A Case of Osteolytic Malignancy in the Setting of Immunocompromise Secondary to HIV

Maneera Chopra
Dr. Pritish Bawa
Dr. Brandon Wang, R1

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MSK Radiology RAD 4014

UTHealth
The University of Texas Health Science Center at Houston
McGovern Medical School

Clinical History

- 47 year old female with a history of HIV on HAART (undetectable viral load) presented to the ER with complaint of L knee pain
  - Pain began 1-2 mo ago with L knee and thigh pain, swelling
  - 2 weeks prior to presentation felt a “pop” and was unable to walk
  - Pain exacerbated by movement
  - Was seen at OSH and was given a brace and discharged, but pain persisted
  - No fevers/chills, no dyspnea, no chest pain, no rashes, no bruising, no edema, and no lymphadenopathy

Physical Exam

VS: T: 98.3 F HR: 89 RR: 18 BP: 127/79 SpO2; 99%

Gen: Pt alert and oriented

HEENT: Head normal, no trauma, no conjunctival injection. EOMI. PERRLA. No oral lesions.

NECK: Neck supple, no lymphadenopathy

CV: RRR, no murmurs

PULM: Clear to auscultation

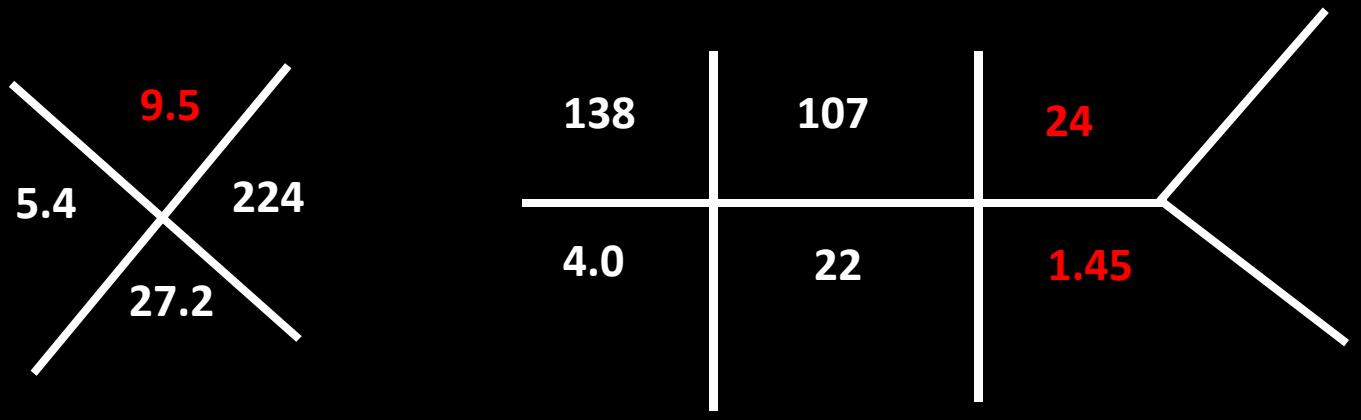
GI: Bowel sounds present, no mass, no tenderness

MSK: Distal left thigh tenderness and some fullness. No edema. No sensory deficits. Full 5/5 strength bilateral upper and lower extremities

NEURO: No focal deficits

SKIN: No rashes, skin lesions

Lab Work



Sed Rate: > 100
PT: 13.3
PTT: 30.5
INR: 1.03

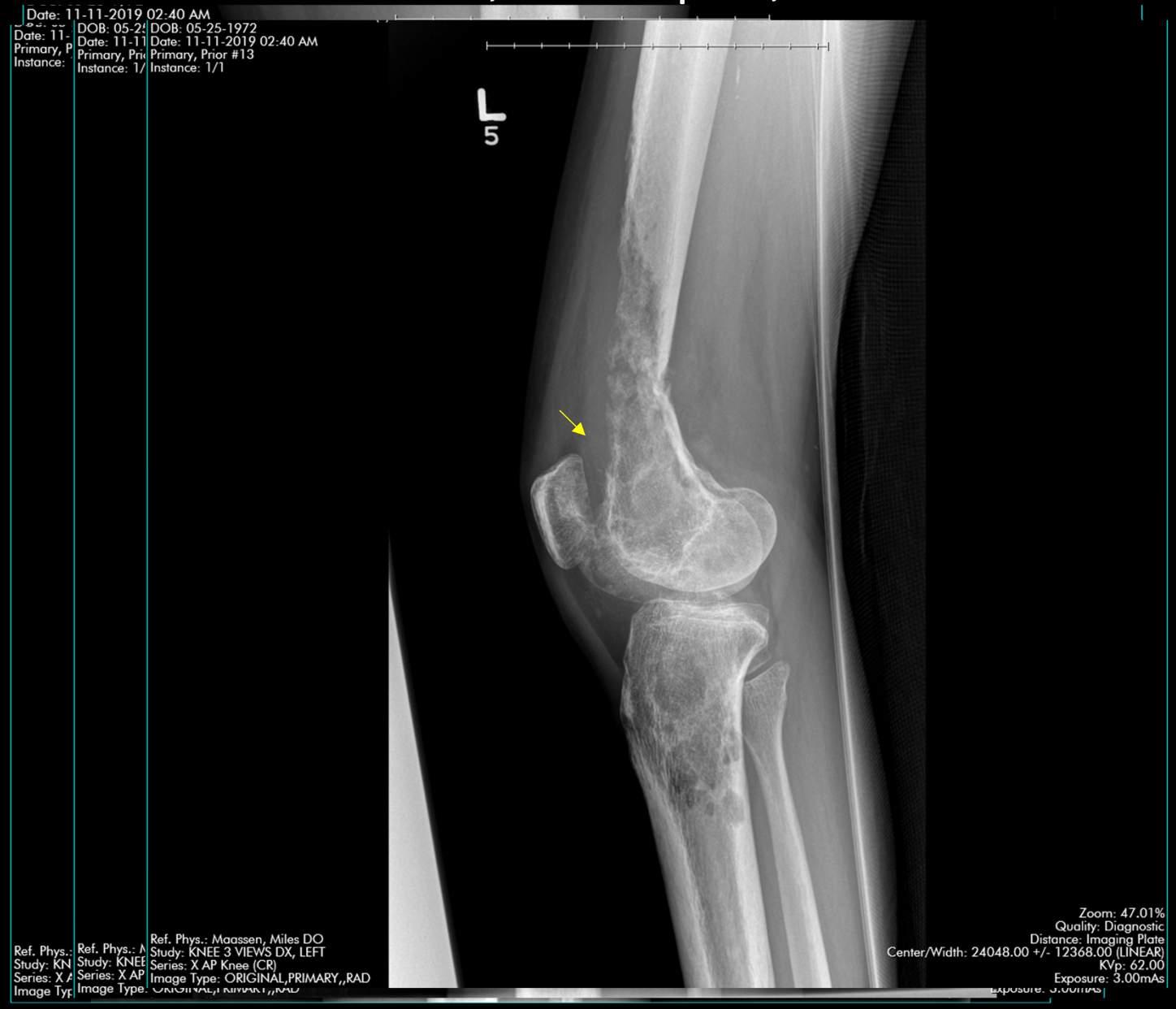
HIV 1: positive
HIV 2: negative

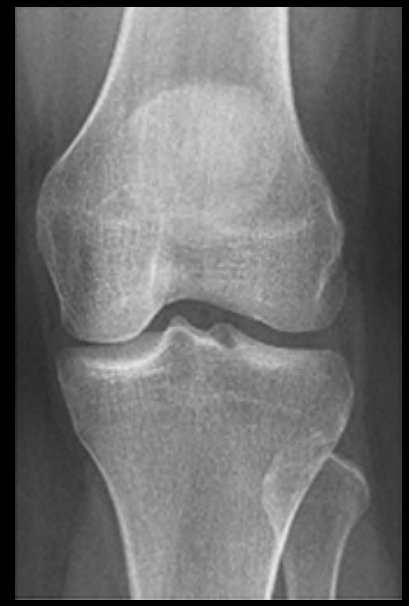
Serum Protein Electrophoresis (SPEP): Total protein elevated, serum albumin within reference, elevations in alpha and alpha-2 fractions. Monoclonal protein present in gamma globulin region

