angioedema and others
---Panniculitis is rare and affects children and more frequently adults
---Recurrent tender nodules on proximal extremities, buttocks and trunk
---+/- ulceration and drainage of oily, clear or serosanguineous fluid
---Associated with fever; may mimic cellulites
---May be precipitated by trauma or excessive physical activity
---Resolve with atrophic scars.

HISTOLOGIC FEATURES:
---Splaying of neutrophils between collagen bundles in reticular dermis
---Septal panniculitis with liquefactive necrosis and collagenolysis of septae and dermis
---Masses of neutrophils and histiocytes in septae
---Lobular panniculitis with fat necrosis and massive neutrophilic inflammation
---Normal fat lobules adjacent to necrotic fat lobules
---+/- transepidermal elimination.

DIFFERENTIAL DIAGNOSIS:
Infectious panniculitis, factitial panniculitis, traumatic panniculitis, neutrophilic panniculitis/subcutaneous Sweet’s syndrome, subcutaneous leukocytoclastic vasculitis, pancreatic panniculitis.

DISCUSSION:
Alpha-1-antitrypsin is the most abundant circulating serine proteinase inhibitor and is involved in a variety of proteolytic functions. There are greater than 90 genetic variants of the alpha-1-antitrypsin allele. Two alleles combine to determine the phenotype of alpha-1-antitrypsin. The most common allele associated with normal levels is PiMM. Homozygous phenotype PiZZ (severe deficiency) is most frequently associated with panniculitis. Heterozygous deficiency with phenotype MZ or MS has also been reported. Deficiency of alpha-1-antitrypsin accelerates activation of lymphocytes and phagocytes producing inflammation and tissue necrosis secondary to protease action.

REFERENCES:

CONTRIBUTED BY LESLIE ROBINSON-BOSTOM, MD
CASE #65 - SLIDE #65

DIAGNOSIS: COLLAGENOUS FIBROMA (DESMOPLASTIC FIBROBLASTOMA)

CLINICAL FEATURES:
--- Firm asymptomatic solitary slowly growing tumor
--- Typically 2-3 cm in diameter, may be as large as 20 cm
--- Predilection for adult males in the fifth or sixth decades
--- Arise in subcutaneous tissue or muscle
--- Rare dermal involvement
--- Most common site is the upper extremities followed by lower extremities and head and neck regions.

HISTOLOGIC FEATURES:
--- Fairly well-demarcated with surrounding soft tissue infiltration (subcutaneous fat or rarely skeletal muscle)
--- Hypocellular, composed of large bland stellate or spindle cells
--- Embedded in a fibromyxoid or dense collagenous stroma
--- Mitoses are rare or absent
--- Necrosis is not present
--- Inconspicuous small vessels +/- perivascular hyalinization
--- Stroma stains with alcian blue at pH 2.5
--- Spindle cells are diffusely positive for vimentin, +/- factor XIIIa
--- Myofibroblastic cells may stain focally with alpha smooth muscle actin, muscle specific actin and rarely keratin
--- Typically negative for desmin, CD34 and S100; rare diffuse staining with S100 has been reported.

DIFFERENTIAL DIAGNOSIS:
--- Myxoid neurofibroma
--- Desmoid tumor/deep fibromatosis
--- Calcifying fibrous pseudotumor
--- Low-grade fibromyxoid sarcoma
--- Nodular fasciitis/hyalinized fasciitis
--- Superficial angiomyxoma
--- Metastatic melanoma.

DISCUSSION:
Collagenous fibroma (desmoplastic fibroblastomas) is a distinctive fibrous soft tissue tumor composed of fibroblasts and myofibroblasts. The slow growth rate and large size favors a Neoplastic process over a reactive proliferation. Cytogenetic findings of abnormalities on the long arm of chromosome II in several cases raises the possibility of a relationship between collagenous fibroma and fibroma of tendon sheath which shows rearrangement in the same region. To date, all tumors have demonstrated benign biologic behavior without recurrence after complete conservative excision.
REFERENCES:
CASE #66 - SLIDE #66

DIAGNOSIS: ADENOMA OF ANOGENITAL MAMMARY-LIKE GLANDS

CLINICAL FEATURES:
---Smooth flesh-colored pedunculated nodule
---Located most frequently in the perianal and vulva areas
---May appear outside of the embryonic milk lines or mammary ridges in the vulva
---Also reported on the thigh, scalp, eyelid and umbilicus
---Clinically resembles hemorrhoids.

HISTOLOGIC FEATURES:
---Architecturally similar to intracanalicular fibroadenomas of the breast
---Dense fibrous or fibromucinous stroma
---Tubular and cystic structures with lobular configuration
---+/- papillary projections
---Deformed and compressed by proliferating stroma
---Ducts are lined by a double layer of epithelial cells (cuboidal and columnar)
---May show apocrine secretion (decapitation)
---Contain progesterone and estrogen receptors.

DIFFERENTIAL DIAGNOSIS:
---Fibroadenoma of the breast
---Hidradenoma papilliferum
---Tubular apocrine adenoma
---Papillary eccrine carcinoma
---Adenocarcinoma
---Syringocystadenoma papilliferum
---Erosive adenomatosis of the nipple
---Lactating adenoma.

DISCUSSION:
Anogenital mammary-like glands are a recently recognized variant of cutaneous adnexal gland with features of modified eccrine and apocrine glands. The glands demonstrate a wide coiled tube from which acini, diverticula and short branches arise. Typically compact simple columnar epithelium with prominent apocrine snouts protrude into the lumen. The surrounding stroma varies from loose fibromyxoid to dense collagenous tissue. True lobuli are seen occasionally resembling those of mammary glands. A variety of lesions can originate from these lesions including lactating glands, lactating adenoma, fibroadenomas, hidrocystoma, hidroadenoma papilliferum, most cases of extramammary Paget’s disease and invasive adenocarcinoma. Lesions in the anogenital area previously reported as apocrine adenoma and apocrine fibroadenomas are most likely variants of adenomas of anogenital mammary-like glands.
REFERENCES:
CLINICAL FEATURES:
--- Typically presents in middle-aged adults with renal disease
--- Symmetrically distributed on the trunk and extremities, spares face
--- May be slowly or rapidly progressive, encasing, woody fibrosis
--- +/- limits range of motion of major joints
--- Cutaneous erythema or brawny induration
--- Cobblestone texture or peau d’orange texture
--- “Amoeboid” projections
--- Yellow plaques on sclera.

HISTOLOGIC FEATURES:
Early lesion – Increase in interstitial dermal fibroblasts with tapered, rounded or angulated nuclei; stain with both CD34 and procollagen; scant inflammation.
Developed lesion – Increased interstitial spindle and epithelioid fibroblasts in dermis and subcutis which expand subcutaneous septa (CD34 and procollagen positive); thickened collagen bundles, increased elastic fibers, variable increased mucin; variable numbers of CD68 positive histiocytes and multinucleated giant cells and factor XIIIa positive dermal dendritic cells; +/- perivascular lymphocytic inflammation; occasional dermal calcinosis.

DIFFERENTIAL DIAGNOSIS:
Scleromyxedema, Scleroderma/morphea, eosinophilic fasciitis, eosinophilia-myalgia syndrome, dermatofibrosarcoma protuberans, spindle cell melanoma.

DISCUSSION:
Nephrogenic fibrosing dermopathy is an acquired idiopathic fibrosing disorder recently described in patients with renal insufficiency. This process was initially termed “scleromyxedema-like disease in dialysis patients” and was renamed when patients who had not previously been treated with dialysis became affected. Over 150 cases have been reported worldwide to the NFD registry at Yale University (http://www.icnfdr.org). No known medication, toxin or infectious agent appears to trigger NFD. However, cases have been reported after recent surgery, a thrombotic event or anasarca. The cause of renal disease, duration and dialysis therapy is not related to the onset or severity of the disease. The bone marrow derived “circulating fibrocytes” which expresses leukocyte and antigen-presentation markers and can induce collagen production may be responsible for this systemic disease.

REFERENCES:

CONTRIBUTED BY LESLIE ROBINSON-BOSTOM, M.D.
CASE #68 - SLIDE #68

**DIAGNOSIS: GRANULAR PARAKERATOSIS**

**CLINICAL FEATURES:**
--- Erythematous or hyperpigmented plaques at intertriginous sites
--- Female predilection
--- Infantile cases in diaper area.

