Alendronate-associated ulnar and tibial fractures: a case report

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ABSTRACT

Bisphosphonates are widely used to prevent osteoporotic fractures. Long-term use has resulted in unexpected subtrochanteric fractures in some elderly patients. We report a patient on long-term alendronate therapy who sustained fractures of the ulna and tibia sequentially over a 7-month period, without any trauma or fall.

Key words: alendronate; diphosphonates; hip fractures; osteoporotic fractures

INTRODUCTION

Bisphosphonates have been widely used to treat osteoporosis and prevent vertebral and femoral neck fractures in post-menopausal women. Nonetheless, alendronate-associated subtrochanteric fractures have been reported, especially in patients on long-term treatment. No other bones have been reported in relation to such fractures. We report a case of sequential fractures of the proximal ulna and tibia over a 7-month period without any trauma or fall in a 76-year-old woman who had taken alendronate on and off for 7 years.

CASE REPORT

In April 2009, a 76-year-old woman presented with pain and swelling over the right forearm after hearing a crack when using her right hand to support herself getting up from a wheelchair. There was no history of any trauma or fall. The patient had taken alendronate on and off for 7 years. Clinical examination revealed a tender swelling over the proximal shaft of the right ulna. Radiographs revealed a non-displaced transverse fracture of the proximal third of the ulna (Fig. 1a). Her comorbidities included colonic diverticulitis, gastroesophageal reflux, hypertension, peptic ulcer disease, and ischaemic heart disease (for which she had had bypass surgery in 1988).

Her serum calcium and phosphate levels were normal, as were her serum parathyroid hormone and...
25-hydroxy vitamin D levels. In June 2009, a bone mineral density test showed a T-score of 0.1 at both the lumbar spine and femoral neck, compared with the previous respective scores of -0.33 and -0.19 in 2004. Alendronate therapy was therefore ceased.

The patient declined surgery; her right arm was splinted in a long-arm fibreglass cast. At the 2-month follow-up, the fracture was noted to be displaced with evidence of non-union (Fig. 1b). The patient declined surgery again.

In December 2009, the patient presented with a 2-day history of pain over the proximal right tibia and inability to bear weight. There was no history of any trauma or fall. Radiographs revealed a crack fracture of the proximal right tibia (Fig. 2a). The serum calcium and phosphate levels were again normal, as were the serum parathyroid hormone and 25-hydroxy vitamin D levels. The patient underwent internal fixation for the tibial fracture (Fig. 2b), but refused any surgery for her non-united ulnar fracture.

**DISCUSSION**

Osteoporosis is a chronic and progressive condition where bone resorption exceeds formation, and results in a reduced bone mass and an increased tendency to fractures. Alendronate is a bisphosphonate widely used to treat osteoporosis. It prevents vertebral and femoral neck fractures in post-menopausal osteoporotic women by inhibiting osteoclast-mediated bone resorption. When discontinued, the physiological effect on bone resorption remains for 5 years, with no increase in the fracture risk.\(^4\) Alendronate therapy may increase bone mineral density, and the effect is sustainable when administered for up to 10 years.\(^5\)

Nonetheless, there are deleterious effects from long-term alendronate therapy. Six of 9 patients who had taken this drug for 3 to 8 years sustained non-traumatic non-spinal fractures, and their healing was delayed for 3 months to 2 years.\(^6\) Long-term alendronate use may overly suppress bone metabolism, decrease bone turnover, increase skeletal microdamage, and lead to development of osteopetrosis, thereby increasing the fracture risk.\(^2\)

In 17 patients who were on alendronate therapy for a mean of 4.8 years and sustained low-energy subtrochanteric fractures,\(^3\) 53% of the patients had bilateral stress reactions or fractures and 76% had prodromal pain. Radiography showed a transverse fracture line with a medial cortical spike and cortical thickening. Only 6 of them had evidence of osteoporosis at the time of the fractures, although they remained taking alendronate.\(^7\) In 5 patients with alendronate-related subtrochanteric fractures,\(^2\) they had prodromal symptoms for 2 and 6 months prior to the fractures. Only one of them was osteoporotic at the time of the fracture based on bone density tests. In spite of normal bone density, these patients had continued taking alendronate.\(^2\)

Unlike the lower limbs, stress fractures of the upper limbs are rare.\(^7\) Stress fractures of the ulna usually occur in athletes who exert excessive forearm rotation during tennis,\(^8\) softball,\(^9\) table tennis\(^10\) and golf.\(^11\) Excessive weight lifting\(^12\) and bodybuilding\(^13\)
also predisposes to stress fractures of the ulna. Repeated flexor profundus muscle contraction in the bowler\textsuperscript{14} and intensive rifle drill training in military recruits\textsuperscript{15} may also lead to this injury. Such fractures also occurred in a young girl on crutches for osteochondritis dissecans of the talus.\textsuperscript{16} Cylindrical weight bearing with the elbow flexed, forearm pronated, and wrist ulna deviated may be a cause of ulnar fractures. During axial loading, the radius carries 82\% and the ulna carries 18\% of the load. However, the load along the ulna increases with wrist flexion, ulnar deviation, and forearm pronation. In our patient, the fractures may be secondary to long-term alendronate use, as her bone mineral density was normal at the time of the fracture and beforehand. Her vitamin D and parathyroid hormone levels were also normal. The ulnar fracture went on to non-union. The risk factors for such atypical fractures include steroid use, long-term use of bisphosphonates, and low bone turnover.\textsuperscript{6}

Tibial fatigue fractures are mostly reported in military recruits, long distance runners, and ballet dancers.\textsuperscript{17} Most insufficiency fractures are associated with osteoporosis or bone loss.\textsuperscript{17} Insufficiency fractures of the proximal tibia have also been reported in the osteoporotic elderly with varus osteoarthritis of the knee.\textsuperscript{18} In our patient, the tibial fracture was associated with alendronate intake and unlikely to have been related to her underlying degenerative joint disorder, as she had been wheelchair bound, and her bone mineral density had been normal. Both the ulnar and tibial fractures occurred suddenly without the prodromal pain, as encountered with subtrochanteric fractures. Radiographs did not show the typical periosteal new bone formation, which is noted with subtrochanteric fractures. Subtrochanteric fractures in patients on long-term alendronate have been well documented, but ulnar or tibial fractures have not.

The bone mineral density in patients on bisphosphonates should be monitored on a regular basis. Treatment should be ceased in consultation with the endocrinologist once the optimal bone density is achieved. Continuation of alendronate even with optimal bone density may increase the risk of pathological fractures by suppressing bone metabolism, decreasing bone turnover, and increasing skeletal microdamage.\textsuperscript{23}

REFERENCES