Pediatric Dermatology: Tumors of Fat, Muscle and Bone

Broward Health Medical Center

10/18/15
Benign Tumors of Fat:
Lipoma

Introduction:
- The most common benign tumors of fat are lipomas. Lipomas are composed of mature lipocytes. They are among the most common neoplasms and represent the most common mesenchymal neoplasms.

Clinical Evaluation:
- Asymptomatic, soft, subcutaneous nodule arising from any site

Associations:
- Bannayan-Riley-Ruvacalba, Gardner’s syndrome, Proteus syndrome, MEN1, Familial multiple lipomatosis, Dercum’s dz, Madelung’s dz, CLOVE syndrome
Lipoma

Pathology:
- Proliferation of normal-appearing adipose in subcutaneous fat, (+) adipophyllin, (+) oil-red-O (must be frozen sections)

Differential Diagnosis:
- Epidermoid cyst
- Dermoid cyst
- Angiolipoma
- Metastatic malignancy
- Abscess
- Leiomyoma

Treatment
- Excision
Angiolipoma

Epidemiology:
- Young adults in their late teens or early twenties. About 5% of cases are familial.

Clinical Evaluation:
- Soft subcutaneous nodules, usually less than 2cm in diameter, may be painful. Tumors are found on the forearms (2/3 of pts), less commonly the trunk and upper arms. An estimated two-thirds of patients have multiple tumors.

Pathology:
- Mature adipose tissue is admixed with a variable number of small vessels occ w/ thrombi.
- No malignant transformation noted.

Differential Diagnosis:
- Angiomyolipoma.
Spindle cell/pleomorphic lipoma

Introduction:
- Represent a group of histologically distinct tumors composed of mature fat cells, a population of spindle cells, and strands of dense collagen. Pleomorphic lipomas also contain an admixture of bizarre, often multinucleated cells (“floret-like cells”)

Epidemiology:
- Majority found in middle-aged to older men

Clinical Evaluation:
- Usually a solitary, slow growing, mobile and painless subcutaneous nodule without epidermal change on posterior neck

Treatment:
- Surgical excision is curative for this benign tumor. It is rare for spindle cell lipomas to recur after complete excision
Spindle cell/pleomorphic lipoma

Pathology:

- **Spindle cell**: (+)CD34 requires the presence of three components (1) mature fat cells; (2) small, uniform spindle cells; and (3) strands of dense, eosinophilic (“ropey”) collagen

- **Pleomorphic**: hyperchromatic adipocytes, bizarre floret giant cells, overlapping nuclei, pseudomalignant appearance, resembles liposarcoma but rare lipoblasts and no necrosis

- Spindle cells in both spindle cell and pleomorphic lipomas are CD34-positive and rarely S100-positive
Hibernoma

Introduction:
- Young adults in their late teens or early twenties. About 5% of cases are familial

Epidemiology:
- Indistinguishable from lipoma, interscapular area, thighs, shoulder, neck, chest, arms and abdominal cavity/retroperitoneum

Pathogenesis:
- Overall unknown, clonal chromosomal abnormalities consist of structural rearrangements of 11q13 and 11q21

Pathology:
- Characteristic tan to deep red-brown color; pronounced lobulation; vascular interlobular septa surround individual lobules
- Characteristic brown fat cells with a small central nucleus and multivacuolated to granular eosinophilic cytoplasm, “Mulberry cells” admixed w/ mature fat cells and pale multivacuolated cells
Hibernoma

Differential Diagnosis:
- Lipoma, Liposarcoma, Neurofibroma, Angiolipoma, Lymphoma, Rhabdomyoma, Rhabdomyosarcoma

Diagnostic Evaluation:
- Core needle biopsy is contraindicated if suspecting hibernoma due to hypervascularity and risk of hemorrhage.
- Ultrasound, CT, MRI can be used to help in diagnosis

Therapy:
- Complete surgical excision
- May be difficult to excise as they often are in close proximity to neurovascular structures
Nevus lipomatosus superficialis

Clinical Features:
- Rare, clustered papules or nodules of **buttocks, hips and thighs** with onset at birth or within first two decades of life

Pathology:
- Adipose in superficial dermis, increased dermal blood vessels

DDX for “adipose in superficial dermis”:
- Proteus syndrome
- Michelin tire baby
- Lipedematous alopecia
- Connective tissue nevus (Clinical)

