SKELETAL COMPLICATIONS IN ONCOLOGY PATIENTS

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Sunrise Session

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Disclosures

- I have no commercial or financial disclosures
Learning Objectives:

- Describe MSK complications in pediatric oncology patients
- Recognize imaging features of MSK complications in oncology
- Discuss role of imaging in diagnosis and management of MSK complications in pediatric oncology
Overview

MSK Complications

Pre - RX
- pathologic Fractures
- Hemorrhage
- Joint effusion
- ALL – Osteopenia/bands

Post - RX

Chemotherapy

Radiation

Surgical
At presentation:

- Pathologic fracture
  - solid tumor
  - Low BMD
- Hemorrhage into soft tissue tumor
- Joint effusion
- Rheumatologic assessment
- NB mets
Acute Lymphoblastic Leukemia

- Most common childhood malignancy
- Improved survival (80% at 5 yrs)
- Increased skeletal morbidity
ALL 4yo – osteopenia + fracture

- Radiographic abN – 69%
  - Metaphyseal bands, lytic lesions
- Osteopenia – 25%
- Fractures – 10%
ALL

2 yo refusal to walk
Severe OP
Metaphyseal bands
Diffuse marrow replacement
Underlying etiologies?

- ALL process associated with a low bone turnover state
- Acquired GH insensitivity
- Leukemic cell secretion:
  - Osteoblast-inhibiting factor
  - Parathyroid hormone-related peptide
- Spongiosa destruction by direct infiltration of leukemic cells
- Mineral homeostasis imbalance
  - 1,25-dihydroxyvitamin D3
  - hypercalciuria
Chemotherapy

- MSK effects are not as evident as radiation
- Changing therapies
- Severity of malignancy

- Methotrexate
- Ifosfamide
- Steroids
Methotrexate

- Folic acid antagonist
- Interferes with osteoblast precursor differentiation

**Radiographic features:**
- Early: metaphyseal lucent bands
- Bone pain, “scurvy-like” changes
- Insufficiency fractures
  - Corner fractures
  - Dense ZPC (white line)
- Radiographs normalize after several months
Ifosfamide

- Alkylating agent derived from cyclophosphamide
- Nephrotoxicity by proximal renal tubule dysfunction, may be irreversible
- Risk factor: nephrectomy
- 10% hypophosphatemic rickets

Classic features:

- Loss of ZPC
- Metaphyseal cupping / flaring
- Physeal widening

Chemo for medulloblastoma
Ifosfamide - Osteopenia

- Alveolar RMS thigh
- Chemo - no rad
- Pathologic #
Glucocorticoids

- Osteonecrosis mechanism
- Osteopenia

- Early osteocyte apoptosis + increased adipocytosis
- Intraosseous pressure
- Vascular perfusion of epiphysis
Glucocorticoids

- Osteonecrosis mechanism
- Osteopenia

- Osteonecrosis risk factors:
  - Pre-Rx: acute leukemic cell infiltration
  - Adolescents
    - ?hormonal, intraosseous pressures at physeal closure
    - >16 yo with hematologic ca – more severe outcome
  - Radiation therapy
  - BMT
  - Dexamethasone > prednisolone
Osteonecrosis – What we know

- **Prevalence**
  - Up to 72% (prospective)
  - Rates lower – asymptomatic

- **Often asymptomatic until advanced**
  - 21% asymptomatic after collapse
  - Lesions >50% articular surface – consistently symptomatic

- **Lesion size correlates poorly with pain severity**
  - role for prospective monitoring
  - >30% surface = worse outcome
  - Hips: 80% of these collapse within 2 years & half need arthroplasty
Osteonecrosis

- 6 yo ALL
- Osteopenia
- Patchy sclerosis

- Poor sensitivity for early detection
- Best use in advanced disease /surgical planning
Osteonecrosis

- **Classic** features:
  - Geographic
  - Sclerotic line dark on all sequences
  - "double line" sign – T2 high intensity inner line

- **MRI**
  - Most sensitive & specific for sequences
  - T and STIR
  - Microstructural ox

- **Sag or axial**
  - Volume involved

- **Perfusion / diffusion**
  - Prelim – aim to identify ON at earlier stage
Osteonecrosis - Differential

- Disease relapse
- Metastatic disease
- Transient non-specific signal abnormalities
  - Contusion, microfracture
Steroid-induced osteopenia

- Eventually went on to path # from severe osteopenia
Radiation

- Integral role in therapy
  - definitive, adjuvant, palliative
  - Osseous tumor vs extraosseous tumor vs WBI
- Damage is dependant on multiple factors:
  - Dose –disturbances greater in younger pts
  - Fractionation –helps to reduce toxicity
  - Field size
  - Age of patient
  - Beam energy
Post Radiation Effects

- Growth disturbances

- Epiphysis is most radiosensitive
- Histologic changes at 300cGy
  - Chondrocyte swelling, fragmentation, degeneration
- Growth retardation at 400cGy
- Permanent changes above 1200cGy
- Timing:
  - 1-2 mo – growth plate widening
  - >6 mo – delayed changes
    - Cartilage degeneration, bone atrophy
    - Combination of osteocyte and vascular injury
  - 8-10 mo – joint space widening

- Location of bone irradiated
  - Metaphyseal - bowing, irregularity, premature physeal fusion
  - Diaphyseal – overtubulation due to periosteal damage
Growth disturbance - Scoliosis