Urine Protein Electrophoresis (UPEP): Urine protein consists primarily of albumin. Faint protein in gamma globulin region which may represent small protein spike

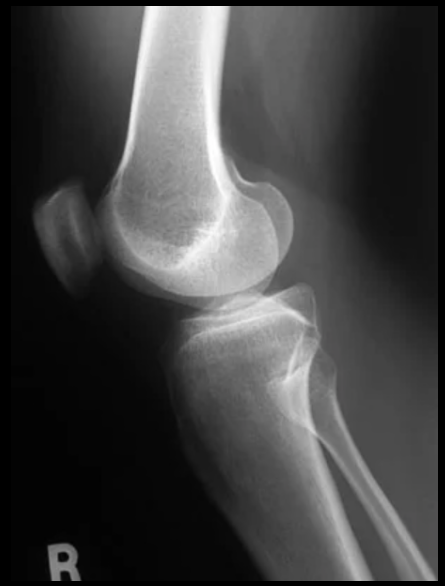
Imaging: XR L Knee 3 Views-AP, Oblique, and Lateral 11/11/2019

1. Osteolytic lesions of left distal femur and proximal tibia (red arrows)
2. Mildly displaced fracture of distal metadiaphysis of left femur (blue arrow)
3. Moderate left knee effusion (yellow arrow)

