From Chest Pain to Multiple Myeloma: Radiology in Practice

Mekeme Utuk, Harvard Medical School Year III
Gillian Lieberman, MD
Our Patient – RB

• RB is a 58yoM with no significant PMH presented to PCP with 2 weeks of vague upper chest pain with some SOB.
## Chest Pain Differential Diagnosis

<table>
<thead>
<tr>
<th>Cardiovascular</th>
<th>Pulmonary</th>
<th>Musculoskeletal</th>
<th>Gastrointestinal</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>– <em>Myocardial ischemia (angina/MI)</em></td>
<td>– Pneumonia</td>
<td>– Cervical or thoracic disc disease or arthritis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>– <em>Pericarditis</em></td>
<td>– Pleuritis</td>
<td>– Shoulder arthritis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>– Aortic stenosis</td>
<td>– Bronchitis</td>
<td>– Costochondritis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>– <em>Pulmonary Embolism</em></td>
<td>– (*Tension) Pneumothorax</td>
<td>– Subacromial bursitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>– <em>Aortic dissection</em></td>
<td>– Tumor</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myocarditis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>– Mitral Valve Prolapse</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>– Pulmonary Hypertension</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>– Right ventricular hypertrophy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pulmonary</th>
<th>Gastrointestinal</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>– Pneumonia</td>
<td>– <em>Esophageal rupture</em></td>
<td>– Anxiety/panic attack</td>
</tr>
<tr>
<td>– Pleuritis</td>
<td>– GERD</td>
<td>– Herpes zoster</td>
</tr>
<tr>
<td>– Bronchitis</td>
<td>– Esophageal spasm</td>
<td>– Breast disorders</td>
</tr>
<tr>
<td>– (*Tension) Pneumothorax</td>
<td>– Peptic Ulcer Dz</td>
<td>– Chest wall tumor</td>
</tr>
<tr>
<td>– Tumor</td>
<td>– Biliary Disease</td>
<td>– Thoracic outlet syndrome</td>
</tr>
<tr>
<td></td>
<td>– Pancreatitis</td>
<td>– Mediastinitis</td>
</tr>
</tbody>
</table>

* = “Don’t miss” diagnosis!!
Back to RB

- PCP initially attributed pain to costochondritis.
- Pain was refractory to NSAIDs.
- An outpt stress test was performed, which was normal.
- Pain persisted for several more days and spread to mid-back.
- Pt went to his local ED, where a CTA was performed to rule out a pulmonary embolism.
Computed Tomography Angiography (CTA)

- Fast, simple, noninvasive technique that provides images with excellent spatial resolution and good soft tissue contrast.
- Using a single contrast medial bolus injection, CTA allows for complete visualization of the entire aorta and its branches.
- The imaging modality of choice in the evaluation of patients with suspected pulmonary embolus.
Review: Great Vessels on CTA

Axial CT+, Arterial Phase

DesA=Descending Aorta
UpLB-L=Left Upper Lobe Bronchus
PA-L=Left Pulmonary Artery
PA-M=Pulmonary Artery Trunk
AscA=Ascending Aorta
SVC=Superior Vena Cava
PA-R=Right Pulmonary Artery
MB-R=Right Main Stem Bronchus
AZY=Azygos Vein

http://www.e-radiography.net/technique/chest/Chest_t4_labelled_medastinum_ct.jpg
Companion Patient #1: PE on CTA

- Unenhanced CT scan demonstrates subtle regions of hyperattenuation.

- Confirmatory CT pulmonary angiogram demonstrates acute pulmonary embolism within the right main and left interlobar pulmonary arteries.

http://radiographics.rsna.org/content/31/5/1425.full.pdf+html
RB’s OSH CTA: No PE found

PACS, BIDMC
Axial CT+, Arterial Phase
• To recap, tests RB has had:
  – Stress test: normal
  – CTA: no pulmonary embolus

• However, other views on CTA did find something significant.
RB’s OSH CTA

Lytic bone lesion: T4 compression fracture

Sagittal view, pre-contrast

Coronal view, post-contrast
Our Patient: Hospital Course

• With the lytic bone lesion seen on CTA, RB was diagnosed with a T4 compression fracture, and transferred to BIDMC for further workup.
## Narrowing the CP Differential

### Cardiovascular:
- *Myocardial ischemia (angina/MI)*
- *Pericarditis*
- Aortic stenosis
- *Pulmonary Embolism*
- Aortic dissection
- Myocarditis
- Mitral Valve Prolapse
- Pulmonary Hypertension
- Right ventricular hypertrophy

### Pulmonary:
- Pneumonia
- Pleuritis
- Bronchitis
- (*Tension) Pneumothorax
- Tumor

### Gastrointestinal:
- *Esophageal rupture*
- GERD
- Esophageal spasm
- Peptic Ulcer Dz
- Biliary Disease
- Pancreatitis

### Musculoskeletal:
- Cervical or thoracic disc disease or arthritis
- Shoulder arthritis
- Costochondritis
- Subacromial bursitis

### Other:
- Anxiety/panic attack
- Herpes zoster
- Breast disorders
- Chest wall tumor
- Thoracic outlet syndrome
- Mediastinitis

