Australasian Dermatopathology Society

Diagnostic pearls and pitfalls concerning dermal histiocytic proliferations

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What Is A Histiocyte?

- Bone marrow-derived skin resident cell delivered to its location as a monocyte
- Macrophages and giant cells
- Dermal dendritic cells
  - Langerhans cells
  - Resident dermal dendritic cells (Factor 13a+)
  - Plasmacytoid dendritic cells
Clinical Information

A 65 year old male with a yellow pink/brown dome-shaped nodule on the right upper shoulder.
Artur Zembowicz, M.D., Ph. D.

Diagnosis
Juvenile xanthogranuloma
**JXG**

**Clinical:**
- Children and neonates, rarely adults
- Any site (head and neck)
- Yellow-brown papule
- Single cutaneous nodule > subcutaneous > visceral
- Xanthogranulomatosis

**Microscopic:**
- Histiocytes (CD68, CD163-positive, S100, CD1a negative)
- Abundant glassy/foamy cytoplasm
- Touton-type GCs
- Eosinophils, neutrophils and lymphocytes
JXG in an Adult

DDX:
✓ Xanthoma (eruptive, other)
✓ Necrobiotic xanthogranuloma
✓ Lipidized (ankle type) dermatofibroma
✓ Giant cell tumor of tendon sheath
✓ Rosai-Dorfman disease
✓ Reticulohistiocytoma

Visceral:
Could be a different disease. Erdheim-Chester disease recently shown to have high percentage of BRAF V600 mutations

Multiple/eruptive:
Paraneoplastic syndrome?
Necrobiotic xanthogranuloma

- M=F
- 6th decade
- Face/periocular>trunk, extremities
- Mucosal lesions, splenomegaly
- ESR, Cryos,
- Leukopenia, hypocomplementemia, anemia

- Red-yellow nodules or plaques
- Ulceration
- Telangiectasias

- 80-90% paraneoplastic syndrome associated with IgG monoclonal gammopathy:
  - Plasma cell dyscrasia, MM, non-Hodgkin lymphoma
Necrobiotic xanthogranuloma
Lipidized dermatofibroma
• 53 y.o. male with poorly delineated brown/yellow nodule on the calf

Ankle-type dermatofibroma
Clinical Information

A 5 year-old boy with a rapidly growing skin nodule on the scalp
Case 16 Diagnosis:

Giant Monomorphous Juvenile Xanthogranuloma

Ziegler et al. 1995
Benign Cephalic Histiocytosis

- Infants <1 year
- Small reddish papules
- Eruptive
- Spontaneously regress

Courtesy Dr. Samuel Moschella, M.D. Lahey Clinic, Burlington, MA
66 year-old male with progressive pancytopenia, 6 month history of progressive generalized rash and recently discovered monoclonal (kappa IgG) gammonathy

Multiple/eruptive xanthogranulomas as a paraneoplastic phenomenon
Clinical Information

A 23 year old female with brownish dome shape papule on her neck; clinician favored a benign lesion.
Didactic Session IX:  
Saturday 11:30-12:00pm

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Diagnosis:  
Reticulohistiocytoma
Reticulohistiocytoma

**Clinical:**
- Young adults (wide range)
- Any site (head and neck)
- Red/yellow-brown papule
- Small (<1 cm papule)
- Face and digits not involved

**Microscopic:**
- Superficial dermal location
- Abundant glassy cytoplasm
- Touton-type GCs
- CD3-positive T cells
- Low mitotic count

**DDX:**
- Multicentric reticulohistiocytosis
- Generalized cutaneous reticulohistiocytosis
- Juvenile xanthogranuloma
- Rosai-Dorfman disease
- LYP/Anaplastic large cell lymphoma
- Epithelioid fibrous histiocytoma
- Histiocytic sarcoma