**HISTOLOGIC FEATURES:**
--- Hyperkeratosis, acanthosis, papillomatosis
--- Confluent parakeratosis
--- Retention of keratohyalin granules within parakeratotic areas.

**DIFFERENTIAL DIAGNOSIS:**
--- Psoriasis
--- Epidermal nevus
--- Dermatophytosis.

**DISCUSSION:**
Granular parakeratosis is an acquired disorder of keratinization, originally described in the axillary region in women. Over the years, the clinical spectrum of this disorder has been expanded to include other intertriginous sites, as well as involvement in children. While the exact pathogenesis is unknown, the location of the lesions suggests that maceration and/or irritation play a role. This histology is striking, showing keratohyalin granules within a parakeratotic stratum corneum. Immunohistochemical and ultrastructural studies indicate a defect in the conversion of profillagrin to filagrin, resulting in failure to degrade keratohyalin granules and to properly aggregate keratin filaments.

**REFERENCES:**

CONTRIBUTED BY MARSHA L. CHAFFINS, M.D.
DIAGNOSIS: SUPERFICIAL MORPHEA

CLINICAL FEATURES:
---Hyper- or hypopigmented patches with minimal induration
---Female predilection
---No systemic involvement.

HISTOLOGIC FEATURES:
---Thickened collagen bundles in upper one-third of the dermis with sparing of the deep reticular dermis
---Mild lymphoplasmacellular inflammation in superficial dermis
---Lack of epidermal changes or interface dermatitis
---Diminished CD34 staining in the sclerotic areas.

DIFFERENTIAL DIAGNOSIS:
---Morphea/lichen sclerosis et atrophicus overlap
---Atrophoderma of Pasini and Pierini.

DISCUSSION:
This diagnosis of morphea may be missed if one requires deep dermal sclerosis and/or inflammation at the dermal subcutaneous interface to be present in the biopsy. Superficial morphea is a distinctive variant that shows superficial sclerosis and inflammation, while sparing the deep reticular dermis.

This condition can be distinguished from morphea/lichen sclerosus et atrophicus overlap by the absence of epidermal involvement. Also superficial morphea shows a parallel arrangement of elastic fibers in the involved areas whereas lichen sclerosus et atrophicus typically loss of elastic fibers in the superficial dermis.

REFERENCES:

CONTRIBUTED BY MARSHA L. CHAFFINS, M.D.
CASE #70 - SLIDE #70

DIAGNOSIS: PROLIFERATIVE NODULE

CLINICAL FEATURES:
---Papules or nodules within giant congenital nevus
---Variable pigmentation
---+/ - ulceration and a history of increased size
---Usually occur in infants, rarely in young children.

HISTOLOGIC FEATURES:
---Nodular area of increased cellularity and larger cells within giant congenital nevus
---Abundant melanin; few mitoses
---Absence of necrosis; +/ - ulceration
---Absence of pagetoid migration of melanocytes
---Proliferative nodule blends with surrounding nevus
---Atypical Proliferative nodules may have an abrupt interface with the surrounding nevus, show more nuclear atypia and more mitotic activity.

DIFFERENTIAL DIAGNOSIS:
Melanoma arising within congenital nevus.

DISCUSSION:
Prior to 2000, there were few articles in the literature on proliferative nodules. However, in recent years these lesions have become more widely recognized and better characterized. Though biopsies of Proliferative nodules can be alarming, carefully applied histologic criteria allow their distinction from melanoma. Immunohistochemical staining for c-kit (CD117) may also have some diagnostic utility, as proliferative nodules usually positive c-kit staining while nevi and melanomas are negative. Molecular and cytogenetic analyses have shown chromosomal aberrations within proliferative nodules, which are different than those occurring in melanoma.

REFERENCES:

CONTRIBUTED BY MARSHA L. CHAFFINS, M.D.
DIAGNOSIS: METASTATIC RENAL CELL CARCINOMA

CLINICAL FEATURES:
Erythematous to purple nodules; trunk, scalp and extremities are most common locations.

HISTOLOGIC FEATURES:
--- Nodular collection of clear cells with atypical nuclear features
--- Vascular stroma
--- Absence of epidermal connection
--- Cytokeratin cocktail positive, S100 negative
--- CD20-, CD7-, RCC+, CD10+
--- PAS positive, diastase sensitive.

DIFFERENTIAL DIAGNOSIS:
--- Clear cell squamous cell carcinoma
--- Hidradenocarcinoma
--- Sebaceous carcinoma
--- Melanoma
--- Vascular tumors.

DISCUSSION:
Metastatic renal cell carcinoma typically has a richly vascular stroma, which can cause confusion both clinically and histologically with benign vascular tumors. Careful inspection of vascular tumors for atypical cells can help prevent this important diagnosis from being overlooked. Renal cell carcinomas frequently show coexpression for vimentin and cytokeratin. Both papillary renal cell carcinoma and clear cell renal cell carcinoma show usually staining for CD10 which is expressed on the brush border of renal tubular epithelial cells and RCC, which is expressed in renal proximal tubular epithelial cells.

REFERENCES:

CONTRIBUTED BY MARSHA L. CHAFFINS, MD
CASE #72 - SLIDE #72

DIAGNOSIS: POLYMORPHOUS LIGHT ERUPTION, PINPOINT PAPULAR VARIANT

CLINICAL FEATURES:
---Pinpoint papules 1-2 mm in diameter on sun-exposed skin
---Eruption appears within a few hours of sun exposure
---Sparing of face and flexural areas
---African-American women.

HISTOLOGIC FEATURES:
---Perivascular lymphocytic inflammation
---Focal lichenoid or interface dermatitis
---Erythrocyte extravasation
---Superficial and deep perivascular lymphoid inflammation
---Papillary dermal edema.

DISCUSSION:
The classic histologic description of polymorphous light eruption is that of superficial and deep lymphoid infiltrates, with prominent papillary dermal edema. However, as the name implies, PMLE can show variable clinical and histologic morphologies. Biopsies of PMLE may reveal epidermal spongiosis, parakeratosis and vacuolar alteration of the basal cell layer. The papulovesicular form often contains prominent epidermal spongiosis. Pinpoint papular PMLE is a distinct variant, which clinically resembles lichen niditus and which occurs primarily in African-American women. The corresponding histologic findings of focal lichenoid inflammation and/or interface dermatitis are characteristic of the pinpoint papular type of PMLE.

REFERENCES:

CONTRIBUTED BY MARSHA L. CHAFFINS, M.D.
CASE #73 - SLIDE #73

DIAGNOSIS: CHRONIC CUTANEOUS LUPUS ERYTHEMATOSUS

CLINICAL FEATURES:
This condition is typically found in adult women and usually is not associated with systemic disease. Fifty percent of patients with disease isolated to skin have alopecia, and some patients have scalp lesions only. Establishing the diagnosis is more difficult when lesions are confined to the scalp, and certainly non-scalp lesions are supportive of the diagnosis. Itching or tenderness may be present. Typical lesions of DLE (erythema, scaling, “follicular plugging”) may be present in the scalp, but “non-inflammatory” disease resembling pseudopelade or alopecia areata may also be present.

HISTOLOGIC FEATURES:
Vacuolar interface alteration of the epidermis and follicular epithelium is typical, although the epidermis may be spared in lesions of CCLE involving the scalp. The interface change is usually vacuolar rather than lichenoid. In other words, lymphocytic inflammation at the DE junction is less prominent. Dyskeratosis and colloid (Civatte) bodies are occasionally seen but less commonly than in LPP. Moderate to dense chronic inflammation, often including plasma cells, is seen in both perivascular and periadnexal locations. When perifollicular inflammation is noted, it usually is most severe at the level of the infundibulum, and inflammatory cells may invade the follicular epithelium. Similar inflammation may be found in and around the follicular tracts that lie below telogen follicles or have been destroyed. Increased dermal mucin is often present and is helpful in differentiating CCLE from LPP. Granular deposits of IgG and C3 (rarely IgM or IgA) at the dermoepidermal junction and/or the junction of the follicular epithelium and dermis are typical of CCLE. Globular deposits of IgM representing colloid bodies may be present, but not as commonly as in LPP.

