Soft Tissue Tumors with Bone and Cartilage Differentiation

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Introduction: Definitions

- “Skeletal” matrix in soft tissue tumors
  - Bone and osteoid
  - Cartilage
  - Other calcium deposits

Osteoid = Matrix synthesized by osteoblasts, mostly type 1 collagen
Bone = Osteoid + calcium hydroxyapatite crystals
Cartilage = Matrix synthesized by chondrocytes, mostly water, proteoglycan, type 2 collagen
Calcifications = calcium salts
  - Crystals: Urate (gout), Pyrophosphate (pseudogout), Hydroxyapatite (calcific tendonitis)
  - Amorphous: Usually CaPO₄ (dystrophic, metastatic, tumoral calcinosis)

Disclosures

I have nothing to disclose.
Introduction: imaging
- For most primary bone tumors, plain films are adequate
- If soft tissue involvement is present, cross-sectional imaging (CT and MRI) become more useful
  - To define source of the tumor
  - To narrow differential diagnosis

Introduction: pearls
- Tumors with cells located centrally and matrix at the periphery - usually benign
- Tumors that leave matrix behind as a front of cells expand into surrounding soft tissue - usually malignant
- Primary conventional chondrosarcoma of soft tissue is “nonexistent”

Skeletal matrix is incidental
- “Dedifferentiated” sarcomas
  - Liposarcoma
  - Malignant peripheral nerve sheath tumor
  - Leiomyosarcoma
- Melanoma
- Soft tissue myoepithelioma (mixed tumor)

Skeletal matrix is definitional
- Bone
  - Myositis ossificans
  - Soft tissue osteosarcoma
  - Ossifying fibromyxoid tumor
- Cartilage
- Soft tissue ABC
**Myositis ossificans**

- **Clinical**
  - Young adults but wide age range
  - Trauma in ~50%, repetitive microtrauma
  - Thigh, arm, digits, mesentery
  - Painful, relatively rapid onset (< 3 months)

- **Radiology**
  - Soft tissue mass → Peripheral mineralization

- **Genetics**
  - USP6 rearrangements (also in nodular fascitis, aneurysmal bone cyst)

- **Prognosis**
  - Simple excision curative

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**Myositis ossificans**

- **Histology:**
  - Zonation: Fasciitis (center) → osteoid → mature bone (periphery)

- **Immunohistochemistry:** SMA in spindle cells

- **Differential diagnosis**
  - Soft tissue osteosarcoma
  - Nodular fasciitis
  - Bizarre parosteal osteochondromatous proliferation (digits)
Myositis ossificans: fasciitis-like center

Myositis ossificans: osteoid

Myositis ossificans: maturing bone
Myositis ossificans: maturing woven bone

Myositis ossificans: mature lamellar bone

Myositis ossificans: mature lamellar bone

Myositis ossificans: aneurysmal bone cyst (ABC)-like area
Myositis ossificans: fracture-callus like area

Clinical
- Peak in 5th decade
- Painful, relatively rapid onset (< 3 months)
- Deep thigh, limb girdles
- Radiation in ~10%

Radiology
- Soft tissue mass → Central or diffuse mineralization

Genetics
- Highly complex, no reproducible changes

Prognosis
- 5 year survival ~25%

Soft tissue osteosarcoma

Histology:
- Diffuse pleomorphism
- Lacelike osteoid between individual cells or clusters
- Atypical mitoses, necrosis

Immunohistochemistry: SATB2, S100 if cartilage present

Differential diagnosis
- Primary bone osteosarcoma with soft tissue extension
- Myositis ossificans
- Malignant ossifying fibromyxoid tumor

Axial T1
Soft tissue osteosarcoma: central bone, peripheral cellularity

Soft tissue osteosarcoma: bone + atypical cells

Soft tissue osteosarcoma: Lace-like osteoid/bone
Soft tissue osteosarcoma: osteoclasts

Soft tissue osteosarcoma: cartilage

Soft tissue osteosarcoma: is this osteoid?