**Immunohistochemistry:**
- CD163
- CD68
- +/- Factor XIIIa, S100, MITF, CD31, CD45

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*Image Reference: Reticulohistiocytoma (Solitary Epithelioid Histiocytoma): A Clinicopathologic and Immunohistochemical Study of 44 Cases*

*Markku Miettinen, MD and John F. Fetsch, MD*
Multicentric reticulohistiocytosis

Courtesy Dr. Samuel Moschella, M.D. Lahey Clinic, Burlington, MA
A 43 year-old Asian-American female with 4 month history of brownish dermal nodule on the chest.
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Diagnosis
Rosai-Dorfman disease
Classic Rosai-Dorfman Disease/Sinus Histiocytosis with Massive Lymphadenopathy (1969)

- Lymph nodes
  - Cervical
- B symptoms
- Autoimmune anemia
- Extranodal (40%): Skin > Other

Pathogenesis:
- Cytokine-mediated activation:
  - autoimmune process
  - lymphoproliferative disorder
  - infection (viral)

- Young adults
- M > F
- AA, Caucasians > Asians
- Self-limited but 10% die due to critical organ involvement

Impox:
- S100+, CD68+, CD163+

Click [here](#) for reference
Cutaneous Rosai-Dorfman Disease/Sinus Histiocytosis with Massive Lymphadenopathy (1969)

- Adults
- F>M
- Caucasians, Asians>AA

- Hyperpigmented plaques
- Often multiple or multifocal
- Progression to systemic or lymph node disease rare

Courtesy Dr. Morayo Adisa, M.D, John H Stroger Hospital of Cook County, Chicago
Clinical Information

36 year-old white female with orbital mass
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Diagnosis
Crystal-storing histiocytosis
Crystal Storing Histiocytosis (Clinical)

- Adults (mean ca. 60 y.o.)
- F=M
- Asians, Caucasian
- 60% Localized: head and neck (eye and orbit)>lung and pleura
- 40% Generalized (bone marrow, liver, lymph nodes, spleen)

- Asymptomatic mass or swelling, sometimes slowly progressing
- 90%: MM, LPL, MGUS
- Rarely chronic inflammatory disease
- Can precede diagnosis

Rare variants:
- Clofazimine-induced
- Charcot-Leiden crystals
- Hereditary cystinosis
- Asymptomatic mass or swelling, sometimes slowly progressing
Crystal Storing Histiocytosis (Histology)

- Histiocytes
- Crystals
- Bland nuclei

- Varying degree of lymphocytes and plasma cells.

- Usually kappa restricted (impox staining variable)

- CD68, CD163+
- S100-
- CD1a-
Clinical Information

36 A 48 year-old Brazilian man with asymptomatic skin colored nodules on the face, ears, knees and elbows.
Didactic Session IX:
Saturday 11:30-12:00pm

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Diagnosis
Lepromatous leprosy
Leprosy: Histology

- Lepromatous
- Indeterminate
- Borderline
- Tuberculoid

Downgrading

High Bacterial load Low
Treated borderline lepromatous
Special stains in leprosy

- Fite
- GMS
- AFB +/-

Treatment effect
Clinical Information

A 34 y.o. F with eyelid swelling and radiographically-confirmed left orbital mass.
Diagnosis
Xanthelasma

Can be tumoral and involve deep soft tissue and orbit
Variants of Fibrous Histiocytoma
Case 15: A 34 year-old female with a skin-colored papule on the right forearm
Case 15 Diagnosis:

Epithelioid fibrous histiocytoma
Epithelioid fibrous histiocytoma
(Epithelioid cell histiocytoma)

- Extremities
- Pink or skin-colored papule
- Both sexes

? Variant of FH:
- No giant, atypical or xanthoma cells
- Papillary dermal location

- Well-circumscribed
- Papillary dermal location with epidermal collarette
- Epithelioid cells with abundant pink cytoplasm, binucleated cells, "spitzoid" appearance

Impox:
- >50%: EMA, Factor XIIIa, D2-40
- CD163 –
- CD68 +/-
Classic fibrous histiocytoma (dermatofibroma)

