

AMSER Case of the Month

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Denosumab induced femoral insufficiency fracture
evaluation and workup



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Patient Presentation

Clinical Presentation: A 74-year-old woman presents to the ED with excruciating left thigh pain radiating to the hip after a fall. She reported chronic shooting nerve pain with certain movements, radiating bilaterally. While walking, an episode of pain caused her to lose balance and fall. She heard a “pop.” Left femur radiographs demonstrate a displaced fracture of the proximal diaphysis of the left femur. The lateral cortical thickening seen on radiographs (Figure 1) was concerning for an atypical femoral fracture, prompting further evaluation of the contralateral (right) femur.

PMH: Hypertension, osteoporosis for 10-15 years, strong family history of osteoporosis, arthritis, annual DEXA screenings through PCP

Medications: Denosumab (Prolia) every 6 months for about 10 years, alendronate (Fosamax) for 4-5 years, tramadol, simvastatin, senna, pregabalin, cyclosporine, daily calcium and Vitamin D supplementation



Atypical femoral fracture (AFF) of the proximal diaphysis of the left femur, prompting evaluation of the right femur

What Imaging Should We Order?

Select the applicable ACR Appropriateness Criteria

Scenario	Scenario ID	Procedure	Adult RRL	Peds RRL	Appropriateness Category
Stress fracture suspected, femur, initial imaging	3197231	● Radiography femur	<0.1 mSv ☼	0.03-0.3 mSv [ped] ☼☼	Usually appropriate
		● Bone scan whole body with SPECT or SPECT/CT femur	1-10 mSv ☼☼☼	3-10 mSv [ped] ☼☼☼☼	May be appropriate
		● US thigh	0 mSv O	0 mSv [ped] O	Usually not appropriate
		● MRI thigh without and with IV contrast	0 mSv O	0 mSv [ped] O	Usually not appropriate
		● MRI thigh without IV contrast	0 mSv O	0 mSv [ped] O	Usually not appropriate
		● CT thigh with IV contrast	0.1-1mSv ☼☼		Usually not appropriate
		● CT thigh without IV contrast	0.1-1mSv ☼☼		Usually not appropriate
		● CT thigh without and with IV contrast	1-10 mSv ☼☼☼		Usually not appropriate

This imaging modality was ordered for the right femur due to a suspicion of atypical femoral fracture, which commonly presents bilaterally.

Findings (unlabeled)

