

Subtrochanteric Femoral Fracture in a Patient on Alendronate Therapy: A Case Report

K.C. Lakati¹, M.B.L. Lutomia²

¹Nakuru Orthopedic Center, ²Egerton University Medical School, Nakuru, Kenya.

Correspondence to: Dr.Lakati, K.C, Email:klakati@yahoo.com

Bisphosphonates are currently widely used in the treatment of osteoporosis. Recent reports have attributed atypical femoral fractures to long term use of bisphosphonates.

We present a case of such a low energy subtrochanteric femur fracture in a lady who was on alendronate therapy for three years. Radiological evaluation revealed features similar to those found in other reported cases, demonstrating that this fracture could have been predicted if the patient was closely monitored.

Introduction

Bisphosphonates have been shown to be effective in preventing fragility fractures in osteoporosis^{1,2}. Recently, reports linking alendronate and other bisphosphonates use to atypical femoral fractures have appeared, thus questioning the safety of these drugs when used for a long time³⁻¹¹. It is postulated that the suppression of bone remodeling by the bisphosphonates leads to accumulation of micro-fractures in lamella bone. Failure to repair these micro-fractures ends up in a low energy clinical fracture^{13,14}.

We present a case, the first such reported in local literature, of a lady who suffered a low energy subtrochanteric femur fracture while on alendronate therapy, with characteristic radiological features similar to those described by other authors elsewhere.

Case report

A 58 year old female, of Asian origin, presented to hospital after she slipped and fell in her bathroom and was unable to get up due to a painful right upper thigh. She was previously well and reported no preceding thigh or groin pain. She had been on alendronate (Fosamax®) 70 mg once weekly and calcium (Calcimax® 1tablet daily) over the previous 3 years. This had been started after a Dual Energy X-ray Absorptiometry (DEXA) scan done during one of her visits to India showed that she had osteoporosis with an average T score of - 2.7(- 2.8 at the neck of femur and -2.6 at the lumbar spine). She had no other chronic illnesses and was not on any other medication.

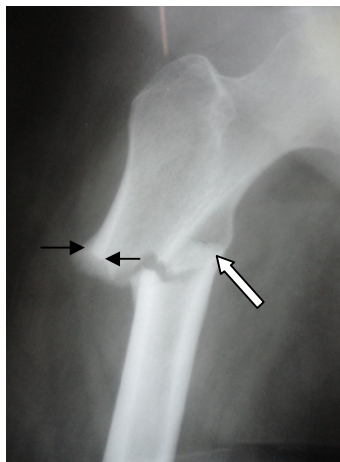


Figure 1. Subtrochanteric fracture, lateral cortical thickening (solid black arrows), medial cortical beaking (white arrow)



Figure 2. Close up Showing Lateral Cortical Thickening and Medial cortical Beaking (White Arrow)



Figure 3. Treatment Using Condylar Blade Plate

Evaluation revealed a displaced transverse subtrochanteric fracture with lateral cortical thickening and medial beaking (Figures 1 and 2). She underwent open reduction and internal fixation of the fracture using a 95° angled blade plate (Figure 3). Alendronate was stopped on admission, but the calcium was continued. On follow up, the fracture united uneventfully.

A repeat DEXA scan after 6 months of stoppage of alendronate revealed that her bone density was normal with an average T score of 1.1(1.0 at the neck of femur and 1.2 at the lumbar spine).

Discussion

The effectiveness of the bisphosphonate alendronate in increasing bone mineral density and reducing fracture risk in osteoporosis is well documented. Liberman et al showed that daily treatment with alendronate increases bone mass in the hips, spine and reduces the incidence of vertebral fractures¹. Cummings et al reported significant reduction in the risk of clinical fractures in patients with low bone mineral density on alendronate². For this reason bisphosphonate use in the treatment of

osteoporosis is now widespread. However, recent reports have cast doubts on the safety of long term use of alendronate and other bisphosphonates. Attention has been drawn to a possible association between bisphosphonate use and atypical femoral fractures. Goh et al³ first reported on low energy subtrochanteric fractures of the femur in patients taking alendronate. In their series of 13 patients with low energy subtrochanteric femur fractures, 9(69%) were found to have been on alendronate. After this, other cases have been reported in various parts of the world.