REFERENCES:

CONTRIBUTED BY LEONARD SPERLING, MD, COL, MC, USA
CLINICAL FEATURES:
Although LPP may affect only the scalp, a history of mucosal or non-scalp lichen planus is supportive of the diagnosis. The condition may evolve slowly and indolently or may be rapid and fulminant. Evidence of inflammation and follicular scarring are present. Lesions may be diffuse throughout the scalp or may affect circumscribed areas. The diagnosis of LPP affecting just the scalp cannot be based on clinical features alone and required good histologic correlation.

HISTOLOGIC FEATURES:
Typical lichen planopilaris shows a bandlike mononuclear cell infiltrate obscuring the interface between follicular epithelium and dermis. The epithelial-adventitial junction often shows prominent hyperkeratosis with individually necrotic, polygonal basal keratinocytes. Colloid or Civatte bodies are occasionally found as part of the interface alteration, but this is less common in follicular than in epidermal LP. Vacular alteration at the interface and hypergranulosis of the infundibulum may be present. Inflammation affects the upper portion of the follicle (infundibulum and isthmus) most severely, but inflammation may extend down the length of the follicle. The perivascular and peri-eccrine lymphocytic infiltrates of the mid- and deep dermis that are typical of discoid lupus erythematosus are absent in lichen planopilaris. Occasionally, interfollicular changes of lichen planus are also present. This feature, when present, strongly supports a diagnosis of lichen planopilaris.

Eventually the infundibulum becomes distended and plugged with keratinous debris. Perifollicular fibrosis and chronic inflammation (without distinct interface changes) may be seen at this later stage of disease. The inflammatory infiltrate seems to “back away” from the zone of fibrosis. Artifactual clefting between the “squamatized” epithelium and the stroma is common, and the epithelium may appear to be “floating” in a clear space. Although these changes are often seen in patients with longstanding lichen planopilaris, they are not diagnostic and can be observed in other forms of inflammatory scarring alopecia.

In time, the follicle is entirely destroyed. At first, retained hair shaft fragments and a granulomatous response is observed, but eventually the follicle is replaced by a column of sclerotic collagen, forming a true “follicular scar.” This represents an end-stage phenomenon that is shared by all forms of inflammatory, scarring alopecia such as discoid lupus erythematosus and central, centrifugal scarring alopecia. Grouped globular immunofluorescence (usually IgM), especially when found adjacent to the follicular epithelium, is the characteristic pattern seen in lichen planopilaris. Linear deposits of immunoreactants are typical of lupus erythematosus. This distinction can be important, because LPP and DLE may resemble each other both clinically and histologically in the setting of scarring alopecia.

REFERENCES:

CONTRIBUTED BY LEONARD SPERLING, MD, COL, MC, USA
DIAGNOSIS: TRICHTILLOMANIA

CLINICAL FEATURES:
Trichotillomania is a form of mechanical alopecia caused by forcefully plucking or twisting the hair. Patients will often deny plucking hair. A history suggestive of emotional stress can often be obtained, especially in adolescents. A minority of patients have severe psychiatric disturbances.

On examination there are markedly thinned but not denuded, irregularly shaped patches of alopecia, often with a bizarre distribution atypical for other forms of alopecia. Short hairs of various lengths are found within the thinned area.

HISTOLOGIC FEATURES:
The act of plucking results in several histologic changes that are highly suggestive or diagnostic of trichotillomania. The appearance of a given follicle will depend on: 1) the amount of damage done to the follicle during plucking, and 2) the amount of time elapsed between the act of plucking and the biopsy. The presence of incomplete and distorted anatomy without inflammation is convincing evidence of follicular injury and the most distinctive histologic feature of trichotillomania.

Follicles respond to the trauma of plucking by entering the catagen and subsequently telogen phases. This is true even for hairs that are badly distorted during plucking. Therefore, a marked increase in catagen and telogen hairs is common in trichotillomania. As mentioned earlier, an increased number of catagen and telogen hairs can also be found in alopecia areata (although inflammation is often present).

Pigment casts, clumps of pigmented hair matrix cells that become “stranded” in the upper follicle as they are torn out, are commonly found in trichotillomania. With time, the casts become compact, black, acellular structures within the interior of a shaftless follicle.

Trichomalacia is also a common finding in trichotillomania. Shafts demonstrating trichomalacia are abnormally small, distorted or bizarre in shape, incompletely keratinized, and show irregular pigmentation. Occasionally trichomalacia is also found in alopecia areata, so this finding is not diagnostic for traumatic alopecia.

The frequency with which the histologic findings of trichotillomania are found will depend on whether biopsy specimens are examined by transverse or vertical sectioning. The changes seen with vertical sections have been extensively reviewed. The AFIP experience has been that when transverse sections are performed, incomplete or distorted follicular anatomy can be found in over 50% of cases. This diagnostic finding is present in less than a quarter of specimens sectioned vertically, even when 20 or more sections are obtained. Typically, multiple findings are present when two or three levels of transversely sectioned specimens are studied.
REFERENCES:

CONTRIBUTED BY LEONARD SPERLING, MD, COL, MC, USA
CLINICAL FEATURES:
The nomenclature for scarring alopecia is confusing to say the least. My attempt at classification can be found in reference number 2 below. Central, centrifugal scarring alopecia has at least four names in the literature: “pseudopelade” (in Caucasians), follicular degeneration syndrome (in African-Americans), folliculitis decalvans (if pustules/acute inflammation are present) and “tufted folliculitis” (if scarring has lead to clustering of hairs). The various names probably represent different clinical presentations of the same condition, namely CCCA. The “pseudopelade” pattern of CCCA should not be confused with pseudopelade of Brocq, an entirely different clinical entity.

Formerly called “hot comb alopecia” or “the follicular degeneration syndrome (FDS),” CCCA occurs predominantly in adult black patients, usually women, with slowly progressive, relatively asymptomatic hair loss involving the crown or vertex. The condition continues to progress despite the cessation of chemical hair relaxers. A small percentage of patients are not black. White patients have been described as having “pseudopelade” or “folliculitis decalvans,” but the term Central, Centrifugal Cicatricial Alopecia encompasses the condition in all races.

Clinically, there is a large, fairly symmetrical patch of hair loss centered over the crown or vertex. The margins show partial alopecia that blends with the surrounding normal scalp. Scarring alopecia is evident by the smooth shiny surface and loss of follicular ostia. A few hairs may persist, “stranded” in an otherwise denuded patch. Inflammatory follicular papules may be present in the marginal zone.

HISTOLOGIC FEATURES:
If the biopsy site is chosen correctly, the histologic findings are diagnostic. If the central, bald zone is sampled, the findings will be those of a “burnt out” scarring alopecia. The most productive area is the peripheral, partially alopecic fringe. Even clinically “normal” scalp may be diseased at the microscopic level. Not every follicle in a given area is involved simultaneously. A 4 mm punch biopsy specimen may contain only one or two “diagnostic” follicles. This is because the involved follicles are selectively destroyed, leaving behind relatively normal follicles. Although an occasional vertical section may sample an involved hair, in most cases transverse sections at several levels are required to establish a definitive diagnosis.

The one unequivocal and diagnostic finding in histologic sections of CCCA is premature desquamation of the inner root sheath. Normally, the inner root sheath desquamates and disappears within the mid- to upper isthmus, which is usually located in the upper half of the dermis. In CCCA, the inner root sheath of an involved follicle desquamates in the lower half of the dermis, sometimes as low as the dermal/subcutaneous junction. In clinically abnormal scalp skin, involved follicles usually demonstrate some or all of the following histologic features; marked thinning of the outer root sheath with close approximation of the hair shaft and dermis; perifollicular, concentric (“onion skin-like”) fibroplasias; a variably dense, perifollicular, mononuclear cell infiltrate, most prominent at the level of the isthmus; and migration of the hair shaft through the outer root sheath into the dermis, with intense, reactive inflammation. The dermal response to extruded hair shaft and follicular contents in initially acute (polymorphonuclear) inflammation. However, as the follicular epithelium is gradually
sealed off and eliminated, a more chronic, mononuclear or granulomatous pattern of inflammation supervenes. Eventually, only a “naked” hair shaft and surrounding mild granulomatous inflammation remain. As the hair shaft is slowly dissolved, a column of fibrous tissue replaces it. To date, the immunofluorescent findings in patients with CCCA have not been studied.

