RADY 403: Ewing Sarcoma

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June 17, 2021
Focused patient history and workup

- 11-year-old with unremarkable past medical history, family history

- Presented to pediatrician after one month of right leg pain in lower leg/calf
  - Dull, achy, non-radiating pain
  - No history of trauma, although is active
  - No erythema, swelling, gait issues
  - Afebrile, no overlying skin abrasions or lesions

- Diagnosed as muscle strain

- Pain continued to worsen
  - Developed new limp with noticeable swelling in right lower leg
  - Minimally responsive to Tylenol
Local radiographs were performed, in line with the ACR Appropriateness Criteria.
List of Imaging Studies

- Frontal and lateral radiographs of right tibia and fibula
- CT-guided biopsy
- MRI of right fibula
- CT chest
- PET CT
Ill-defined, expansile, lytic lesion of the mid fibula with a moth-eaten appearance and Codman's triangle. Codman's Triangle. Medullary involvement and possible soft tissue component.
Bony spicules extending horizontally

Tibia, distal femur appear uninvolved

Knee and ankle joints are unremarkable

Poorly defined, expansile, lytic lesion

Bony spicules extending horizontally
CT-Guided FNA and Core Needle Biopsy of Right Fibula Lesion

Lateral approach to the lesion for FNA (x2) and Core Needle Biopsy (x2)

Hair-on-end periosteal reaction
## ACR Appropriateness Criteria

### Suspect primary bone tumor. Lesion on radiographs. Indeterminate or aggressive appearance for malignancy. Next imaging study.

<table>
<thead>
<tr>
<th>Name</th>
<th>Category</th>
<th>Adult RRL</th>
<th>Peds RRL</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRI area of interest without and with IV contrast</td>
<td>Usually appropriate</td>
<td>O 0 mSv</td>
<td>O 0 mSv [ped]</td>
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<tr>
<td>CT area of interest without and with IV contrast</td>
<td>May be appropriate (Disagreement)</td>
<td>Varies</td>
<td>Varies</td>
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<tr>
<td>CT area of interest without IV contrast</td>
<td>May be appropriate</td>
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<td>Varies</td>
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<tr>
<td>MRI area of interest without IV contrast</td>
<td>May be appropriate</td>
<td>O 0 mSv</td>
<td>O 0 mSv [ped]</td>
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<tr>
<td>Bone scan whole body with SPECT or SPECT/CT area of interest</td>
<td>May be appropriate</td>
<td>1-10 mSv</td>
<td>3-10 mSv [ped]</td>
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<tr>
<td>FDG-PET/CT whole body</td>
<td>May be appropriate</td>
<td>10-30 mSv</td>
<td>3-10 mSv [ped]</td>
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<tr>
<td>US area of interest</td>
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<td>O 0 mSv</td>
<td>O 0 mSv [ped]</td>
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<tr>
<td>Radiography skeletal survey</td>
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<td>0.3-3 mSv [ped]</td>
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<td>CT area of interest with IV contrast</td>
<td>Usually not appropriate</td>
<td>Varies</td>
<td>Varies</td>
</tr>
<tr>
<td>Bone scan whole body</td>
<td>Usually not appropriate</td>
<td>1-10 mSv</td>
<td>3-10 mSv [ped]</td>
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There is a heterogeneous T2 hyperintense, T1 isointense, enhancing lesion in the diaphysis of the mid fibula.

Abnormal signal intensity and enhancement in the tibialis posterior, flexor hallucis longus, peroneus longus/brevis with disruption of the interosseous membrane.
3 mm LUL ground glass opacity, likely atelectasis
No distant sites of abnormal uptake to suggest distant metastases

Right fibula metadiaphyseal osseous lesion with aggressive periosteal reaction and localized muscle invasion

Avid FDG uptake in the tibialis posterior, flexor hallucis longus, peroneus longus and brevis

Metastasis Workup: FDG PET/CT

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<tbody>
<tr>
<td>CT chest without IV contrast</td>
<td>Usually appropriate</td>
<td>1-10 mSv</td>
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<tr>
<td>FDG-PET/CT whole body</td>
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<td>10-30 mSv</td>
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<tr>
<td>Radiography chest</td>
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<td>1-10 mSv</td>
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<td>1-10 mSv</td>
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Ewing Sarcoma: Background

- Second most common primary pediatric bone tumor (osteosarcoma)
  - 3% of all pediatric tumors

- Generally occurs in second decade of life (mean age of 11 years)
  - Males > females

- Aggressive, small, round, blue-cell tumor

- Genetics
  - Arise from a precursor cell capable of neuroectodermal differentiation
  - 11;22 translocation
  - PAS+ and CD99+

Histology slide showing sheets of small, round, uniform cells with scant clear cytoplasm, divided into irregular lobules by fibrous strands

Courtesy of https://www.pathologyoutlines.com/topic/bonewing.html

Courtesy of https://www.talkbasket.net/85740-patrick-ewing-michael-jordan-still-trash-talks-me-to-this-day
Ewing Sarcoma: Clinical Features

- Most common locations: femur > ilium > tibia > humerus > fibula > ribs > sacrum
  - Can develop in any bone, although long bones most common
  - Soft tissue involvement is more common in older patients

