Bilateral Femur Fractures Associated With Short-term Bisphosphonate Use

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abstract

Bisphosphonates are the most commonly prescribed drugs to treat osteoporosis because they have been proposed to prevent bone loss. Nevertheless, in up to 0.1% of patients, long-term use may cause atypical stress or insufficiency femoral fractures. Bilateral femoral shaft fractures have been reported after long-term use of bisphosphonates; however, there is limited evidence of the effect of short-term use. The current study reports a case of bilateral femoral fractures after a low-energy fall in a 56-year-old woman and provides a review of the literature on bilateral femoral shaft fractures after long-term use of bisphosphonates. Patients should be educated about the potential for stress fractures with the use of this treatment. In patients with thigh pain, a thorough history and physical examination, including the contralateral thigh, may be beneficial to detect bilateral traumatic or atypical stress fracture patterns. More studies with larger sample sizes are necessary to better identify patients who may be at risk for fracture, including histomorphometric evidence of low bone turnover in patients with unfortunate bilateral cases. [Orthopedics. 2015; 38(2):e139-e142.]
Osteoporosis, especially in postmenopausal women and elderly men, is a global challenge because of its potential for complicated morbidities and economic burdens on the health care system. Bisphosphonates are the most commonly prescribed drugs to treat osteoporosis and similar diseases because they have been proposed to prevent bone loss. As implied by the name, bisphosphonates have 2 phosphate groups and are similar in structure to pyrophosphate. On the structural level, their long and short side chains determine their potency and pharmacokinetics, respectively. These drugs also may reduce the risk of osteoporotic fracture in patients who have had previous fractures.

Although bisphosphonates have an important role in the treatment of osteoporosis, there are known risks associated with their use, such as osteonecrosis of the jaw and insufficiency femoral fractures. They also may be associated with atypical stress or insufficiency femoral fractures in approximately 70 to 100 per 100,000 patients. Nevertheless, the occurrence of bilateral femoral fractures after long-term use of bisphosphonates has not been widely evaluated. The current case report describes a patient with bilateral femoral fractures after a fall and provides a review of the literature on bilateral fractures after the use of bisphosphonates.

**Case Report**

A 56-year-old postmenopausal woman presented to the emergency department approximately 2 hours after sustaining a fall from standing height (Figures 1-4). She had severe right thigh pain, swelling, and decreased hip range of motion. Medical history was significant for shortness of breath, unsteady gait, frequent falls, and severe osteoporosis for which she had been treated with ibandronate and calcium supplements for more than 5 years. She was postmenopausal for 8 years and received hormone replacement therapy for 6 years after the onset of menopause at age 48 years. She had no risk factors for pathologic fractures, did not smoke, and did not use alcohol or illicit drugs. However, she had vague bilateral thigh weakness with a severe limp for approximately 3 years before the current fall. Body mass index was 25 kg/m².

Plain radiographs of the pelvis, right hip, and right femur showed a right transverse midshaft femur fracture with moderate angulation and some impaction. The fracture edges were sclerotic, suggestive of displacement of chronic stress fracture. Because the patient had a history of vague left lower-extremity weakness, anteroposterior and lateral radiographs of the left femur were obtained on the morning after admission. Plain radiographs showed a thin, well-defined, yet incomplete midshaft fracture. The cortex was thickened and sclerotic, consistent with another chronic stress fracture. The patient underwent whole-body bone scan to exclude malignancy in light of the finding of bilateral femoral fractures. Whole-body 3-phase bone scan showed...
an area of increased uptake in the midshaft of the right femur, corresponding to the transverse fracture. A small focal area of increased uptake in the midshaft of the left femur was also noted, corresponding to that fracture. Also noted was increased uptake in the first tarsometatarsal region of the left foot, consistent with posttraumatic or arthritic changes. Minimally irregular uptake was noted in the thoracic spine, consistent with a pattern of degenerative change.

The patient underwent staged bilateral closed reduction and internal fixation with a cephalomedullary device. She tolerated the procedures well and had no postoperative medical or surgical complications. Pathologic analysis of bone fragments removed during the procedure showed no granuloma or malignancy. The patient was discharged after a 4-day hospital stay and had an uneventful recovery.

**Discussion**

The estimated incidence of unilateral bisphosphonate-associated femoral fractures is 70 to 100 per 100,000 patients. Proposed mechanisms include suppression of bone turnover, accumulation of microfractures, reduced capacity for energy absorption, increased fragility of osteoporotic bone, and targeted bone remodeling through death of osteocytes.

This combination of factors may predispose patients to a higher risk of long bone fracture. For patients who have symptomatic hip pain, plain radiographs can be used to evaluate for lateral femoral cortex thickening or fracture with a short oblique or transverse line. Approximately 50% of oral or intravenous bisphosphonate is excreted by the kidney; however, the remainder has a very high affinity for calcium and bone surfaces and is rapidly adsorbed into the bone tissue. Because the estimated half-life of bisphosphonates is approximately 10 years, their effects may continue long after the cessation of therapy (drug holiday).

Bilateral femur fractures have been reported in patients with long-term bisphosphonate use. However, in this case, the authors report this complication in a patient with short-term use of this drug. Goddard et al reported atraumatic bilateral femur fractures in a 67-year-old woman with a history of femoral diaphyseal fracture 3 years earlier, use of hormone replacement therapy, and long-term use of bisphosphonates (alendronate 70 mg for 10 years and ibandronate 150 mg for 1 year). She was treated with cephalomedullary rod fixation. However, at 6-month follow-up, the patient had clinical and radiographic signs of delayed union. Dynamization was performed by removing the distal interlocking screws. At 1-year follow-up, the fracture had healed completely.

Puah and Tan described a case of bilateral femur fracture after a fall in a 64-year-old woman who had a history of osteoporosis with bisphosphonate use, asthma with prednisone use, diabetes mellitus, and breast cancer. The patient had a stress fracture of the right femoral shaft approximately 67 months earlier, and at that time she was advised to stop taking alendronate. At 5-year follow-up, she was prescribed letrozole with ibandronate by her oncologist. She continued to take this drug for 7 months, at which time she had a fall. She was treated with bilateral plate fixation, and the fractures healed uneventfully.

Jo et al described an atypical stress fracture of the bilateral femur in a 75-year-old woman with a history of hypertension,
spinal stenosis, and osteoporosis. She had been treated with alendronate 70 mg for 8 years. Plain radiographs of the femora showed bilateral lateral cortical thickening with transverse fracture of the right femur. Whole-body bone scan showed an additional fracture of the left femur. The patient was treated with open reduction and internal fixation with a plate and screw of the right femur and intramedullary nail and cables of the left femoral shaft. Treatment with alendronate was discontinued.

The patient’s outcome was good, without acute complications.

**CONCLUSION**

Patients who receive long-term bisphosphonate therapy because of osteoporosis should be evaluated for potential fall risk. In addition, they should be educated about the potential for stress fractures with long-term use of this treatment. In patients with thigh pain, a thorough history and physical examination, including the contralateral thigh, may be beneficial to detect bilateral traumatic or atypical stress fracture patterns. Long-term bisphosphonate users may benefit from counseling with an endocrinologist to adjust bisphosphonate therapy. More studies with larger sample sizes are necessary to better identify patients who may be at risk for fracture, including histomorphometric evidence of low bone turnover in patients with bilateral fractures. The current patient had vague symptoms only 2 years after initiation of ibandronate treatment. It is important to determine how soon after the start of treatment fractures or other adverse events may occur and when these patients should be further evaluated.

**REFERENCES**