Malignant Lesions in Kids: Ewing’s Sarcoma and Osteosarcoma

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Outline

- Presentation
- Radiology
- Histology
- Genetics
- Treatment and Outcomes
Ewing Sarcoma

- First described by James Ewing as “diffuse endothelioma of bone”

- Now Ewing’s Sarcoma Family of Tumours

- Round cell tumors with varying degrees of neuroectodermal differentiation
Ewing Sarcoma

- 2nd most common primary malignant bone tumour in children
- 1% of all childhood tumours
- M:F ratio is 3:2
- Peak incidence: males 10-14 y.o., females 5-9 y.o.
Location

- Found most commonly in:
  - Femur and Flat bones
    - Pelvis
    - Scapula
  - Also: tibia, humerus, fibula
Clinical Presentation

- Pain
- Swelling
- Erythema
- Fever due to cytokine production
- Tumour in pelvis may present with gait abnormalities, bowel or bladder dysfunction or back pain
Radiographic Presentation

- Aggressive
  - diaphyseal/metadiaphyseal
- Permeative
- Poorly marginated
- “onion skin” periosteal reaction
- Often have soft-tissue mass
Radiographic Presentation

- Radiographic Differential Diagnosis:
  - Lymphoma
  - Leukemia
  - Osteosarcoma
  - Osteomyelitis
  - Eosinophilic Granuloma
MRI

- Usually reveals large soft tissue mass
- Extent of bone marrow edema
Molecular Genetics

- 85% $t(11:22)$
  - Creates EWS-FLI1 gene
  - Leads to oncogenic protein

- 10% $t(21:22)$
  - EWS-ERG

* Guaranteed OITE material
Workup

- Local staging – MRI primary site
- Systemic staging
  - CT (or xray) chest
  - Bone scan
- Labs – LDH, Alk Phos
Workup

- Biopsy always required for Dx

- **Bone marrow Biopsy X 3** – looking for micromets
Histology

- High Grade – Lots of cells
- Small round blue cells
- Large nuclei with scant cytoplasm
- Small round blue cells
- Also
- Small round blue cells…
Histology
Histology
SRBC Tumours

DDX:

- Ewings
- Lymphoma
- Myeloma
- Small cell osteosarcoma
- Osteomyelitis
- Histiocytosis (EG)
- Neuroblastoma
- Rhabdomyosarcoma
- Metastatic disease: small cell lung
Diagnosis

- As always depends on clinical, radiographic, histologic correlation

- Immunohistochemistry - CD-99 positive
Treatment

- Pre-op – neoadjuvant chemotherapy
  - ↓ LDH, ↓ soft tissue mass (measure %)
  - Response usually better with type I EWS-Fli1 fusion

- Local control with surgery or radiation
  - Local relapse rates lower with surgery, overall survival no demonstrated difference
Treatment

- Radiation an option when:
  - surgery leads to unacceptable morbidity or mortality
  - Positive margins post op
  - Mets

- Post op Chemo
Negative Prognostic Factors

- Non pulmonary mets
- <90% necrosis after chemotherapy
- Axial primary
- Age > 20 yrs
- Non Type – EWS-FII1
Outcome

- Pelvic ES with Mets
  - 5 yr event free survival ~ 10-20%

- Metastatic at presentation
  - 5 yr event free survival ~ 25%

- Localized at presentation
  - 5 yr event free survival ~ 75%
Osteosarcoma

- **Definition:**
  - Malignant neoplasm...that produces osteoid
  - Most common *primary* neoplasm of bone
    (ES was 2nd most common)
  - Not the most common malignancy of bone
Introduction
Introduction

Table 1
Osteosarcoma Types

Central
  High-grade
    Conventional
  Telangiectatic
  Small cell
  Epithelioid
  Osteoblastoma-like
  Chondroblastoma-like
  Fibrohistiocytic
  Giant cell-rich
  Low-grade
    Low-grade central
      Fibrous dysplasia-like
      Desmoplastic fibroma-like
  Surface
    Low-grade
    Parosteal
    Intermediate-grade
      Periosteal
    High-grade
      Dedifferentiated parosteal
      High-grade surface
  Intracortical
  Gnathic
  Extraskeletal
    High-grade
    Low-grade
Epidemiology

- **Bimodal**
  - 2\(^{nd}\) decades - primary
  - 2\(^{nd}\) peak in elderly – secondary

