Subtrochanteric Femoral Insufficiency Fracture in Woman on Bisphosphonate Therapy for Glucocorticoid-Induced Osteoporosis

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Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging; MDP, methylene disphosphonate; IV, intravenous; PTH, parathyroid hormone; SSBT, severely suppressed bone turnover

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Abstract

We present the case of an 85-year-old woman who sustained a subtrochanteric femoral shaft insufficiency fracture after receiving bisphosphonate therapy for osteoporosis. After more than 6 years of taking risedronate sodium (Actonel) and daily supplemental calcium carbonate and vitamin D, the patient developed right anterior thigh pain that was worse with weight-bearing. A small, pyramidal ridge of cortical bone was demonstrated by radiographs and CT along the antero-lateral subtrochanteric region of the right femoral shaft. On MRI, there was focally increased T2 signal in the adjacent bone marrow. Radionuclide bone scan showed moderately-intense, focally-increased uptake. The lesion was recognized as a potential stress riser for fracture; however, before a prophylactic intramedullary rod could be placed, the patient suffered a low-energy insufficiency fracture through the lesion. In the setting of bisphosphonate therapy for osteoporosis, a painful pyramidal projection of cortical bone in the subtrochanteric femoral shaft should be recognized as an impending insufficiency fracture and treated expeditiously.

Introduction

We present the case of an insufficiency fracture of the proximal femoral shaft in an 85-year-old woman who was receiving bisphosphonate therapy to reduce the fracture risk secondary to severe osteoporosis which was likely multi-factorial in etiology with advanced age, postmenopausal state, and prolonged use of glucocorticoid medications all likely being contributory. This fracture is
identical in presentation and appearance to other cases of insufficiency fractures of the proximal femoral shaft described in patients who developed severe suppression of bone turnover with prolonged oral bisphosphonate therapy. Abnormal bone remodeling due to prolonged osteoclast suppression appears to lead to insufficiency fractures of the subtrochanteric femoral shaft. It is ironic that medications known to increase bone density by decreasing the activity of osteoclasts, could in certain patients, contribute to severe suppression of bone turnover characterized by inadequate remodeling and the formation of insufficiency fractures.

Case Report

An 85-year-old woman presented with limp and anterior right thigh pain. After more than 6 years of taking risedronate sodium (Actonel) at a dose of 35mg/week, as well as supplemental calcium carbonate and Vitamin D, the patient complained of 2-3 months of persistent anterior right thigh pain that was worse with weight bearing. This pain was different from previous episodes of pain related to spinal stenosis and polymyalgia rheumatica. Her past medical history was significant for osteoporosis with prior fractures of the pelvis, spine, and both ankles, polymyalgia rheumatica, and disc degeneration with spinal stenosis. She had taken oral corticosteroids for polymyalgia rheumatica for many years with a daily dose alternating between 7.5 and 10 mg of prednisone. On physical exam, her pain was non-radiating, and her gait was antalgic. Initially, an MRI was performed at an outside institution, and the patient was subsequently referred to our institution for further evaluation. The MRI report described focally increased T2 signal in the right lateral femur. At our institution, a CT was performed as well as radiographs, and a bone scan. Radiographic evaluation of the femur demonstrated a focal pyramidal-shaped projection of bone on the lateral cortex (Fig. 1). The bone scan performed following injection Tc99m methylene disphosphonate (MDP) (Fig. 2) revealed a moderately-intense focus of increased uptake at the subtrochanteric region of the right femur and a degenerative pattern of activity in the spine, shoulders, knees, and wrists without evidence of other lesions concerning for metastatic disease. CT demonstrated a focal beak of cortical thickening on the lateral cortex (Fig. 3), and 3-dimensional reformations showed the lesion to be a domed roughly-pyramidal ridge, similar to a volcano such as Mt. Rainier (Fig 4). Although no fracture line was evident, this lesion was recognized as potential riser for fracture and the patient was referred to orthopedics. The patient hesitated at their recommendation for biopsy and prophylactic placement of an intramedullary rod to prevent fracture completion.
Figure 1. 85-year-old woman on bisphosphonate therapy. Radiographic evaluation of the femur demonstrated mild, diffuse cortical thickening and a focal, domed, conical, projection along the lateral cortex (arrow).

Figure 2. 85-year-old woman on bisphosphonate therapy. Tc99m MDP bone scan shows a focus of moderately intense uptake at the subtrochanteric region of the right femur (arrows) and a degenerative pattern of activity in the spine, shoulders, knees, and wrists, without evidence of metastatic disease.