Soft tissue osteosarcoma: SATB2
**SATB2**
- Special AT-rich sequence binding protein 2, 2q33
- Regulates osteoblast differentiation, skeletal development, brain development, cleft palate
- Expressed by osteoblasts and colonic epithelial cells
- *Sensitivity* 89% for extraskeletal osteosarcoma
- *Specificity*:
  - 91% in soft tissue (vs. UPS)
  - 45-50% in bone (vs. UPS and fibrosarcoma)

**Myositis ossificans or osteosarcoma?**

<table>
<thead>
<tr>
<th></th>
<th>Myositis ossificans</th>
<th>Extraskeletal Osteosarcoma</th>
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<tr>
<td>Clinical</td>
<td>Young adults, trauma</td>
<td>Older adults, radiation</td>
</tr>
<tr>
<td>Size</td>
<td>&lt;6 cm</td>
<td>&gt;10 cm</td>
</tr>
<tr>
<td>Bone</td>
<td>Periphery</td>
<td>Central</td>
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<tr>
<td>Atypia</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Mitotic activity</td>
<td>+</td>
<td>+ (Atypical)</td>
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<tr>
<td>Necrosis</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Genetics</td>
<td>PHF1 rearrangement (benign)</td>
<td>del22 (malignant)</td>
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**Ossifying fibromyxoid tumor**
- *Clinical*
  - Median 6th decade
  - Thigh, head/neck, trunk, attached to tendon
  - Painless, slow growing
- *Radiology*
  - Soft tissue mass → incomplete rim of bone
- *Genetics*
  - *PHF1* rearrangement (benign)
  - del22 (malignant)
- *Prognosis*
  - Late recurrence (decades)
  - Malignant OFMT → metastasis
Ossifying fibromyxoid tumor

- **Histology:**
  - Thin, incomplete shell of bone (70% of cases)
  - Lobulated, myxoid
  - Ovoid cells, evenly distributed or in cords
  - Mitoses ≤ 2 / 50 hpf

- **Immunohistochemistry:**
  - S100 (70%), INI1 loss (mosaic)
  - SATB2 negative

- **Differential diagnosis**
  - Malignant OFMT: Hypercellular, more mitoses, central bone, pleomorphic
  - Soft tissue osteosarcoma
  - Myositis ossificans
  - Epithelioid schwannoma
OFMT: Cords of cells, myxoid stroma

Ossifying fibromyxoid tumor: round cells, vague cords

Ossifying fibromyxoid tumor: Spindled cells, myxoid stroma

Malignant OFMT: central bone

Malignant OFMT: Diffuse atypia, mitoses
Bone or cartilage is definitional

Soft tissue chondroma

- **Clinical:**
  - 3rd-5th decade
  - Fingers, hands, feet
  - Pain, stiffness, decreased ROM
- **Radiology**
  - Plain film shows cloudy or ring calcifications
  - Can erode cortex
  - MRI, lobulated, bright on T2
- **Prognosis:**
  - Local excision usually curative
  - Recurrence <5%
  - "No" malignant transformation (<1%)

Synovial chondromatosis:

distinguishing features from soft tissue chondroma

- **Clinical:**
  - Large joints especially knee, shoulder
- **Radiology**
  - Plain film shows multiple cloudy or ring calcifications
- **Prognosis:**
  - Recurrence more common (20%)
  - Rare, malignant transformation (<2%)

Soft tissue chondroma

Photo courtesy Dr. Kenneth Yim, SCVMC
Synovial chondromatosis

- **Histology:**
  - Nodule of cartilage
  - Evenly spaced chondrocytes
  - Calcifications, endochondral ossification
  - Nuclear enlargement, hyperchromasia, binucleation common
  - No mitoses

- **Differential diagnosis**
  - Synovial chondromatosis
  - Secondary chondrosarcoma
  - Chondro-osseous loose body
  - Chondrosarcoma arising from adjacent bone

