CUTANEOUS PSEUDONEOPLASTIC MESENCHYMAL LESIONS ("PSEUDOSARCOMAS")

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The images of disease that are seen by clinicians, radiologists, & pathologists are often quite different, and this fact pertains especially to “pseudotumors.”

- A palpable “lump” in the breast felt by a surgeon, but not corresponding to any mammographic abnormality or any proliferative lesion on fine needle aspiration [Probable anatomical variation]

- Observation of histologically atypical squamoid cell nests in a biopsy of the oral mucosa done for evaluation of a non-neoplastic process without radiographic abnormalities [Organ of Chievitz]
PSEUDONEOPLASTIC PROLIFERATIONS: Anatomic Distribution & Clinical Frequency

- Virtually all body sites are potential hosts to at least some pseudoneoplastic proliferations.
- Those locations where “pseudotumors” are seen with greatest frequency include the lung, urinary tract, skin, & gastrointestinal tract.
- The latter point undoubtedly reflects the relative impact of common etiologic causes of pseudoneoplastic proliferations on the organ sites in question.
LESIONS THAT ARE RELATED ETIOLOGICALLY TO TRAUMA & REPAIR
Variations on a Theme: Cutaneous Pseudosarcomatous Over-reactions to Injury

- Proliferating Scar
- Acroangiodermatitis
- Posttraumatic Spindle-Cell Proliferation
- Reaction to Monsel Solution
- Nodular Fasciitis

Pseudosarcomatous Polyp
Two unusual acquired polypoid skin lesions exhibited prominent histological atypia, but were biologically benign. Both patients were elderly females. The lesions clinically mimicked fibroepithelial polyp or nevus lipomatosus. Both had been present for about 20 years. One lesion was located on the back, the other on the posterior thigh. Each lesion exhibited dilated, hyalinized vessels in the dermis with focal fibrin deposits, myxoid stroma, and a population of bizarre, pleomorphic spindle to stellate cells, some of which were multinucleated. Occasional atypical mitoses were present. One lesion had abundant admixed fat.

Immunohistochemical staining was strongly positive only for vimentin. The lesions share features with degenerating angiofibroma and vaginal pseudosarcomatous polyp. As in those lesions, the atypia is most probably reactive and degenerative.
Pseudosarcomatous polyp
Pseudosarcomatous polyp
Nodular & proliferative fasciitis
Proliferating vascular scars & “acroangiodermatitis”
Postoperative-posttraumatic spindle cell nodules
Reactions to Monsel’s solution
NODULAR FASCIITIS (NF): Clinical Features

- Most often observed in areas of soft tissue that are prone to injury, in line with the premise that NF is an idiosyncratic proliferative reaction to trauma.

- As such, it is understandable that young individuals (< 25 yrs of age; male dominance) are preferentially affected by nodular fasciitis.

- RAPID growth of lesion over days to weeks... too rapid to be malignant!

- Also reported in salivary glands, mouth, nasal cavity, and scalp.
Nodular fasciitis
• Analogous to similar lesions seen in the genitourinary tract after recent surgery
• Clinically has the appearance of polypoid granulation tissue or pyogenic granuloma
• Microscopically, PSCN shows random proliferation of spindle cells with variable nuclear atypia and brisk mitotic activity
• Red cell extravasation & stromal edema— analogous to nodular fasciitis in deeper tissue
• May demonstrate aberrant immunoreactivity for keratin, leading to potential misdiagnosis as sarcomatoid carcinoma; also DES+/MSA+
Excision of junctional nevus 1 mo. prior

Postop spindle cell nodule
Aberrant keratin immunostaining

Postop spindle cell nodule

“Aberrant” keratin immunostaining
Reactions to Monsel Solution

- Monsel solution is ferric subsulphate solution, used as a styptic for minor surgical procedures
- In selected patients, it idiosyncratically incites a proliferative fibroblastic response that may simulate a neoplasm
Monsel reaction

Perl Stain
Reaction to Monsel Solution (RMS)

• Clues to the diagnosis of RMS:
  – Knowledge of recent surgical procedure (biopsy, excision) at the site of the current lesion
  – Presence of foreign-body-type giant cells
  – Large deposits of iron in the lesion, stainable with Perl’s method
Acroangiodermatitis: Clinical