Figure 3. 85-year-old woman on bisphosphonate therapy. 3D surface rendered CT reformation demonstrates the cortical ridge at the antero-lateral aspect of the femur at the junction of the proximal and middle thirds (arrow).
Nearly one month later, on her way to an appointment to discuss additional treatment options for this lesion, the patient stumbled on a curb. With this minimal trauma, the insufficiency fracture completed. Radiographs of the fracture showed a severely-angulated, simple, transverse, subtrochanteric femoral shaft fracture at the junction of the proximal and middle thirds (Fig 5). Following closed reduction, the fracture is seen to extend through the middle of the cortical ridge seen on the earlier radiograph (Fig. 6).

**Figure 4.** The volcanic mountain peak, Mt. Rainier, as viewed from Puget Sound offshore Seattle, Washington. (Courtesy Mahesh Thapa, M.D., starvingphotographer.com.)

**Figure 5.** 85-year-old woman on bisphosphonate therapy. Post-fracture radiograph depicts a severely-angulated, simple, transverse, subtrochanteric femoral shaft fracture at the junction of the proximal and middle thirds that extends through the middle of the triangular cortical ridge seen on the earlier studies. Old, healed fractures of the superior and inferior rami of the left obturator ring are also evident (arrows).
Figure 6. 85-year-old woman on bisphosphonate therapy. Proximal femoral shaft fracture following closed reduction of the marked angular deformity, the simple transverse fracture extends through the beak-shaped region of the insufficiency fracture (arrow). Mild diffuse cortical thickening is also present.

The patient underwent surgical reduction and internal fixation. A relatively long and thick reconstruction nail with two pins in the femoral neck was utilized due to the osteoporotic capaciousness of her intramedullary canal and to prevent formation of proximal femoral neck and distal femoral shaft stress risers which could lead to subsequent fractures. At the time of surgery, a curetted bone specimen was obtained by reaming for intramedullary rod placement. Histological examination of this specimen confirmed the absence of malignant disease.

Due to prolonged bisphosphonate usage and both chronic and ongoing glucocorticoid use, she was considered at risk for poor fracture healing, and her medications were adjusted to optimize healing. Medical necessity required that her steroid medication be continued; however, her bisphosphonate medication, risedronate sodium (Actonel), was discontinued. Her calcium and vitamin D supplementation were continued unchanged, and an anabolic agent, recombinant human parathyroid hormone, teriparatide (Forteo), was initiated at 20 micrograms daily by subcutaneous injection.

Follow up radiographs of the fracture site obtained ten (Fig. 7) and nineteen weeks (Fig. 8) after surgery demonstrated abundant fracture callus and were deemed consistent with appropriate interval fracture healing. The patient has recovered uneventfully.
**Figure 7.** 85-year-old woman on bisphosphonate therapy. Subtrochanteric femur fracture 10 weeks post operative fixation with an 11mm x 40cm reconstruction rod with 75 and 85mm screws proximally and a 65 mm locking screw distally (not included in this image). Exuberant callus is present at the fracture site (arrows).

**Figure 8.** 85-year-old woman on bisphosphonate therapy. Subtrochanteric femur fracture 19 weeks post operative fixation. (A) AP and lateral (B) lateral views with exuberant callus at the fracture site (arrows) in the proximal femoral diaphysis, compatible with appropriate healing.

**Discussion**

The femoral shaft is the strongest portion of the most resilient bone in the body, and therefore, subtrochanteric shaft fracture is associated with violent force or underlying bony abnormality to include tumor, Paget disease, excessive exercise, hypophosphatemic osteomalacia, pycnodysostosis,
fluorosis, or severe osteoporosis. [1-9] Osteoporotic femoral fractures are associated with a higher degree of comminution [10].

In 2005, Odvina et al. identified a group of 9 patients who developed spontaneous non-spinal fractures while on long-term alendronate. These non-traumatic fractures involved skeletal areas rich in cortical bone such as the femoral shaft, pubic bone, and ischium, and were considered atypical for osteoporotic fractures [11]. Bone biopsies in all demonstrated severe suppression of bone turnover (SSBT). The patients also on estrogen or glucocorticoids presented with fractures after a shorter duration of bisphosphonate therapy. Post-fracture continuation of bisphosphonate therapy was also associated with delayed fracture healing [11].

In 2007, an apparent increase in the number of subtrochanteric femur fractures in women between the ages of 50 and 70, many of whom had received alendronate for 3 or more years prompted Goh et al. to further evaluate these fractures. In a series of 13 patients with low energy subtrochanteric fractures, patients on alendronate had a higher incidence of simple transverse or short oblique fractures (89%) as opposed to the patients with osteoporosis not receiving bisphosphonates (0%) [12]. Approximately 55-76% of the patients with bisphosphonate-related fractures had prodromal pain prior to fracture completion whereas none of the patients with fractures due solely to severe osteoporosis in the absence of long-term alendronate had prodromal pain [12, 13]. Their further retrospective review determined a radiographically-identifiable insufficiency fracture configuration characterized by focal, lateral cortical thickening of the subtrochanteric femur with subsequent development of a transverse fracture through the lesion [13]. Additionally, 53% had bilateral findings of stress reaction or fracture [13].