REFERENCES:

CONTRIBUTED BY LEONARD SPERLING, MD, COL, MC, USA
DIAGNOSIS: ALOPECIA AREATA, STABLE “NON-INFLAMMATORY” TYPE

CLINICAL FEATURES:
Alopecia areata has a spectrum of severity ranging from a small solitary patch of hair loss to disease affecting every hair on the body. The clinical spectrum of disease severity is matched by a histologic spectrum of abnormalities. Recent hair loss may appear very different histologically than longstanding disease.

HISTOLOGIC FEATURES:
In early (acute) disease, the following features are commonly seen: normal total numbers of hairs; increased number of catagen and telogen follicles; mononuclear cell infiltrate around the bulbs of some terminal anagen and catagen hairs; hair matrix changes such as intercellular edema, exocytosis of inflammatory cells, nuclear pyknosis, cellular necrosis and vacuole formation; trichomalacia and marked narrowing of hair shafts.

In longstanding (“chronic”) alopecia areata, there are normal or nearly normal numbers of follicles, but almost all are miniaturized; the majority of hairs are in catagen or telogen phases; the peribulbar infiltrate may be scanty or absent, and is usually associated with anagen hairs only; and the miniaturized anagen hairs may fail to exhibit any hair shaft production. These rather atypical miniaturized hairs have been termed “nanogen hairs,” and are characteristic of alopecia areata. Peribulbar inflammation tends to subside as affected follicles enter the telogen phase, but occasionally a few inflammatory cells can still be found around telogen hairs.

The miniaturized follicles are often missed on routine vertical sectioning, and transverse sections greatly increase the chance of seeing all or most affected hairs. Below each miniaturized follicle is a collapsed fibrous root sheath. Inflammatory cells and clumps of melanin may be found in and around some, but not all, of the collapsed sheaths. Non-inflamed fibrous root sheaths are morphologically similar to the “fibrous streamers” described in androgenetic alopecia.

REFERENCES:

CONTRIBUTED BY LEONARD SPERLING, MD, COL, MC, USA
CASE #78 - SLIDE #78

DIAGNOSIS: FIRE ANT BITE

CLINICAL FEATURES:
---When disturbed, the small imported fire ant will swarm from its nest and actively attach intruders with a painful bite/sting.
---One to three days later a small sterile pustule with a red halo appears at the site. The pustule is asymptomatic and resolves in about a week.

HISTOLOGIC FEATURES:
---There is a large wedge-shaped subcorneal pustule with underlying ulceration and dermal necrosis. Eosinophils are numerous in the surrounding dermis.
---In sections adjacent to the pustule there is subepidermal edema and a superficial and deep perivascular and interstitial mixed inflammatory infiltrate with numerous eosinophils.

DIFFERENTIAL DIAGNOSIS:
---Bowel bypass syndrome
---Suppurative folliculitis
---Other arthropod bites with secondary infection.

DISCUSSION:
This is an all-too-common lesion to anyone living in the southern United States where over 300 million acres are infested with the imported fire ant [order Hymenoptera, genus Solenopsis, especially S. invicta (red) and S. richteri (black)] beginning at the port of Mobile, Alabama in the early 1900s and now extending north to Virginia and west to California. Compared to the native ants these species are more aggressive, the bite/sting more painful, and the resulting pustule more distinctive. More than 50% of persons living in endemic areas report being stung each year. Most lesions are nuisances requiring no treatment, but rare persons become allergic to the fire ant venom and develop exaggerated local reactions or even anaphylaxis to subsequent stings. There is also potential neurotoxicity, including seizures or neuropathy. Increasingly, there are reports of indoor attacks by foraging ants on patients in hospitals or nursing homes where immobilized or impaired patients may sustain hundreds of stings, and there is at least one account of a neglected newborn baby who nearly died from a similar attack. RAST serologic tests and skin testing using isolated allergens or whole body extracts can detect allergy, and immunotherapy can reduce the risk of subsequent systemic reactions.

REFERENCES:

CONTRIBUTED BY EMILY F. OMURA, M.D.
CASE #79 - SLIDE #79

DIAGNOSIS: LEISHMANIASIS (IN A SOLIDER RETURNING FROM IRAQ)

CLINICAL FEATURES:
---A 27 year-old soldier stationed in Iraq from 3/03 to 9/03 developed several red non-ulcerated asymptomatic nodules over the wrist and forearm four months after returning to the U.S. Intralesional steroid injection caused initial improvement with later recurrence and ulceration. Eventual healing with scarring occurred.
---The key to diagnosis is awareness of a patient’s military/travel history to an endemic area with lesions on exposed/unprotected skin.
---Unusual cutaneous presentations include annular, zosteriform, sporotrichoid, erysipeloid and recidivous forms.

HISTOLOGIC FEATURES:
---There is irregular epidermal hyperplasia. In the dermis there is necrotizing granulomatous inflammation with epithelioid histiocytes palisading around a deep focus of necrosis, hemorrhage, plasma cells and a few neutrophils. A few parasitized histiocytes are present in the necrotic area with intracytoplasmic round organisms with eccentrically located kinetoplasts and no capsule.
---The earlier biopsy containing perivascular granulomas without necrosis or visible organisms will also be shown.

DIFFERENTIAL DIAGNOSIS:
---Histoplasmosis
---Sporotrichosis
---Lupus vulgaris
---Leprosy, cat scratch disease, other infections.

DISCUSSION:
Over 500 cases of cutaneous leishmaniasis have been seen since the invasion of Iraq, most from 8/03 to 11/03 (2004). The diagnosis in returning personnel is challenging because of the delayed onset, the small number of parasites that may be present in cutaneous lesions and the lack of experience with the disease in the U.S. If biopsy and/or a Giemsa-stained smear from an ulcer edge or culture is not diagnostic, polymerase chain reaction to detect Leishmania DNA is the most sensitive single diagnostic procedure; it was done in this case by Walter Reed Hospital and confirmed L. major.

REFERENCES:

CONTRIBUTED BY EMILY F. OMURA, M.D.
DIAGNOSIS: CUTANEOUS ROSAI-DORFMAN DISEASE

CLINICAL FEATURES:
---A 46 year-old woman noted an asymptomatic 8 cm plaque with multiple purplish nodules of three months duration over one thigh. There was no palpable lymphadenopathy.
---This disease was originally described by Rosai and Dorfman as “sinus histiocytosis with massive lymphadenopathy” in 1969. In 1978 cutaneous manifestations were noted in many patients, and subsequently cases confined to the skin have been recognized. All ages are affected. Skin lesions are usually papular or nodular but vary tremendously in number, site and color from a solitary red-brown nodule on the scalp to widespread numerous small red-yellow papules resembling xanthomas.

HISTOLOGIC FEATURES:
---Slight hyperkeratosis and hypergranulosis
---Beneath a thin Grenz zone, there is a dense diffuse mixed inflammatory infiltrate, obscuring normal structures, composed of histiocytes with abundant foamy of vacuolated cytoplasm, clumps of plasma cells, hemosiderin and scattered neutrophils and eosinophils.
---Main finding: lymphocytes and plasma cells within the cytoplasm of some histiocytes (emperipolesis), occasionally marked, with a “bag of coins” look
---Histiocytes are S100 protein and CD68 positive, but CD1a negative, and no Birbeck granules are present on EM.

DISCUSSION:
Rosai-Dorfman disease is an uncommon entity of unknown cause affecting lymph nodes, plus a variety of extranodal sites in 30-40% of cases, of which the skin is the most common. Purely cutaneous disease is rare but may be a distinct entity with no progression to systemic disease and with eventual spontaneous resolution or lack of recurrence after surgical removal. Other reported extranodal sites range widely, including a lytic pseudotumor of bone, a giant intracranial lesion, thyroid, thymus, breast, pleura, retina, lachrymal gland, meninges, etc. Emperipolesis and the unusual staining characteristics of the histiocytes make the diagnosis. The histology resembles a reactive inflammatory pseudotumor, but the etiology is at present unknown, despite EM, cultures and serologic investigations.