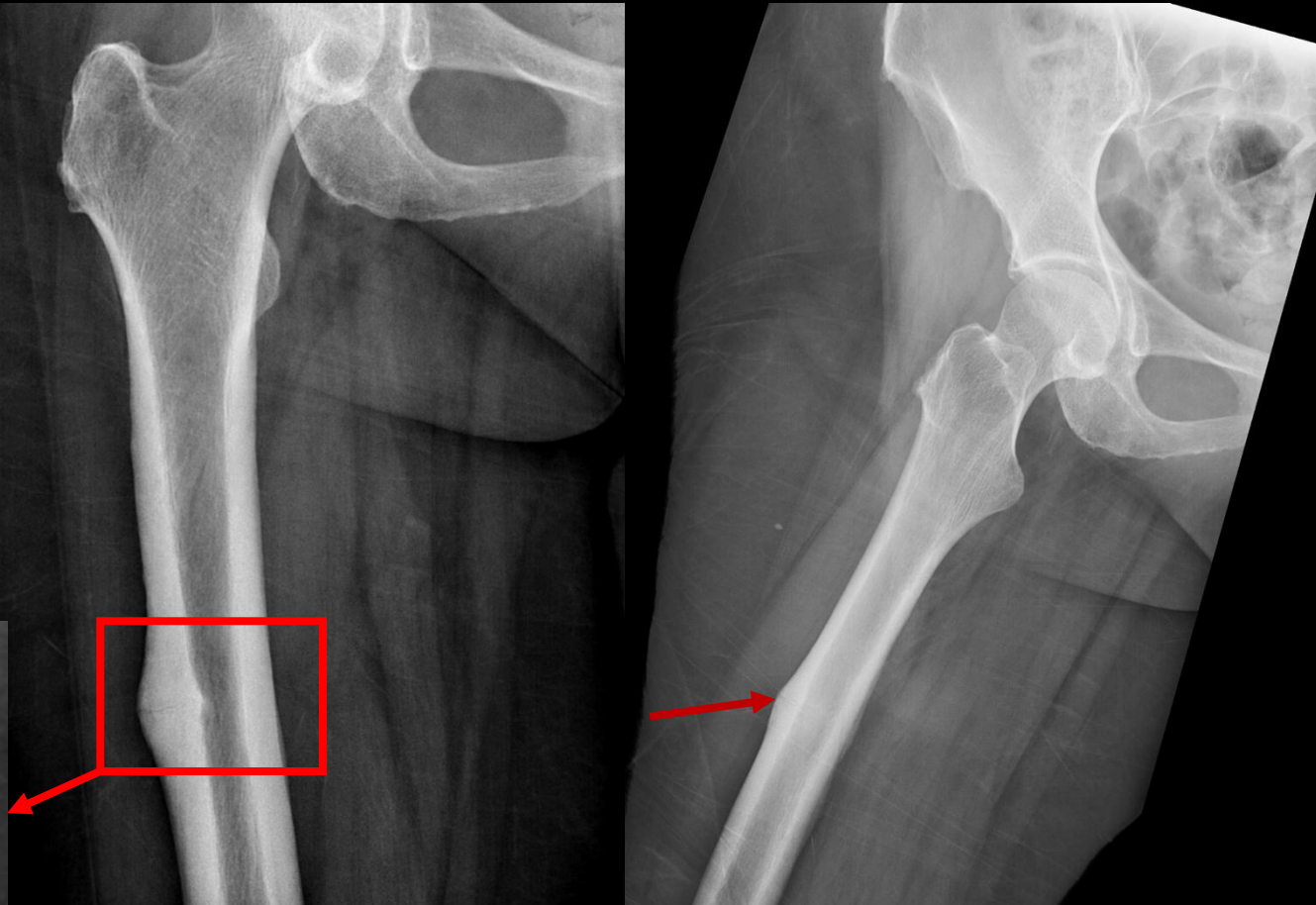
Zoomed-in View



Radiographs of
the right femur
(AP and frog
lateral views)

Findings (labeled)

Zoomed-in View



Red arrow indicates hypertrophic reactive changes with linear fracture lucency transversing the hypertrophied lateral cortex.

The following criteria of AFFs are met¹:

- Transverse fracture line is located in the more proximal diaphyseal region
- Lateral cortex is involved
- Transverse oblique fracture line
- No comminution
- No precipitating trauma

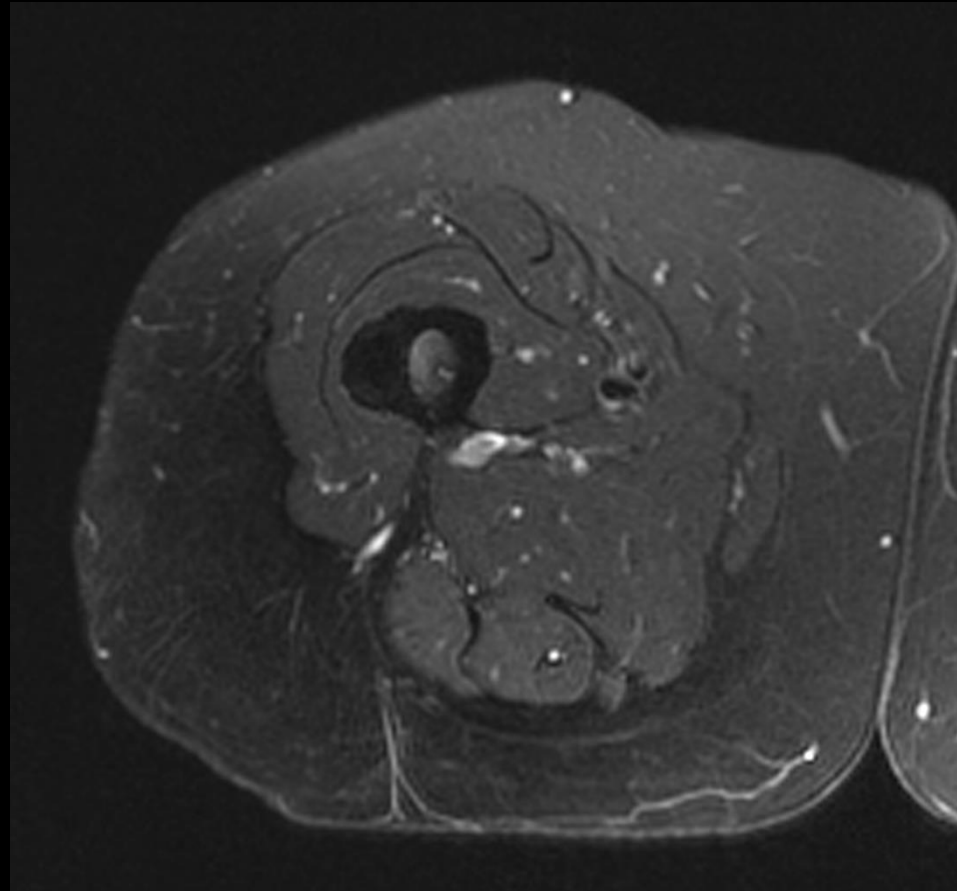
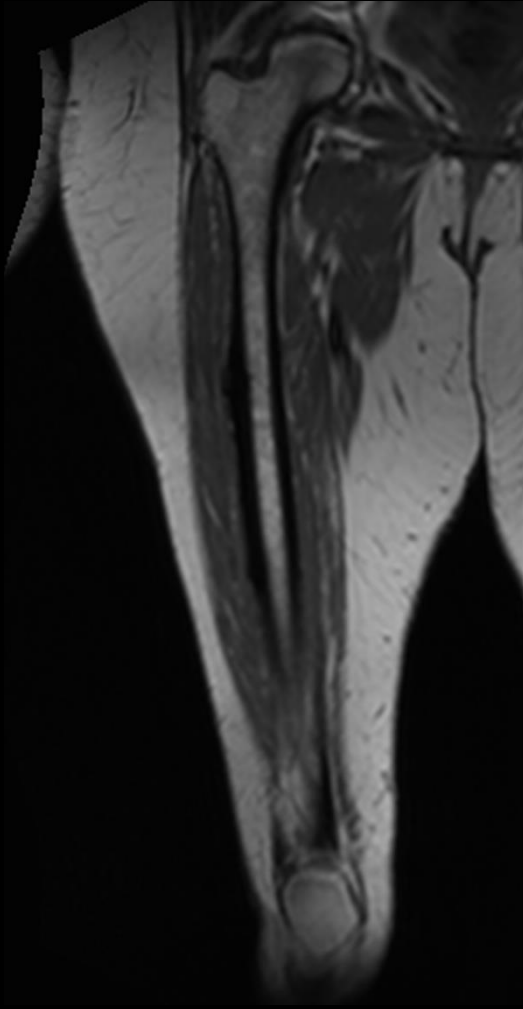
Select the applicable ACR Appropriateness Criteria