Kwek et al⁴ reported on 17 patients with low energy subtrochanteric femur fractures, all of whom were on bisphosphonates (16 on Alendronate, 1 on Risedronate). In a retrospective case control study, Lenart et al showed that the rate of bisphosphonate use was higher in patients with low energy subtrochanteric femur fractures than matched controls with intertrochanteric and femoral neck fractures⁵. This finding alludes to the possibility of a causal relationship between bisphosphonate use and low energy femur fractures.

These fractures typically occur in the subtrochanteric region, or shaft of the femur, though they have been reported in other areas of the skeleton. Radiographic features include a transverse or a short oblique pattern, lateral cortical thickening and medial cortical beaking. This fracture pattern has been described as “simple with thick cortices”¹¹. All the patients (100%) reported by Kwek et al had all the above radiological features⁴. In a study by Neviasser et al, 76% of the patients on alendronate had the same fracture pattern. They concluded that alendronate use was a risk factor for the fracture pattern and that the pattern was 98% specific to alendronate users⁶. All(100 %) patients retrospectively reviewed by Capeci et al with low energy sub-trochanteric fractures who were on alendronate had the same fracture pattern⁹. Other case reports have shown the same fracture pattern^{6,7,8,9,10,11}. These fractures are typically preceded by prodromal symptoms of thigh or groin pain or discomfort, lasting from weeks to years^{3,4,8}.

Though no direct link has been made between bisphosphonate use and these atypical fractures, it has been postulated that there is accumulation of “micro-damage” within the lamellar bone due the suppression of bone turn-over by the drugs. Failure to repair such micro-damage finally ends up in a stress fracture. In animal studies, it has been shown that trabecular bone remodeling is strongly suppressed by bisphosphonates. This is associated with accumulation of micro-damage in trabecular bone at all sites and lamellar bone toughness is reduced by about 20% with bisphosphonate treatment¹³. Cortical stress reactions associated with prolonged antiresorptive therapy have been shown to have an increased risk for progression to complete stress fractures¹⁴. Though these fractures have been reported in patients on bisphosphonate treatment for two years, studies have shown that the longer the duration of bisphosphonate use, the higher the risk of developing the fractures, and the more likely that it is the peculiar “simple with thick cortices” pattern⁵.

Despite the risk of developing these fractures while on bisphosphonate therapy, the risk is low. In a retrospective study of over 3,000 patients on bisphosphonates, Schilcher found only 5 who developed stress fractures, giving an incidence density of 1/1000 per year¹². This is decidedly low compared to the number of clinically significant osteoporotic fractures prevented by bisphosphonates. As prolonged bisphosphonate use increases the risk of these fractures, therapy can be stopped after five years of continuous use, with a drug holiday of up to twelve months. It has been shown that fracture risk does not significantly increase on stopping treatment after five years of use¹⁵.

In the US, the FDA recommends that physicians be aware of these atypical fractures, and aggressively rule out femoral fractures in patients who present with groin or thigh pain while on bisphosphonates, and stoppage of the same should a fracture occur. The FDA also recommends that physicians reevaluate whether continued treatment is needed for those patients who have been treated for more than five years¹⁶.

Currently there are no local guidelines concerning the duration of bisphosphonate use and the risk of developing the atypical fractures. Given that many cases of bisphosphonate associated fractures are being reported as early as after two years of therapy, it would seem prudent to initiate surveillance for prodromal symptoms and signs at two years. Radiological assessment using plain radiographs and CT scans in patients with hip, groin or thigh pain will help pick out those at risk. Regular follow up with DEXA scans every 6 months would help the physician to know when bone density has normalized after which the bisphosphonate therapy may be halted. Re-initiation of therapy may be guided by further DEXA evaluations.

Evidently, further research is required to clearly define the relationship between bisphosphonate use and these fractures, and to set guidelines on duration of treatment and drug holidays. Meanwhile physicians must be aware of the risk of these fractures among patients on long term bisphosphonate treatment.

