Cutaneous Myxoid Tumors

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Myxoid tumors
- Dermatopathologists rely on pattern recognition
- Myxoid tumors:
  - Accumulation of myxoid stroma
  - Diagnosis defining pattern subtle
  - Careful attention to detail allows diagnosis

43-year-old man presents with a nodule on the chest

Superficial angiomyxoma/ cutaneous myxoma
- Clinical features
  - More common in males
  - Trunk, lower extremities and head/neck
  - Multiple lesions associated with Carney's complex:
    - Lentigines, blue nevi, cutaneous and cardiac myxoma, endocrine overactivity, mutation in PRKAR1A
    - Benign with some local recurrences
Superficial angiomyxoma/cutaneous myxoma

Microscopic features
- Multinodular, lobular
- Prominent arborizing, thin-walled vessels
- Bland spindled cells
- Neutrophils commonly present
- Entrapped epithelial structures

Differential diagnosis
Focal dermal mucinosis
- Focal collection of dermal mucin in upper dermis
- Vasculature less prominent
- Stromal neutrophils absent
- Intercalates between collagen bundles
- Difficult

Case
41-year-old man presented with a firm subcutaneous mass on the posterior neck
Spindle Cell Lipoma

Clinical
- Middle aged and older men
- Head and neck, shoulders, upper back
- Painless mass
- Rarely multiple

Spindle Cell Lipoma

Classic Microscopic Features
- Short fascicles in 'school of fish' pattern
- Bland spindled cells
- Ropey collagen
- Myxoid stroma (common) and in some cases prominent
- Admixed mature fat cells
- CD34+
- Loss of 13q (Loss of RB1 expression)
- Some cases have no or only a small amount of fat
Spindle cell lipoma
• Always consider this diagnosis in lesions from the upper back, posterior head and neck of middle aged and older men
• Caveat: spindle cell lipomas in women have broader range of clinical locations
• Cutaneous solitary fibrous tumor very rare

Identification of Recurrent NAB2-STAT6 Gene Fusions in Solitary Fibrous Tumor by Integrative Sequencing

STATE rabbit monoclonal antibody is a robust diagnostic tool for the distinction of solitary fibrous tumour from its mistica

34/34 SFT STAT6 +
0/10 Spindle cell lipomas
A 56-year-old man presented with a recurrent spindle cell lipoma of the scalp

Diagnosis?
Myxoid Dermatofibrosarcoma Protuberans

- Rare case reports
- Two larger series

Myxoid DFSP

- **Clinical Features**
  - Middle aged patients (9 mo – 74 yrs)
  - Extremities, head and neck, groin, trunk
  - Clinical diagnosis:
    - Benign cyst
    - Lipoma
    - Pyogenic granuloma
    - Enlarged lymph node

- **Microscopic features**
  - Bland spindled to stellate cells
  - Random pattern
  - Uniform cellularity
  - No rosy collagen
  - Vasculature, variable thin-walled vessels
  - CD34+

Giant cell fibroblastoma

- Present in ~10% of cases
- Pseudovascular spaces lined by tumor cells
- Multinucleated tumor cells

Myxoid DFSP

- Conventional DFSP
  - Present in >60% of cases
  - May be focal
  - Adequate sampling

- **Differential Diagnosis**
  - **Myxoid DFSP**
    - Clinical overlap
    - Spindled to stellate cells
    - Random pattern
    - No rosy collagen
    - CD34+
    - t(17;22) rearrangement of PDGFRB
  - **Myxoid Spindle cell lipoma**
    - Clinical overlap
    - Spindled cells
    - Often fascicles
    - Ropy collagen
    - CD34+
    - Loss of 13q
DDx: Myxoid Liposarcoma

**Clinical features**
- Middle aged adults
- Deep soft tissue mass (almost never occurs above the fascia as a primary tumor)

**Microscopic features**
- Uniform round to spindled cells
- Lipoblasts
- Myxoid pools
- Delicate branching vasculature

Myxoid Liposarcoma Vs. Myxoid DFSP

<table>
<thead>
<tr>
<th>Myxoid Liposarcoma</th>
<th>Myxoid DFSP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deep</td>
<td>Superficial</td>
</tr>
<tr>
<td>Plexiform vasculature</td>
<td>Variable vasculature</td>
</tr>
<tr>
<td>Round to spindled cells</td>
<td>Spindled to stellate cells</td>
</tr>
<tr>
<td>Lipoblasts</td>
<td>No lipoblasts</td>
</tr>
<tr>
<td>t(12;16)</td>
<td>t(17;22)</td>
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67-year-old man with a calf mass. A punch biopsy was performed.
Diagnosis?