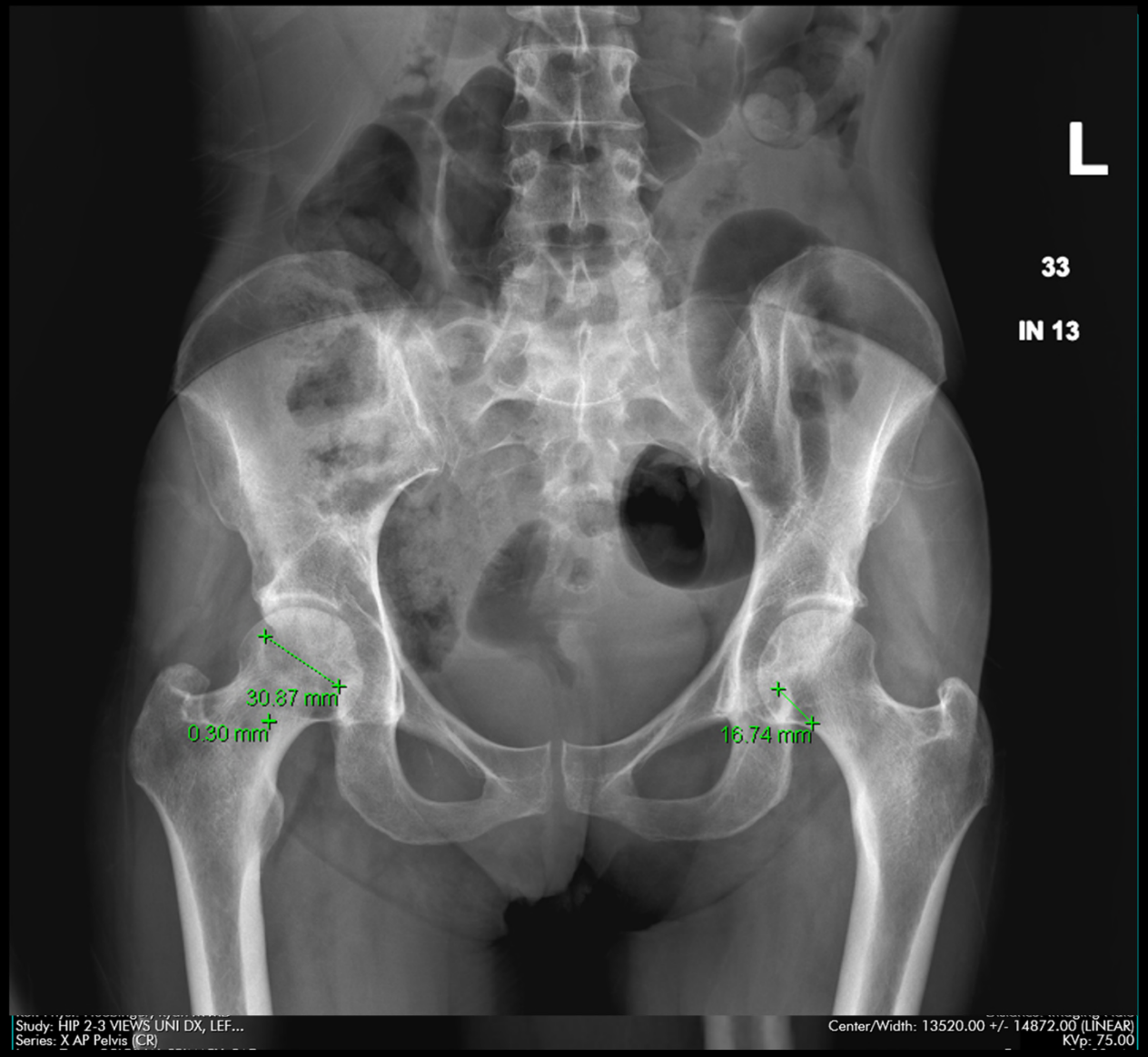


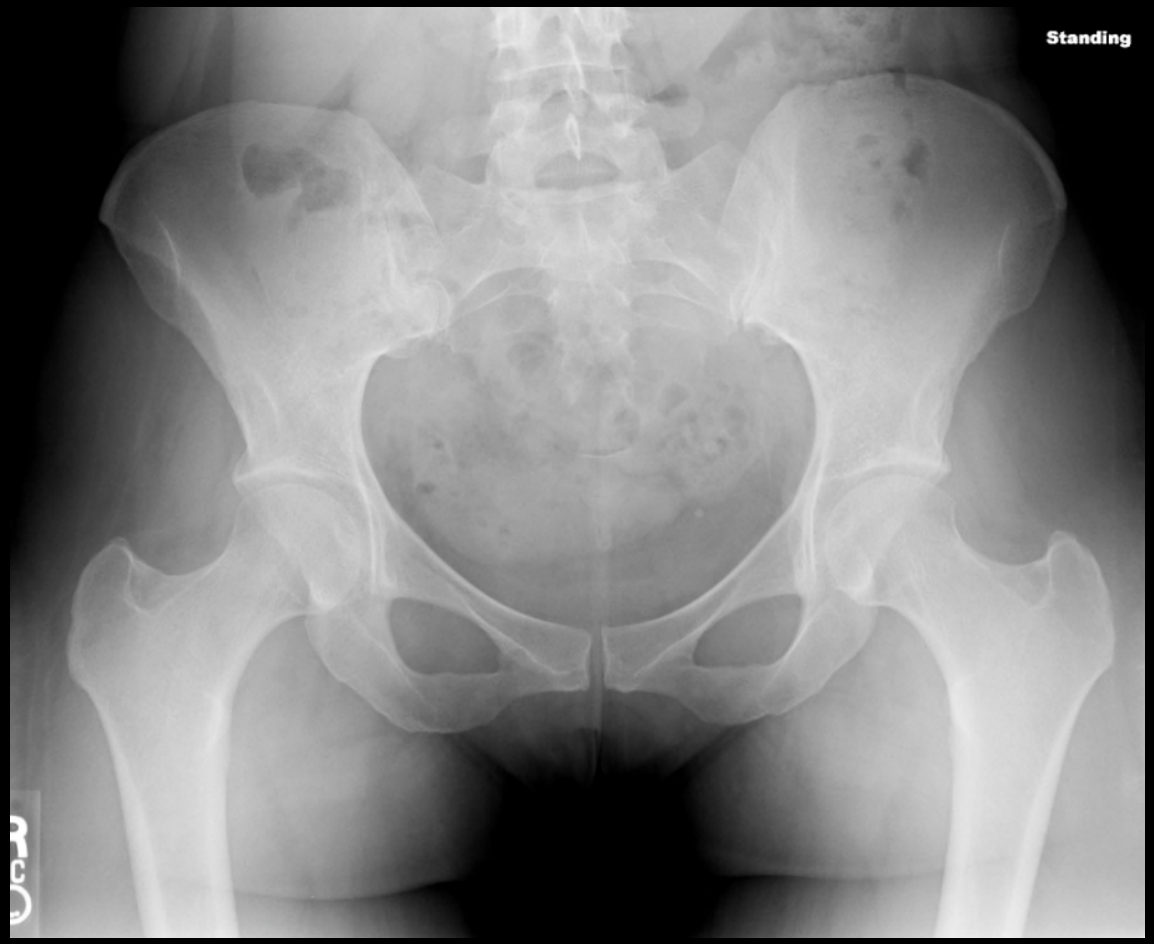


XR Normal Knee



Imaging: XR L Hip 2 Views-AP Pelvis 11/11/2019

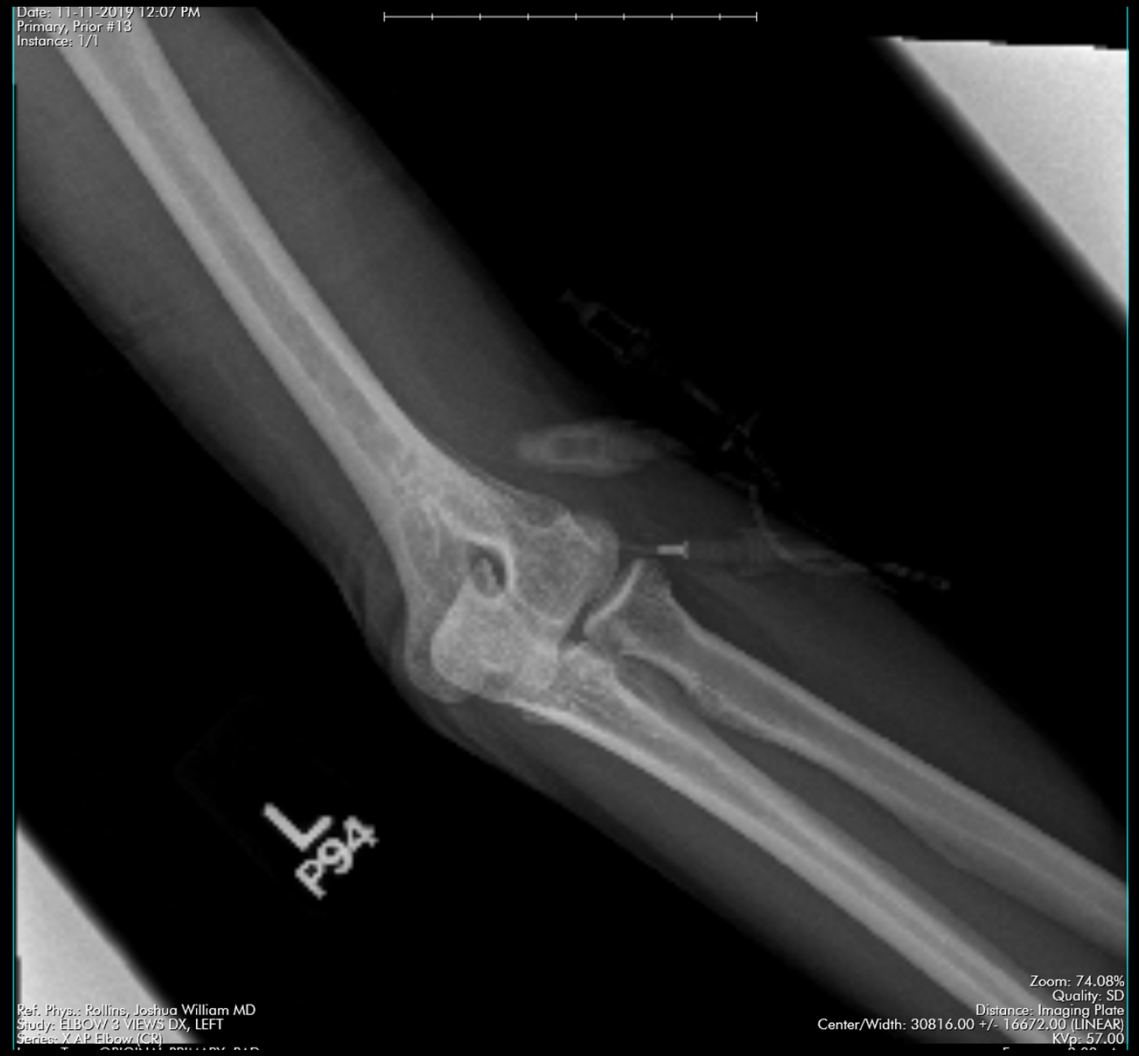