* = “Don’t miss” diagnosis!!
Lytic Bone Lesion DDx

FOG MACHINES:

| F | = Fibrous Dysplasia |
| O | = Osteoblastoma    |
| G | = Giant Cell Tumor |
| M | = Metastasis/Myeloma|
| A | = Aneurysmal Bone Cyst|
| C | = Chondroblastoma  |
| H | = Hyperparathyroidism (brown tumors) / Hemangioma |
| I | = Infection        |
| N | = Non-ossifying Fibroma |
| E | = Eosinophilic Granuloma / Enchondroma |
| S | = Solitary Bone Cyst |
Let’s take a step back and review how to approach bone lesions in general.
A Simple Approach to Bone Lesions

- Age
- Location
- Margins
- Periosteal Reaction
- Matrix
- Number
- Soft Tissue
Bone Lesions by Age

Our Patient: 58yo

http://www.radiologyassistant.nl/en/494e15cbf0d8d
Bone Lesions by Location

- Our Patient: T4 lesion

http://www.radiologyassistant.nl/en/494e15cbf0d8d
Bone Lesions by Margins and Periosteal Reaction

• **Margin**: helps indicate whether a lesion is benign or malignant
  - **Geographic**: well-defined margin from normal bone; usually benign
  - **Moth-Eaten**
  - **Permeative**: most aggressive; poorly demarcated; usually malignant

Burgener, et al. Bone and Joint Disorders. 2nd Ed.

• **Periosteal Reaction**: non-specific reaction that occurs whenever bone is irritated (e.g. by tumor, trauma, infection)

http://www.radiologyassistant.nl/en/494e15cbe0d8d
Bone Lesions by Matrix

• **Matrix:**
  – Opacity:
    • Lytic (black)
    • Sclerotic (white)
    • Mixed
  – Calcification pattern: gives clues regarding the lesion’s tissue of origin
    • **Osteoid matrix:** “cloud-like”
    • **Chondroid matrix:** “arcs and rings”
Bone Lesions by Number and Soft Tissue

- **Number**
  - Most bone tumors are solitary
  - Multiple osteolytic lesions-
    - **FEEMHI:**
      - Fibrous dysplasia
      - Enchondromas
      - Eosinophilic Granuloma
      - Metastases and myeloma
      - Hyperparathyroidism
      - Infection

- **Soft tissue involvement generally indicates aggressive lesions (i.e. malignant)**
Our Patient: Narrow the DDx

- 58yoM
- T4 compression fracture

| F  | = Fibrous Dysplasia |
| O  | = Osteoblastoma     |
| G  | = Giant Cell Tumor  |
| M  | = Metastasis/Myeloma|
| A  | = Aneurysmal Bone Cyst |
| C  | = Chondroblastoma   |
| H  | = Hyperparathyroidism (brown tumors) / Hemangioma |
| I  | = Infection         |
| N  | = Non-ossifying Fibroma |
| E  | = Eosinophilic Granuloma / Enchondroma |
| S  | = Solitary Bone Cyst |
• After being transferred to BIDMC, RB had more imaging done.

Let’s review some spinal anatomy, and then continue with RB’s findings.
Review: Spinal Anatomy

http://www.trialsightmedia.com/exhibit_store/images/thoracicspine.jpg

Axial T1 MRI, pre-contrast
PACS, BIDMC


Lumbar MRI showing spinal stenosis at L3-4 level due to disc herniation

Sagittal T1 MRI
Our Patient: Spinal MRI

- Pathologic fracture at T4 level with compression of the vertebral body and retropulsion and enhancing epidural and paraspinal soft tissue.
- Spinal canal is narrowed by ~50%
- No other areas of bony abnormalities

All images  PACS, BIDMC
Our Patient: Additional workup

- RB also had a CT chest, abdomen, and pelvis to look for a primary tumor.
- No primary tumor was found.
- Up to date on all age-related cancer screenings (colon, prostate)
- Thus, diagnosis is likely myeloma, not metastasis
Multiple Myeloma: Facts

• Neoplastic proliferation of a single line of plasma cells that make a monoclonal immunoglobulin.
• Increased incidence >50yo, African Americans
• Unclear etiology
  – It is known that neoplastic plasma cells release osteoclast activating factor, which causes the stereotypical osteolytic lesions
• Clinical features:
  – Bone pain, fractures, and vertebral collapse secondary to osteolytic lesions
  – Pathologic fractures
  – Hypercalcemia
  – Anemia (2/2 bone marrow infiltration)
  – Renal failure (2/2 hypercalcemia and immunoglobulin precipitation in renal tubules, which causes Bence-Jones protein casts)
  – Recurrent infections (2/2 decreased humoral immunity)
    • 70% of MM patients will die of infection (usually lung or urinary tract)
Multiple Myeloma: More Facts

• **Treatment**
  – Indications: hypercalcemia, bone pain, spinal cord compression
  – General treatment plan:
    • Systemic CTX
    • Radiation therapy (if no response to CTX, or disabling pain)
    • Autologous peripheral blood stem cell transplant > BMT

