

CASE REPORT



Atypical femoral fracture in the setting of alendronate treatment for osteoporosis: a case report and literature review

Eric D. Van Baarsel, Vandan Patel, Yazeed Kesbeh, Huthayfa Kahf and Nicholas Alonzo

School of Medicine, University of California, Riverside, CA, USA

ABSTRACT

Osteoporosis leads to reduced bone mass and disrupted bone architecture. Bisphosphonates are used to treat osteoporosis by inhibiting bone resorption. Chronic bisphosphonate use has been associated with adverse effects including atypical femoral fractures (AFF). We report the case of a 63-year-old woman with a history of osteoporosis treated with alendronate, who presented with bilateral hip and groin pain. Radiography detected a chronic-appearing callus in the left hip concerning for a chronic stress fracture versus malignancy. Initial imaging could not rule out malignancy, prompting positron emission tomography (PET) and bone biopsy. PET scan was negative for malignancy and biopsy found changes consistent with chronic bisphosphonate use. This prompted prophylactic intramedullary nailing of the femur. This case highlights the importance of considering AFF in patients with a history of hip pain in the setting of chronic BPs use and reviews criteria within the literature to manage patients with AFFs.

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1. Introduction

Osteoporosis is a disease characterized by decreased bone mass and increased bone fragility due to disruption of the bone microarchitecture and deterioration of bone tissue[1]. It is the most common bone disease in humans and its prevalence continues to rise with the aging population. It has been estimated that over 200 million people are affected by osteoporosis worldwide, with over 44 million in the USA alone[2]. Osteoporosis is most common in Caucasians, the elderly, and women[1]. Advanced age is the best predictor of the disease, but other factors such as smoking, glucocorticoid overuse, early menopause, low body weight, and maternal factors all play a role in the pathogenesis of osteoporosis[2].

Reduced bone mass and disrupted bone architecture in osteoporosis leads to the presence of porous bones that are more susceptible to skeletal and non-skeletal fractures, termed fragility fractures. These fragility fractures can occur with low-impact. All fractures are associated with considerable morbidity, a decreased quality of life, and increased mortality[2]. The resultant decrease in mobility, increase in hospitalizations, and increase in nursing home requirements impose a significant financial burden on the patient and health care services[2]. Therefore, early diagnosis and treatment is crucial to reduce the overall health and financial burden imposed by osteoporosis.

In 1995 the USA Food and Drug Administration approved alendronate as the first drug in the bisphosphonate (BPs) class to be used to prevent fractures

caused by osteoporosis. BPs have a structure similar to pyrophosphate and act by attaching to hydroxyapatite binding sites on bone, particularly in areas of high resorption. As bone is resorbed by osteoclasts, the bisphosphonate is released and impairs the osteoclast's ability to further resorb bone[3]. Though effective in inhibiting bone resorption, prolonged use of bisphosphonates has been associated with certain serious adverse effects including AFFs and osteonecrosis of the jaw. Here we present a case of an AFF in a 63-year-old female in the setting of alendronate treatment for osteoporosis.

2. Case presentation

A 63-year old female with a past medical history of osteoporosis presented with a multiple year history of bilateral hip pain, with more significant pain on the left. The patient endorsed a previous history of alendronate use several years prior to presentation. Unfortunately, the patient was a poor historian and could not recall the details of how long she underwent alendronate therapy. Her pain was primarily located in her groin and lateral hip, described as sharp and burning, and was worse with movement. The patient denied any significant trauma. Physical examination was positive for generalized tenderness to palpation over the trochanteric regions bilaterally and mild pain within the bilateral groins upon internal rotation. Initial radiographic findings found mild degenerative changes to the bilateral hips with the lateral aspect of the left femur containing

a subtrochanteric chronic-appearing callus concerning for an incomplete chronic stress fracture versus malignancy (Figure 1, Figure 2). The suspicious finding prompted magnetic resonance imaging (MRI) which found a 2.4 cm sclerotic density along the left proximal lateral femur with low signal in both T1 and T2. Further evaluation with bone scintigraphy found focal uptake within the bilateral proximal femurs, left greater than right, seen only on delayed imaging. From these results, the differential diagnosis included both benign and malignant etiologies prompting analysis with PET scan and computed tomography (CT) guided biopsy. PET scan found no significant fluoroxyglucose uptake to suggest malignancy or metastatic disease. CT guided biopsy found small fragments of sclerotic bone compatible with changes seen in chronic bisphosphonate use. With malignancy ruled out, the patient was diagnosed with an incomplete AFF and a prophylactic trochanteric femoral nail was placed to prevent a future complete fracture of the proximal femur.



Figure 1. Anterior posterior X-ray of left femur demonstrating zone of sclerosis within the proximal femur.



Figure 2. Anterior posterior X-ray of bilateral hips displayed increased cortical thickness of the bilateral femoral diaphyses with partially visualized zone of sclerosis within the proximal lateral left femur.