Normal AP pelvis radiograph

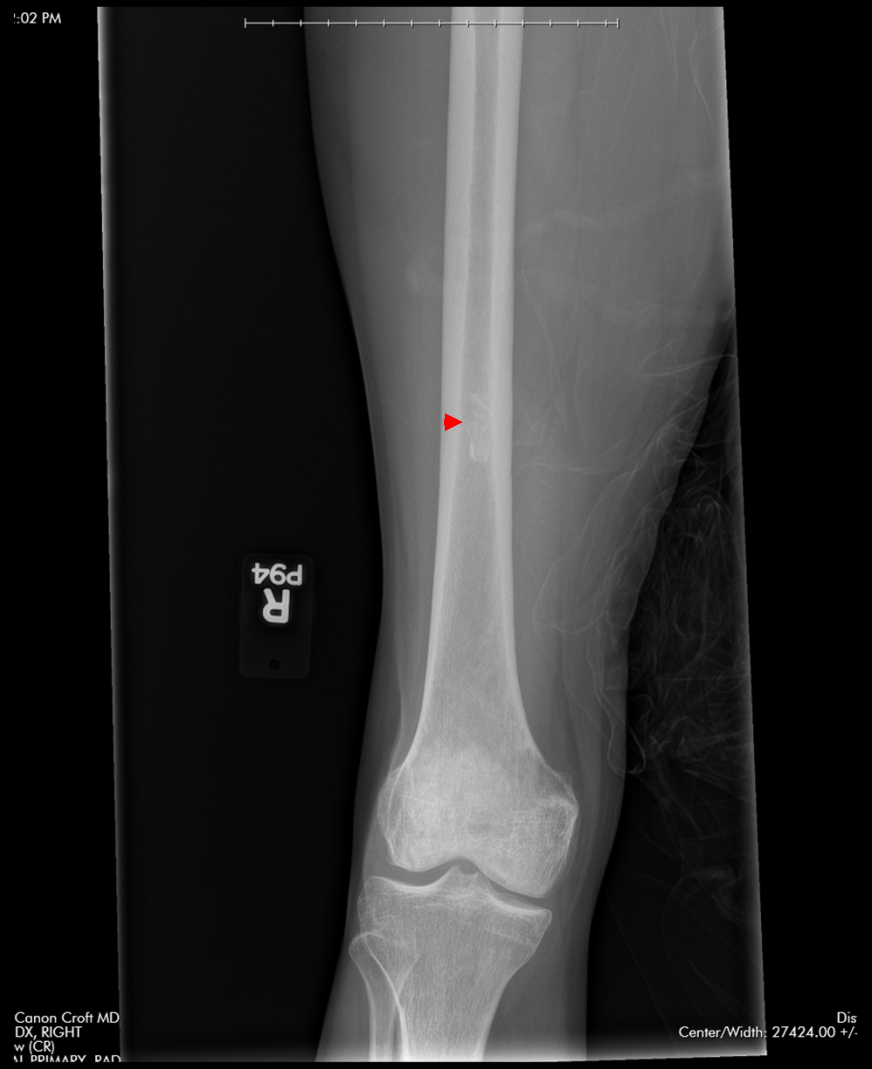
1. Osteolytic lesions of the left femoral neck (1.7 cm) and right femoral head (3 cm)
2. Osteolytic lesion suspected of the R medial acetabulum