Treatment
- Excision
**Lipoblastoma/lipoblastomatosis**

**Introduction:**
- Benign neoplasm of immature fat cells that typically occurs on extremities
- Circumscribed form = lipoblastoma, diffuse = lipoblastomatosis

**Epidemiology:**
- Young children, M>F

**Pathology:**
- Cannot be distinguished from myxoid liposarcoma; poorly circumscribed or encapsulated subcutaneous tumor of immature fat cells w/ lipoblasts (lipid vacuoles displace the nuclei), mucinous stroma

**Differential Diagnosis:**
- Liposarcoma - Lack of cellular atypia and rare mitoses help to distinguish it histologically from liposarcoma

**Treatment:**
- May recur after excision but do not metastasize
Malignant Tumors of Fat: Liposarcoma/Atypical Lipomatous Tumor

Introduction:
- Uncommon soft tissue sarcoma, five histopathologic subtypes
- Range in behavior from locally aggressive tumors to highly malignant depending on the subtype

Key Points:
- Comprise < 5% of all soft tissue sarcomas in children
- Rarely arise in children younger than 10 years of age
- Arise de novo and not in pre-existing lipomas
Liposarcoma/Atypical Lipomatous Tumor

Clinical Presentation:
- Affects dermis > subcutis
- Dome-shaped or polypoid
- LE > UE, retroperitoneum
- 1-20 cm in size

Differential Diagnosis:
- Lipoblastoma, lipoblastomatosis, spindle cell/pleomorphic lipoma

Histopathology:
- Presence of lipoblasts
- Five subtypes:
  - Well-differentiated
  - Myxoid
  - Round cell
  - Pleomorphic
  - Dedifferentiated
Liposarcoma/Atypical Lipomatous Tumor

Treatment/Prognosis:

- Wide excision performed with the use of proper imaging techniques to rule out growth into underlying muscle and fascial planes
- Post operative radiotherapy and chemotherapy have been used
- Prognosis depends on histologic subtype
- High-grade pleomorphic tumors can metastasize to lungs
Malignant Tumors of Muscle: Rhabdomyosarcoma

Introduction:
- Rhabdomyosarcoma (RMS) is the most common soft tissue sarcoma in children. Various forms include: embryonal, botryoid, alveolar, and undifferentiated type. Localized disease has over 80% 5-year survival, however metastatic rates are less than 30%

Clinical Evaluation:
- RMS usually presents with an expanding mass. Pain and swelling are the most common symptoms and are location dependent

Radiologic Evaluation:
- Studies include: MRI, CT, PET scan, Ultrasonography, Echocardiography and bone scans
Rhabdomyosarcoma

Pathology:
- Small round blue cells with positive staining for desmin, vimentin, myoglobin, actin and transcription factor myoD

Treatment:
- Chemotherapy, radiation therapy and surgical removal.
Leiomyosarcoma

Epidemiology:
- Extremely rare in children, < 1% of primary sarcomas in children less than 20
- EBV-associated leiomyosarcomas (EBV-LMS) in HIV patients
- Gastrointestinal or other visceral locations most common

Staining:
- (+) Actin, (+) Desmin, (-) cytokeratin, (-) s100, (-) CD68

Treatment/Prognosis:
- Treatment of dermal tumors is simple excision; subcutaneous is wide excision with careful examination of all surgical margins
- Usually low-grade morphology with better prognosis than adult
- Subcutaneous tumors metastasize in 25-40% of patients

<table>
<thead>
<tr>
<th>Clinical features</th>
<th>Most Common location</th>
<th>DDX</th>
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<tbody>
<tr>
<td>Firm skin-colored to red-brown dermal or subcutaneous nodules, may have overlying ulceration + pain</td>
<td>Trunk (back, abdomen and chest wall), lower limb, neck</td>
<td>Infantile myofibromatosis, rhabdomyosarcoma, synovial sarcoma</td>
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## Benign Bone Tumors: Bone-forming tumors

