Paget Disease

Mark D. Murphey, MD, FACR

Paget Disease: Clinical Characteristics
- Described in 1877 by Sir James Paget
- Osteitis deformans
- Common disease (some researchers believe it is decreasing in frequency by up to 50%)
  - 3%–4% over age 40
  - 10% over age 80
- More common in men (3:2 ratio)
- Common in Great Britain and descendents (US, Australia)
  - Also continental Europe
- Uncommon in Asia and Africa
- Many patients asymptomatic (20%)
- Tendency to increase in age, decrease in severity, more monostotic

Paget Disease: Clinical Presentation
- Pain (11%–54%)
- Osseous bowing and enlargement
- Neurologic symptoms
- High output congestive failure
- Lab
  - Serum alkaline phosphatase (blastic phase)
  - Urinary and blood hydroxyproline (lytic phase)

Paget Disease: Etiology
- Unknown
- Possible etiologies
  - Infection: slow virus theory
  - Intranuclear inclusions: paramyxovirus (measles)
  - Autoimmune
  - Connective tissue disease
  - Genetic
  - Neoplastic

Paget Disease: Pathology
- Initially osteoclastic resorption
- Subsequently osteoblastic response (active)
  - Excessive and disorganized
  - “Mosaic” or “jigsaw” pattern
  - Marrow: fibrovascular reaction
  - Marrow: fat (inactive)

Paget Disease: Skeletal Distribution
- Calvarium, spine (lumbosacral), and pelvis (25%–75%)
- Proximal long bones (25%–30%)
- Humerus (31%), scapula (24%), clavicle (11%)
- Initially monostotic (10%–35%) most polyostotic (65%–90%)

Paget Disease: Radiologic Evaluation
- Radiographs: diagnosis
- Bone scan: assess areas involved
- CT/MRI: assess complications or unusual cases

Figure 1 A & B
Marrow replacement by fibrovascular tissue in active Paget disease (left image) versus fat in marrow with inactive disease (right image).

Figure 2
Paget disease: skeletal distribution.
Paget Disease: Radiologic Stages
- Active
  - Lytic: osteoclastic activity
  - Mixed: majority of cases
- Inactive
  - Mixed: majority of cases
  - Blastic: osteoblastic activity
- Usually progresses through these phases but not always
  - Recrudescent lytic phase in patients at rest; simulates tumor

Paget Disease: Radiologic Lytic Phase
(Figures 3 to 5)
- Skull: large well-defined areas; involve both inner (more prominent) and outer tables of frontal/occipital bones (osteoporosis circumscripta) and cross suture lines
- Long bones: subchondral location with advancing wedge/“V” shape – “blade of grass”/“candle flame” appearance

Paget Disease: Radiographs – Mixed/Blastic Disease
- Sclerosis and lucency
- Trabecular and cortical thickening
  - Along the lines of stress
  - But some disorganization
- Bone enlargement

Paget Disease: Radiographs – Mixed/Blastic Disease
(Figures 6 to 9)
- Skull: “cotton-wool” appearance obscures inner and outer tables (“tam-o-shanter”), often spares facial bones
- Spine: vertebral body “picture frame” – ivory vertebral body; posterior elements may be involved

Figure 3 A, B, C & D
Pictorial representations of skeletal distribution of Paget disease in the skull (osteoporosis circumscripta) and long bone (“blade of grass” appearance).

Figure 4 A & B
Osteoporosis circumscripta with sharply margined large area of bone lysis.

Figure 5 A & B
Lytic phase of Paget disease with sharp margins and subchondral extension.

Figure 6
“Cotton-wool” appearance on radiograph with multifocal areas of sclerosis and thickening of the diploic space anteriorly.
Ivory Vertebral Body: Differential Diagnosis

- Blastic metastasis: breast, prostate, adenocarcinoma gastrointestinal (GI) tract, carcinoid, transitional cell carcinoma bladder
- Lymphoma
- Chronic infection
- Chordoma

Paget Disease: Radiographs – Mixed/Blastic Phase

- Pelvis: asymmetric involvement
  - Thickened iliopectineal line
  - Enlarged pubic rami and ischium
- Long bones: epiphyseal involvement
  - Rarely diaphyseal (tibia)
  - Enlarged bone

Figure 9 A & B
Ivory vertebral body in Paget disease on radiograph and intense uptake on radionuclide bone scan.

Figure 10
Paget disease with coarsened trabecular pattern and thickening of the iliopectineal line involving the entire hemipelvis.

Figure 7 A to F
Mixed lytic/blastic Paget disease in skull with diploic space expansion and hyperemic bone on CT, gross specimen, and histology.