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Soft tissue chondroma

- **Histology:**
  - Nodules of cartilage
  - Rimmed by synovium
  - Chondrocyte clustering

- **Differential diagnosis**
  - Soft tissue chondroma

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**Synovial chondromatosis:**

distinguishing features from soft tissue chondroma

- **Histology:**
  - Nodules of cartilage
  - Rimmed by synovium
  - Chondrocyte clustering

- **Differential diagnosis**
  - Soft tissue chondroma
Soft tissue chondroma

Soft tissue chondroma: calcified matrix, degenerative atypia
Synovial chondromatosis: multiple nodules, eroding articular cartilage

Synovial chondromatosis (synovial capsule)

Synovial chondromatosis: Chondrocyte clustering

Chondro-osseous loose body

**Synonym:** Joint mouse

**Clinical**
- Middle aged
- Knee, hip joint
- Osteoarthritis, osteochondral fracture, osteonecrosis

**Radiology**
- Ring or cloudy calcification on plain film
- Osteoarthritis or other underlying disease visible

**Prognosis:**
- Non-neoplastic
- Excision curative
Chondro-osseous loose body

**Histology:**
- Concentric layering, peripheral cartilage
- Residual features of articular cartilage: tidemark
- Central bone, osteonecrosis
- Chondrocytes arranged randomly, clusters or single file rows

**Differential diagnosis**
- Soft tissue chondroma, synovial chondromatosis
- Osteochondroma

Chondro-osseous loose body:
- Hyaline and fibrocartilage, irregular calcifications

Chondro-osseous loose body:
- Transition from articular cartilage to necrotic bone
Mesenchymal chondrosarcoma

- **Clinical:**
  - 2nd-3rd decade
  - 1/3rd in somatic soft tissue, rarely meninges
- **Radiology**
  - Circumscribed
  - Variable amount of stippled calcifications
- **Genetics**
  - HEY1-NCAO2 fusion
- **Prognosis:**
  - Protracted, late metastasis (decades)

Mesenchymal chondrosarcoma

- **Histology:**
  - Biphasic: abrupt or gradual
    - Primitive small round blue cell tumor, HPC-like vessels
    - Hyaline cartilage
- **Immunophenotype**
  - Small round cells: CD99, SOX9
  - Cartilage: S100
- **Differential diagnosis**
  - Ewing sarcoma
  - Dedifferentiated chondrosarcoma
  - Chondroblastic osteosarcoma
Mesenchymal chondrosarcoma: biphasic

Small round blue cells

Hyaline cartilage

WHO2013: tumor of uncertain histotype

Clinical
- 6th decade
- Deep soft tissue of extremities, trunk, abdomen

Radiology
- Nonspecific, not calcified

Genetics
- t(9;22) EWSR1-NR4A3 fusion
- Other NR4A3 fusions

Prognosis:
- Long survival, late metastasis (decades) but relentless

Extrasketal myxoid “chondrosarcoma”
Extraskeletal myxoid "chondrosarcoma"

**Histology:**
- No hyaline cartilage
- Myxoid lobules divided by fibrous septae
- Cords and chains of plump spindled to round cells
- Mitotic activity <2 /10

**Immunophenotype**
- Synaptophysin

**Differential diagnosis**
- Soft tissue mixed tumor (myoepithelioma)
- Soft tissue chondroma
- Chordoma with soft tissue extension
Take-home messages

- In soft tissue osteosarcoma, bone is central and malignant cells are peripheral.
- In benign bone-forming lesions, bone is usually peripheral and cells are central.
- Primary hyaline chondrosarcoma of soft tissue is nonexistent.
  - Soft tissue extension from bone.
  - Transformation of a benign soft tissue cartilage tumor.
- Extraskeletal myxoid "chondrosarcoma" is a translocation sarcoma of uncertain histotype.