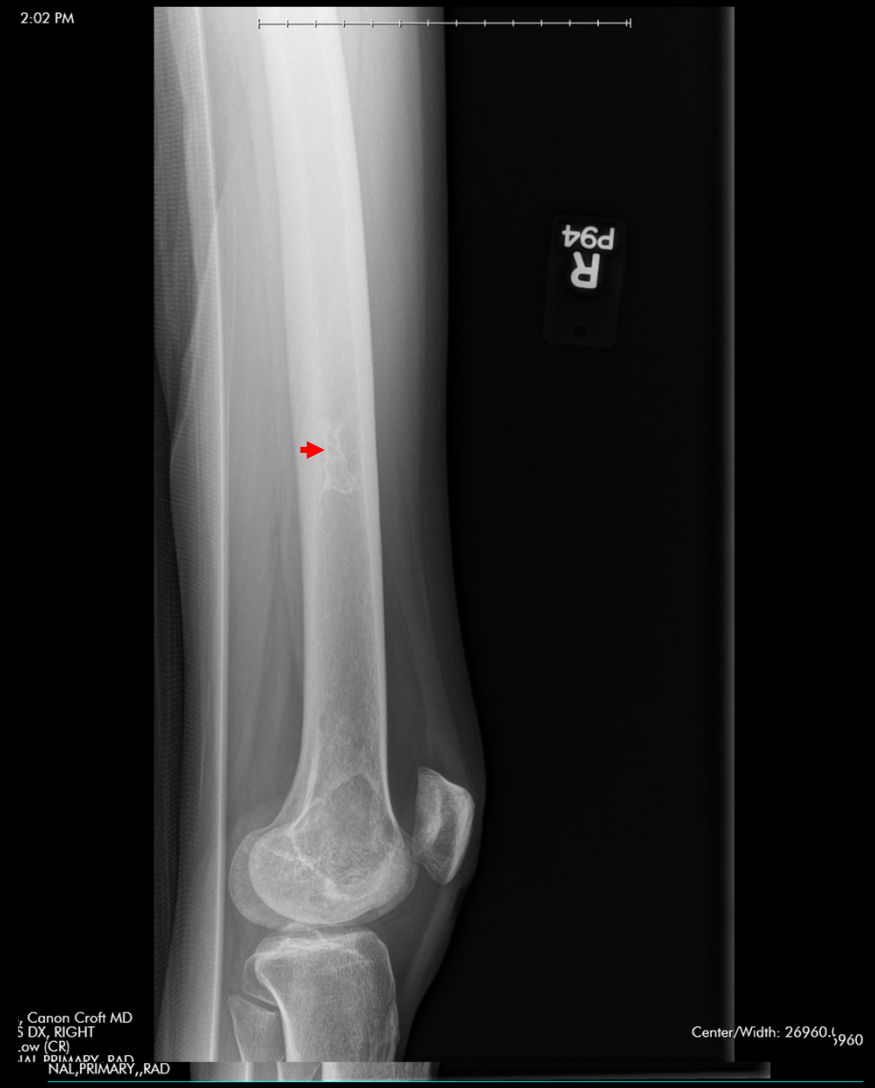
Imaging: XR Elbow 2 Views 11/11/2019



Imaging: Femur Series 11/11/2019

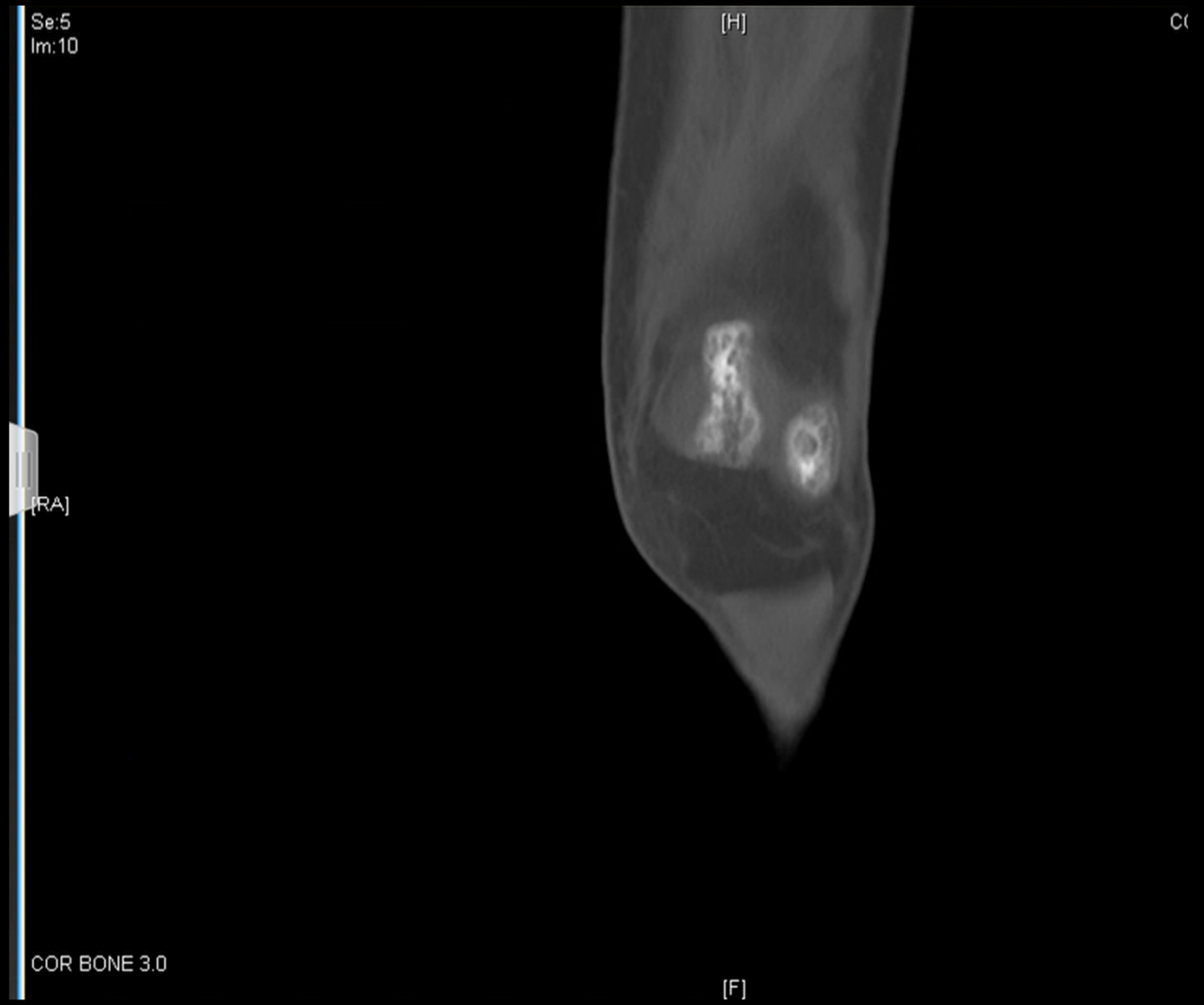
1. Small area of lucency at the medial aspect of R distal femur suspicious for early lesion in this region without risk for impending pathologic fracture (red arrowhead)



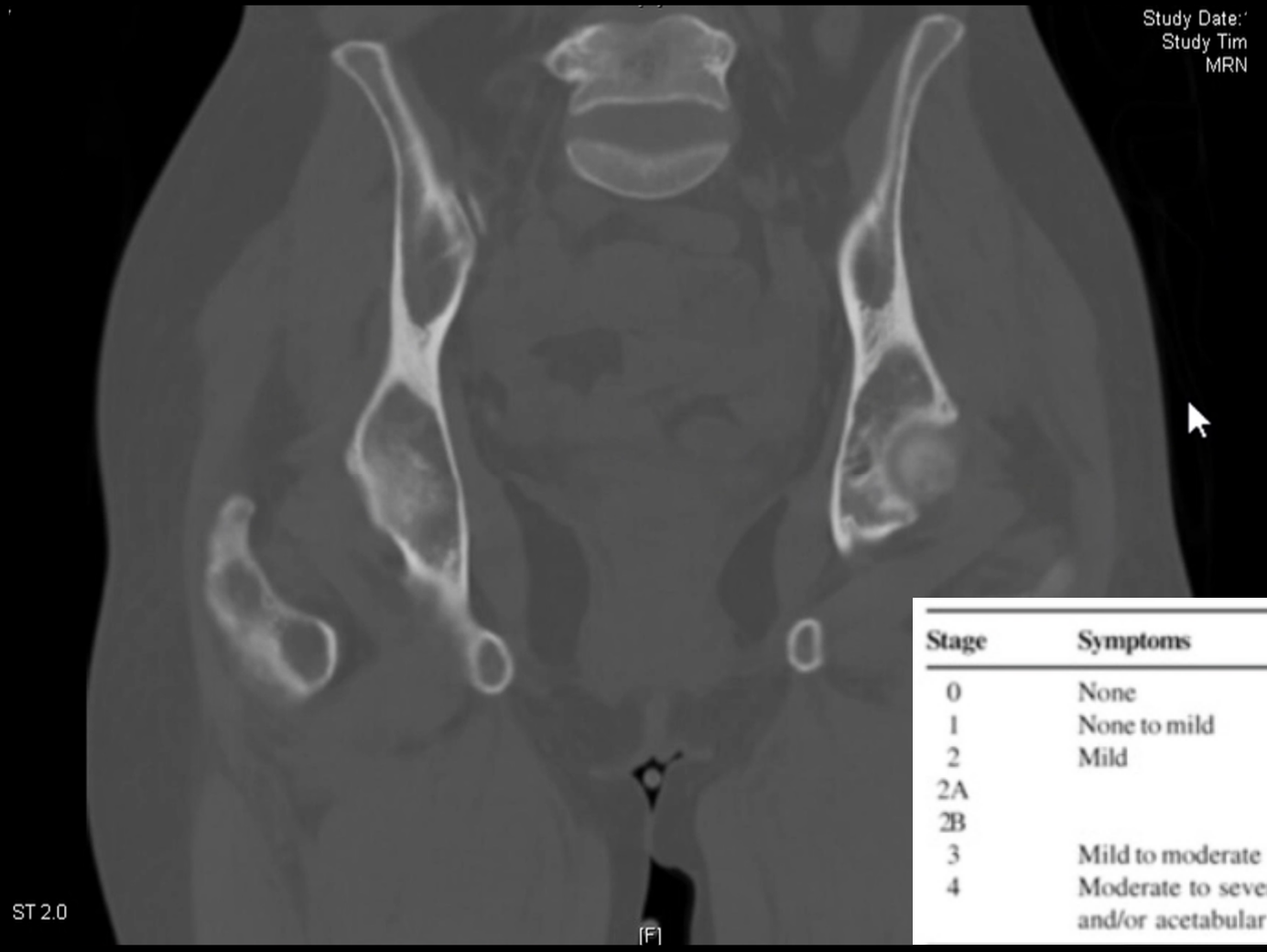


Imaging: L Knee CT-Sagittal and Coronal views 11/12/2019

1. Unchanged alignment of mildly displaced obliquely oriented pathologic fracture of distal femur
2. Extensive lytic lesions involving the distal L femur and proximal tibia extending to the articular surface with associated cortical destruction and circumferential soft tissue mass.