REFERENCES:
CLINICAL FEATURES:
--- A 47 year-old white man had pink edematous papules coalescent into plaques of the trunk and extremities for two weeks; clinical impression was “rule out urticarial, drug eruption.”
--- Osler’s “great imitator” may present with lesions of almost any morphology except blisters. Helpful: palm and sole “nickels and dimes,” moth-eaten alopecia and soft mucosal plaques.

HISTOLOGIC FEATURES:
--- Compact hyperkeratosis with parakeratosis and a few collections of PMNs
--- Moderate psoriasiform epidermal hyperplasia with lymphocytes scattered in lower epidermis
--- A dense lichenoid and superficial and deep perivascular and perifollicular mononuclear cell infiltrate, with numerous plasma cells.
--- The features may vary: plasma cells may be few, the inflammation may be neutrophilic or granulomatous including palisaded granulomas, and ulceration may occur.

DIFFERENTIAL DIAGNOSIS:
Mucha-Haberman disease, mycosis fungoides, psoriasis, lichen planus, lupus erythematosus.

DISCUSSION:
The diagnosis is frequently difficult because of the diverse clinical and histologic features that may occur and the low yield of silver stains, but the simplicity and virtually 100% sensitivity of serology has heretofore saved many a situation and been the gold standard. However, there is an increasing incidence of seronegative secondary syphilis in HIV patients, making it important for us to re-hone our skills in histologic interpretation of the various stages of the lesions. This biopsy illustrates the classic pattern of epidermal hyperplasia with exocytosis of lymphocytes and a bandlike and superficial and deep perivascular infiltrate rich in plasma cells. The main differential diagnosis of this pattern: Mucha-Habermann disease, with necrotic keratinocytes and mycosis fungoides, with atypical lymphocytes in the epidermis and fibrosis of the papillary dermis; neither has numerous plasma cells. A recent improvement for spirochete detection in formalin-fixed tissue is an immunoperoxidase stain using a monoclonal antibody to T. pallidum with a reported 71% sensitivity, compared to an optimistic 41% sensitivity for silver stains.

REFERENCES:

CONTRIBUTED BY EMILY F. OMURA, M.D.
CASE #82 - SLIDE #82

DIAGNOSIS: ACQUIRED TUFTED ANGIOMA

CLINICAL FEATURES:
---A 19 month-old girl had a slowly enlarging 10 X 5 cm apparently asymptomatic indurated pink plaque over the abdomen with several small nodules within the plaque and with slight peripheral hypertrichosis. A platelet count was normal.
---This acquired vascular tumor occurs mostly in children and young adults; congenital and older ages of onset have been described as well as familial cases. The lesion may be tender. Most cases do not regress as “strawberry” hemangiomas do.

HISTOLOGIC FEATURES:
---There are multiple separated cellular lobules (“tufts” or “cannonballs”) throughout the dermis composed of densely aggregated large endothelial cells with spindled or oval nuclei and small capillary-sized vascular lumena.
---Mitotic figures are present but no atypical mitoses or nuclear atypia.
---The surrounding dermis is somewhat dense without inflammation or edema.

DIFFERENTIAL DIAGNOSIS:
---Congenital hemangioma
---Kaposi’s sarcoma or low-grade angiosarcoma
---Kaposiform hemangioendothelioma.

DISCUSSION:
This case illustrates the typical presentation and histology of a distinctive benign progressive angioma described by Wilson Jones in 1989. Tenderness, hypertrichosis and a lack of regression distinguish it from the more common “strawberry” hemangioma. Since the descriptions of acquired tufted angioma and kaposiform hemangioendothelioma, it has become apparent that Kasabach-Merritt phenomenon (the association of a vascular tumor and life-threatening thrombocytopenic coagulopathy) occurs in these lesions rather than in ordinary congenital hemangiomas of infancy. Both lesions show lymphatic differentiation on immunostaining.

REFERENCES:

CONTRIBUTED BY EMILY F. OMURA, M.D.
CASE #83 - SLIDE #83

DIAGNOSIS: REACTION TO SILICONE BREAST IMPLANT

CLINICAL FEATURES:
Rupture of a silicone-gel breast implant may be contained within the fibrous scar or capsule that forms around the implant or extracapsular, breaching the capsule. Patients may be asymptomatic, may have localized discomfort or may note a firmness or mass adjacent to the implant.

HISTOLOGIC FEATURES:
Silicones can produce a range of histologic reactions, depending mainly on the form of the silicone (liquid, gel or solid elastomer type) and the amount in the tissues. Silicone elastomer particles elicit a marked granulomatous foreign body reaction. Liquid and gel silicone have similar light microscopic features except that small amounts of gel may remain in vacuoles.
---Round to oval vacuoles of varying size
---Vacuoles usually appear empty (silicone liquid lost in processing)
---Vacuoles sometimes surrounded by histiocytes
---Histiocytes possibly show multivacuolated (foamy) cytoplasm
---Multinucleate giant cells occasionally seen
---Variable fibroblastic response.

DIFFERENTIAL DIAGNOSIS:
Paraffinoma and other injectable materials; sclerosing lipogranuloma.

DISCUSSION:
Breast implant composed of silicone gel enveloped in a silicone rubber elastomer were introduced in 1963. Silicone-gel breast implants have been widely used for breast augmentation and reconstruction after mastectomy. An estimated one to two million U.S. women have undergone mammoplasty, 20% for reconstruction after mastectomy and 80% for cosmetic augmentation. The frequency of rupture of silicone-gel-filled breast prostheses is unknown, but it is generally accepted that silicone breast implants “bleed” and actual rupture is not necessary to identify silicone in the periprosthetic capsule.

REFERENCES:

CONTRIBUTED BY ANTOINETTE HOOD, M.D.
CLINICAL FEATURES:
The vast majority of lesions has been present for years and are brought to clinical attention as a result of persistent nail changes. The main clinical findings include yellow longitudinal band, splinter hemorrhages and longitudinal ridging with a tendency toward transverse overcurvature. Nail avulsion exposes a villous tumor arising in the matrix; the nail appears as a thickened and somewhat flattened funnel with filamentous digitations of matrix lodged within multiple holes or channels within the proximal nail plate.

HISTOLOGIC FEATURES:
---Epithelial and stromal components with a proximal and distal region
---The proximal region is situated beneath the proximal nail fold and a distal zone with nail matrix epithelium raised in characteristic “glove-finger” projections.
---Stromal component in the proximal region is organized into two layers
   ---A highly cellular superficial layer is highly cellular with fibrillary collagen
   ---A deeper layer composed of thicker bundles of collagen.

DIFFERENTIAL DIAGNOSIS:
Fibrokeratoma; squamous cell carcinoma in situ.

DISCUSSION:
Onychomatricoma is a rare tumor of the nail bed, originating within the matrix, producing characteristic yellowing and deformity of the nail patch with corrugation and canalization. First described by Baran and Kint in 1992, twenty-eight cases have been described in the literature, with four in the United States.

REFERENCES:
CASE #85 - SLIDE #85

DIAGNOSIS: DERMATOFIBROMA WITH MONSTER CELLS

CLINICAL FEATURES:
Typically presents as papules or nodules on the extremities.

HISTOLOGIC FEATURES:
---Overlying epidermis shows the elongated rete ridges
---Intradermal proliferation of spindle cells and histiocytic cells
---Border infiltrative and ill-defined
---Collagen bundles entrapped by proliferating cells
---Multinucleate giant cells, foamy histiocytic cells
---“Monster cells” characterized by large atypical nuclei.

DISCUSSION:
Monster cells are seen in the early histiocytic stage of dermatofibroma when lipophages and siderophages are usually present in large numbers. Histologic variants of benign fibrous histiocytoma/dermatofibroma include the following:
- Cellular fibrous histiocytoma
- Epithelioid fibrous histiocytoma
- Aneurysmal fibrous histiocytoma
- Clear cell dermatofibroma
- Palisaded fibrous histiocytoma
- Myxoid dermatofibroma
- Lipidized fibrous histiocytoma
- Dermatofibroma with granular cell changes.