- Also known as “dermatitis hemostatica,” & “pseudo-Kaposi’s sarcoma”
- Proliferative response to stasis dermatitis, seen in older individuals
- Clinically– and sometimes– histologically confused with KS
Acroangiodermatitis: Histologic

- Proliferating venule-sized vessels, admixed with extravasated erythrocytes, hemosiderin, and stromal spindle cells

- No "promontory sign, dilated lymphatics, plasma cell infiltrates, or eosinophilic globules, as seen in KS"
HISTOLOGICAL FEATURES OF MESENCHYMAL PROLIFERATIONS THAT TEND TO EXCLUDE A DIAGNOSIS OF A REPARATIVE LESION

- Marked nuclear hyperchromasia or pleomorphism in proliferating cells
- Spontaneous ulceration of overlying skin or mucosa by the lesion
- Pathologically-shaped mitoses
- Prominent spontaneous intralesional geographic necrosis
Reparative Spindle-Cell Proliferations in the Skin---
*Immunophenotype*

- *Vimentin (+)*
- *Muscle-specific actin (+)*
- *Alpha-isoform actin (+)*
  - *Desmin (+/-)*
- *S100 protein (-)*
  - *CD57 (-)*
- *Collagen type IV (+/-)*
  - *CD68/163 (+/-)*
- *Nuclear beta-catenin (-)*
MESENCHYMAL PROLIFERATIONS WITH IDENTICAL IMMUNOPHENOTYPES

• Nodular fasciitis & related lesions
  • “Myofibroblastoma”
• Leiomyoma & Leiomyosarcoma
  • Fibromatose (except for desmoid– nuclear beta-catenin)
Nuclear Beta-catenin in Desmoid Fibromatosis
LESIONS THAT ARE RELATED ETIOLOGICALLY TO INFECTION
BACILLARY ANGIOMATOSIS:  
**Clinical Features**

- Recognized in HIV+ patients in 1983
- Cutaneous red-violet nodules and papules
- Mistaken clinically for Kaposi’s sarcoma, but pathologically for epithelioid hemangioma
- Eminently treatable with antibiotics; causative organism is currently classified as a *Bartonella sp.* (formerly *Rochilamaeae*)
Bacillary angiomatosis
BACILLARY ANGIOMATOSIS: Histological Features

• Histologically-identical to verruga peruana of Bartonellosis (Carrion’s disease)
  • Simulates epithelioid (a.k.a. histiocytoid) hemangioma or low-grade angiosarcoma
  • Lobules of epithelioid endothelial cells forming variably-distinct intercellular lumina
    • Interspersed neutrophils common
  • Proliferating epithelioid endothelial cells often contain numerous Warthin-Starry+ bacilliform bacteria
• Fibroblastic & histiocytic proliferations are seen in the skin and viscera in association with infections by *M. leprae, M. avium-intracellulare*, and, rarely, other mycobacteria
• Cytoplasm of proliferating cells is frequently “foamy” or granular
• Lesions may be well-demarcated or pseudoinfiltrative
• Histochemical stains for AFB (e.g., Ziehl-Neelsen; Fite) are floridly positive
Mycobacterial pseudotumor

Histoid lepromatous leprosy

Mycobacterial pseudotumor
Mycobacterial pseudotumor

Fite Stain
IDIOPATHIC & IMMUNOLOGICAL PSEUDOSARCOMATOUS SKIN LESIONS
Isolated Necrobiotic Granulomas of the Skin

• Some examples of deep granuloma annulare & rheumatoid nodule demonstrate nuclear atypia & mitotic activity in constituent histiocytic cells, simulating the appearance of epithelioid sarcoma

• Central areas of necrosis/necrobiosis also possible in GA and RN

• Immunohistologic differences:
  
  * **Epithelioid sarcoma:**
    • $CK^+/EMA^+/CD45^-/CD34^+/-/CD163^-/-$

  * **Granulomas:**
    • $CK^-/EMA^-/CD45^+/CD34^-/CD163^+$
Granuloma annulare
Epithelioid sarcoma
Granuloma annulare: Colloidal iron stain

CD163 immunostain
Epithelioid sarcoma: Keratin immunostain

EMA immunostain
PSEUDONEOPLASTIC DISORDERS: Methods for Avoiding Misdiagnosis

1. Close collegial interaction, with detailed sharing of all available clinicopathologic information—physical & historical findings, radiographic data, and macroscopic & histopathologic observations

2. Special focus on diagnostic disagreements between specialists involved in the care of a given patient