Figure 8 A & B
“Picture frame” appearance of Paget disease of the spine (multiple levels) on radiograph and coronal macrosection.
Paget Disease: Bone Scintigraphy
- Active disease: marked uptake
  - Dynamic and static images
- Abnormal before radiographs
- Overview of disease: look at distribution
- Monitor disease and therapy

Paget Disease: CT/MRI Noncomplicated Disease
- Not usually needed for diagnosis
- CT: thickened trabeculae
  - Bone enlargement
  - Lytic areas

Paget Disease: MRI Noncomplicated Disease
- T1-weighted images
  - Cortical and trabecular thickening
  - Enlarged bone
  - Low signal (sclerosis)
  - Yellow marrow/fat (inactive disease)
  - Heterogeneous signal (active disease)
  - Marrow replacement nonmasslike
- T2-weighted images
  - Low signal (sclerosis)
  - Fat signal intensity (inactive disease)
  - Heterogeneous intermediate/high signal (fibrovascular marrow – active disease)
  - No focal mass (marrow or soft tissue)
Paget Disease: Osseous Deformity
[Figure 19]
- Effects of bone softening
- Bowing common in long bones
- Acetabuli protrusio
- Basilar invagination – 30% of patients with skull involvement

Paget Disease: Fractures
[Figure 20]
- Partial or complete (insufficiency)
- True acute fractures
- Horizontal lucencies (“banana fracture”)
- Convex surface of bone
- Single or multiple
- Often symptomatic
- Sites: femur, humerus, pelvis
- Spine: central compressions
- May heal but high nonunion rate
- At risk for sarcoma (biopsy?)

Paget Disease: Neurologic Symptoms
[Figure 21]
- Symptoms: impingement of cranial and spinal nerves (spinal stenosis 33%)
- Caused by skull and spine involvement (hydrocephalus)
- Bone enlargement, fractures, bone softening with basilar invagination
- Increased osseous vascularity with cord hypoxia also vertebrobasilar insufficiency
- CT/MRI for evaluation

Paget Disease: Complications
- Osseous deformity
- Fractures
- Neurologic symptoms
- Arthropathy
- Neoplasm
Paget Disease: Arthropathy
- Rheumatic diseases with poor association: rheumatoid arthritis, calcium pyrophosphate deposition (CPPD), ankylosing spondylitis
- Gout: higher incidence hyperuricemia (40%) from increased cell turnover
- Osteoarthritis
  - Hip and knee most common
  - Abnormal mechanics from deformity
  - Bone weakening
  - Hip narrowing can be axial
- Soft tissue calcification
  - Tendinopathy with vitamin D treatment

Paget Disease: Neoplasm
- Sarcomatous transformation
  - 1% of patients with Paget disease
  - 5%-10% of patients with extensive disease
- Patients 55–80 years old
- Common sites: femur, pelvis, humerus
- Osteosarcoma (50%-60%)
- Malignant fibrous histiocytoma (MFH)/Fibrosarcoma (20%-25%)
- Chondrosarcoma (10%)
- Lymphoma and angiosarcoma (1%-3%)
- Giant cell tumor (GCT)
- Metastasis, myeloma, leukemia

Paget Disease: Neoplasm – Radiology
[Figures 22 to 24]
- Bone destruction predominates
- Cortical involvement and soft tissue mass
- No periosteal reaction
- Persistent nonhealing fracture
- Compare with old radiographs
- Bone scan: photopenic area
- Gallium scan: increased uptake
- MRI
  - T1-weighted: masslike marrow replacement
  - T2-weighted: focal mass of high intensity
  - Soft tissue mass
Paget Disease: Neoplasm
- GCT: skull or facial bones
  - More often benign
  - Rarely multiple (familial)
  - Lytic expansile lesion
- Metastasis: likely related to hyperemia

Hereditary Hyperphosphatasia: Juvenile Paget Disease
- Described in 1956 by Bakwin/Eliger
- Autosomal recessive
- Disorder of infants/children
- Elevated alkaline and acid phosphatase, uric acid

Juvenile Paget Disease: Radiographic Findings
- Generalized cortical thickening
- All bones including skull involved
- Osteopenia and bowing
- Epiphyses may be spared
- Patients severely deformed

Paget Disease: Differential Diagnosis
- Diffuse sclerosis: chronic renal failure (CRF), myelofibrosis, metastasis, lymphoma, sickle cell anemia
- Trabecular thickening: hemangioma, chronic infection, osteomalacia, fluorosis
- Polyostotic lesions: CRF (hyperparathyroidism), Langerhans cell histiocytosis, unusual infection, metastasis, fibrous dysplasia, lymphoma, Gaucher disease, mastocytosis

Paget Disease: Treatment
- Calcitonin: inhibits resorption
- Bisphosphonates: inhibits bone resorption and production; may restore bone histology/radiology
- Mithramycin: cytotoxic antibiotic
- Often relieve pain

Paget Disease: Summary
- Common disease: 3%–4%
- Diagnosis: radiographs
  - Lytic: well-defined, subchondral (“V” or wedge shape – “candle flame” appearance)
  - Thickened trabeculae and cortex
  - Osseous enlargement
- Bone scan: overview
- Complications: fracture, osseous deformity, neurologic symptoms, arthritis, neoplasm
- CT/MRI used to evaluate complications
- CT/MRI: noncomplicated case
  - Bone enlargement
  - Trabecular thickening
  - T1-weighted: low signal (sclerosis), yellow marrow, heterogeneous nonmasslike marrow replacement
  - T2-weighted: low signal (sclerosis), yellow marrow, heterogeneous high signal, no focal mass
- CT/MRI: complicated case
  - CT: focal bone destruction/soft tissue mass
  - T1-weighted: masslike marrow replacement
  - T2-weighted: focal mass in marrow with high signal and soft tissue mass

Paget Disease: Radiology Posttreatment
- Often subtle or no change
- Occasionally improved radiographs
- Watch for fractures: may increase with bisphosphonates
- Bone scans are best treatment indicator
References