Soft Tissue Cytopathology: A Practical Approach
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What does the clinician want to know?
• Is the lesion of mesenchymal origin or not?
• Is it benign or malignant?
• If it is malignant:
  – Is it a small round cell tumor & if so what type?
  – Is this soft tissue neoplasm of low or high-grade?

Practical diagnostic categories used in soft tissue cytopathology
Practical approach to interpret FNA of soft tissue lesions involves:
1. Predominant cell type present
2. Background pattern recognition

<table>
<thead>
<tr>
<th>Cell Type</th>
<th>Stroma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipomatus</td>
<td>Myxoid</td>
</tr>
<tr>
<td>Spindle cells</td>
<td>Other</td>
</tr>
<tr>
<td>Giant cells</td>
<td></td>
</tr>
<tr>
<td>Round cells</td>
<td></td>
</tr>
<tr>
<td>Epithelioid</td>
<td></td>
</tr>
<tr>
<td>Pleomorphic</td>
<td></td>
</tr>
</tbody>
</table>

Lipomatous
Myxoid sarcoma
Epithelioid
Clear cell sarcoma
CASE #1

- 45yr Man
- Thigh mass (fatty)
- CNB with TP (DQ stain)

DQ Mag 20x

ALT - Floret cells
Adipocytic Lesions

- Lipoma - most common soft tissue neoplasm
- Liposarcoma - most common adult soft tissue sarcoma
- Benign features:
  - Large, univacuolated adipocytes of uniform size
  - Small, bland nuclei without atypia
- Malignant features:
  - Lipoblasts, pleomorphic giant cells or round cells
  - Vascular myxoid stroma
- Pitfalls: Lipophages & pseudo-lipoblasts
- Fat easily destroyed (oil globules) & lost with preparation

Lipoma & Variants

- Angiolipoma (prominent vessels)
- Myolipoma (smooth muscle)
- Angiomyolipoma (vessels + smooth muscle)
- Myelolipoma (hematopoietic elements)
- Chondroid lipoma (chondromyxoid matrix)
- Spindle cell lipoma (CD34+ spindle cells)
- Pleomorphic lipoma
- Intramuscular lipoma

Lipoma
Angiolipoma

Myelolipoma

Lipoblasts

- Typically multivacuolated
- Can be monovacuolated
- Hyperchromatic nuclei
- Irregular (scalloped) nuclei
- Nucleoli not typically seen
Myxoid Liposarcoma
Lipoblasts are often present

Univacuolated
Multivacuolated

Myxoid Liposarcoma
Characteristic branching (crow's feet) vessels
Myxoid/Round Cell Liposarcoma
Fleshy areas (arrows) indicate progression to high-grade round cell sarcoma

Myxoid/Round Cell Liposarcoma
Progression from myxoid to round cell liposarcoma

Round cell liposarcoma
**CASE #2**

- 88yr Female
- Thigh mass
- CNB with TP (DQ stain)

**Spindle Cell Lesions**

<table>
<thead>
<tr>
<th>Benign Entities</th>
<th>Nodular fascitis (pseudosarcomas), schwannoma, neurofibroma, spindle cell lipoma/fibrolipoma, leiomyoma, fibromatosis, granulomatous inflammation, extra-dural meningioma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignant tumors</td>
<td>Low-grade fibromyxoid sarcoma, DFSP, fibrosarcoma, leiomyosarcoma, synovial sarcoma, malignant peripheral nerve sheath tumors (MPNST), Kaposi sarcoma, some angiosarcomas, some liposarcomas, gastrointestinal stromal tumors (GIST), metastatic spindle cell carcinoma, spindle cell melanoma</td>
</tr>
</tbody>
</table>

**Hemangiopericytoma Pattern**

- Solitary fibrous tumor
- Synovial sarcoma
- Myopericytoma
- Mesenchymal chondrosarcoma
- Malignant peripheral nerve sheath tumor

Branching dilated (staghorn) blood vessels
SOLITARY FIBROUS TUMOR

• Previously these were called "hemangiopericytoma"
• Pleural & occurs at other sites
• Cellular to fibrous tumors
• Hyper- and hypocellular areas
• "Patternless" tumors
• Dilated branching vessels
• Immunohistochemistry:
  – STAT6+, CD34+ (90%), CD99+ (70%), EMA+ (30%), bcl-2+ (30%), and actin+ (20%)

MYOFIBROBLASTIC PSEUDOSARCOMAS

• Nodular fascitis and variants:
  – Proliferative fascitis & myositis
  – Intravascular fascitis
  – Ischemic fascitis ("atypical decubitis fibroplasia")
  – Fasciitis ossificans
• Pseudosarcomatous myofibroblastic proliferation:
  – e.g. Post-operative spindle cell nodule
Nodular fasciitis

Proliferative fasciitis

Synovial sarcoma
NON-MESENCHYMAL SPINDLE CELL NEOPLASMS

- Spindle cell carcinoma
- Spindle cell/desmoplastic melanoma
- Spindle cell/desmoplastic mesothelioma
- Others (metastatic gliosarcoma, extracranial meningioma, myeloid sarcoma, interdigitating dendritic cell sarcoma, mast cell neoplasms)

