IMAGING OF EWING SARCOMA AND LANGERHANS CELL HISTIOCYTOSIS

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LEARNING OBJECTIVES

• Identify the demographic and distribution patterns of Ewing sarcoma and Langerhans cell histiocytosis

• Recognize the spectrum of imaging appearances of Ewing sarcoma and Langerhans cell histiocytosis with pathologic correlation
EWING SARCOMA

HISTORY

• Highly malignant primary bone sarcoma

• Ewing provided first comprehensive description in 1921, designating it “diffuse endothelioma” of bone

• Later (1924) termed “endothelial myeloma” of bone and “Ewing tumor” by Codman
James Ewing MD:
1866 - 1943

- Osteomyelitis at 14
- Bed rest 2-years
- 1st Professor of Pathology Cornell University 1899
- Co-founder American Cancer Society
EWING SARCOMA
INCIDENCE/DISTRIBUTION

• Approximately 5% of all biopsied tumors
• Long bones involved most commonly
• Usually major long bones, femur most common (22%-25%), humerus (8%-10%) and fibula (8%-10%)
• In flat bones, most common pelvis (20%) followed by ribs (11%)
EWING SARCOMA DEMOGRAPHICS

- 90% of patients present at 5-30 years
- Peak incidence 10 to 15 years
- Range 5 months to 83 years
- Slight male predominance (1.5:1)
- Pain/swelling most common symptom
- Constitutional signs to include local heat, fever, anemia and leukocytosis
EWING SARCOMA

DEMOGRAPHICS

- Chromosomal translocation in > 90%;
  \textit{t}(11;22) most common; others
  \textit{t}(21;22), \textit{t}(7;22)

- Predilection for Caucasians (95%)

- Usually solitary and nonfamilial; 10%
  are reported to be multiple at
  presentation
EWING SARCOMA
PATHOLOGY

- Large tumors 5-10 cm in size; extraosseous component often larger than intraosseous
- Characterized by sheets of monotonous malignant "round cells"
- Indistinct cytoplasmic borders
- Frequent areas of necrosis and hemorrhage
- Virtually all PAS positive (glycogen)
- Ewing family includes Ewing sarcoma and primitive neuroectodermal tumor (PNET)
Sheets of monotonous malignant “round cells“ with indistinct cytoplasm; areas of necrosis and hemorrhage are frequent.
EWING SARCOMA
RADIOGRAPHS

• Distribution: metadiaphysis 59%, diaphysis 35%, metaphysis 5%, epiphysis <1%
• Lesions medullary, central > eccentric
• Aggressive bone destruction (permeative) 97% - 3% normal radiograph
• Cortical destruction 42%; Soft tissue mass 56%
• Sclerosis 32% (93% intraosseous component) - Most common in flat bone lesions
EWING SARCOMA RADIOGRAPHS

- Periosteal reaction 58%-85%
- “Onion skin” appearance due to cyclic pattern of periosteal irritation 55%
- Perpendicular striations due to rapid continuous lifting of periosteum 30%
- Cortical thickening 6%-20%
- Pathologic fracture in 10%-15%
- Marked increased uptake bone scintigraphy/PET
Ewing sarcoma. Radiograph. Note the metadiaphyseal location and absence of identifiable matrix mineralization.
Scintigraphy. Focal increased tracer accumulation on flow study.
Scintigraphy. Focal increased tracer accumulation on blood pool images.
Scintigraphy. Focal increased tracer accumulation on delayed static images.
EWING SARCOMA
CT FEATURES

- CT bone destruction with tissue similar to mildly lower attenuation to muscle
  - Cortical destruction 83% (focal 17%, along vascular channels 30%, both 36%, intact 17%)
  - Soft tissue mass 96% asymmetric about cortex
  - Sclerosis/mineralization 39% (80% intraosseous); more common in flat bone lesions
EWING SARCOMA
MRI FEATURES

- MR marrow replacement on T1W with low to intermediate signal intensity (95%) on T1W and T2W (68%; 32% high signal intensity)
- Soft tissue mass 96% usually asymmetric about cortex; Neurovascular encasement 20%; Joint involved (29%)
- Contrast enhancement 100% usually diffuse
- Cortical destruction 92%
  - Focal 22%, along vascular channels 40%, both 34%, intact 4%
MR imaging. Typical features. MR shows large heterogeneous circumferential soft tissue mass. Soft tissue changes seen to better advantage on MR. Coronal T1-weighted (left) and T2-weighted (right) images.
Ewing sarcoma. Flat bone. Radiograph.
EWING SARCOMA EXTRASKELETAL

- Similar demographics/pathology to bone lesions, except less male predilection, average age 20 yrs.
- Location: paravertebral region (32%), lower extremities (26%), chest wall (18%), pelvis/hip (11%), retroperitoneum (11%), and upper extremities (3%)
- Chest/chest wall (Askin tumor) – Large masses may opacify entire chest with pleural effusion/rib involvement
- Nonspecific imaging appearance with soft tissue mass; may see high flow vessels on MR; may involve bone surface and calcification (10%-30%)
EWING SARCOMA
TREATMENT/PROGNOSIS

- Ablative surgery, chemotherapy and radiation therapy
- About 30% present with metastases
- Metastases typically to lungs (85%), bones (69%), pleura (46%), CNS (12%)
- The 5-year survival rate for patients without metastases at presentation: 55%-70%
LANGERHANS CELL HISTIOCYTOSIS (LCH)

