

AMSER Case of the Month

September 2025

91 y.o. male with left lower extremity pain

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Patient Presentation

91-Year-Old male presents to the Emergency Department with left hip pain

- PMHx: Prostate cancer with bone metastases, hypertension
- HPI: Presents with left lower extremity pain for 2 weeks, localized to the left hip. Reports progressive weakness and increasing difficulty with activities of daily living. Pain is exacerbated by weight-bearing. No history of recent falls or trauma. Completed fourth cycle of radiation therapy one month ago. Family reports worsening fatigue and weakness following previous treatment.
- Physical Exam: Normal lower extremity physical exam
- ROS: negative for fever, chills, upper respiratory symptoms, chest pain, shortness of breath, abdominal pain, urinary or bowel incontinence or retention
- Medications: calcium citrate, Vit D, denosumab, enzalutamide, gabapentin, leuprolide, and losartan

Pertinent Labs

- None

What Imaging Should We Order?

ACR Appropriateness Criteria

Variant 1: Adult. Suspect stress fracture, excluding vertebrae. Initial imaging.

Procedure	Appropriateness Category	Relative Radiation Level
Radiography area of interest	Usually Appropriate	Varies
Bone scan whole body with SPECT or SPECT/CT area of interest	May Be Appropriate (Disagreement)	☢☢☢
US area of interest	Usually Not Appropriate	○
MRI area of interest without and with IV contrast	Usually Not Appropriate	○
MRI area of interest without IV contrast	Usually Not Appropriate	○
CT area of interest with IV contrast	Usually Not Appropriate	Varies
CT area of interest without and with IV contrast	Usually Not Appropriate	Varies
CT area of interest without IV contrast	Usually Not Appropriate	Varies

This imaging modality was ordered by the ER physician

Findings (unlabeled)



Findings (labeled)



AP view of pelvis

Severe degenerative changes with joint space narrowing, subchondral sclerosis and osteophyte formation

Otherwise, no acute findings

Findings (unlabeled)

