Plasmacytoma

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Our Index Patient - Y.B.

• YB is a 43yo F with unremarkable past medical history
• Presented to her PCP in complaining of lower back/left hip pain after a fall on the ice. Pain did not respond to conservative management with NSAIDs
• Over two months her symptoms progressed. Pain was severe, associated with left leg parasthesias and shooting radicular pain. Walking became difficult.
• She presented to the BIDMC ED where L-spine plain films were taken
# Differential Diagnosis: Low back pain

<table>
<thead>
<tr>
<th>Mechanical (97%)</th>
<th>Visceral (2%)</th>
<th>Miscellaneous (1%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lumbar strain</td>
<td>Endometriosis</td>
<td>Multiple myeloma</td>
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<tr>
<td>Degenerative disks disease</td>
<td>Nephrolithiasis</td>
<td>Metastatic disease</td>
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<td>Herniated disk</td>
<td>Pyelonephritis</td>
<td>Lymphoma and leukemia</td>
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<td>Spinal stenosis</td>
<td>Aortic aneurysm</td>
<td>Spinal cord tumors</td>
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<td>Compression fracture</td>
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<td>Osteomyelitis</td>
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- Ankylosing spondylitis
- Paget's disease

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"Red flags" for a potentially serious underlying cause for low back pain

- Recent significant trauma
- Unexplained weight loss/fever
- Immunosuppression
- History of cancer
- IV drug use
- Osteoporosis
- Age >70
  - Focal neurologic deficit
  - Progressive or disabling symptoms
  - Duration greater than 6 weeks
Pelvic Skeletal Anatomy Review

Gray’s Anatomy
www.bartleby.com
YB: Plasmacytoma on L-Spine Plain Radiograph

- Well circumscribed radiolucent/lytic lesion at left sacroiliac joint
- Partially obscured by overlying bowel gas
Differential Diagnosis: Lytic Bone Lesions

- F fibrous dysplasia
- O osteoblastoma
- G giant cell tumor
- M metastasis/multiple myeloma
- A aneurysmal bone cyst
- C chondroblastoma
- H hyperparathyroidism – brown tumor
- I infection
- N non-ossifying fibroma
- E enchondroma/eosinophilic granuloma
- S solitary bone cyst
BONE TUMORS

How can we narrow this differential? Let’s quickly review the key principles in approaching bone tumors:
How to Approach Bone Lesions

1. Age of patient
2. Location/distribution of tumor
3. Margins
4. Periosteal reaction
5. Opacity/Mineralization
6. Number of lesions
7. Soft tissue component
Age of Patient and Bone Lesions

- **<20**
  - Simple bone cyst
  - Aneurysmal Bone Cyst
  - Osteoblastoma
  - Osteoid Osteoma
  - Osteochondroma (exostosis)
  - Fibrous dysplasia
  - Eosinophilic granuloma

- **20-40**
  - Enchondroma
  - Giant cell tumor
  - Chondroblastoma

- **40 and above**
  - Paget’s Disease
  - Myeloma
  - Lymphoma
  - Chordoma
  - Malignant Fibrous Histiocytoma
  - Chondrosarcoma
  - Metastasis
    - Lytic
      - Kidney
      - Lung
      - Colon
      - Melanoma
      - Thyroid
    - Blastic
      - Breast
      - Prostate
Common Skeletal Sites of Bone Tumors

**Hands and Feet**
- Multiple Myeloma
- Enchondroma

**Axial Skeleton**
- Metastatic disease
- Lymphoma
- Chordoma

**Long Bones**

**Epiphysis**
- Chondroblastoma
- Giant Cell Tumor

**Metaphysis**
- Osteosarcoma
- Chondrosarcoma
- Fibrosarcoma
- Osteoblastoma
- Fibrous Dysplasia
- Bone Cyst
- Aneurysmal Bone Cyst

**Diaphysis**
- Non Ossifying Fibroma
- Osteochondroma
- Ewing’s
- Lymphoma
- Myeloma
- Fibrous Dysplasia
- Enchondroma
- Osteoid Osteoma

http://chs.westport.k12.ct.us/mjvl/anatomy/skeletal/femur.jpg

http://chs.westport.k12.ct.us/mjvl/anatomy/skeletal/femur.jpg
Periosteal Reactions & Tumor Margins

- Periosteal Reaction: appearance of the periosteal reaction can indicate aggressive behavior of a bony lesion
  - i.e. onion peel, Codman’s Triangle, sunburst patterns.