Myxofibrosarcoma

**Clinical**
- Superficial sarcoma
- Usually in older patients
- Thigh most common location
- Rare in head and neck area

**Microscopic features**
- Infiltrative: often extend along subcutaneous septae
- Myxoid tumors
- Relatively hypocellular
- Hyperchromatic spindled cells with mild to moderate atypia
- Curvilinear vasculature
- Tumor cells often aggregate around vessels
- Pseudolipoblasts
- Mitotic rate often low
Myxofibrosarcoma

- Some cases are intermediate or high grade sarcomas
- Recurrent cases often undergo histologic progression
- Higher grade tumors show different histologic features from classic (grade 1) myxofibrosarcoma

Myxofibrosarcoma grade 2,3

- More cellular
- More atypia
- Fibrous areas
- More solid areas of tumor proliferation
- More mitotic activity
- Necrosis

Immunophenotype: no consistent pattern
Cytogenetics: no consistent abnormality

Behavior:
- Frequent recurrence (20-70%)
- Recurrences frequently undergo histologic progression
- Metastatic risk low for grade 1 tumors (<10%)
- Metastatic risk increases in higher grade tumors (20-40%)

Epithelioid Myxofibrosarcoma

- Clinical presentation similar to conventional myxofibrosarcoma
- Histologic features
  - Multinodular tumor
  - Myxoid stroma
  - Curvilinear blood vessels
  - Epithelioid cells with eosinophilic cytoplasm
Epithelioid myxofibrosarcoma
- More aggressive than conventional myxofibrosarcoma
- Recurrence rate >70%
- Metastatic rate 50%
  - Visceral and lymph nodes

Myxofibrosarcoma vs. Myxoid DFSP
- Myxofibrosarcoma
  - Curvilinear vessels
  - More nuclear atypia
  - Less uniform cellularity
  - Pseudolipoblasts
  - No characteristic cytogenetics
- Myxoid DFSP
  - Delicate vessels
  - Bland nuclei (GCF multinucleated cells)
  - Uniform cellularity
  - t(17;22)

DDx: Myxoinflammatory fibroblastic sarcoma
- Clinical features
  - Middle-aged adults
  - Most common on distal extremities
  - Fingers and hands most common location
  - Clinically can mimic ganglion cyst or other benign acral tumors
- Microscopic features
  - Multinodular, poorly-circumscribed mass
  - Myxoid and hyalinized lobules admixed with dense inflammatory aggregates
  - Amount of components varies from case to case
  - Scattered giant bizarre pleomorphic cells with prominent nuclei that resemble Reed-Sternberg cells or virally infected cells
  - Low mitotic rate (<2/50 HPFs)
Differential diagnosis

<table>
<thead>
<tr>
<th>MIFS</th>
<th>Myofibrosarcoma</th>
</tr>
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<tbody>
<tr>
<td>Acral</td>
<td>Non-acral</td>
</tr>
<tr>
<td>Inflammation prominent</td>
<td>No significant inflammation</td>
</tr>
<tr>
<td>Reed-Sternberg like cells</td>
<td>Reed-Sternberg like cells absent</td>
</tr>
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Case

A 4-year-old girl presented with a flank mass
Immunostains
- S100 protein negative
- CD34 negative
- EMA negative
- Cytokeratin negative

Low Grade Fibromyxoid Sarcoma
- 1986: First described by Evans
  - 2 cases of deceptively bland sarcomas with paradoxically aggressive behavior
- 1993: 12 additional cases
  - Similarly bland features
  - Aggressive behavior:
    - Metastasis in 7/12
    - 4 DOD
    - 3 AWD

Hyalinizing Spindle Cell Tumor with Giant Collagen Rosettes
- Described in 1997 (Lane et al, AJSP 1997)
- Clinical and histologic similarities to LGFMS
- A variant of LGFMS
- Relationship with LGFMS supported by presence of focal rosettes and small collagen rosettes in cases of LGFMS (Folpe et al, AJSP 2000)
Cytogenetics
- Both HSTGR and LGFMS share common cytogenetic abnormality
  - t(7;16)(q34;p11)
  - Fusion of FUS/CREB3L2
  - FUS: RNA-binding protein
  - CREB3L2: member of OASIS B-ZIP family of transcription factors