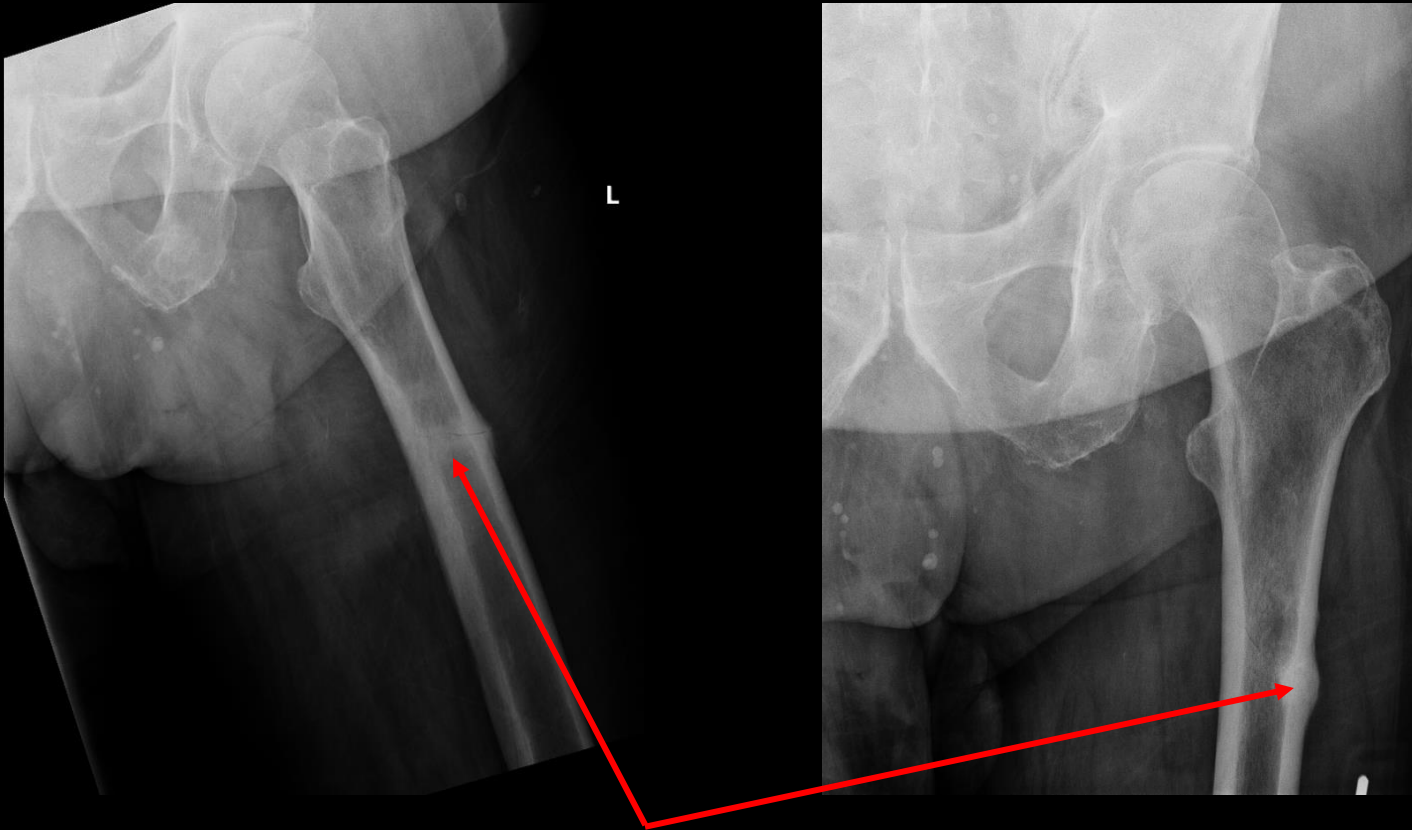


Findings (labeled)

Left femur

Lateral view

AP view



Linear lucency of the left femoral proximal diaphysis with lateral periosteal/callus formation → subacute, nondisplaced fracture likely associated with denosumab use

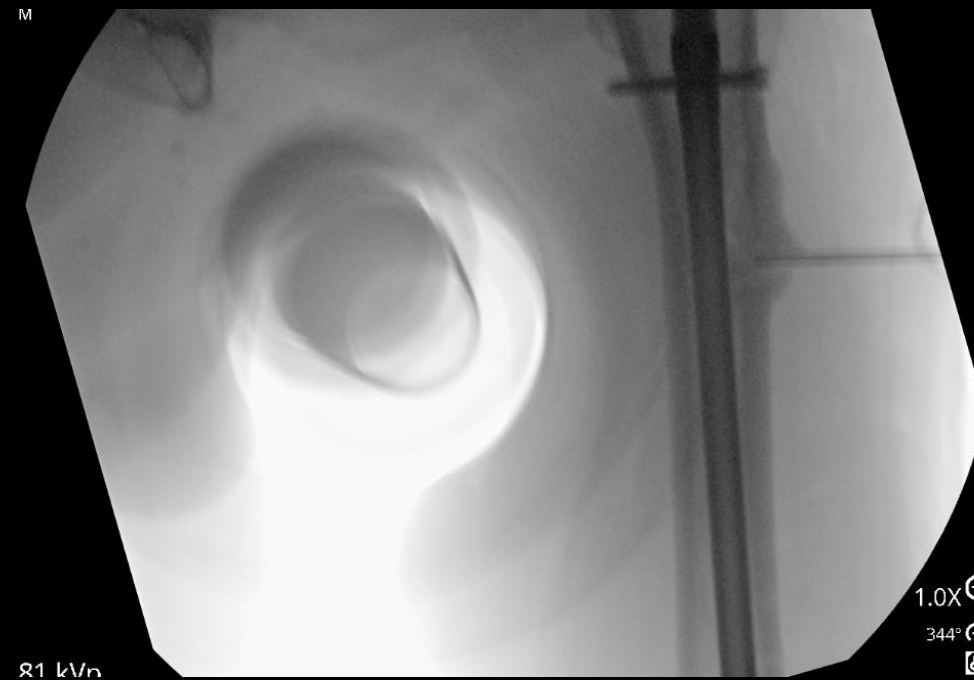
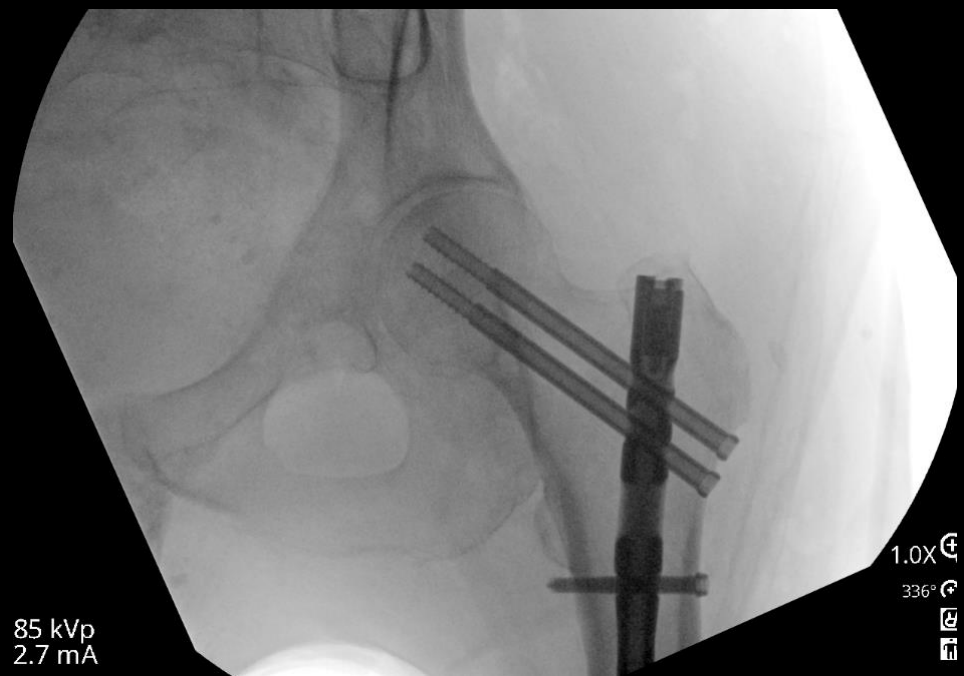
Right femur