3. Discussion

For greater than two decades, BPs have been extensively prescribed to patients with a history of osteoporosis and have been shown to reduce risk of vertebral and femoral neck fractures due to their ability to maintain bone density [4,5]. However, concerns have been raised that chronic BPs treatment may cause over suppression of bone turnover. It has been proposed that severe suppression of bone turnover may occur with chronic BPs therapy resulting in increased skeletal fragility and diminished ability to repair skeletal microcracks[6]. Furthermore in 2007, Goh and others reported an association between AFFs and long-term alendronate therapy. Five of nine patients in that study reported pain or discomfort in the proximal affected limb, groin and/or in the lateral aspect of the thigh. Radiographs found that the majority of these patients had type-A subtrochanteric fractures with good cortical bone stock with thickening in the lateral femoral cortex[7].

Soon after this study, the American Society for Bone and Mineral Research (ASBMR) published reports in 2010 and 2013 defining unique characteristics of AFFs distinct from fractures caused by typical osteoporotic femur fractures [8,9]. The ASBMR Task Force stated that for a fracture to classify as an AFF, the fracture must be located within the femoral diaphysis distal to the lesser trochanter but proximal to the supracondylar flare. Major features of AFFs were defined, of which four of five must be present. Additionally, minor features associated with AFFs were reported, but these features are not mandatory for the diagnosis of AFF

Table 1. ASBMR task force 2013 revised case definition of AFFs. Four of five major features should be observed; minor criteria may be observed but are not necessary for diagnosis.

Major Features

- Fracture is associated with minimal or no trauma (eg, fall from standing height or less)
- Fracture line originates at the lateral cortex, and is substantially transverse in its orientation, although it may become oblique as it progresses medially across the femur
- Complete fractures extend through both cortices and may be associated with a medial spike; incomplete features involve only the lateral cortex
- The fracture is noncomminuted or minimally comminuted
- Localized periosteal or endosteal thickening of the lateral cortex is present at the fracture site ('beaking' or 'flaring')

Minor Features

- Generalized increased in cortical thickness of the femoral diaphysis
- Unilateral or bilateral prodromal symptoms such as a dull or aching pain in the groin or thigh
- Bilateral incomplete or complete femoral diaphysis fractures
- Delayed fracture healing

ASBMR = American Society for Bone and Mineral Research; AFF = atypical femur fracture. Excludes fractures of the femoral neck, intertrochanteric fractures with spiral subtrochanteric extension, periprosthetic fractures, and pathological fractures associated with primary or metastatic bone tumors and miscellaneous bone diseases (eg, Paget's disease, fibrous dysplasia).

(Table 1)[9]. Radiographic imaging of our patient found a left femoral subtrochanteric noncomminuted horizontal chronic stress fracture of the lateral cortex that was not associated with any significant trauma (Figure 1, Figure 2). Additionally, the patient had prodromal symptoms in the groin and thigh along with generalized increased cortical thickness of the bilateral femoral diaphyses (Figure 2). Therefore, the radiographic findings coupled with the patient's history satisfied five of five major features and two minor features defined by the ASBMR task force.

All patients diagnosed with AFF should discontinue BPs use and begin taking calcium and vitamin D supplements[10]. It has been observed that risk of AFF will drop by 70% per year once BPs are stopped [11]. Despite these efforts, patients who discontinue BPs therapy have a 19.3% incidence of contralateral AFF in the next three years compared with 41.2% if BPs are continued [10,12]. Radiographs of the contralateral femur should be a priority even in the absence of prodromal symptoms as AFF affects the contralateral leg in 28% of cases [9,10]. Adequate study of the contralateral femur prior to surgical treatment of the affected leg is preferred to help guide management [10]. Intramedullary (IM) nailing is often done for both complete and incomplete AFF with the latter being to prevent a complete fracture in the future [10]. The drug teriparatide has also been shown to be effective in both complete and incomplete AFF as it promotes callus formation even in cases of nonunion while also reducing healing time[13]. In our patient's case, once malignancy was ruled out, it was decided to prophylactically place a trochanteric femoral nail in the limb containing the AFF as a preventive measure.

4. Conclusion

Osteoporosis is prevalent both worldwide and in the USA. As these numbers continue to increase, more patients will be placed on long term BPs to help prevent the detrimental consequences of osteoporosis. Despite the apparent increase in AFFs in patients on chronic alendronate therapy, studies have shown rates of AFFs in these patients are only 11 per 100,000 per year; however, hip fracture rates have been shown to be decreased by 20–50%[14]. With the risks and benefits of long-term bisphosphonate use in mind, patients should still be encouraged to undergo bisphosphonate therapy. However, clinicians should be aware of the potential development of excessive suppression of bone turnover and the development of AFF. Patients with history of chronic bisphosphonate therapy (particularly those for more than 3 to 10 years) who develop limb or groin pain should be evaluated to rule out possible AFFs [8,9,15]. For patients with a vague history of BPs use (such as the one described herein), malignancy or other bone disease should be ruled out before the diagnosis of AFF can be given. If pathological causes of fracture have been excluded, and four of five major features defined by the ASBMR are satisfied, AFF can be diagnosed and appropriate management should be initiated.

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