ABSTRACT

Recent literature shows an association between long-term bisphosphonate therapy and low-energy fractures of the subtrochanteric femur. It is thought that the pharmacology of bisphosphonates and stress characteristics of the subtrochanteric femur predispose patients on long-term therapy to fracture. There are few reports in the literature of bisphosphonate-associated periprosthetic fractures with the characteristic fracture pattern. We report a case in a patient with a 10-year history of sustained bisphosphonate use. The patient is a 79-year-old female that developed new thigh pain 9 years following a cemented total hip arthroplasty. Radiographs revealed lateral cortical thickening and a transverse periprosthetic stress fracture of the lateral femoral cortex at the level of the distal stem. This fracture appears consistent with a bisphosphonate-associated insufficiency fracture, demonstrating that this pattern is not isolated to nonarthroplasty patients.

Keywords: Bisphosphonate, Femur fracture, Periprosthetic fracture, Insufficiency fracture.

INTRODUCTION

Recent reports have shown a strong association between long-term bisphosphonate therapy and low-energy femur fractures.1-7 These reports include subtrochanteric, diaphyseal and bilateral femur fractures.8 However, there are few reports in the literature of periprosthetic femur fractures in patients on long-term bisphosphonate therapy.9,10 Bisphosphonates have been shown to reduce the risk of fragility fractures, including vertebral and femoral neck fractures in postmenopausal osteoporotic patients.11-13 However, the unique pharmacology of bisphosphonates and stress characteristics of the subtrochanteric femur appears to place patients on long-term therapy at an increased risk of subtrochanteric and proximal-third diaphyseal fractures. We present a patient with a 10-year history of continued bisphosphonate use that sustained a periprosthetic femoral stress fracture after total hip arthroplasty.

CASE REPORT

A 79-year-old female with a history of hypothyroidism, chronic obstructive pulmonary disease, osteoporosis, and bilateral total knee replacements, underwent an uncomplicated right total hip arthroplasty with a cemented stem and uncemented cup at our institution in 2001. She began treatment for her osteoporosis in 2000 with alendronate and later changed to ibandronate in 2008, for a total of 10-year of continuous therapy.

One year following her surgery she complained of new-onset right hip and thigh pain. Radiographs revealed a fracture in the proximal cement mantle with a new radiolucency at the distal femoral stem concerning for possible early prosthetic loosening. An infection work-up was negative. The patient experienced gradual symptomatic improvement without intervention. Four years postoperatively the patient had good function with intermittent thigh pain. Radiographs showed a subtle varus position of the stem with lateral migration of the stem tip, and radiolucencies around the distal cement mantle and the lateral shoulder (Fig. 1). Aseptic loosening was suspected, but due to her stable radiographs and minimal pain no treatment was recommended.

At 9 years postoperatively, she presented to clinic complaining of daily right thigh pain and difficulty with ambulation requiring the assistance of a walker. She denied any recent fall or other inciting trauma. Radiographs revealed a periprosthetic stress fracture with cortical thickening of the lateral femoral cortex at the level of the distal femoral stem (Fig. 2).

She was offered a revision of the femoral component, but she elected to pursue conservative treatment, consisting of protected weight bearing. Over the next 3 months her symptoms progressed and new radiographs revealed medial extension and widening of the known fracture (Fig. 3).

She elected to undergo revision of her femoral component with a long, fully porous-coated femoral stem, strut graft, cerclage cables, and exchange of the acetabular polyethylene liner. Her bisphosphonate therapy was discontinued at admission as her fracture pattern raised concern for a bisphosphonate-associated fracture. A lateral cortical window was used for cement removal. At follow-up 5 months postrevision, radiographs show stable alignment of her uncemented femoral stem with minimal healing across the fracture site and cortical window (Fig. 4).

Due to reports of bilateral insufficiency fractures in patients on long-term bisphosphonate therapy,8,14,15 radiographs of the contralateral femur and a bone scan were obtained, both of which were negative for fracture.
DISCUSSION

Bisphosphonates bind preferentially to hydroxyapatite at the site of bone resorption and inhibit osteoclast function by inducing apoptosis and blocking cholesterol synthesis. Short-term use of bisphosphonates inhibits bone resorption and can increase bone mineral density. Long-term use of bisphosphonates, estimated at 5 years or more, inhibits bone remodeling, which is critical for the repair of physiologic microdamage.5,8,17,18