AP view



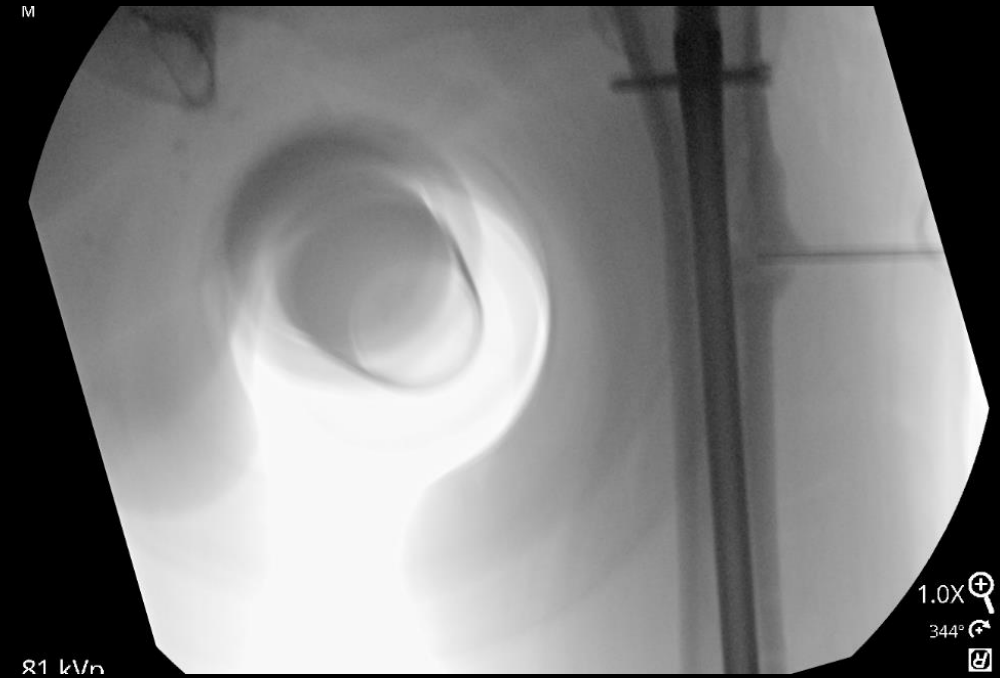
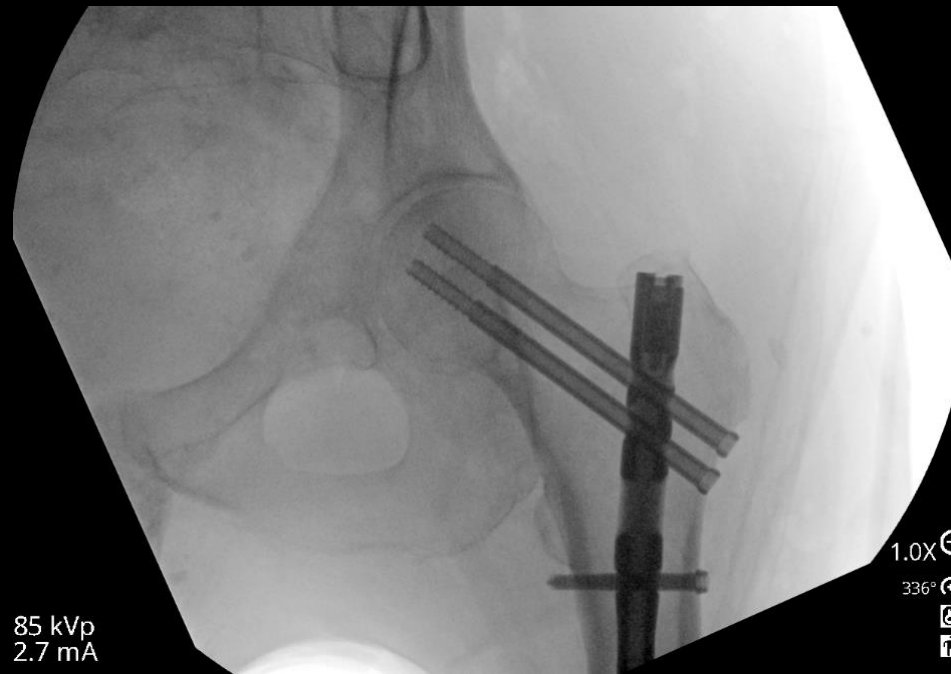
No acute findings