Clinical Features
- Primarily affects young to middle-aged adults
  - 10-20% of cases present in children
- Predominantly present as deep soft tissue mass
  - 20% present as superficial tumors of subcutis or dermis (Billings, et al AJSP 2005)
  - Superficial tumors relatively common in children (~40% of superficial tumors)

Histologic features
- Immunohistochemistry/FISH
  - More a tool of exclusion
  - Vimentin +
  - Actins +/-
  - EMA +/- (30%)
  - S100 +/-
  - CD34 – (rare focal positivity)
  - Desmin –
  - Exception: MUC-4 positive >90%

LGFMS vs. Perineurioma
- LGFMS
  - Swirling growth pattern
  - Fibrous and myxoid (often abrupt)
  - Slight atypia
  - EMA -90%
  - MUC4+ (>95%)
  - t(7;16)(FUS-CREB3)
- Perineurioma
  - Swirling growth pattern
  - Fibrous and myxoid (not usually abrupt)
  - No atypia
  - EMA 100%
  - MUC4+ (0%)
  - t(7;16) absent

Low-Grade Fibromyxoid Sarcoma: A Clinicopathologic Study of 33 Cases With Long-Term Follow-Up
- 21 patients recurrences after intervals up to 15 years (median 3.5 yrs)
- 15 with metastasis after periods up to 45 years (median 5 yrs)
- Still aggressive
- Patients need lifelong follow-up
Perineurioma

LGFMS vs. Myxofibrosarcoma

**LGFMS**
- Whorled to fascicular
- Pushing border
- Myxoid/collagenous
- Less atypia
- Rosettes sometimes
- MUC4+
- t(7;16)

**Myxofibrosarcoma**
- Random to fascicular
- Infiltrative
- Purely myxoid (grade 1)
- More atypia
- Rosettes absent
- MUC4-
- No consistent cytogenetics

Ossifying fibromyxoid tumor (OFMT)

**Clinical features**
- Adult patients, M>F
- Extremities
- Arises in subcutis or deep soft tissue

**Microscopic features**
- Circumscribed
- Peripheral shell of bone in up to 80% of cases
- Uniform round to spindled cells
- Arranged in cords, nests or sheets
- Fibrous to myxoid stroma
- May have dense collagen that transitions to osteoid

**OFMT**

**Microscopic features**
- Vascular often prominent
- My have hyalinized blood vessels

**Immunophenotype**
- S100 protein positive in 70-80% of cases
- Focal desmin positivity in ~20%
- Usually negative for cytokeratins
- Sometimes focal MUC4+

**Cytogenetics**
- Rearrangements of PHF1 on chromosome 6 in ~60-80%
Malignant OFMT

- High nuclear grade or high cellularity
- Mitotic rate > 2/50 HPFs
- If only one atypical feature, classify lesion as atypical OFMT
- Typical and atypical OFMT
  - Indolent; metastatic rate <6%
- Malignant OFMT
  - Often have areas of conventional OFMT
  - Metastatic rate ~60%

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Differential diagnosis

Myoepithelioma/myoepithelial carcinoma
**Differential diagnosis**

**OFMT**
- Encapsulated, often with bone
- Cells more uniformly arranged
- Immuno: S100+ (70-80%), occasionally positive for actin, p63, SMA; negative for keratins and SOX-10

**Myoepithelioma/myoepithelial carcinoma**
- Non-encapsulated
- Less uniform pattern of cells
- Immuno variably+: S100, CK, EMA, calponin, SMA, SOX-10

**OFMT vs LGFMS**
- OFMT has capsule and often shell of bone
- Tumor cells often more round to oval
- Cord and nested pattern
- Evenly fibrous and myxoid stroma
- S100+, MUC4- (rarely focal+)
- PHF1 rearrangement

- LGFMS circumscribed but not capsule
- Tumor cells spindled, not round
- Fascicles and swirling pattern
- Abrupt changes from fibrous to myxoid stroma
- MUC4+, S100-
- FUS rearrangement
Epithelioid schwannoma
- Histologic variant of schwannoma
- Largely epithelioid morphology
- S100 protein and SOX10 positive

OFMT vs Epithelioid Schwannoma
- OFMT
  - Shell of bone
  - Capsule
  - More evenly cellular
  - Hyalinized vessels less common
  - S100+
  - SOX10-
- Epithelioid Schwannoma
  - No bone
  - Capsule
  - Antoni A and B
  - Hyalinized vessels common
  - S100+
  - SOX10+