Scenario	Scenario ID	Procedure	Adult RRL	Peds RRL	Appropriateness Category
Stress fracture suspected, femur, osteoporosis or bisphosphonate therapy, radiography indeterminate, next imaging study	3197297	● MRI thigh without IV contrast	0 mSv O	0 mSv [ped] O	Usually appropriate
		● CT thigh without IV contrast	0.1-1 mSv ☼☼		May be appropriate
		● Bone scan whole body with SPECT or SPECT/CT femur	1-10 mSv ☼☼☼	3-10 mSv [ped] ☼☼☼☼	May be appropriate
		● US thigh	0 mSv O	0 mSv [ped] O	Usually not appropriate
		● Radiography femur repeat in 10-14 days	<0.1 mSv ☼	0.03-0.3 mSv [ped] ☼☼	Usually not appropriate
		● MRI thigh without and with IV contrast	0 mSv O	0 mSv [ped] O	Usually not appropriate
		● CT thigh with IV contrast	0.1-1 mSv ☼☼		Usually not appropriate
		● CT thigh without and with IV contrast	1-10 mSv ☼☼☼		Usually not appropriate



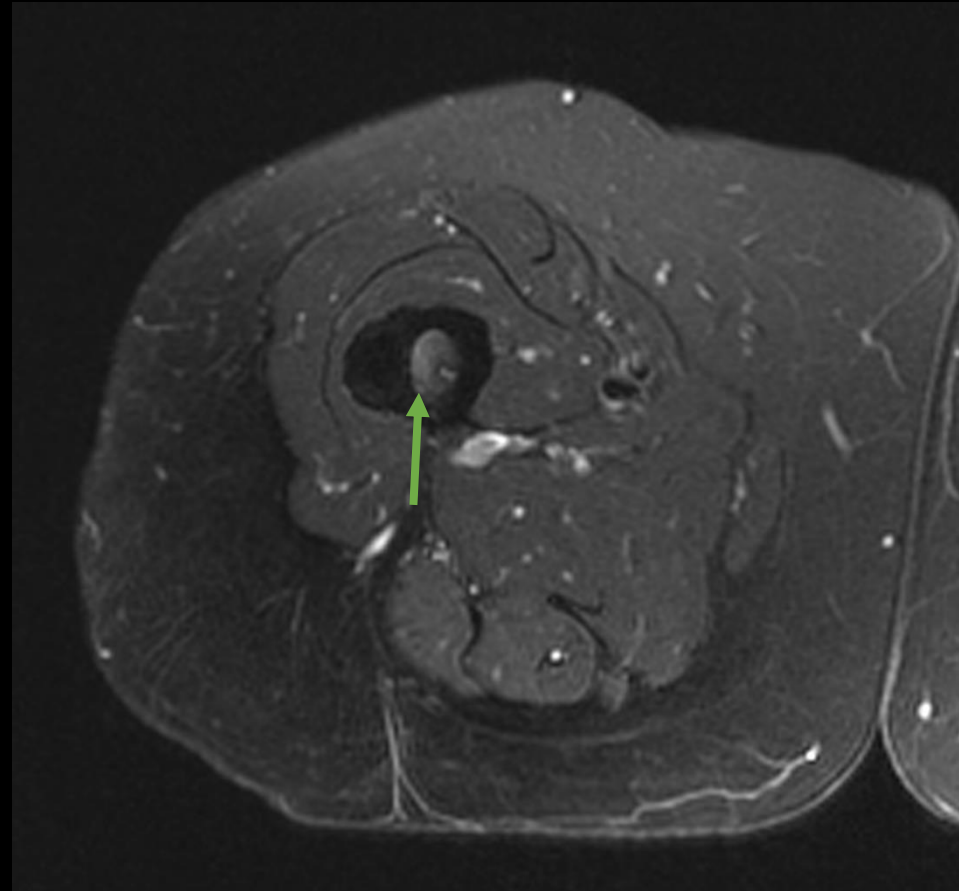
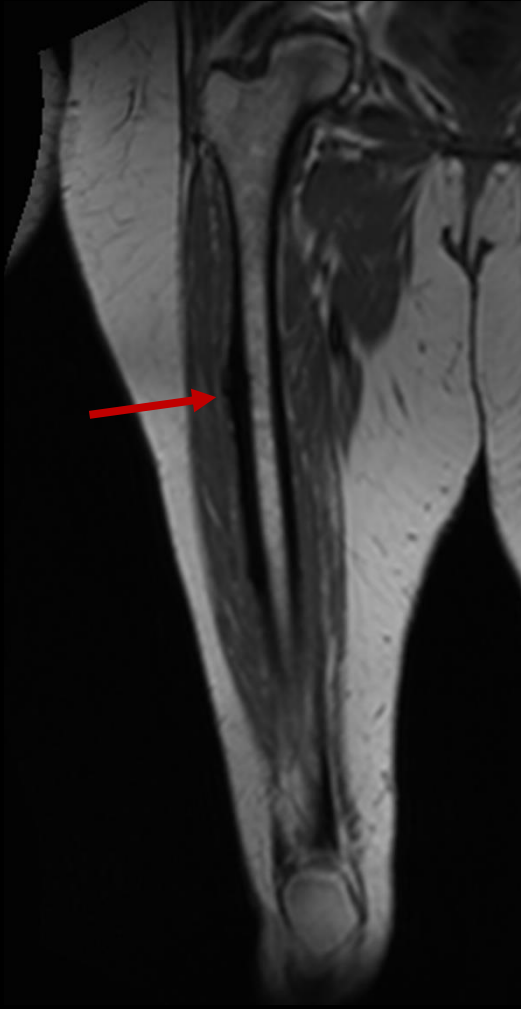
This imaging modality was ordered for the right femur to assist with surgical planning.

Findings (unlabeled)



Coronal T1
(left) and axial
fat saturated T2
(right) MRI
images of the
right femur

Findings (labeled)



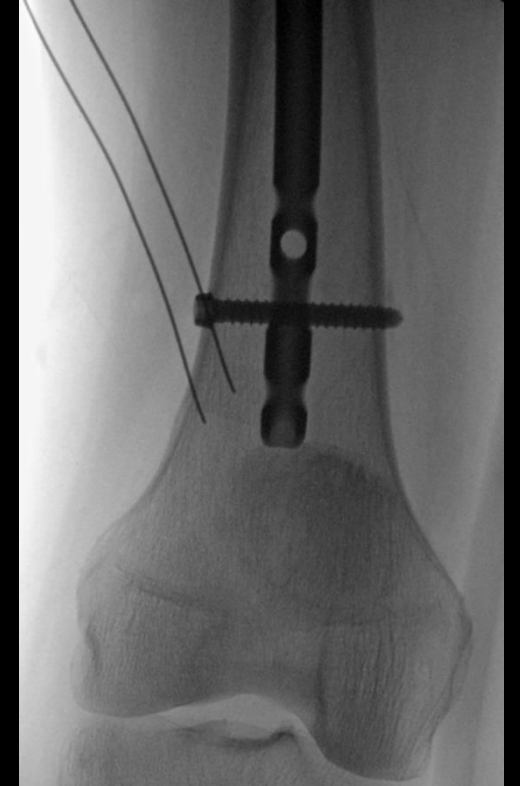
MRI confirms focal cortical thickening along the lateral cortex of the mid right femoral diaphysis (red arrow). There is underlying mild subcortical bone marrow edema (green arrow). The transverse fracture line is not readily visible.