Findings (unlabeled)



Findings (labeled)

Post-surgical fluoroscopic images of the left femur



Internal fixation with a long cephalomedullary nail extending from the proximal femur into the diaphysis. Hardware is appropriately positioned.

Final Dx:

Denosumab-related insufficiency fracture

Case Discussion

- Atypical femoral fractures are a subtype of insufficiency fractures, resulting from normal stressors on abnormal bone.
 - Most commonly associated with long-term bisphosphonate use
- Denosumab is a monoclonal antibody that inhibits RANKL (Receptor Activator of Nuclear factor Kappa-B Ligand), thereby preventing osteoclast recruitment and bone resorption¹
- Microcracks in bone are identified and repaired through a process called targeted remodeling, which relies on osteoclasts being recruited via RANKL signaling¹

Case Discussion

- Denosumab disrupts target remodeling, allowing microcracks to coalesce into stress fractures – similar to the mechanism proposed for bisphosphonates²
- Unlike bisphosphonates, denosumab's effects are reversible between doses, allowing partial recovery of bone remodeling and a lower risk of atypical fractures with intermittent exposure²
- Denosumab carries a similar risk of atypical femoral fractures as bisphosphonates via RANKL inhibition, but its fracture prevention benefits outweigh risk in appropriately selected patients²
 - May be indicated in osteoporosis, cancer-related bone loss, bone metastases at high fracture risk, etc.

Case Discussion

- Imaging of the contralateral femur is recommended, as 20–64% of patients with atypical femoral fractures show similar findings bilaterally³
- Proximal femoral diaphyseal fractures occurring after low-energy trauma should raise concern for long-term bisphosphonate or denosumab use⁴

References:

- [1] Aspenberg P. Denosumab and atypical femoral fractures. *Acta Orthop*. 2014;85(1):1. doi:10.3109/17453674.2013.859423. PMID: 24171676. PMCID: PMC3940980.
- [2] Kwek EB, Koh JS, Howe TS. More on atypical fractures of the femoral diaphysis. *N Engl J Med*. 2008;359(3):316–317; author reply 317–318.
- [3] Lenart BA, Lorch DG, Lane JM. Atypical fractures of the femoral diaphysis in postmenopausal women taking alendronate. *N Engl J Med*. 2008;358(12):1304–1306.
- [4] Shane E, Burr D, Abrahamsen B, et al. Atypical subtrochanteric and diaphyseal femoral fractures: second report of a task force of the American Society for Bone and Mineral Research. *AJR*. 2010;196(1):W52–W57. doi:10.2214/AJR.09.3383