- Extremities
- Women
- Mid dermal

- Mid dermal
- Spindle cell or histiocytoid cells
- Storiform +/- fascicular arrangement
- Entrapped collagen at the periphery of the lesions
- Epidermal hyperplasia

Impox:
- No specific panel
- +/- Factor XIIIa, SMA, CD68
Morphological variants of FH

- Epithelioid
- Aneurysmal
- Cellular/Atypical
- Lipidized (ankle type)
Deep fibrous histiocytoma

- Extremities > H&N
- M>F
- SQ or visceral
- Well-circumscribed
- Resemble cellular df (+/- aneurysmal, atypical changes)
- Mitotically active
- 20% recur
- 5% metastasize
Recurrence in fibrous histiocytoma

- Cellular
- Aneurysmal
- Atypical
- Deep subcutaneous

20%
No histological differences between metastatic and benign fibrous histiocytoma

Metastatic FH

- 36 cases

- Metastatic FH

- No histological differences

- 5/7 abnormal CGH

- Increased risk:
  - Large size
  - Early, multiple recurrences

Metastasizing “Benign” Cutaneous Fibrous Histiocytoma
A Clinicopathologic Analysis of 16 Cases
Leona A. Doyle, MD and Christopher D.M. Fletcher, MD, FRCPath

Abstract: Cutaneous fibrous histiocytoma (FH) is considered a benign tumor; however, certain types of FH have been shown to have a tendency for local recurrence, and there are rare reported cases of metastasis. In this study, 16 cases of morphologically benign FH with local and distant metastases were identified in our files. Pathologic features of primary, recurrent, and metastatic tumors, as well as clinical outcome, were evaluated. Nine were male and 7 were female patients; mean age was 42 years (range, 3 to 68 years). Primary tumors arose on the leg in 5 patients, buttock in 1, trunk in 3, shoulder in 3, neck in 2, and finger in 1. The primary site in 1 case was unknown. Fifteen primary tumors available for review involved the dermis, 6 extended into the superficial subcutis. Tumor size ranged from 1 to 5 cm (median 3.2 cm). Histologically, primary tumors showed:

- Early, multiple recurrences

Malignant dermatofibroma:
clinical, immunohistochemical, and molecular analysis of seven cases

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Dermatofibroma (cutaneous fibrous histiocytoma) represents a common benign mesenchymal tumor, and numerous morphologic variants have been described. Some variants of dermatofibroma are characterized by an increased risk of local recurrences, and there are a few reported metastasizing cases. Unfortunately, an aggressive behavior cannot be predicted reliably by morphology at the moment, and we evaluated the value of array-comparative genomic hybridization (CGH) in this setting. Seven cases of clinically aggressive dermatofibromas were identified, and pathologic and molecular features were evaluated. The neoplasms occurred in four female and in three male patients (mean age was 32 years, range 2-65 years), and arose on the shoulder, buttock, temple, lateral neck, thigh, ankle, and chest. The size of the neoplasms ranged from 1 to 9 cm (mean: 3 cm). An infiltration of the subcutis was seen in five cases. Two neoplasms were completely excised, whereas an incomplete or marginal excision was reported in the remaining cases. Local recurrences were seen in six cases (time to the first recurrence ranged from 6 months to 8 years after diagnosis in a history. Histologically, the primary tumor aneurysmal dermatofibroma (one case) and pleomorphic sarcoma (one case) were described by our group in five cases. Interestingly, malignant dermatofibroma (one case) was seen in one case. Chromosomal aberrations by array-CGH tool in the recognition of cases of dermatofibroma (one case).

Keywords: dermatofibroma, clinical, immunohistochemical, molecular analysis
Malignant dermatofibroma: clinicopathological, immunohistochemical, and molecular analysis of seven cases

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Keywords: soft tissue tumor, metastasis, fibrous histiocytoma.