- Eosinophic granuloma
- Hand-Schüller-Christian disease
- Letterer-Siwe disease
PAUL LANGERHANS: 1847-1888

- In 1868, he stained human skin with gold chloride, and described the dendritic cell that bears his name.
- In 1869, discovered pancreatic cell islands.
- Acquired TB 1874, relocated to Madeira.
LANGERHANS CELL HISTIOCYTOSIS
HISTORY

• 1940: Jaffe & Lichtenstein - eosinophilic granuloma (EG)

• 1941: Farber, Green & Farber - EG could be solitary or multiple

• 1953: Lichtenstein - proposed the name histiocytosis X for the inflammatory histiocytoses
LANGERHANS CELL HISTIOCYTOSIS CLASSIFICATION

• 1987: Writing Group of the Histiocyte Society endorsed the term Langerhans cell histiocytosis (LCH)

• 1997: Histiocyte Society grouped LCH according to the number of sites and types of tissues/organs involved and the presence or absence of involved organ failure
• Single system (one organ system): single site or multifocal (eosinophilic granuloma - EG)

• Multisystem (two or more organ systems): further separated into patients with or without “risk organ involvement”
  - Hand-Schuller-Christian and Letterer Siwe

• Risk organ involvement: liver, spleen, hematopoietic system or lungs
LANGERHANS CELL HISTIOCYTOSIS
INCIDENCE/DISTRIBUTION

- LCH involves bone most commonly; about 1% of all biopsied osseous tumors
- Solitary LCH 2x multifocal LCH
- About 70% involve flat bones, most commonly skull (25%), pelvis (20%)
- In long bones, femur then humerus
- Hands and feet rare in solitary disease
LANGERHANS CELL HISTIOCYTOSIS

CLINICAL FEATURES

- About 90% are 5-15 years (average 10-12)
- Male:female about 2:1
- More than 95% of patients are white
- Most patients present with pain/tenderness
- Fever may be present and presentation may suggest osteomyelitis
LANGERHANS CELL HISTIOCYTOSIS

PATHOLOGIC FEATURES

- Characterized by a collection of histiocytes
- Histiocytes are either oval, lobulated or reniform, with clefts or indentations
- Eosinophils may be seen singly, in sheets, clusters or not at all
- Birbeck bodies on electron microscopy (EM)
Histiocytosis. Note histiocytes with reniform shape and clefts. Scattered eosinophils are seen.
Histiocytosis. EM. Note Birbeck bodies.
LANGERHANS CELL HISTIOCYTOSIS
RADIOLOGIC FEATURES

• May be permeative destruction in early phase (< 5-10 years of age patients) less aggressive over time
• “Cloaking” periosteal reaction
• More sharply delineated over time, although lesion may still be enlarging as time progresses
• Hole within a hole appearance
• Lesions may a rind of sclerosis
LANGERHANS CELL HISTIOCYTOSIS
RADIOLOGIC FEATURES

- Bone scintigraphy may not show intense radionuclide uptake
- MR marrow replacement on T1W and high signal on T2W
  - Associated surrounding edema cloaking about cortex
- Soft tissue mass 5%-10% of patients (axial skeleton and flat bones)
LANGERHANS CELL HISTIOCYTOSIS
RADIOLOGIC FEATURES

- Skull: beveled edge, button sequestrum
- Common cause of mastoid lesion
- Common cause of rib or clavicular lesions in young patients
- Spine: vertebra plana
- Mandible/maxilla: floating teeth
Skull. Beveled edge.
Skull. Beveled edge.
Skull. Button sequestrum.
Skull. Button sequestrum.
Clavicular lesion. Radiograph (top image) and macrosection (bottom image).
Vertebra.

Plana.
MRI. Spine. Single lesion. T1 weighted (left) and T2-weighted (right) images.
Floating teeth.
HAND-SCHULLER-CHRISTIAN LCH CHRONIC DISSEMINATED

- Initially described by Hand (1893), then by Schuller (1916); Christian (1920)
- Classic triad: destructive skeletal lesions, exophthalmos and diabetes insipidus
- Histologically identical to lesions of EG
- About 10% of patients with unifocal EG will develop multifocal and extraskeletal disease
Patients are young, usually less than 5 years
Classic triad in 10%-15%, <50% have diabetes insipidus, exophthalmos about 25%
Any bone may be involved, 90% have cranial involvement, 7% hand or foot lesions
Hepatosplenomegaly and adenopathy
Anemia, fever, neurologic complaints
Fatal in about 15%, morbidity may be high
LETTERER-SIWE
LCH ACUTE DISSEMINATED

• Initial reported by Letterer in 1924 (one case) and Siwe in 1933 (7 cases)
• Usually develops within the first year of life
• Disease disseminated and bone lesions small
• Symptomatology may be severe
• Fatal in about 95% of those who develop disease before 1 year of age
LANGERHANS CELL HISTIOCYTOSIS
PROGNOSIS/TREATMENT

• Benign course – observation
• May regress spontaneously
• Bisphosphonates
• Simple curettage
• Intralesional or systemic prednisone
• Large lesions/vertebral lesions may be treated with low dose radiation therapy (700-1000 cGy)
• Radiofrequency ablation
• Aggressive systemic disease with chemotherapy
Ewing Sarcoma and LCH Conclusions

- Review the imaging appearances of Ewing sarcoma and the osseous Langerhans cell histiocytosis
- Demonstrate how the radiologic images reflect the underlying pathophysiology
- Recognize appropriate differentiating features
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