- Margins
  - **Geographic**: sharp margin and narrow transition zone
  - **Moth Eaten/Permeative**: small, ill-defined areas of bone destruction

Lesion Opacity, Mineralization, Number, and Tissue Component

- Opacity: mixed, lytic, sclerotic
- Mineralization: pattern can indicated tissue of origin
  - Cartilage - arc like mineralization
  - Bone - fluffy/cloudlike
- Number: primary bone tumors tend to be solitary
- Soft tissue component: suggests a malignancy
RETURNING TO OUR PATIENT: YB
Narrowing the Differential

• Given our discussion, we can narrow our differential for YB

The most common causes of a lytic lesion of the axial skeleton in a 43 year old patient are:

M metastasis/multiple myeloma

In our patient YB, the cause of her lytic pelvic lesion is a related condition called Plasmacytoma

PACS, BIDMC
Multiple Myeloma

- Clonal B-cell neoplasm
- Bone destruction caused by increased osteoclastic bone resorption
- Up to 90% of myeloma patients have lytic bone lesions
  - Usually of axial skeleton and proximal aspects of long bones
- Patients usually present with fatigue and bone pain, as well as hypercalcemia and renal insufficiency due to effect of monoclonal light chains in renal tubules
- Laboratory abnormalities include:
  - Monoclonal M protein (usually IgG)
    - >3g/dl in serum and 1g/24h in urine
    - >10% abnormal plasma cells in bone marrow biopsy
- Treatment
  - corticosteroids, chemotherapy (thalidomide-based) and bisphosphonates, local radiation, vertebroplasty/kyphoplasty, stem cell transplant
Plasmacytoma

• “Plasmacytoma” is a solitary plasma cell tumor without evidence of systemic spread by serum/marrow analysis or imaging
  – Bone marrow plasma cell infiltration ≤10%
  – No additional osteolytic bone lesions
  – No anemia, hypercalcemia, or renal disease caused by myeloma
  – Low concentrations of serum/urine monoclonal proteins
  – Normal immunoglobulin levels

• 50 – 60% patients will develop MM, most in three years or less

• YB’s Data
  – Bone marrow biopsy showed 10% plasma cells
  – Serum IgG kappa M protein spike of 2200mg/dL
  – Urine light chains 260mg/day
  – These findings are consistent with her diagnosis of plasmacytoma
Staging of Multiple Myeloma

• Durie & Salmon

Based on amount of:
1. M protein
2. Serum Hb
3. Serum Ca
4. Renal function
5. Number of lytic bone lesions by skeletal survey

• Durie & Salmon PLUS

<table>
<thead>
<tr>
<th>Classification</th>
<th>Whole body MRI and/or PET</th>
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<tr>
<td>MGUS</td>
<td>Negative</td>
</tr>
<tr>
<td>Stage IA</td>
<td>Normal skeletal survey or one lesion (smouldering)</td>
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<tr>
<td>Stage IB</td>
<td>&lt; five focal lesions or mild diffuse disease</td>
</tr>
<tr>
<td>Stage IIA/B</td>
<td>5-20 focal lesions or moderate diffuse disease</td>
</tr>
<tr>
<td>Stage IIIA/B</td>
<td>&gt;20 focal lesions or severe diffuse disease</td>
</tr>
</tbody>
</table>
Imaging Options in Multiple Myeloma

- Skeletal Survey
- CT
- MRI
- Bone Scan
- PET scan
- Interventional Procedures
  - Biopsy
  - Vertebroplasty/Kyphoplasty
Let’s Review Some Examples Of these Imaging Modalities in Our Patient and Several Companion Patients
Role of Skeletal Survey In Multiple Myeloma

- "Standard" for staging and follow-up of bone involvement in MM
  - Frontal and lateral skull
  - Cervical, thoracic, and lumbar spine
  - Frontal rib cage, humeri, femura, knees, pelvis