Imaging: Pelvic CT-Coronal View 11/12/2019



1. Bilateral femoral head AVN with minimal articular surface collapse on the right (Ficat stage III) and no articular surface collapse on the left (Ficat stage II)

Stage	Symptoms	X-ray
0	None	Normal
1	None to mild	Normal
2	Mild	Change in density
2A		Sclerosis or cysts
2B		Applanation (crescent sign)
3	Mild to moderate	Loss of sphericity
4	Moderate to severe and/or acetabular changes	Reduction of the articular space

Key Imaging Findings

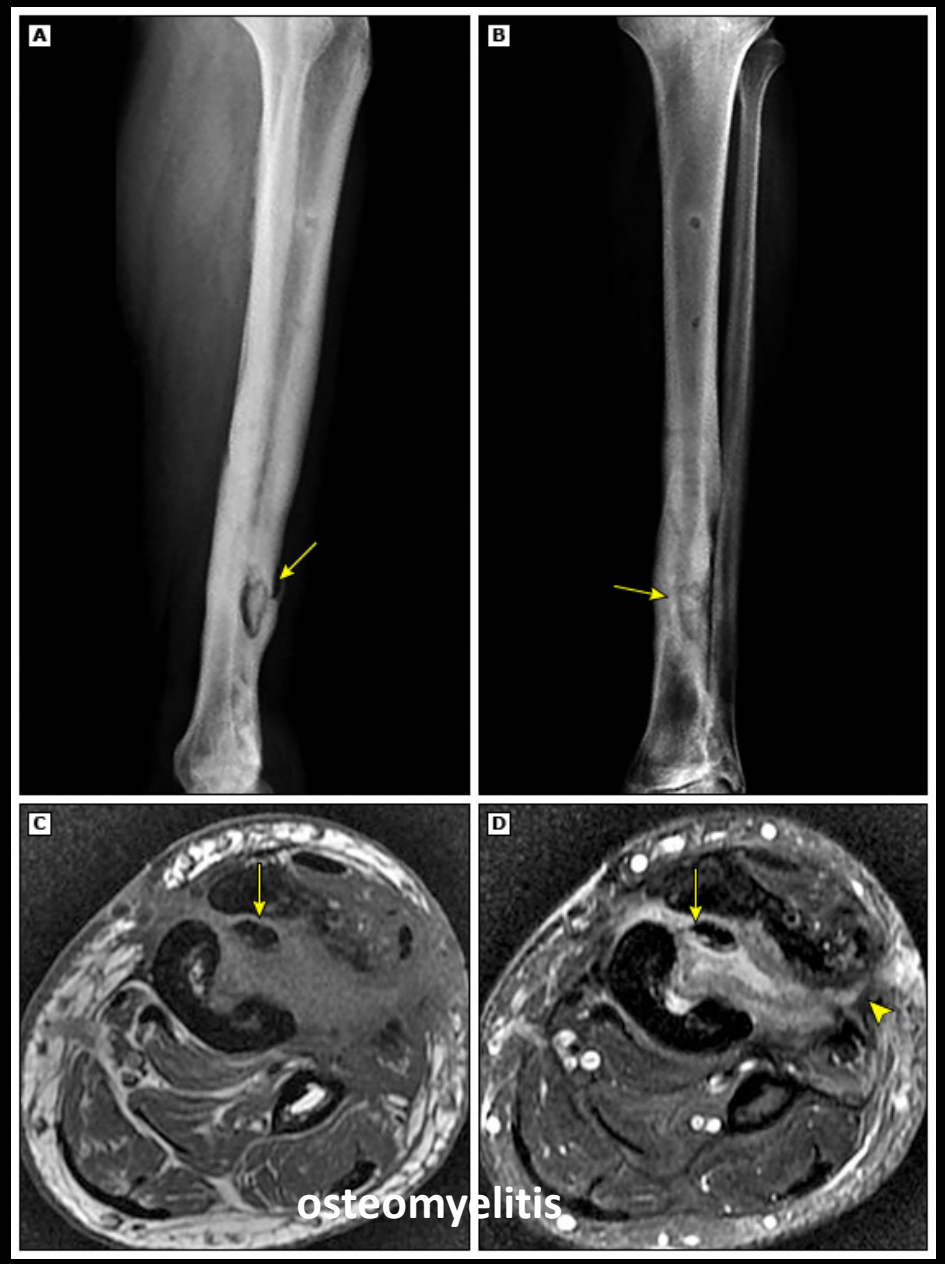
- 47 year old woman with localized knee pain and swelling with imaging showing lesions of the proximal tibia and distal femur, pathological fracture of the distal L femur, and avascular necrosis of the bilateral femoral heads.

Differential Diagnosis:

- Vascular
  - Avascular necrosis
- Neoplastic
  - Metastasis
    - Breast
    - Lung
  - Multiple Myeloma
  - Lymphoma of the Bone
- Infectious
  - Osteomyelitis
  - Bacillary Angiomatosis (Cat Scratch Disease)
- Benign
  - Osteoid osteoma
  - Aneurysmal bone cyst
  - Fibroma
- Endocrine
  - Hyperparathyroidism

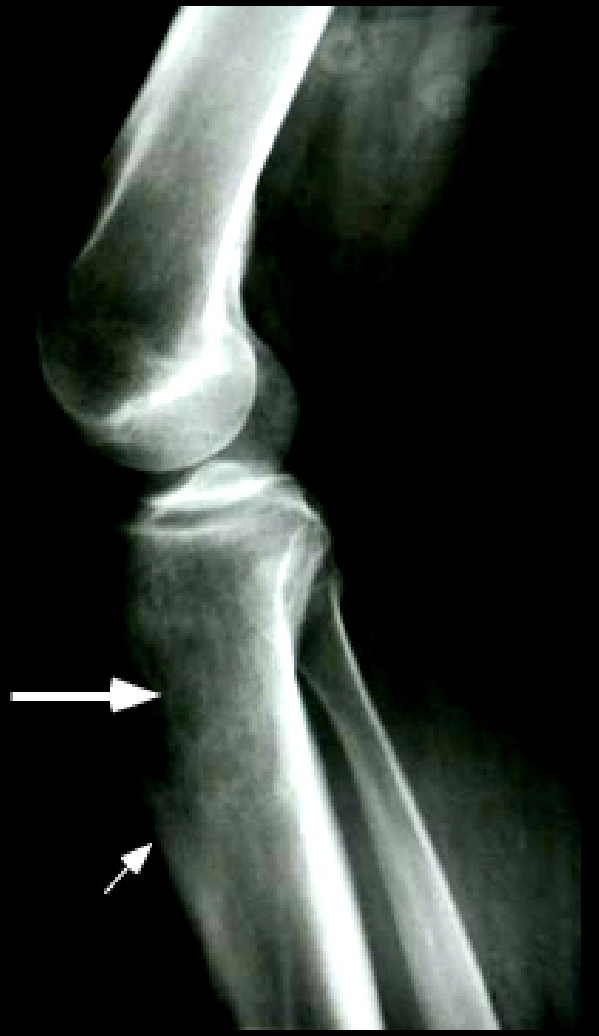
Differential Diagnosis

- Chronic Osteomyelitis
  - Clinical signs include dull pain, local edema and erythema, and sometimes systemic symptoms
  - Radiographic
    - Soft tissue swelling
    - Cortical loss and bone destruction
    - Periosteal reaction
    - Lytic changes in later stages
    - Nonhealing fractures