REFERENCES:

CONTRIBUTED BY ANTOINETTE HOOD, M.D.
CASE #86 - SLIDE #86

DIAGNOSIS: SOFT TISSUE GIANT CELL TUMOR
(OF LOW MALIGNANT POTENTIAL)

CLINICAL FEATURES:
Soft tissue giant cell tumors typically present as multinodular masses in the skin or subcutis of young to middle-aged adults, although occasional cases may present as more deeply seated masses or in children. Tumors have significant capacities for local recurrences but only metastasize in extremely rare instances. The locally recurring potential of these tumors is most likely related to the multinodular growth pattern, and wide excision is curative in most cases.

HISTOLOGIC FEATURES:
---Multinodular masses in deep dermis and subcutis
---Peripheral surrounding shell of metaplastic, woven bone
---Individual tumor nodules comprised of a mixture of osteoclastic giant cells, bland mononuclear cells and short fascicles of bland spindled cells
---Mitotic figures numerous; atypical mitoses uncommon.

DIFFERENTIAL DIAGNOSIS:
The histologic differential diagnosis of soft tissue giant cell tumor is broad and includes both benign and malignant entities. Sarcomas that may be confused with soft tissue giant cell tumor include malignant giant cell tumors of soft parts (giant cell-rich variant of malignant fibrous histiocytoma), extraskeletal osteosarcoma and various other osteoclastic-rich malignancies. Benign tumors that may be mistaken for soft tissue giant cell tumors include tenosynovial giant cell tumors or giant cell-rich forms of nodular fasciitis.

DISCUSSION:
This tumor was first described in 1972 by Salm and Sissons who noted a close resemblance between a subset of giant cell rich soft tissue tumors and giant cell tumors of bone. Subsequent publications have established it as a distinct entity. Dermatologists and dermatopathologists must be aware of this tumor and its potential for recurrence if not completely excised.

REFERENCES:

CONTRIBUTED BY ANTOINETTE HOOD, M.D.
CASE #87 - SLIDE #87

DIAGNOSIS: AGGRESSIVE ANGIOMYXOMA

CLINICAL FEATURES:
This neoplasm predominantly affects reproductive-age women with a peak incidence during the third decade of life. The female/male ratio is more than 6:1, but the tumor has been increasingly recognizing as arising in men.

HISTOLOGIC FEATURES:
---Tumor composed of widely scattered spindle- and stellate-cells with ill-defined cytoplasm
---Varially sized, thin- or thick-walled vascular channels
     ---perivascular hyalinization and medial hypertrophy
---Myxoid stroma rich in collagen fibers
---Mast cells often prominent
---Immunohistochemical findings: cells show diffuse staining for vimentin, focal or diffuse staining for desmin and smooth muscle actin; S100 protein and cytokeratins are negative.

DIFFERENTIAL DIAGNOSIS:
The histologic differential diagnosis includes other benign and malignant myxoid neoplasms such as angiomyofibroblastoma, a neoplasm that arises in the subcutaneous tissues of the vulva, vagina and rarely the scrotum; cutaneous myxoma; myxoid neurofibroma; myxoid leiomyoma; myxoid Liposarcoma and myxofibrosarcoma.

DISCUSSION:
Aggressive angiomyxoma is a term coined by Steeper and Rosai in 1983 for a morphologically distinctive, slow-growing neoplasm that occurs chiefly in the genital, perineal and pelvic regions of adult women. Despite its bland histologic features, it has a propensity for local recurrence.

REFERENCES:

CONTRIBUTED BY ANTOINETTE HOOD, M.D.
Clinical and Histopathologic Findings
Cellular neurothekeomas are rare cutaneous tumors of disputed etiology. These tumors usually present on the head, neck and upper extremities. They are more commonly seen in children and young adults with a predilection for females. Clinically, they present as a long-standing asymptomatic nodule that can measure up to 6 cm or more in diameter. Evidence that cellular neurothekeomas show nerve sheath differentiation is lacking, and several authors have proposed that they are of fibrohistiocytic origin. Despite sometimes showing atypical cytologic features, cellular neurothekeomas consistently behave in a benign fashion and only occasionally recur. Histologically, they show a poorly defined, micronodular or lobulated growth pattern in the dermis with frequent extension into the superficial subcutis. These lobules are composed of epithelioid to spindled cells with abundant, pale, eosinophilic cytoplasm with vesicular nuclei and mild or no cytologic atypia; however, up to 25% of cases show marked pleomorphism. Typical mitotic figures are seen sometimes. Myxoid changes can be prominent. These tumors are strongly positive for NKI-C3, NSE, S100A6, PGP9.5 and MITF-1, and nearly 60% show expression of SMA. None of these markers are specific for cellular neurothekeomas. They are negative for S100p, HMB-45, and MART-1. The histopathology of these tumors can sometimes mimic a melanocytic neoplasm; thus, S100p should always be performed to rule out this possibility.

References
CLINICAL FEATURES:
Infection of the lung by Penicillium marneffei, mainly in Southeast Asia in patients with AIDS, disseminates to other organs later. Acneiform papules resemble Molluscum contagiosum clinically. Papules are often umbilicated, as in this patient, and cryptococcosis also comes to min. This patient lived in a refugee camp for ten years and arrived in the US febrile, hypotensive and septic, with lymphadenopathy and splenomegaly. His CD4 count was 70, and he was not taking any medications prior to admission. He completely recovered after treatment with systemic antifungals and HAART therapy.

HISTOLOGIC FEATURES:
---Diffuse suppurative granulomatous inflammation
---Necrosis prominent with sparse inflammation in patients with poor immunity
---Yeast with diameter of 3 microns in histiocytes, up to 8 microns when extracellular, dividing by fission without buds, appearing elongated and septate
---Positive staining of yeast with PAS and GMS, but not with mucicarmine.

DIFFERENTIAL DIAGNOSIS:
---Histoplasmosis may be nearly impossible to distinguish on biopsy. It usually is uniformly two to four microns and does not get up to eight microns. The geographic location of infection (SE Asia) is very helpful in penicilliosis, and the presence of binary fission of the yeast without buds is also helpful. The yeast of penicilliosis also becomes more sausage-shaped with blunt ends like in this biopsy.
---Cryptococcosis is also common with AIDS and clinically presents with similar umbilicated papules on the face, but has a more rounded 5-20 micron yeast that buds. There is an often gelatinous appearance of the biopsy, and there is mucin in the capsule.

DISCUSSION:
The fungus was grown in culture in this patient. It is dimorphic in culture unlike other members of the Penicillium genus. It appears in yeast form in vivo. It also has a unique red color of the reverse. The bamboo rat might be the reservoir of infection.

REFERENCES:

CONTRIBUTED BY RONALD P. RAPINI, M.D.
CASE #90 - SLIDE #90

DIAGNOSIS: GELFOAM FOREIGN BODY

CLINICAL FEATURES:
Gelfoam (gelatin sponge) is generally used by dermatologists and other physicians for hemostasis. Special tampon-like plus are sold for punch biopsies, for use in lieu of suturing. Gelfoam powder can be sprinkled on wounds, and foam-like pads can be applied to open wounds.

HISTOLOGIC FEATURES:
Gelfoam has an eosinophilic trabecular claw-like appearance.

DIFFERENTIAL DIAGNOSIS:
Other foreign materials do not have this same appearance. Some examples of other foreign materials will be shown at the conference.

DISCUSSION:
I don’t see many examples as exuberant like this particular case in my dermpath practice, but in some geographic areas where Gelfoam is used more commonly, it might be commonly seen. Some Mohs surgeons like to use it.

REFERENCES:
CASE #91 - SLIDE #91

DIAGNOSIS: CYTOMEGALOVIRUS AND FUNGUS CO-INFECTION

CLINICAL FEATURES:
CMV is widely prevalent in its latent state in the general population and mainly reacti
vates when there is immunosuppression. Fever occurs along with infection of many internal organs, especially causing pneumonitis, hepatitis, encephalitis, chorioretinitis and gastroenteritis. A wide variety of skin manifestations includes blueberry muffin babies (dermal hematopoiesis), ulcers (especially perianal and mouth), mononucleosis-like syndrome (especially after ampicillin), morbilliform eruption, urticarial, purpura, bullae or verrucous lesions.