### Osteoid Osteoma

<table>
<thead>
<tr>
<th>Clinical features</th>
<th>Most common locations</th>
<th>Plain radiographic features</th>
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</thead>
<tbody>
<tr>
<td>• 10 to 20 years</td>
<td>• Cortex of the metaphysis or diaphysis (less common) of the proximal femur&lt;br&gt;• proximal tibia&lt;br&gt;• distal femur&lt;br&gt;• spine&lt;br&gt;• proximal humerus&lt;br&gt;• phalanges</td>
<td>• Small round intracortical lucency (nidus) with sclerotic margin&lt;br&gt;• special imaging studies (bone scan, CT, or MRI) often needed for spine</td>
</tr>
<tr>
<td>• M &gt; F</td>
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<tr>
<td>• Nocturnal pain promptly relieved by NSAIDs; limp, scoliosis</td>
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# Bone-forming tumors

## Osteoblastoma

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<th>Most common locations</th>
<th>Plain radiographic features</th>
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<tbody>
<tr>
<td>Any age (usually 10 to 20 years)</td>
<td>Posterior elements of the spine or sacrum; less commonly occurs in the metaphysis of the proximal femur or tibia</td>
<td>Variable (often requires CT or MRI for diagnosis)</td>
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<td>M &gt; F</td>
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<tr>
<td>Chronic pain; less responsive to NSAIDs than osteoid osteoma; spine lesions may cause neurologic symptoms</td>
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### Osteochondroma & hereditary multiple osteochondromas

## Clinical features
- 10 to 20 yrs
- M > F
- Pain, functional problems, deformity, pathologic fracture, palpable near the ends of long bones
- Risk of malignant transformation to chondrosarcoma in adults (in HME)

## Most common locations
- Metaphysis of the distal femur, proximal tibia, and proximal humerus

## Plain radiographic features
- Bony spur arising from the surface of the cortex; the cortex of the spur is continuous with the cortex of underlying bone
Enchondromatosis (Ollier syndrome, including Maffucci syndrome*)

Clinical features
- <10 years
- Intracranial enchondromas may cause headache and cranial nerve deficit
- Risk of malignant transformation to chondrosarcoma and increased risk of nonsarcomatous neoplasms

Most common locations
- Metaphysis, diaphysis of any bone

Plain radiographic features
- Oval, well-circumscribed central (medullary), lucent lesions with or without matrix calcifications or expansion of the cortex
Fibrous Lesions

### Fibrous Dysplasia

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<th>Plain Radiographic Features</th>
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<tbody>
<tr>
<td>Portions of bone replaced by fibrous connective tissue</td>
<td>Any bone, MC: Proximal femur, Tibia, Ribs, Skull</td>
<td>Lytic lesion in the metaphysis or diaphysis with a &quot;ground glass&quot; appearance, Expansion of the bone and possible bowing</td>
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<td>Originates in medullary cavity</td>
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<td>Single or multiple</td>
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<td>Teens or 20s</td>
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<td>Most asymptomatic</td>
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## Langerhans cell histiocytosis

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<th>Plain Radiographic Features</th>
</tr>
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<tbody>
<tr>
<td>Any age (most common 5 to 10 years)</td>
<td>Skull, ribs, pelvis, long bones, mandible, vertebrae</td>
<td>Well-defined lytic lesion with or without sclerotic margins; variable periosteal reaction; flattening of vertebral body; &quot;floating&quot; teeth (with mandibular involvement)</td>
</tr>
<tr>
<td>M &gt; F</td>
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<tr>
<td>Painful swelling of affected site, pathologic fracture, proptosis, thirst, refractory otitis media</td>
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# Miscellaneous Bone Tumors

## Giant cell tumor

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<th>Plain Radiographic Features</th>
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<tr>
<td>Young adults (peak incidence in 20s to 30s) F &gt; M Pain, swelling, limitation of joint movement, pathologic fracture</td>
<td>• Epiphysis of the distal femur, proximal tibia, distal radius, sacrum</td>
<td>• Expansile, eccentric, lytic lesion in epiphysis and adjacent metaphysis, may extend to subchondral plate; absence of matrix calcification and periosteal reaction</td>
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[Image orthoinfo.aaos.org]
Malignant Tumors of Bone

Introduction:

- Most common malignant tumors of bone in pediatric population 1\textsuperscript{st} - Osteosarcoma, 2\textsuperscript{nd} - Ewing’s sarcoma

Clinical Evaluation:

- Osteosarcoma MC presents with pain (pathologic fracture uncommon)
- Ewing’s sarcoma MC presents with pain of hips, back with localized swelling

Radiographic Findings:

- Osteosarcoma: Sunburst pattern, Codman’s triangle
- Ewing’s sarcoma: Onion-skin periosteal reaction, lytic lesion of pelvis
Osteosarcoma

Etiology:

- May arise as a de novo lesion or develop secondarily to a known premalignant lesion such as Paget disease, osteogenesis imperfecta, bone lesion, chronic osteomyelitis, fibrous dysplasia, giant cell tumor, osteoblastoma or radiation therapy.
- Some familial cases: esp in familial bilateral retinoblastoma.
- Increased risk with inherited diseases - Rothmund-Thompson, Li-Fraumeni syndrome, Bloom syndrome.