In 2008, Neviaser et al. evaluated 70 low energy fractures of the femoral shaft and identified that the simple transverse fracture pattern with unicortical beak was 98% specific for alendronate use and was more likely to be seen in patients with long term use; an average of 6.9 years of alendronate use in patients with this fracture type compared with 2.5 years in patients on alendronate but not displaying this fracture pattern [15].

In 2008, Visekruna et al. described severely suppressed bone turnover (SSBT) and atypical skeletal fragility with proximal femoral metadiaphyseal/subtrochanteric fractures in 3 patients on long term bisphosphonate therapy, all three of whom were receiving another medication (estrogen, glucocorticoid, or raloxifene) that likely further suppressed bone remodeling beyond the effect of the alendronate alone [16]. Given the prolonged residence time of bisphosphonate medications in bone, their non-metabolized nature, and their ability to cause irreversible osteoclast failure, Visekruna et al. raise concern that although beneficial in most patients, certain susceptible patients may experience atypical skeletal fragility related to oral bisphosphonates, particularly when administered with other anti-remodeling agents. They further suggested a potential role for teriparatide to facilitate fracture healing in this scenario of suppressed bone remodeling [16]. Recombinant human parathyroid hormone PTH (1-34); teriparatide (Forteo) can be systemically administered to increase bone as it promotes osteoblastogenesis and decreases osteoblast apoptosis [17-19].

After postmenopausal and senile osteoporosis, glucocorticoid-induced osteoporosis is the third most common etiology of osteoporosis [20]. Common expressions of glucocorticoid-induced osteoporosis include fractures of the spine and ribs and osteonecrosis of the femoral heads [20]. Glucocorticoid medications contribute to osteopenia by several mechanisms, including early osteoclast stimulation and chronic osteoblast suppression [19]. It seems reasonable that teriparatide, may be beneficial in cases of glucocorticoid-induced osteoporosis and has been demonstrated to increase bone density in these patients [18].
There is potential for insufficiency fractures in patients on long term, high dose, or IV bisphosphonates; particularly if there are other co-administered medications or factors that inhibit bone remodeling. In the setting of bisphosphonate therapy for osteoporosis, a painful pyramidal projection of cortical bone in the subtrochanteric femoral shaft should be recognized as an impending/incomplete insufficiency fracture and treated expeditiously to reduce the risk of fracture completion.

It is necessary to balance the important benefit of bisphosphonate therapy in osteoporotic against the potential risk of over-suppression and subsequent insufficiency fracture. Optimal protocols for the dosage and duration of bisphosphonate therapy and preferred clinical management of a patient with an impending or completed insufficiency fracture while on bisphosphonates or other anti-remodeling medications deserve additional consideration. Because bisphosphonates are not metabolized, have a long dwell time, and may adversely affect fracture healing in some patients for months or even years after discontinuation, additional steps in addition to bisphosphonate discontinuation may be needed to promote fracture healing [11, 21, 22, 23, 24, 25].

This case is a paradigm of a new pattern of fractures noted in patients on bisphosphonates. It demonstrates characteristic radiographic features which may help identify patients at risk for impending fractures and suggests a possible role for teriparatide in treatment. Our patient appears to represent a “textbook presentation” of insufficiency fracture related to prolonged bisphosphonate medication on a background of severe glucocorticoid-induced osteoporosis. She presented with prodromal pain, a volcano-shaped conical ridge at the lateral subtrochanteric femur, and a subsequent simple transverse fracture with low energy mechanism. These findings are not characteristic of an osteoporotic fracture (due to the prodromal pain and lack of comminution), nor is the subtrochanteric femur a standard site for glucocorticoid-induced complications which primarily involve fractures of the ribs and spine, and osteonecrosis of the femoral head.

This case further highlights a paucity of data addressing the clinical management of these lesions. It is unknown which patients will best benefit from prophylactic placement of an intramedullary rod to prevent fracture completion and in which cases a less-invasive pharmaceutical modality may achieve fracture healing. Given our current understanding of this syndrome of insufficiency fracture in the setting of severely suppressed bone turnover, the discontinuation of bisphosphonate medication, and use of teriparatide seem to be the best actions; however, in years to come, more information will certainly refine the understanding and management of these patients.

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