References

1. Liberman UA ,Weiss SR ,Broll J, Minne HW, Quan H ,Bell NH, Rodriguez-Portales J ,Downs RW Jr, Dequcker J, Favus. Effect of oral alendronate on bone mineral density and the incidence of fractures in postmenopausal osteoporosis. The Alendronate Phase III Osteoporosis Treatment Study Group. *N Eng J Med* 1995: 333:1437-1443
2. Cummings SR, Black DM, Thompson DE ,Applegate WB, Barret-Connor E, Musliner TA, Palermo L,Prineas R, Rubin SM, Scott JC, Vogt T, Wallace R, Yates J, LaCroix AZ.Effect of alendronate on risk of fracture in women with low bone density but without vertebral fractures: Results from the Fracture Intervention Trial.*JAMA* 1998: 280(24):2077-2082
3. Goh SK, Yang KY, Koh JS, Wong MK, Chua SY, Chua DT, Howe TS.Subtrochanteric insufficiency fractures in patients on alendronate therapy: a caution..*J Bone J Surg Br* 2007;89(3):349-353
4. Kwek EB, Goh SK, Koh JS, Png MA, Howe TS. An emerging pattern of subtrochanteric stress fractures: a long term complication of alendronate therapy? *Injury* 2008;39(2):224-231
5. Lenart BA, Neviaser AS, Lyman S, Chang CC, Edobor-Osula F, Steele B, van der Meulen MCH, Lorich DG, Lane JM. Association of low energy femoral fractures with prolonged bisphosphonate use: a case control study. *Osteoporos Int*:2009;20:1353-1362
6. Neviaser AS, Lane JM, Lenart BA, Edobor-Osula F, Lorich DG. Low energy femoral shaft fractures associated with alendronate use. *J Orthop Trauma* 2008; 22:346-350.
7. Sayed-Noor AS, Sjoden GO. Subtrochanteric displaced insufficiency fracture after long-term alendronate therapy-a case report. *Acta Orthopaedica* 2008;79(4):565-567
8. Edwards MH, McCrae FC, Young-Min SA. Alendronate-related femoral diaphysis fracture-what should be done to predict and prevent subsequent fracture of contralateral side? *Osteoporos Int*:2010;21:701-703
9. Capeci CM, Tejwani NC.Bilateral low energy simultaneous or sequential femoral fractures in patients on long term alendronate therapy. *J Bone J Surg Am* 2009;91:2556-2561
10. Ali T, Jay RH, Spontaneous femoral shaft fracture after long-term alendronate. *Age and ageing* 2009;38:625-626
11. Cheung RHK, Leung KK, Lee KC, Chow TC. Sequential non-traumatic femoral shaft fractures in a patient on long-term alendronate. *Hong Kong Med J* 2007;13:485-489
12. Schilcher J, Aspenberg P.Incidence of stress fractures of the femoral shaft in women treated with bisphosphonate. *Acta Orthopaedica* 2009;80(4):413-415

13. Mashiba T, Turner CH, Hirano T, Forwood MR, Johnston CC, Burr DB. Effects of suppressed bone turnover by bisphosphonates on microdamage accumulation and biomechanical properties in clinically relevant skeletal sites in beagles. *Bone* 2001;28:524-531
14. Koh JSB, Goh SK, Png MA, Kwek EBK, Howe TS .Femoral cortical stress lesions in long-term bisphosphonate therapy: A herald of impending fracture? *J Orthop Trauma* 2010;24:75-81
15. Black DM, Schwarz AV, Ensrud KE, Cauley JA, Levis S, Quandt SA, Satterfield S, Wallace RB, Bauer DC, Palermo L, Wehren LE, Lombardi A, Santora AC, Cummings SR. Effects of continuing or stopping alendronate after 5 years of treatment. The Fracture Intervention Trial Long Term Extension (FLEX): A randomized trial. *JAMA* 2006;296(24):2927-2938
16. www.accessdata.fda.gov/scripts/cdrh/cfdocs/psn/transcript.cfm?show=106