UNCLASSIFIED SPINDLE CELL SARCOMA

- 5-10% of spindle cell sarcomas remain unclassifiable
- Avoid calling these fibrosarcoma
- This typically includes:
  - MPNST
  - Post-radiation sarcomas
- Myogenic differentiation implies a worse prognosis

CASE #3

- 22yr Male
- Knee tumor
- CNB with TP
Giant Cell Lesions

- Predominance of multinucleated giant cells
- Giant cells can be reactive or tumorous
  - Reactive: Multiple, uniform, bland nuclei (e.g. foreign-body giant cells)
  - Malignant: Hyperchromatic atypical nuclei (pleomorphic tumor cells)
- Giant-rich malignancies contain reactive osteoclastic cells
- Megakaryocytes can be seen in myelolipoma & extramedullary hematopoietic tumors
Giant Cell Lesions

<table>
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<th>Benign</th>
<th>Malignant</th>
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<tr>
<td>Localized tenosynovial</td>
<td>Soft tissue giant cell tumor of low malignant potential, pleomorphic sarcomas (undifferentiated pleomorphic sarcoma or MFH), pleomorphic liposarcoma, dedifferentiated liposarcoma, pleomorphic leiomyosarcoma, giant cell-rich osteosarcoma, giant cell tumor of bone, metastatic giant cell carcinoma, melanoma, anaplastic large cell lymphoma, Hodgkin lymphoma (RS cells)</td>
</tr>
<tr>
<td>giant cell tumor (giant cell tumor of tendon sheath or nodular tenosynovitis), diffuse type tenosynovial giant cell tumor (pigmented villonodular synovitis), myositis ossificans, nodular fasciitis</td>
<td></td>
</tr>
</tbody>
</table>

Gout

CASE #4
- 59yr Female
- Thigh mass
- CNB with TP (DQ stain)

LIVE VIEW
Small Round Cell Tumors

| Mesenchymal | Neuroblastoma, Ewing sarcoma/PNET, desmoplastic small round cell tumor (DSRCT), rhabdomyosarcoma, poorly differentiated synovial sarcoma, extraskeletal mesenchymal chondrosarcoma, small cell osteosarcoma |
| Non-Mesenchymal | Small cell carcinoma, basaloid squamous cell carcinoma, Merkel cell carcinoma, lymphoma/leukemia, germ cell tumor, melanoma with small cell morphology, hepatoblastoma, Wilms tumor, retinoblastoma |

Ewing sarcoma

- Cellular isolated cells
- 2-3x small lymphocytes
- Light (viable) cells
- Dark (dying) cells
- Nuclear molding
- Tigroid background
- Pseudorosettes
CASE #5

- 38yr Man
- Mid arm mass
- FNA
Arm mass (DCQ)

Cell block. Granular cell tumor

Cell block 5100x
Epithelioid Cell Lesions

- Rhabdomyoma
- Granular cell tumor
- Epithelioid sarcoma
- Epithelioid variant of leiomyosarcoma
- Malignant peripheral nerve sheath tumor
- Epithelioid variant of angiosarcoma
- Epithelioid hemangiendothelioma
- Malignant extrarenal rhabdoid tumor
- Pleomorphic rhabdomyosarcoma
- Clear cell sarcoma of soft tissue
- Alveolar soft part sarcoma
- Metastases (melanoma, carcinoma, mesothelioma)
- Hematolymphoid tumors (lymphoma, plasmacytoma, myeloid sarcoma)

Epithelioid sarcoma

Keratin+ & CD34+

Pleomorphic Lesions

- There are several pleomorphic sarcomas (rhabdomyosarcoma, leiomyosarcoma, liposarcoma, chondrosarcoma)
- Pleomorphic undifferentiated sarcoma (PLUS)
  - High-grade (pleomorphic MFH)
  - Most common sarcoma >40 years
  - Hypercellular smears with necrosis
  - Marked nuclear atypia (anaplasia)
  - Giant cells (bizarre cells)
  - Numerous mitoses including atypical forms
CASE #7

- 50yr Man
- Knee cyst
- FNA
Differential Diagnosis of Myxoid Lesions

<table>
<thead>
<tr>
<th>Hypocellular Benign Entities</th>
<th>Myxoma, seroma, ganglion cyst, nodular fasciitis</th>
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<td>Cellular Benign Entities</td>
<td>Nodular fasciitis, cellular myxoma, schwannoma, neurofibroma, benign mesenchymal tumors with myxoid change (fibrolipoma etc)</td>
</tr>
<tr>
<td>Malignant Entities</td>
<td>Myxofibrosarcoma, myxoid liposarcoma, extraskeletal myxoid chondrosarcoma, low-grade fibromyxoid sarcoma, sarcoma with myxoid features, chordoma and parachordoma, myoepithelial tumors of soft tissue, metastatic mucinous carcinomas</td>
</tr>
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Myxoid Stroma

Gross Pathology (Myxoma)

Histopathology (Myxoid Liposarcoma)

Myxoid Tumors with Pleomorphism

- Myxofibrosarcoma
- Myoepithelial carcinoma
- Myxoinflammatory fibroblastic sarcoma
Myxofibrosarcoma (low grade)

Myxofibrosarcoma (high grade)

Examples of Myxoid Variants

Dermatofibrosarcoma protuberans  Solitary fibrous tumor