Epidemiology:

- Most common non-hematologic primary malignant tumors of bone in both children and adults.
- Bimodal age distribution 10-25 yo, and >60 yo.
- Metaphysis of long bones, MC distal femur (75%).
Osteosarcoma

Radiographic findings:

- Large infiltrating metaphyseal lesion arising in medullary bone with a mixed lytic and sclerotic appearance. Can be purely osteolytic (about 30% of patients), purely osteoblastic (about 45% of patients), or both.
- **Codman’s triangle**: Elevation of the periosteum
- **Sunburst pattern**: Extension of tumor through the periosteum may result in sunburst appearance (~60% of patients)

Associated dermatologic disorders:

- **Rothmund-Thompson syndrome** (AR, RECQL4, photosensitive genodermatosis, poikiloderma, hypoplastic thumbs)
- **Li-Fraumeni syndrome** (AD, P53 mutation, multiple malignancies)
- **Bloom syndrome** (AR, RECQL2, RECQL3, photosensitive, decreased IgM)
- **Neutrophilic eccrine hidradenitis**
Ewing’s Sarcoma

Etiology:
- Translocation mutation t(11;22) fuses one of many observed combinations of exons from EWS and FLI1 forming fusion message, MC: EWS exon 7 fused to FLI1 exon 6 (type 1 translocation) found in 50-64% of ewing sarcomas

Epidemiology:
- 2nd MC primary malignant bone tumor in adolescents and young adults, annual incidence of 1 in 1 million, 50% of Ewing sarcomas in pts aged 10-20, peaking in later teenage years, higher incidence in Caucasians (9x higher)

Clinical presentation:
- Patients usually present with pain, palpable mass, back pain may indicate a paraspinal, retroperitoneal, or deep pelvic tumor. Most commonly found in axial skeleton, particularly in the pelvis
- Systemic sx: fever, weight loss can occur and may indicate metastatic dz

Radiographic findings:
- Peri-osteal “onion-skinning” reaction, lytic or sclerotic primary bone lesions

Associated dermatologic disorders:
- Can have petichiae or purpura secondary to tumor induced thrombocytopenia
Which of the following statements is false regarding infantile myofibromatosis?

A) Visceral involvement carries a high mortality rate within months d/t compromise of vital organ function

B) With ONLY soft tissue and bony involvement there is a very good prognosis

C) Lesions are only rarely present at birth

D) Although this entity is rare, it is the most common of the juvenile fibromatoses

E) Tumors tend to regress

Answer: 50% of lesions are present at birth and more present with in the first 2 years of life

This syndrome illustrated by the photo on the right has characteristic venous malformations of the distal extremities. For which of the following neoplasms are these patients at risk of developing?

- A. lung CA
- B. adrenal CA
- C. chondrosarcomas
- D. enchondromas
- E. C & D
- F. A & C
- G. All of the above

Answer: E. Benign enchondromas which can compromise bone strength and lead to chondrosarcomas.

What is the defect responsible for Mafucci’s syndrome?

- A. ALK1
- B. PTH/PTHrP
- C. TIE2
- D. LMX1B

Answer: B
Osteosarcomas are associated with all of the following syndromes except

A) Rothmund-Thompson syndrome
B) Li-Fraumeni syndrome
C) Bloom syndrome
D) Blue rubber bleb syndrome
Polyostotic Fibrous Dysplasia

- What is another name for polyostotic fibrous dysplasia and what is its genetic mutation?
  - McCune-Albright syndrome
  - GNAS 1 mutation
- Large café-au-lait macules
  - Geographic borders
- Precocious puberty
- Pathologic fractures
- Endocrine abnormalities
  - Hyperparathyroidism
  - Hyperthyroidism
- Acromegaly
10. Images courtesy of Ronald P. Rapini, MD and Richard Kempson, MD.