HISTOLOGIC FEATURES:
---Epidermis normal, verrucous or ulcerated
---Vascular dilation with large cytomegalic endothelial cells
---Intranuclear and intracytoplasmic inclusion bodies (halo around intranuclear inclusions forming an “owl’s eye” appearance)
---Variable perivascular lymphocytes or neutrophils
---Positive CMV immunostain (readily available commercially)
---Viral particles indistinguishable from other herpes viruses by electron microscopy.

DIFFERENTIAL DIAGNOSIS:
Once the characteristic cells are identified, there is not much that remains in the differential diagnosis. When in doubt, immunostaining, serology or PCR can be done. Large endothelial cells may be seen in various vascular proliferations like angiolymphoid hyperplasia and other reactive inflammatory conditions, but this rarely causes difficulty, and inclusion bodies are not found and the clinical setting is different.

DISCUSSION:
I checked all of the recuts, and CMV cells were present on all, along with plenty of fungus infection. Serologic testing for CMV is widely available. The virus can be cultured from urine, blood or tissue. The specific cytomegalic cells are more likely to be found in the ulcers rather than in the more nonspecific rashes.

REFERENCES:

CONTRIBUTED BY RONALD P. RAPINI, M.D.
CASE #92 - SLIDE #92

DIAGNOSIS: SPOROTRICHOSIS WITH ASTEROID BODIES

CLINICAL FEATURES:
Sporotrichum schenckii produces nodules and pustules, especially on the hands, fingers and forearms, after primary inoculation, especially from rose thorns or sphagnum moss. Nodules may spread in a linear pattern up the lymphatics, rarely disseminating into joints or systemically.

HISTOLOGIC FEATURES:
---Pseudoepitheliomatous hyperplasia; often with intraepidermal neutrophilic microabscesses or ulceration
---Diffuse mixed dermal infiltrate of neutrophils (often abscesses), histiocytes, plasma cells and multinucleated giant cells.
---Round, oval or cigar-shaped spores range from 3-8 microns but are often difficult to find, even with PAS and GMS stains. In some cases, as in this case there may be “sporothrix asteroids” with a yeast form surrounded by radiating eosinophilic rays of immune complexes, sort of like a smaller scale Splendore-Hoepli phenomenon that occurs with actinomycosis.

DIFFERENTIAL DIAGNOSIS:
---Clinically sporotrichoid lesions include Sporotrichosis, leishmaniasis, atypical mycobacterial infection, nocardiosis, tularemia and ordinary Staphylococcal furunculosis. The mnemonic “SLANT” has been used.
---Other disease with pseudoepitheliomatous hyperplasia with microabscesses include other deep fungi and acid-fast bacillus infections, halogenoderms and variants of pyoderma gangrenosum.

DISCUSSION:
There is a beautiful picture of Sporothrix asteroid formation with a microabscess in the second edition of the textbook Skin Pathology by Weedon on page 674, that is identical to this case. I personally checked every recut slide, and all of them had one of these organisms that I circled. Weedon points out that the traditional view is that fungal elements are infrequently demonstrated in human cases of Sporotrichosis, but that he as able to find them in 37 of 39 of his own cases. He admits that his cases were mostly not of the lymphangitic type. In my own experience in cases that are more lymphangitic in immunosuppressed patients, organisms are sometimes numerous. Sporotrichosis is generally relatively easy to grow in culture and is not fastidious.

REFERENCES:

CONTRIBUTED BY RONALD P. RAPINI, M.D.
CASE #93 - SLIDE #93

DIAGNOSIS: LOCALIZED ARGYRIA FROM EAR PIERCING

CLINICAL FEATURES:
This patient presented with a blue macule on the upper ear after ear piercing of the cartilaginous portion of the ear with a silver earring. Localized argyria may also occur with traumatic implantation of silver from metal working, acupuncture, photography developing or from tropical exposure to silver-containing compounds (particularly on mucosal surfaces). The lesions are typically asymptomatic blue-gray macules.

HISTOLOGIC FEATURES:
---Fine black pigment granules along the basement membrane zone of the DE junction and around the eccrine coil
---Fine black pigment granules highlight the oxytalan fibers (fine elastic fibers oriented perpendicular to the surface within the papillary dermis)
---Fine black pigment granules within blood vessel walls and free within the dermis
---Absence of significant inflammation
---Fails to sustain with Fontana-Masson or Perl’s iron stain.

DIFFERENTIAL DIAGNOSIS:
---Minocycline pigmentation
---Pseudo-ochronosis
---Nevus of It/Ota
---Blue nevus
---Post-inflammatory pigmentary abnormality.

DISCUSSION:
Localized argyria presents as a blue gray area of macular pigmentation following prolonged contact with silver-containing compounds on mucosal surfaces or after traumatic implantation of silver in the skin. The latter is becoming more common as ear piercing is being performed with silver earrings. Fine black granules are found along the basement membrane zone, around eccrine glands, within endothelial cells, on elastic fibers, in macrophages and free within the dermis. The distribution of the granules on histologic examination, fine black morphology and lack of staining with Fontana-Masson (along with the clinical history) all help in making the diagnosis. A pseudo-ochronosis pattern has been described. The histopathologic features are similar to generalized argyria.

REFERENCES:

CONTRIBUTED BY LISA M. COHEN, M.D.
DIAGNOSIS: CUTANEOUS ANGIOSARCOMA

CLINICAL FEATURES:
--- Uncommon tumor (less than 1% of sarcomas)
--- Elderly patient
--- Males more commonly affected
--- Red to violaceous bruise-like patch or nodular lesion on the head or neck (predilection for the scalp and upper forehead)
--- Rapidly increases in size and may be very large at presentation
--- May also occur on the breast after irradiation or on the arm after chronic lymphedema
--- Aggressive tumor with poor prognosis.

HISTOLOGIC FEATURES:
--- Poorly-differentiated high grade spindle cell tumor
--- Tumor cells are oriented in fascicles and randomly throughout the dermis
--- High mitotic rate and marked pleomorphism and atypia
--- Abundant red blood cells between spindle cells
--- Clue is to look for spindle cells that dissect collagen bundles giving a “cracked” appearance
--- Small newly-formed blood vessels with atypical endothelial cells and papillary projections
--- Immunoperoxidase stains positive for CD31, CD34, factor VIII-related antigen, vimentin.

DIFFERENTIAL DIAGNOSIS:
Other spindle cell malignancies: spindle cell squamous cell carcinoma, spindle cell melanoma, atypical fibroxanthoma, cutaneous leiomyosarcoma (“atypical intradermal smooth muscle neoplasm”), tumor stage Kaposi’s sarcoma.

DISCUSSION:
Cutaneous angiosarcoma is an aggressive malignancy of the endothelial cell. Depending on the location and the clinical setting, variants include cutaneous angiosarcoma (unassociated with lymphedema), cutaneous angiosarcoma associated with lymphedema, angiosarcoma of the breast, radiation-induced angiosarcoma, and angiosarcoma of deep soft tissue. The most common presentation for the former is a red to purple rapidly expanding patch on the face or scalp of an elderly patient. Lesions may be very large at presentation, the average diameter being 5.3 cm. The other clinical setting is in post-irradiation sites, such as the breast, or on an extremity after chronic lymphedema (Stewart-Treves syndrome). Two histologic patterns include anastomosing well-formed blood vessels lined by plump atypical endothelial cells with papillary projections that dissect collagen bundles or a diffuse poorly-differentiated high grade spindle cell tumor (as in this case). Some lesions show a mixed pattern. Two clues to the diagnosis in the latter are abundant hemorrhage and a “cracked” appearance within the tumor where blood vessels dissect collagen bundles. Prognosis is poor (10-25% five-year survival) with a correlation with large size, deep invasion, high mitotic count, positive surgical margins, tumor recurrence and metastasis.
REFERENCES:

CONTRIBUTED BY LISA M. COHEN, M.D.
CASE #95 - SLIDE #95

DIAGNOSIS: MYXOID PLEOMORPHIC FIBROMA

CLINICAL FEATURES:
---Slowly growing flesh-colored dome-shaped papule
---Most commonly located on an extremity
---Slight female predominance, peak incidence 5th decade.