• **Prognosis is poor:**
  – Median survival 2-4y with treatment; a few months w/o treatment.
  – 10% 5y survival rate
Diagnosing Multiple Myeloma

• Diagnostic Criteria:
  – Bone marrow with $\geq 10\%$ abnormal plasma cells, plus either:
    • Monoclonal (M-) protein in the serum
    • M-protein in the urine
    • Lytic bone lesions (usually skull or axial skeleton)

• Radiographic Studies:
  – Skeletal Survey (plan radiographs)
  – CT, MRI, and PET scans are more sensitive than radiographs. However, their use is reserved for patients with:
    • Bone pain w/ a normal skeletal survey
    • Compression fractures
    • Neurologic deficits possibly 2/2 cord compression
Let’s review these different imaging modalities while continuing with RB’s workup.
MM Imaging: Skeletal Survey

- Initial modality for staging and monitoring disease progression
- Skeletal survey can show “punched-out” lytic lesions, diffuse osteopenia, or fractures

Companion Pt #2:
67yoF with MM

Axial Skull
Right humerus

RB’s Skull
No significant findings on SS (besides T4 lesion)
MM imaging: CT

- Faster and more sensitive than bone survey
  - Can visualize lytic lesions <5mm
- Excellent for evaluating bone stability and fractures

Companion Pt #3:
66yoF with MM

RB’s CT:
No significant findings
(besides T4 lesion)
MM Imaging: MRI

- More sensitive than bone scan.
- No ionizing radiation (unlike CT)
- Can detect bone marrow lesions in MM pts with no findings on skeletal survey
- Many MR sequences are used
  - **T1:** HYPOintense lesion w/in hyperintense BM
  - **STIR/T2:** HYERintense lesion w/in hypointense BM
  - Gadolimium: see post-contrast enhancement of MM lesions in BM


RB’s MRI: No significant findings (besides T4 lesion)
MM imaging: FDG PET

- FDG (Fluorodeoxyglucose): a glucose analogue
- PET (Position Emission Tomography): nuclear imaging modality that creates 3D images of functional processes in the body
  - Detects gamma rays emitted by a positron-emitting radionuclide tracer
  - Tracer is ligated to biologically active molecule (e.g. FDG)
- FDG PET: The concentration of tracer imaged represent metabolic activity in the tissue via glucose uptake
  - Helpful in monitoring treatment progression
**MM Imaging: FDG PET cont’d**

**Companion Pt #4**

- Note uptake in spine and chest area

- 3mo after BMT
- Note decreased FDG uptake, which indicates a positive response to treatment.

- RB did not undergo FDG PET

Our Patient: Recap

- **OSH:**
  - CTA

- **Day 1 of admission:**
  - MRI on C/T/L Spine
  - Skeletal Survey
  - CT of Chest, Abdomen, Pelvis

- **Only significant finding:**
  - T4 lytic lesion and compression fracture
Our Patient: Significant Labs

- Hgb 15.5, Hct 44.8 → no anemia
- Ca 9.5 → no hypercalcemia
- BUN 12, Crt 1 → no renal failure
- Negative SPEP and UPEP → no M-protein
- No Bence-Jones protein excretion

Is this really
Multiple Myeloma??
Potential Diagnosis: Solitary Plasmacytoma of Bone

- Like MM, SPB is a neoplastic proliferation of plasma cells.
- Histologically identical to MM
- Diagnostic criteria:
  - Solitary bone lesion with clonal plasma cells seen on bx
  - Normal BM with no clonal plasma cells
  - Normal skeletal survey and MRI of spine, except for solitary lesion
  - No anemia, hypercalcemia, or renal insufficiency
Our Patient: Rest of Hospital Course

• Day 6 Surgery:
  – T4 vertebrectomy
  – T3-T5 fusion

• Day 8 Surgery:
  – T1-T8 fusion
  – Transpedicular decompression
  – Multiple thoracic laminotomies
  – Iliac Crest BM Bx

Thoracic spine radiograph in the OR, s/p T1-T8 fusion
Our Patient: Updates

- T4 lesion pathology did show clonal plasma cells
- Unfortunately, BM bx showed clonal plasma cell dyscrasia
  - This ruled out SPB and confirmed MM
- Received several cycles of radiation treatment
- ~5mo after initial presentation, underwent autologous peripheral stem cell transplant
- Currently awaiting f/u BM bx to evaluate transplant response
Take-Home Points

• Chest pain ≠ Cardiac or Pulmonary diagnosis
  → Keep a broad DDx
• When evaluating bone lesions, age and location are very important
  – MM: >50yo, Skull/axial skeleton
• MM: Anemia, Hypercalcemia, Renal Failure
  – But not every patient will have read the text books
• When considering multiple myeloma, also consider solitary plasmacytoma of bone
• Imaging and biopsies are imperative to proper management
  – CC → CTA → MRI → Skeletal Survey → CT → Bx → Diagnosis → Tx all within 8 days!
References

Acknowledgements

• David Glazier, MD
• Mai-Lan Ho, MD
• Gillian Lieberman, MD
• Claire Odom
• Dr. James Brush, MD
• David Feinbloom, MD
• Anthony Breu, MD