

> THE PATIENT

67-year-old woman

> SIGNS & SYMPTOMS

- Bilateral thigh and knee pain
- Leg weakness
- No history of trauma

> THE CASE

A 67-year-old woman presented to our orthopaedic clinic with a 2-year history of bilateral thigh and knee pain and weakness of her legs. She had no history of trauma, and the pain, which was localized to the distal anterior thighs and patellofemoral area, was 7/10 at rest and worse with standing and walking.

Her medical history was significant for osteoporosis (diagnosed in 2004), hypertension, hypothyroidism, gastroesophageal reflux disease, and menopause (age 54). Her original dual-energy x-ray absorptiometry (DEXA) scan did not reveal the presence of any previous fractures. She was started on calcium and vitamin D supplementation and oral alendronate (70 mg once a week). She took alendronate for 4 years until 2008, when it was stopped due to nausea. She was then started on zoledronic acid (5 mg IV annually). She received 5 infusions of zoledronic acid between 2008 and 2013; she did not have an infusion in 2012. Her medication list also included lisinopril, omeprazole, naproxen, cyclobenzaprine, and a multivitamin. She had normal renal function (estimated glomerular filtration rate >60 mL/min/1.73 m²) and she did not drink alcohol or use tobacco.

In the 2 years prior to her visit to our clinic, she had been evaluated by her primary care provider, an orthopedic sports medicine specialist, 2 spinal surgeons, and a physiatrist. She had also undergone 30 physical therapy sessions. Bilateral femur radiographs (FIGURE 1) ordered by her orthopedist 6 months earlier demonstrated no evidence of fracture, but did show an incidental enchondroma in the right distal diaphysis and bilateral thickening of the lateral femoral cortices.

Finally, with no relief in sight, her obstetrician suggested that she might be experiencing myalgias attributable to her zoledronic acid infusions. She was subsequently referred to us.

■ **The physical exam** revealed a thin female with a body mass index of 21. She had mild tenderness on palpation of the bilateral anterior thighs and knees. There was no pain with hip or knee range of motion and minimal pain in the bilateral lower extremities with axial loading. The patient had normal sensation, did not have an antalgic gait, and exhibited 5/5 strength bilaterally in all distributions of the lower extremities.

THE DIAGNOSIS

Due to continued pain despite negative x-rays, we obtained a 3-phase bone scan of the pelvis and bilateral femurs. Delayed images showed moderately increased activity in the mid-right and mid-left lateral femoral diaphyses at the cortex and confirmed stress fractures (FIGURE 2).

DISCUSSION

Bisphosphonates are considered first-line therapy for osteoporosis, according to current evidence-based guidelines.¹ These medications inhibit osteoclast activity and can bind to

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FIGURE 1

No evidence of fracture?



Bilateral femoral x-rays, taken 6 months prior to surgery, showed no evidence of fracture, dislocation, or pathologic calcifications. However, early findings of atypical femoral fractures can be seen, including lateral cortex thickening and beaking (see arrows). An incidental 3.3-cm enchondroma is noted in the right distal diaphysis.

the bone for more than 10 years.^{2,3} (In women with bone mineral density scores ≤ -2.5 , the number needed to treat is 21.^{1,4})

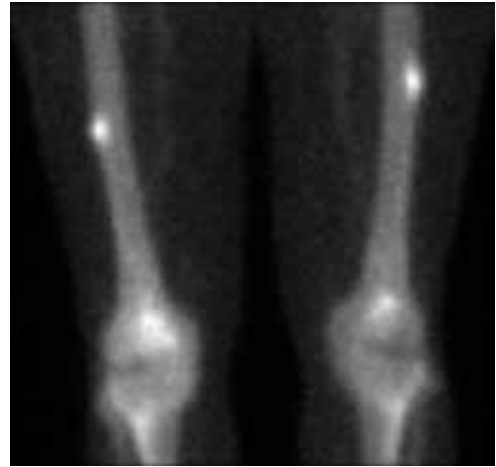
Patients taking bisphosphonates, however, are susceptible to atypical femoral fractures (AFFs), which are stress or insufficiency fractures associated with minimal or no trauma.⁵ The pathophysiology remains unknown at this time, but AFFs may result from changes in bone remodeling that occur when a bone experiences repetitive micro-trauma, leading to lateral cortical thickening of the femur.^{6,7} Incidence of AFFs in patients taking bisphosphonates is estimated to be between 3.2 and 50 cases per 100,000 person-years; however, this risk increases to approximately 100 per 100,000 person-years with long-term use.⁵ Other risk factors include low body weight, advancing age, rheumatoid arthritis, long-term glucocorticoid therapy, and excessive alcohol and cigarette use.⁸

What you'll see

Symptoms typically include unilateral or bilateral prodromal pain with a sharp or achy

FIGURE 2

A 3-phase bone scan was more revealing



A 3-phase bone scan showed increased activity in the mid-right and mid-left lateral femoral diaphyses at the cortex, which was suggestive of stress fractures.

character that is localized to the mid-thigh, upper thigh, or groin.⁹ If an AFF is suspected, we recommend performing a bilateral exam and obtaining radiographs.

If characteristic features are found (eg, signs of focal cortical thickening or beaking) and pain arises in the opposite limb, obtain a radiograph of the contralateral femur. If radiographs are negative but suspicion remains, order magnetic resonance imaging or a bone scan, to identify a cortical fracture line, bone and marrow edema, or hyperemia.⁵

Begin treatment by discontinuing bisphosphonates

Upon identification of an AFF, discontinue bisphosphonates and initiate calcium and vitamin D supplementation.⁵ Prophylactic surgical fixation may also be necessary to accelerate healing and prevent fracture propagation and further pain.

■ **Our patient.** Due to the longevity of the symptoms and the bilateral stress fractures noted on the bone scan, our patient chose to proceed with intramedullary nailing of the bilateral femurs (FIGURES 3 and 4). On postop Day 1, she was able to ambulate using a walker and to participate in bilateral weight-bearing

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> If radiographs are negative, but suspicion remains, an MRI or a bone scan should be ordered.

FIGURE 3

Bilateral intramedullary nailing



The patient underwent fixation with intramedullary nailing for bilateral atypical femoral fractures.

FIGURE 4

More pronounced beaking



Postoperative bilateral femoral x-rays demonstrated further lateral femoral cortex thickening and more pronounced beaking (see arrows).

(as tolerated). She was discharged to a skilled nursing facility, where she progressed to full weight-bearing without aid. On follow-up (one year postop), the patient reported no residual leg pain and was able to work out 5 days per week. Radiographs of her femurs demonstrated healed fractures and stable position of the intramedullary nails.

THE TAKEAWAY

An increased suspicion for AFFs due to bisphosphonate use can lead to earlier diag-

nosis and decreased morbidity for patients. Use of femoral imaging can promote detection and reduce financial burden.

To help prevent AFFs from occurring, we recommend reevaluating the need for continued bisphosphonate therapy after 2 to 5 years of treatment. Continued surveillance is also advisable throughout the duration of their use.

JFP

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