HISTOLOGIC FEATURES:
---Exophytic to polypoid lesion with hypocellular fibrotic stroma
---Dilated blood vessels
---Admixture of ordinary fibroblasts and plump bizarrely atypical fibroblasts sparsely distributed throughout the dermis
---Atypical fibroblasts have large pleomorphic nuclei and floret-type giant cells
---Lack of significant mitotic activity
---In this case, mucin deposition throughout (very rare in most pleomorphic fibromas)
---Mitotic figures are rare
---Spindle cells stain positively for vimentin and CD 34.

DIFFERENTIAL DIAGNOSIS:
---Pleomorphic malignant fibrous histiocytoma
---Myxofibrosarcoma
---Superficial angiomyxoma
---Myxoid leiomyosarcoma
---Neurofibroma with atypia
---Dermatofibroma with monster cells.

DISCUSSION:
In general, pleomorphic fibroma presents as a small papule most commonly on an extremity. The usual clinical impression is nevus versus neurofibroma, and an atypical lesion is not usually suspected clinically. The hallmark of this lesion is scattered large bizarrely atypical fibroblasts and multinucleated cells that are embedded in a collagenous stroma, with little to absent mitotic activity. Although mucin may be rarely present, this case is unusual in that the stroma is diffusely myxoid (rarely reported in the literature). Given the abundance of mucin and the presence of atypical spindle cells, the differential diagnosis includes a variety of sarcomas that can have mucin. The small size of the lesion and sharp circumscription, in conjunction with the clinical presentation, is consistent with this diagnosis.

REFERENCES:

CONTRIBUTED BY LISA M. COHEN, M.D.
CASE #96 - SLIDE #96

DIAGNOSIS: ACUTE GENERALIZED EXANTHEMATOUS PUSTULOSIS

CLINICAL FEATURES:
--Abrupt onset of a generalized pustular eruption
---Sterile, nonfollicular pustules are distributed on an erythematous base with predilection for the skin folds and face
---The eruption is most often due to medication (particularly beta-lactam antibiotics).

HISTOLOGIC FEATURES:
---Subcorneal and spongiform pustules containing neutrophils and eosinophils
---Superficial and deep perivascular dermatitis containing eosinophils
---Papillary dermal edema
---Special stains are negative for bacteria and fungi.

DIFFERENTIAL DIAGNOSIS:
---Pustular drug eruption
---Psoriasis-like drug eruption
---Scabies
---Subcorneal pustular dermatosis
---Immune bullous disorder (IgA pemphigus).

DISCUSSION:
The entity is a type of drug eruption associated with a wide variety of medications including antibiotics, ibuprofen, hydroxychloroquine and others. On occasion, a viral infection can precipitate the eruption. The clinical presentation is characteristic, atypically presenting with dozens to hundreds of sterile pustules on a diffusely erythematous edematous base. The lesions are often concentrated in skin folds and may extensively involve the face. Fever and neutrophilia are common. The eruption resolves spontaneously over several days to two weeks when the medication is withdrawn. The histopathology is characterized by subcorneal and/or intraepidermal pustules with eosinophils and a perivascular dermal infiltrate. Vasculitis may be observed. Scattered necrotic keratinocytes are often seen.

REFERENCES:

CONTRIBUTED BY LISA M. COHEN, M.D.
**CASE #97 - SLIDE #97**

**DIAGNOSIS: EPITHELIOID HEMANGIOMA, PENILE TYPE**

**Clinical Features**
Patients are usually adults (median age 45) who present with a solitary mass. The site may be anywhere on the penis, but is often dorsal and superficial. Lesions are often painful. Size ranged from <0.5 cm to 2.5 cm (median 1.2 cm) in the largest series to date. Behavior is uniformly benign with very long follow-up available in a number of reported cases.

**Histopathologic Features**
- Circumscribed nodular or lobular proliferation of epithelioid endothelial cells.
- Often associated with vessels with mural damage.
- Inflammatory infiltrate present, eosinophils usually prominent.
- Intraluminal proliferation.
- “Atypical” examples show poor canalization, leading to an impression of solid sheets of epithelioid cells.
- Large, but uniform nuclei with open chromatin and distinct central nucleoli.
- Mitotic rate usually very low, atypical forms absent.
- CD31+, CD34-, cytokeratin +/- immunophenotype.

**References**

**CONTRIBUTED BY KRISTOPHER MCKAY, MD**
Clinical Features
Low grade fibromyxoid sarcoma typically occurs as a deep soft tissue mass in the extremities of adults. However, a subset of cases occurs in children where they tend to be more superficially located in the subcutis or even dermis (thus, it is an important tumor for dermatopathologists to be familiar). This case did occur in a child but was deeply located within the muscle. Despite the banal histologic appearance, nearly half of cases of LGFMS metastasize, usually to the lungs. Local recurrence may also be an issue. Recurrence and/or metastasis often occur many years after diagnosis (metastases have been reported almost 50 years later!).

Histologic Features
• Monotonous bland spindle cells (pleomorphism/nuclear atypia VERY RARE).
• Zones of alternating cellularity.
• Cells often arranged in a whorled pattern.
• Variably myxoid and fibrous/hyalinized background.
• Often prominent curved vessels.
• Collagen rosettes (very useful finding) may be seen (but are not featured in this case).
• Expresses MUC4 by immunohistochemistry in most cases (sensitive and specific).

References
CLINICAL PRESENTATION:
---Firm nontender nodule less than 2 cm in diameter
---Usually present within first year of life, one-third present at birth
---Fingers affected more frequently than toes, thumb and great toes spared
---Lesions may be multiple, affecting more than one digit on same hand/foot
---Local recurrence is common, seen in >60% cases.

KEY HISTOLOGIC FEATURES:
---Nodular aggregates of spindle cells, sometimes trapping adnexae
---Characteristic small round perinuclear inclusions in cytoplasm of fibroblasts
---Inclusions are eosinophilic and resemble erythrocytes
---Inclusions are red by Masson Trichrome, purple by PTAH and do not stain by PAS or Alcian blue.

DIFFERENTIAL DIAGNOSIS:
---Acquired digital fibrokeratoma
---Palmar fibromatosis
---Infantile myofibromatosis
---Angiofibroma.

COMMENTS:
The inclusion bodies in this lesion are diagnostic and have led to the alternate name “inclusion body fibromatosis.” Although there is an initial period of growth in these tumors, many tend to regress spontaneously if followed over time. There is a recent report of treating infantile digital fibroma successfully with Intralesional fluorouracil rather than with surgery. The lesions are thought to derive from myofibroblasts, and the inclusions are suspected to contain bundles of actin myofilaments. There may be a relationship to trauma in some cases, and histologically, similar lesions have been reported in adults following trauma in other sites.

REFERENCES:

CONTRIBUTED BY JENNIFER M. McNIFF, M.D.
CASE #100 - SLIDE #100

DIAGNOSIS: FIRBOUS HAMARTOMA OF INFANCY

CLINICAL FEATURES:
---Typically develops in first two years of life
---Small rapidly growing nodule of subcutis or deep dermis
---About one quarter may be present at birth
---More common boys than girls
---Axillae and inguinal regions often affected, uncommon on hands and feet
---Often several centimeters in diameter.

KEY HISTOLOGIC FEATURES:
---Three distinct components giving an “organoid appearance”
   ---Trabeculae of spindle cells and collagen
   ---Loose round areas with basophilic mucoid matrix
   ---Variable amounts of mature fat, often abundant.
---Fibrous spindle cell areas may stain for actin
---Loose myxoid areas stain for mucin.

DIFFERENTIAL DIAGNOSIS:
---Infantile fibromatosis (usually more deeply situated, lacks “organoid pattern”)
---Myofibromatosis (often multinodular, hemangiopericytoma-like pattern
---Calcifying aponeurotic fibroma (acral, older children)
---Giant cell fibroblastomas (more widespread myxoid areas, giant cells).

COMMENTS:
Fibrous hamartoma of infancy have a very characteristic pattern when all three tissue components are present. In more fibrous examples, this lesion may be confused with other fibrous tumors of childhood listed above. Distinction is important because this is a benign lesion, cured by local excision. There is a low but definite rate of recurrence, estimated to be about 16%, but recurrences are indolent and cured by excision. The nature of the cells, in particular the myxoid organoid areas, remains obscure.

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CONTRIBUTED BY JENNIFER M. McNIFF, M.D.
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