- Advantages
  - Does not require potentially nephrotoxic contrast

- Disadvantages
  - Can only reveal lytic disease when significant amount of bone is lost (30% of cancellous bone)
  - Requires multiple views and uncomfortable positioning
  - Involvement of vertebral bodies difficult to assess
    - In one study 50% of patients with MRI-proven vertebral disease had negative plain films
    - Lytic bone lesions on skeletal survey do not regress with response to treatment
In our patient, the normal skeletal survey is consistent with diagnosis of plasmacytoma.
Companion Patient #1:
Lytic Lesions Of Multiple Myeloma On Skeletal Survey

Multiple lytic lesions of skull

“Scalloped” erosions into cortical bone
The Role of CT in Multiple Myeloma

- Gold standard for detecting the stability of bone and predicting risk of fracture
  - Spinal compression fractures occur in up to 70% of patients with MM

- **Advantages**
  - Very sensitive for the detection of small lytic lesions (<5mm)
  - Rapid acquisition of full body imaging without need for repositioning

- **Disadvantages**
  - Increased exposure to radiation compared to other modalities
Our Patient YB:
Plasmacytoma On Pelvic CT

Findings:
Large left sacral mass with extension into SI joint/iliac bone, paraspinal muscles. Mass is of homogenous soft tissue density. Infiltrative process highly suspicious for malignancy.
Our Patient YB:
CT Of Pathologic Fracture

- YB was getting into bed and while rolling onto her right side she heard a “crack” and complained of severe pain. Urgent repeat imaging showed the following:

Prior Axial CT Pelvis, C-

Pathologic fracture
MRI Findings of Multiple Myeloma

- Most sensitive method to detect myeloma and related conditions such as plasacytoma
- MRI marrow infiltrates are displayed before osseous destructions occur
- Can be used to determine exact location/size of lesions, sites of marrow involvement, and response to treatment
  - Chemotherapy will cause reduction in T2 signal intensity and reduced contrast enhancement on MRI
- Frequently used sequences
  - T1: hypointense lesion in hyperintense marrow
  - T2/STIR: hyperintense lesion in hypointense marrow
  - Fat-suppression: improves visualization of marrow involvement
  - Gadolinium: MM involved marrow enhances post contrast

- Age of patient must be taken into account when determining normal marrow characteristics. Ex: older patients have a higher percentage fatty marrow
Our Patient YB: MRI Of Pelvic Plasmacytoma

- **FINDINGS:**
  5cm x 5cm lesion of left sacrum.
  Involvement of S1-S3 nerve roots as well as paraspinal musculature by soft tissue component. No additional foci of involvement or primary site identified in pelvis.
Our Patient YB: Plasmacytoma on MRI Sequences
T1 Hypointense, T2 Hyperintense, Post Contrast Enhancement

* Plasmacytoma

Axial T1 MRI, C-

Axial T1 MRI, C-

Axial T2 MRI, C-

Axial T1 MRI, C+

All images PACS, BIDMC
Patterns of Multiple Myeloma Bone involvement

• Solitary lesion (plasmacytoma)
• Focal destruction by tumor nodules
  – Arise from the inside (cancellous bone) giving a “scalloped” appearance as they erode the cortical bone
• Diffuse bone marrow involvement
  – Normal marrow completely replaced by disease process
  – Can have salt-and-pepper appearance if less than 20% plasma cells
  – Can present as severe osteoporosis
• Extraosseous soft tissue myeloma
  – Usually in nasopharyngeal area
  – Soft tissue involvement either by extraosseous disease or extension from a bone indicates a poor prognosis
Companion Patient #2:
Multiple Myeloma Bone Marrow Involvement On MRI

Diffuse heterogeneous abnormal signal in bone marrow
- Lesions are T1 hypointense and T2 hyperintense
Companion Patient #3:
Extraocceous Plasmacytoma ON MRI

- Nasaopharynx and nasal cavity soft tissue mass, identified on pathology as plasmacytoma
- Skeletal survey for this patient was negative
Use of Bone Scan in Multiple Myeloma