- Presentation
  - Pain and swelling of the affected limb
  - Local findings (warmth and tenderness)
  - Can present with constitutional signs and symptoms (fever, elevated erythrocyte sedimentation rate, leukocytosis, weight loss)
    - 10-20% of patients
    - Associated with advanced disease

- 20-30% of patients have metastasis at time of presentation
  - Lung in 50%, bone in 25% and bone marrow in 20%

- Differential diagnosis: Osteosarcoma, lymphoma, infection, eosinophilic granuloma

Case courtesy of Dr Hani Makky Al Salam, Radiopaedia.org, rID: 7876
Ewing Sarcoma: Radiographic Findings

- Distribution in the long and flat bones
- Centered in the medullary cavity
- “Moth-eaten” appearance
- Lytic lesions with poorly defined margins and permeative pattern
  - Can appear predominantly sclerotic in 15% of cases
  - Bone necrosis can appear radiodense
- “Onion skin” periosteum (non-specific)
  - Extrudes through Haversian Canals, elevating the periosteum in a lamellated fashion
- Large soft-tissue component with little calcification
  - Especially in older patients
  - Difficult to appreciate on plain radiography

Courtesy of https://radiologyassistant.nl/musculoskeletal/bone-tumors/osteolytic-ill-defined#ewings-sarcoma
Ewing Sarcoma: Radiographic Findings

- Onion-skinning of periosteum
- Long bone distribution
- Moth eaten appearance
- Medullary involvement
- Lytic lesions with poorly defined margins and a permeative pattern. They are often located in the diaphysis and metadiaphysis.
Ewing Sarcoma: Imaging Findings

Onion-skinning of periosteum

Moth eaten appearance

Lytic lesions with poorly defined margins and a permeative pattern. They are often located in the diaphysis and metadiaphysis.
Ewing Sarcoma: Imaging Findings

- **MRI**
  - Demonstrates extent of primary osseous lesion and soft tissue, bone marrow involvement
  - Informs the therapeutic approach
  - T1WI: homogenous, intermediate signal intensity
  - T2WI: homogenous, low-intermediate signal intensity
    - High signal intensity predominates in 32% of Ewing sarcomas of bone on T2-weighted images
  - Contrast enhancement is usually seen, and is usually either diffuse or peripheral nodular in pattern
- **CT**
  - Chest CT often performed for detection of metastatic disease
  - Similar appearance of radiography, with aggressive bone destruction and a large associated soft-tissue mass
- **FDG PET/PET-CT**
  - Demonstrate extent of disease and evaluate treatment response
  - Up to 100% sensitivity for detecting sites of disease at staging and recurrence
    - Specificity 82%, accuracy 96%
  - White arrowheads demonstrate cortical involvement as intermediate-intensity channels extending through low-signal-intensity cortex.
  - Up to 100% sensitivity for detecting sites of disease at staging and recurrence
  - Specificity 82%, accuracy 96%
Ewing Sarcoma: Prognosis

- 5-year survival is 70% for localized disease and 30% for metastatic disease
  - Historically, even in localized lesions with adequate tumor resection, 5-year survival was only 10%
    - Began to assume that all patients with Ewing Sarcoma have micrometastases and treat as such

- The most favorable prognostic factors at the time of initial diagnosis are tumor responsiveness to preoperative chemotherapy, and the presence of the most common type of Ewing sarcoma fusion transcript (EWS-FLI1)

- Adverse prognostic indicators at the time of initial diagnosis include:
  - Metastatic disease
    - Eight year survival rate of 30%
  - Flat bone involvement (pelvis)
  - Large tumor size (>8 cm)
  - Older patient age (>15 years) at presentation
  - Elevated LDH
  - Poor tumor response to preoperative chemotherapy

Case courtesy of Dr. Mahmoud Yacoub Alabd, Radiopaedia.org, rID: 41035
Ewing Sarcoma: Management

- Multidisciplinary management is key
  - Multi-drug induction chemotherapy
    - 4-8 cycles
  - Local treatment of primary tumor
    - Surgery, radiotherapy, or both
      - Goal of surgery: wide surgical margin with attempt at limb salvage
      - Limb reconstruction with bone allograft or metallic implant; joint prosthesis if epiphysis is involved in resection
  - Consolidation chemotherapy

- Favorable findings on follow up radiographs:
  - Maturation of periosteal reaction
  - Coarsening of the bone trabeculae
  - Reconstitution of the cortex
  - Increasing osseous sclerosis and progressive mineralization
  - Decrease in the size of the soft-tissue component of the lesion
Patient Treatment and Outcome

- 32 months s/p completion of therapy
- Followed up every three months with leg and chest radiographs and leg MRI
  - Post-treatment imaging is important
- No evidence of recurrence
- Doing well clinically
More common in males

At radiography, Ewing sarcoma of bone reveals aggressive features, reflecting its high-grade nature

Initial imaging of choice is plain radiograph of area of interest
- Moth-eaten lytic lesion in long bones
- Diaphyseal/metadiaphyseal involvement
- "Onion-skin" appearance

30% metastatic at presentation with significantly worse outcomes
- Commonly metastasizes to lungs and bone marrow
  - Assess with chest CT and PET scan

Management includes chemo, then surgery/radiation, then consolidation chemo
References