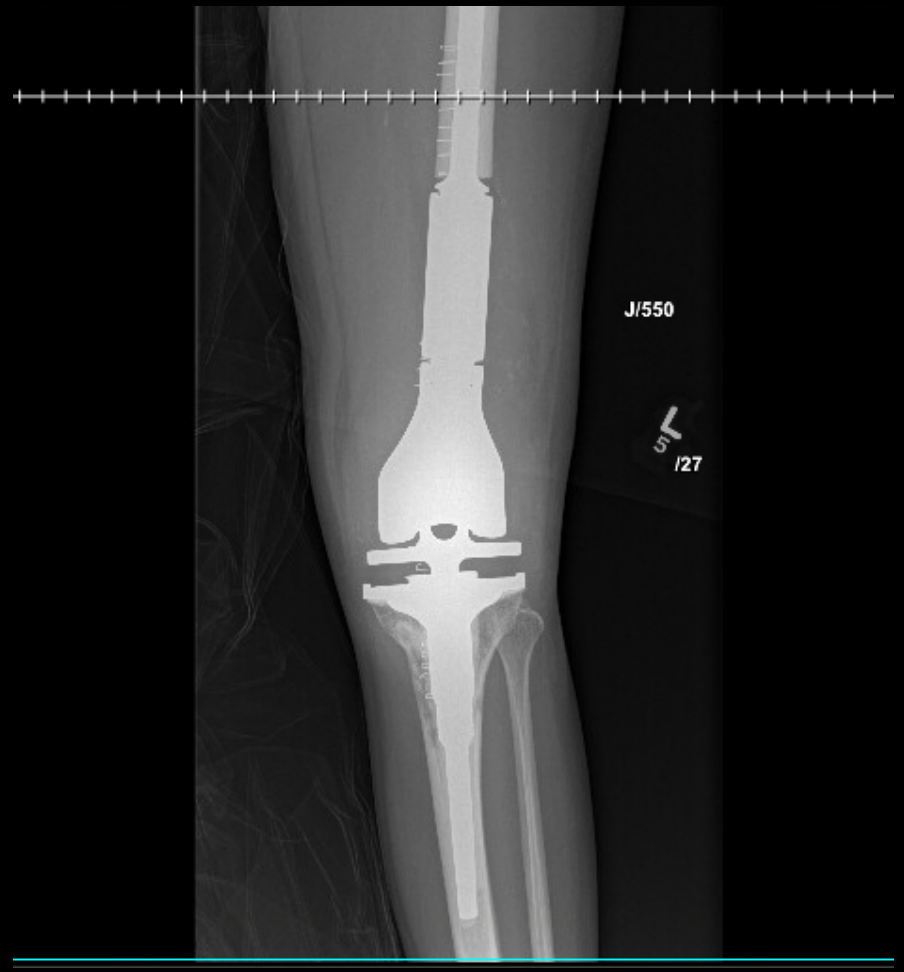
Differential Diagnosis

- Non-Hodgkin's Lymphoma of the Bone
  - Solitary or multiple destructive bony lesions
  - Rare, most patients > 30 years old, mostly women
  - Presents as bone pain, "B" symptoms, and sometimes palpable mass
  - Axial skeleton (weight bearing bones) > appendicular skeleton
  - Radiographic
    - Lytic or radiolucent lesions, often at metadiaphyseal region
    - Non-calcified Soft tissue mass
    - Cortical bone erosion and widened diaphysis
- Multiple Myeloma
  - Neoplastic proliferation of plasma cells forming monoclonal Ig
  - Presents with bone pain, increased total serum protein, anemia, hypercalcemia, and other systemic signs and symptoms
  - Occurs in older adults > 60
  - Radiographic
    - Cross sectional imaging (such as CT or MRI) preferred over plain radiographs
    - Lytic "punched out" lesions, diffuse osteopenia, and fractures



Final Diagnosis

- Patient underwent bone biopsy which showed solitary plasmacytoma of the bone indicating Multiple Myeloma
  - HOWEVER, patient had known history of Non-Hodgkin's Lymphoma at St. Luke's hospital
  - Imaging and biopsy of knee suggests Multiple Myeloma
- Orthopedics performed radical L total knee resection and arthroplasty on 11/12
- MRI brain w and w/o contrast on 12/02 concerning for schwannoma vs lymphoma
- CT Chest on 12/03 showed subpleural metastases, hilar and mediastinal masses
- CT Abdomen/Pelvis on 12/03 showed soft tissue densities of porta hepatis, enlargement of bilateral ovaries, and bilateral inguinal lymphadenopathy
- Patient had a port placed with plans to begin chemotherapy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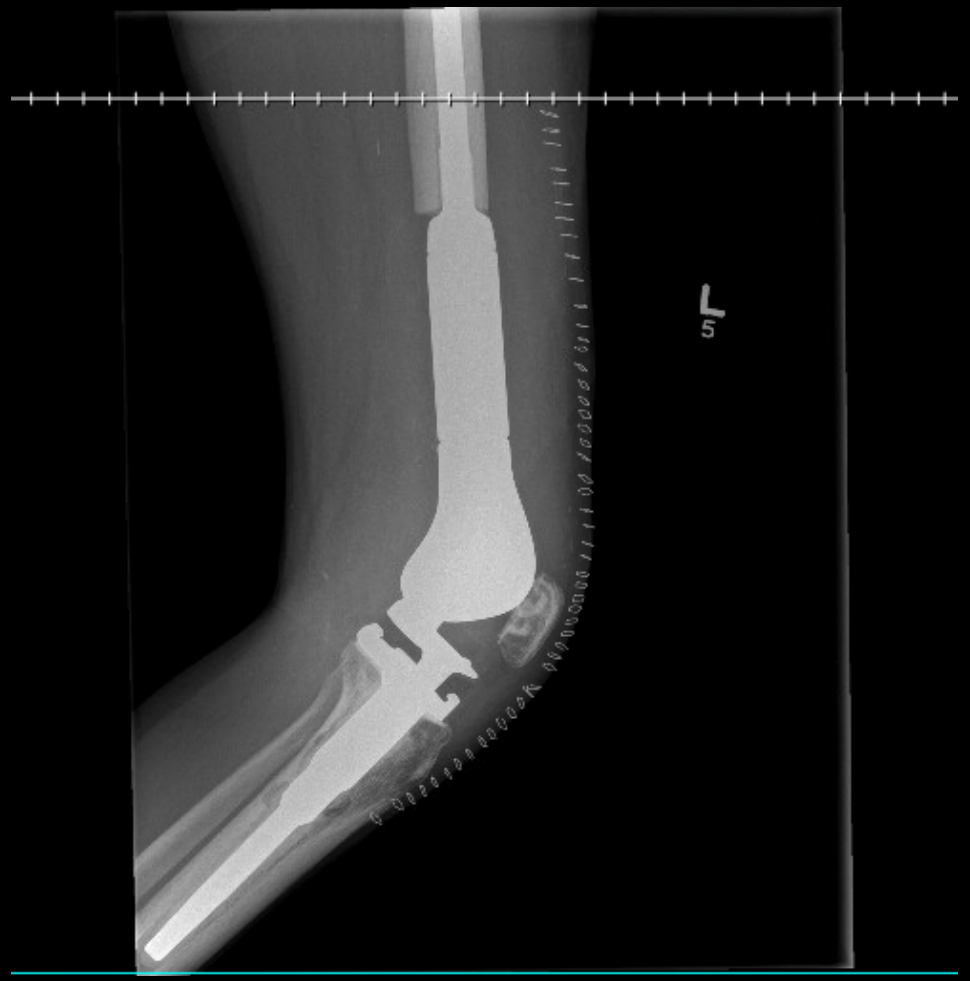
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Pathology Report

Diagnosis

Distal femur, proximal tibia, patella, radical resection:
-Plasma cell neoplasm

Comment

Immunohistochemical stains with appropriate controls were performed on block 1H. CD138 is diffusely positive. Kappa and lambda demonstrate kappa light-chain restriction. CD56 is not aberrantly expressed. The proliferation rate by Ki67 is 10-15%; however, please note that this might be inaccurate due to the use of decalcification.