A major factor in the inhibition of bone remodeling is the long half-life of bisphosphonates in bone, estimated at 10 years.13 This impaired remodeling has been demonstrated histologically in animal models and includes increased mineralization, decreased osteoid production, and a reduction in resorption surfaces. As a result of decreased remodeling, a 2 to 7 fold increase in the accumulation of physiologic microdamage occurs in bone. Ultimately, this microdamage impairs the mechanical properties of bone, leading to a 20% reduction in toughness, increased brittleness, and subsequent propagation of stress fractures that would otherwise be repaired.17,18 These effects are seen in regions of high physiologic stress prone to microdamage accumulation, such as the subtrochanteric femur. As a result, a characteristic ‘simple with thick cortices’ pattern of subtrochanteric femur fractures has been described in patients on long-term bisphosphonate therapy.4

Despite recent literature in support of the link between chronic bisphosphonate therapy and subtrochanteric fractures, there is still skepticism among some groups. A recent meta-analysis did not show a significant increase in the risk of fractures associated with bisphosphonate use.20 This meta-analysis included three large randomized studies and found a rate of 2.3 fractures per 10,000 patient-years...
with hazard ratios that, although all higher than 1.0, had large confidence intervals. The authors concluded that the study was underpowered to provide a definitive conclusion with regard to the association between chronic bisphosphonate use and subtrochanteric femur fractures.20

In our case, we believe the transverse femoral shaft fracture had characteristics of an insufficiency stress fracture and was unrelated to early loosening of the femoral stem with mild varus angulation. After initial femoral stem migration, the patient remained active and relatively pain free without radiographic progression over an extended time period. There is one case report19 in the literature of a lateral femoral insufficiency fracture in total hip arthroplasty caused by varus angulation and osteopenia, and two reports9,10 describing periprosthetic insufficiency fractures after long-term alendronate therapy.

Gill et al19 reported on lateral femoral insufficiency fractures in total hip arthroplasty thought to be related to osteopenia and varus positioning of the femoral component. The similarity between the cases described by Gill et al and our patient is the progressive varus position of the stem and the presence of a fracture in pathologic bone. Varus stem malalignment leads to stress concentration at the distal and lateral aspect of the stem and femur and can lead to cement fracture, component loosening and stress reaction or fracture.21–23 While our patient had a varus stem position, there was also progressive cortical thickening due to pathologic bone remodeling, unlike the cases described above that had osteopenia and thin cortical bone.

The unique thickened lateral femoral cortex and transverse subtrochanteric or diaphyseal insufficiency fracture pattern previously described in association with chronic bisphosphonate use9 is thought to be a result of two factors. First, suppressed bone turnover leads to poor healing of physiologic microdamage, resulting in a thickened femoral cortex.2,3 Second, the large tension force imposed on the lateral subtrochanteric and proximal diaphyseal femur contributes to the transverse fracture pattern.1,3,6 Furthermore, a high-offset stem was used in our case, which increases strain and the bending moment on the implant.24

When managing patients with bisphosphonate-associated insufficiency fractures, it is important to recognize the long half-life of bisphosphonates and the resulting depression of bone turnover, even after drug cessation.25 Patients can be taken off bisphosphonates after chronic use with little short-term effect on both bone turnover and osteoporosis prevention. Our patient stopped her long-term bisphosphonate therapy at the time of revision surgery. Radiographic follow-up at five months post-operatively show slow healing of both the cortical window and periprosthetic femoral fracture, possibly a result of chronic bisphosphonate therapy (Fig. 4). Serial bone density quantification data or bone turnover data such as N-telopeptide levels were not obtained, but may have proved useful in justifying the above-mentioned slow healing response seen in our patient.

The literature supports the use of reamed intramedullary nailing of nonperiprosthetic, subtrochanteric femoral insufficiency fractures. In addition, medical consultation and management consisting of vitamin D, calcium and teriparatide can be initiated.15 However, there is a paucity of literature to direct treatment of periprosthetic femoral insufficiency fractures. Following the Vancouver classification for femoral periprosthetic fracture,26 our patient had a type B2 fracture (i.e. fracture at the level of the distal stem with a loose implant) and therefore was revised with an uncemented long-stem prosthesis. An allograft strut was used to augment construct stability.

Femoral periprosthetic insufficiency fractures associated with bisphosphonate use are uncommon. Although our case was complicated by early loosening and varus femoral stem malalignment, the lateral cortical thickening, clinical presentation, fracture pattern, and slow healing are consistent with a bisphosphonate-associated femoral insufficiency fracture. Our report supports the relationship between long-term bisphosphonate therapy, reduced bone turnover and insufficiency fractures and demonstrates that this unique fracture pattern is not isolated to nonarthroplasty patients. Suppression of bone remodeling, even after cessation of chronic bisphosphonate use, can impair healing after revision surgery.

REFERENCES


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