- **Incidence:** 900 cases annually USA

- ↑ Frequency ↑ Bone Growth
Etiology

- Unknown
- Predisposing factors
  - Familial retinoblastoma
  - Paget’s disease
  - Li-Fraumeni syndrome
  - Radiation Osteitis
Molecular Characterization

- 70% have a chromosomal abnormality
- Abnormalities much more heterogeneous than Ewing’s
Clinical Presentation

- Pain
- Tender mass
- Pathologic fracture
- 80% in long bones
- 90% metaphyseal

- Not generally associated with fever otherwise very similar to Ewing’s
Radiographic Presentation

- Keep classic locations in mind
- Intramedullary
- Osteoid matrix
- Very aggressive periosteal reaction
- Often diagnostic but can sometimes be subtle

Classic

Codman’s Triangle
Sunbursting
Radiographic Presentation

- Aggressive cortical reaction
- Osteoid matrix
- Circumferential
- May cause ‘apple core’ appearance
- Medullary canal not involved (EXTRAMEDULLARY)

Periosteal
Radiographic Presentation

- Popliteal location classic
- Mineralized
- No aggressive periosteal reaction low grade and not much periosteum here
- INTRAMEDULLARY/CORTICAL

Parosteal
Radiographic Presentation

Dedifferentiated Parosteal

[Image of knee X-rays]
Radiographic Presentation

Radiographic Differential Diagnosis:

- Lymphoma
- Leukemia
- Ewing’s Sarcoma
- Osteomyelitis
- Eosinophilic Granuloma

Intramedullary osteosarcoma
### Localization

<table>
<thead>
<tr>
<th>Classic</th>
<th>Periosteal</th>
<th>Parosteal</th>
</tr>
</thead>
<tbody>
<tr>
<td>“lacy”</td>
<td>(Extramedullary/diaphyseal)</td>
<td>(Intramedullary/metaphyseal) “school of fish”</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Bone</th>
<th>Classic</th>
<th>Periosteal</th>
<th>Parosteal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distal Femur</td>
<td>Tibia</td>
<td>Distal Femur (posterior)</td>
<td></td>
</tr>
<tr>
<td>Prox. Tibia</td>
<td>Femur</td>
<td>Prox. Humerus</td>
<td></td>
</tr>
<tr>
<td>Prox. Humerus</td>
<td></td>
<td>Prox. Tibia</td>
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</table>

### Grade

- Aggressive
- Less Aggressive
Workup

- Local and systemic staging similar to Ewings Sarcoma
  - MRI extremity
  - CT or xray lungs
  - Whole body bone scan
  - Alk phos, LDH
  - Biopsy

- No need for bone marrow biopsies
MRI

- MRI used to define extent disease
Histology

- **Classic Osteosarcoma**
- “Lacy” osteoid
  - Unmineralized bone matrix - pink
- **Cell**
  - Anaplastic
  - Pleomorphic
Periosteal Osteosarcoma - Histology

- Well differentiated, uncalcified cartilage
- Often called juxtacortical chondrosarcoma
- Focal areas of osteoid deposition
Periosteal Osteosarcoma -
Histology
Parosteal – Histology
Parosteal – Histology

- “fish” are spindle cells
- Not pleomorphic
- Indicative of lower grade
Treatment for Classic and Periosteal

- Neoadjuvant Chemotherapy decrease tumour size and presumptively for micrometastasis
- Wide resection
- Adjuvant chemotherapy (protocol dependent on response to preop chemo)
Treatment: Parosteal

- Wide resection only!
  - No chemo because less aggressive and can be cured with wide resection, so no need for adjuvant therapy.
Prognosis

- Cancer March 2006, Bacci et al.
- 789 patients over 15 years
- 5 yr EFS 60.1% with surgery and chemo
  (Often appears as 70% in multiple choice)
Test Your Knowledge

- Aggressive proximal tibial lesion in a 13 yr male

- What immunohistochemical markers would you expect?
  - CD-99 Positive
    “thank you Wayne Gretzky 99”
Test Your Knowledge

- Would this biopsy come from an intramedullary or extramedullary lesion?
  - Intramedullary / Metaphyseal
Test Your Knowledge

- Is this bone or cartilage?
  - Bone
  - Classic Osteosarcoma

- Would this more likely be associated with sunbursting or onion skinning?
  - Sunbursting
Test Your Knowledge

- What colour would the biopsy be?
  - Pink for Bone
  - Parosteal
Test Your Knowledge

- What is a school of sharks called?
Thank You