Tumor Summary

Specimen (Note A)
Bone (specify site): Femur

Procedure
Resection

+ Tumor Size
+ Greatest dimension:6 x 4.5 x 3.5 cm

+ Subtype Based on the World Health Organization (WHO) Classification (Note D)
Solitary plasmacytoma of bone

Immunophenotype and Light Chain Type
Kappa light chain

+ CD56: Not detected

+ CD138: Detected

Discussion-Non-Hodgkin's Lymphoma

- Non-Hodgkin lymphoma consists of diverse group of neoplasms: B cell variants, T cell variants, and natural killer cells
- Infections associated with NHL include HIV, HTLV-1, EBV, Hep C, Hep B, Borrelia Burgdorferi, and Chlamydia psittaci
- Aggressive lymphomas can present with waxing/waning lymphadenopathy, B symptoms, elevated LDH and uric acid, hepatosplenomegaly, and cytopenias
- SPEP may detect monoclonal immunoglobulin with large M spikes
- Approximately 50% of patients develop extranodal disease, and 10-35% of patients have primary extranodal lymphoma at diagnosis

Continued discussion-Non-Hodgkin's Lymphoma

- Patients with lymphoma involving the bone staged in the same way as any patient with non-Hodgkin lymphoma to identify patients with stage 1E disease who might be treated with limited chemotherapy and involved field radiation therapy, rather than chemotherapy alone

Revised staging system for primary nodal lymphomas (Lugano classification)

Stage	Involvement	Extranodal (E) status
Limited		
I	One node or a group of adjacent nodes	Single extranodal lesions without nodal involvement
II	Two or more nodal groups on the same side of the diaphragm	Stage I or II by nodal extent with limited contiguous extranodal involvement
II bulky*	II as above with "bulky" disease	Not applicable
Advanced		
III	Nodes on both sides of the diaphragm; nodes above the diaphragm with spleen involvement	Not applicable
IV	Additional noncontiguous extralymphatic involvement	Not applicable

Extent of disease is determined by positron emission tomograph/computed tomography (PET/CT) for avid lymphomas and CT for nonavid histologies. Tonsils, Waldeyer's ring, and spleen are considered nodal tissue.

Treatment-Non-Hodgkin's Lymphoma

- Usually involves chemotherapy +/- radiation therapy with metastatic disease
  - Multiagent chemotherapy with CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone +/- rituximab)
  - Radiation therapy dose of 30-60 Gy
- Surgical interventions involve stabilization of pathologic fractures

Multiple Myeloma

- Four main patterns
  - Disseminated:“punched-out” lytic lesions of axial skeleton
  - Diffuse skeletal osteopenia
  - Solitary plasmacytoma or expansile lesion of pelvis or vertebral bodies
  - Osteosclerosing myeloma
- Radiographic features
  - Lytic lesions that are well-circumscribed
  - Generalized osteopenia
  - Pathological fractures
- Treatment and Prognosis
  - Incurable disease, chemotherapy can slow progression
  - Chemotherapy agents: thalidomide, bortezomib, anthracyclines
  - Stem cell transplant and bone marrow ablation
  - Presence of extraosseous myeloma implies a poorer prognosis

ACR appropriateness Criteria

Variant 5: **Suspect primary bone tumor. Lesion on radiographs. Indeterminate or aggressive appearance for malignancy. Next imaging study.**

Procedure	Appropriateness Category	Relative Radiation Level
MRI area of interest without and with IV contrast	Usually Appropriate	O
MRI area of interest without IV contrast	May Be Appropriate	O
CT area of interest without and with IV contrast	May Be Appropriate (Disagreement)	Varies
CT area of interest without IV contrast	May Be Appropriate	Varies
FDG-PET/CT whole body	May Be Appropriate	☢☢☢☢
Tc-99m bone scan whole body with SPECT/CT area of interest	May Be Appropriate	☢☢☢
Tc-99m bone scan whole body	Usually Not Appropriate	☢☢☢
CT area of interest with IV contrast	Usually Not Appropriate	Varies
Radiography skeletal survey	Usually Not Appropriate	☢☢☢
US area of interest	Usually Not Appropriate	O

ACR appropriateness Criteria

CT Area of Interest

CT continues to play a role in the evaluation of indeterminate bone lesions discovered on radiographs, particularly in lesions with mineralized matrix or in suspected cases of osteoid osteoma (see Variant 4). Both MRI and CT have been used to evaluate the degree of cortical involvement in chondroid lesions [20]. In comparison with radiographs and MRI, CT has been shown to better delineate the presence of cortical destruction and the character of matrix mineralization patterns in patients with clear cell chondrosarcoma [21]. In a retrospective review of 40 pathologically confirmed telangiectatic osteosarcomas, Murphey et al [22] noted that CT was the optimal imaging modality for demonstration of subtle matrix mineralization seen in 85% of cases in the intraosseous or soft-tissue components of the lesion. Not all studies conclude that one modality, CT or MRI, is better than the other. A multi-institutional collaborative study assessing the relative accuracy of CT and MRI in the local staging of primary malignant musculoskeletal neoplasms showed no statistically significant difference between CT and MRI in determining tumor involvement of muscle, bone, joints, or neurovascular structures. Furthermore, the combined interpretation of CT and MRI did not significantly improve accuracy [23]. Advanced CT techniques, such as dual-energy CT, have shown promise in differentiating malignant from nonmalignant tumors, although further research in this area is needed [24]. MRI is generally considered the preferred imaging modality for staging of bone tumors. Some cases may benefit from both MRI and CT because these modalities provide complementary information regarding soft-tissue (often better evaluated on MRI) and matrix mineralization (often better evaluated on CT).

There is no relevant literature regarding the specific use of CT with IV contrast or CT without and with IV contrast in the evaluation of suspected primary bone tumor with radiographs indeterminate for malignancy. However, if contrast is given, CT without and with IV contrast is preferred because it allows differentiation of areas of contrast enhancement from areas of osseous matrix production.

Take Home Points

- Although multiple myeloma was the patient's diagnosis after biopsy, primary Non-Hodgkin's lymphoma of the bone is a rare disease that should be considered in a patient with localized bone pain, swelling, and history of HIV
- Radiographic findings of NHL include "moth-eaten" appearance, osteolytic lesions, pathologic fractures, and cortical destruction, which is similar to MM
- Early identification of bone tumors is important to improve prognosis

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Questions?