- Scoliosis concave to port
- Due to asymmetric vertebral body growth & muscle fibrosis
- Worse outcome <2yo
- Field inhomogeneity
- Occurs in up to 80%
  - 40% are >20°
- Doses
  - 10-20 Gy – bone in bone within a year
  - 20-30 Gy – scalloped, endplate irregularity
- Scoliosis can occur with <15 Gy and usually after 5 years

Multiple recurrences paraspinal neuroblastoma

5 years later
Endplate Changes

Teen with paravertebral Ewing sarcoma
Growth disturbance - LLD

- Ewing
- Neoadjuvant rad
- Physeal arrest
Growth disturbance – “rickets”

- Radiation of physis
- Metaphyseal fraying
- Physeal widening
- Usually occurs within 1 yr after rad
- May also result in LLD
Physeal widening

Pre radiation

Post radiation
Growth disturbance – chest wall

- Chest – rib cage deformity, reduced lung volume
- Pelvis- iliac hypoplasia, acetabular dysplasia, coxa vara/valga
Post Radiation - growth plate injury

- SCFE
- Usually within 3 yrs
  - But can be up to 8 yrs later
- Post rad growth plate widening and “rickets-like” changes may occur without slip
- Seen at low doses
  - TBI 12 Gy

Pre teen radiation for Ewings
Radiation osteitis

- Injury to osteoblasts
- Late vascular changes
- Threshold 30 Gy
- Cell death 50 Gy
- More rare in children given modern radiation methods
- Occurs 2-3 years after rad vs sarcoma with longer latency period

- Imaging features:
  - Osteopenic
  - Coarse trabeculae
  - Patchy sclerosis

Sclerosis following rad for Ewing mets
Ewing’s

Initial study

5 years later

Post rad – short femoral neck - radiation osteitis

SCFE
Ewing’s

Pre-rad

Post-rad
Radiation osteitis & SCFE
AVN post rad for Ewing mets

- Mostly associated with steroid use
- Cases reported 1-13 years after rad
- Doses 30 – 40 Gy
Secondary Tumors

Benign
- Osteochondromas are most common
- Histologically identical to those occurring spontaneously
  - Undifferentiated cartilage migrates to metaphysis
- Osteoblastoma rare

Malignant
- >90% OSA + fibrosarcoma
- 1/3 arise in pre-existing lesions
  - GCT, Ewing, lymphoma
- Osteoradionecrosis seen in up to ½ of cases
- Differentiation between secondary and recurrent primary tumor = biopsy
Secondary tumors - osteochondroma

5 years after treatment for ovarian RMS

Initial study
Secondary tumors - osteochondroma

- WBI for BMT in ALL
- Higher rate in kids <2 at time of radiation
- Dose: 16 – 64 Gy
- Most arise within 5 years
- Prevalence higher with TBI compared to local radiation
NB mets, radiation osteitis, physeal injury and varus, osteochondroma
Secondary Tumors

- **Benign**
  - Osteochondromas are most common
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- **Malignant**
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Secondary tumors - osa

- **Criteria:**
  - Long latency (avg 11-14 yrs)
  - Arises within radiation field
  - Histologically proven sarcoma that is distinct from original lesion

- **Dose:**
  - Minimum >30 Gy
  - Kids are more susceptible

Teen with rib osteogenic sarcoma after radiation Rx for Wilms
Overlap of radiation portals

- Wilms tumor and lung met
- OSA
Normal pattern – marrow conversion

Post-radiation marrow changes

- Hematopoietic elements damaged
- Fatty replacement
- MR
  - Increased STIR signal (1-2 weeks)
  - Later: increased T1
  - Complete fatty conversion (6-8wks)

- Marrow regeneration more likely in kids
  - Dose <30 Gy likely
    - >50 Gy - irreversible
  - Time – 1-2 years

Ewing’s sarcoma
Post Chemotherapy - marrow

- MR: within days - high T2 signal & low T1
  - Hematopoietic cell ablation with BME
- Later:
  - Marrow recovery back to normal pattern
  - Fatty or fibrotic replacement
G-CSF

- Hematopoietic growth factor
- Reduce treatment complications
- Allows more intensive chemotherapy
- Typically delivered for 10-14 d after a cycle

MRI:
- Reconversion: fatty → red marrow
- Various patterns: homogeneous & diffuse vs patchy
- Low T1, mild increased STIR
G-CSF Effects

ALL, end consolidation, BMA

Few months later... pattern resolved
G-CSF Effects

- May simulate metastatic disease
  - Foci can be active on bone scan
  - Foci can mildly enhance on MRI
Post surgical complications

- 90% limb salvage techniques
- Tumor recurrence rate similar in both

Surgery (25%)
- Adjuvant chemo (33%)

Amputation
- Neoadjuvant chemo + surgery with large cement mantle (82%)

McDonald et al.
Limb salvage

- Most common complication = infection
Limb salvage

- Hardware failure
  - Non-union
  - Loosening of implant results in micromotion
  - Abnormal cyclic loading
Limb salvage

- Rotationplasty – 4mo post op OSA
- Severe osteopenia
- Insufficiency fracture
Limb salvage- graft failure

Teen OSA, VFG, slow healing proximally, fracture 4m after hardware removal
Limb salvage - graft failure
Pseudocomplication

- Familiarity with large variety of endoprosthesis used
Amputation - stump neuroma
Osteomyelitis - Ewing
Summary:

- Child
- Presentation
- Inactivity
- Peak bone mass
- Surgery
- Fracture
- BMT
- Chemo
- Radiation
THANK YOU!