Final Diagnosis:

Denosumab-associated atypical femoral fracture

Management

- Surgical management included immediate surgery to stabilize the potential impending right femoral shaft fracture with an intramedullary implant
- The patient continued calcium and vitamin D supplementation
- Additionally, the patient was discontinued on Prolia and recommended to follow up with Endocrinology for alternative treatment options for osteoporosis
- Patient was subsequently managed with Evenity (romosozumab) injections monthly



Fluoroscopic images demonstrating intramedullary implant placement for prophylactic stabilization of the right femur. An image at the site of fracture was not obtained.

Role of Advanced Imaging

- Per ACR Appropriateness Criteria, radiography of the femur is the most appropriate initial imaging for a suspected stress fracture
- Additionally, the most appropriate next imaging study for a patient with high risk for fracture completion is an MRI of the area of interest without IV contrast
- In our case example, although radiographs of the right femur suggested an atypical femoral fracture, a follow up MRI was ordered by the orthopedic surgeon for confirmation and surgical planning
- If the cortical bone is unremarkable or if there is no horizontal lucency within the cortex on radiographs, an occult stress fracture may be present and advanced imaging with MRI would be indicated for diagnosis¹
- A transverse low signal intensity line within the cortex on T1 weighted images can be identified on MRI, to help confirm the diagnosis of an atypical femoral insufficiency fracture¹
- MRI can better differentiate between active stress reaction and healed prior stress changes by detecting bone marrow edema in the setting of an acute fracture, which can help guide the decision between conservative management and prophylactic fixation

Case Discussion

- Atypical femoral fractures (AFFs) are frequently associated with long term treatment for osteoporosis, most commonly with bisphosphate use²
- Denosumab, which is a monoclonal antibody that prevents bone breakdown, has also been reported to be associated with AFFs and present similarly to bisphosphonate induced femoral insufficiency³
- Bisphosphonates, most commonly alendronate, is used as a treatment for osteoporosis by inhibiting the activity of osteoclast-mediated bone resorption⁴
- Long term suppression of bone remodeling may allow microdamage to accumulate, contributing to the atypical femoral fractures⁴
- Although an association exists between long-term bisphosphonate use and AFFs, causation has not been definitively established and the risk remains low²
- AFFs commonly occur in the subtrochanteric or femoral diaphyseal region⁵

Case Discussion

- According to a previous study, AFF incidence decreased by about 50% in the first year after discontinuation of bisphosphonates and 80% after 2 or more years of discontinuation⁶
- Since the patient's alendronate use occurred more than 10 years prior, recent denosumab more likely contribute to the development of the AFF in this patient
- To satisfy the case definition of AFF, the fracture must be located along the femoral diaphysis from just distal to the lesser trochanter to just proximal of the supracondylar flare and 4 of 5 of the major features must be present⁶:
 1. Fracture is associated with minimal or no trauma
 2. Fracture line originates at the lateral cortex and is transverse in its orientation
 3. Complete fractures extend through both cortices; incomplete fractures only involve the lateral cortex
 4. Fracture is noncomminuted or minimally comminuted
 5. Localized periosteal or endosteal thickening is present at the fracture site
- Our case meets all 5 of the major features of AFFs
- AFFs have a bilateral occurrence of 20-30%⁷

References:

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3. Alabbasi A, Moloney DP, Murariu CM, Khan SU. Bisphosphonate break without the bisphosphonate: atypical femoral fracture with denosumab. *BMJ Case Reports CP.* 2025;18(6):e265400. doi:10.1136/BCR-2025-265400
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5. Caldaci A, Panebianco P, Condorelli S, et al. Impact of Prolonged Bisphosphonate Therapy on Atypical Femoral Fractures: Insights from a Single-Center Experience. *J Pers Med.* 2025;15(12):565. doi:10.3390/JPM15120565
6. Black DM, Condra K, Adams AL, Eastell R. Bisphosphonates and the risk of atypical femur fractures. *Bone.* 2022;156:116297. doi:10.1016/J.BONE.2021.116297
7. Mohamed A, Fuad U, Abdelazim M, Elasad A, Bhamidipati P. Bisphosphonate-Related Atypical F
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