- 99m Techetium labeled diphosphonate compounds incorporated into forming bone
- Insensitive in multiple myeloma and plasmacytoma because there is no increased osteoblastic activity (unlike in bone metastasis of most tumors)
- Lesions seen on bone scan are frequently complications of multiple myeloma
  - i.e. Osteoblastic response to compression fracture
Our Patient YB:
Plasmacytoma On Bone Scan

Large photopenic lesion of left sacrum.
Let’s View Some Cases Of Patients with Similar Radiographic Findings
What other conditions can mimic multiple myeloma and plasmacytoma?
Companion Patient #4: Lung Metastasis on CT and Bone Scan

Lytic lesion in vertebral body, similar to those seen in our plasmacytoma patient YB

"Hot" focus of increased tracer uptake on bone scan
Companion Patient #4: Primary Lung Tumor On CT

Cause of lytic lesion and bone scan abnormality, primary lung tumor, can be seen on further chest imaging.
Companion Patient #5:
Thyroid Metastasis on CT and Bone Scan

Multiple lytic lesions throughout pelvis, could this be a case of multiple myeloma?

Areas of decreased tracer uptake in sarcum and left hemi pelvis.

“Cold” lesions on bone scan, similar to those seen on our plasmacytoma patient YB’s bone scan.
Companion Patient #5:
Thyroid Primary Tumor Revealed As Cause of Lytic Lesions on Further Imaging

CT revealed hypodense nodule in left lobe of thyroid gland

Thyroid ultrasound showed large hypoechoic left thyroid lobe nodule that was hypervascular on color Doppler, suspicious for neoplasm.
FDG Tumor Imaging/PET Scan and Multiple Myeloma

- PET uses positron emission by 18-fluorine-fluoro-deoxyglucose to detect tumors with high metabolic activity
- Has been shown to be more sensitive than plain radiographs and can detect additional missed lesions
- Can localize sites of extraosseous disease
- Main limitation is spatial resolution
  - Cannot detect lytic lesions < 1cm
  - PET/CT imaging reduced this limitation
- FDG uptake is usually reduced after successful chemotherapy or stem cell transplant
Finally, Let’s Discuss the Role of Image Guided Interventions in Multiple Myeloma and Plasmacytoma
Companion Patient #6
Vertebroplasty for Compression Fracture

Although companion patient #6 does not have multiple myeloma, vertebroplasty can also be used to alleviate pain associated with vertebral compression fractures in multiple myeloma.

Under fluoroscopic guidance a small amount of cement (PMMA) or polymethylmethacrylate is injected into vertebral body. Cement is mixed with radio-opaque substance such as barium to allow it to be seen on x-ray.
Our Patient YB:
CT-Guided Biopsy Of Plasmacytoma

CT guidance has led to a 20% increased yield for positive cytology when compared to random iliac crest biopsies in multiple myeloma.

In YB’s case - Pathology revealed findings similar to the following:

http://www2.umdnj.edu/pathpweb/images/myeloma_smear.jpg
Companion Patient #7: Ct-Guided Biopsy of Renal Cell Metastasis

Lytic lesion of left sacrum of unknown etiology. Patient referred for IR guided biopsy. CT abdomen/pelvis reveals prior nephrectomy for distant RCC. Pathology showed metastatic renal cell carcinoma.
Goals of Radiologist in Multiple Myeloma

1. Determine extent of skeletal involvement
2. Supply information for staging
3. Assess stability of involved bones and risk for fracture
4. Perform pain relieving procedures
5. Assess treatment response
Update on Patient YB: She Is Currently Receiving Radiation Therapy to Plasmacytoma Site and has Achieved Good Pain Relief
Conclusions: What Lessons to take away from the case of YB

- Tumor metastasis are much more common than multiple myeloma/plasmacytoma, but the two occur in the same patient population and can be difficult to distinguish

- Factors in favor of MM include:
  - Sharply delineated lytic lesions of skull and long bone diaphysis
  - Scalloping (erosion of long bone from inner surface)
  - Negative bone scan or “cold” lesions
  - No primary tumor site evident
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References

• Dimopoulos M et al. International myeloma working group consensus statement and guidelines regarding the current role of imaging techniques in the diagnosis and monitoring of multiple myeloma. Leukemia advance online publication 2009 May 7.