Atypical Fractures on Long Term Bisphosphonates Therapy

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Abstract
Bisphosphonates reduce fractures risk in patients with osteoporosis. A new pattern of fractures is now being noted in patients on prolonged bisphosphonate therapy. We report a case of an atypical femoral fracture with preceding pain and highlight the characteristics of these fractures.

Case Report
A 69 years old Caucasian lady presented with a non-traumatic right hip fracture while going down the stairs. She had a background history of osteoporosis, diagnosed 6 years ago, and was on alendronate since. DXA scans results since diagnosis are shown in Table 1. Risk factors for osteoporosis were early menopause, 20 pack years of smoking and thyroid disease. She was also on calcium and vitamin D supplements, levothyroxine and statin therapy. She was not on steroids or PPI therapy. Figure 1b shows her x-ray following the fracture.

A pelvic X-Ray was obtained a month prior to her fracture because of pain in the anterior thigh on the right side. This revealed no fracture (Figure 1a). A few findings suggested a diagnosis of bisphosphonate-associated fracture: a prodomome of pain at the site of fracture, cortical thickening of femoral bone, location at the subtrochanteric area and shape of the fracture being transverse with medial spike. The patient underwent intra-medullary nailing of the femur. Bisphosphonate therapy was ceased. She was commenced on strontium with a view to commence PTH therapy. MRI of the contralateral hip revealed no evidence of cortical thickening or microfractures. She received intensive physiotherapy and made a good recovery.

Discussion
Fractures occur in one in two women and in one in four men with osteoporosis, and bisphosphonates reduce this risk. Bisphosphonates improve DXA scores and reduce fracture rates beyond 5 years in non-high risk patients, while showing reduced rates of clinical vertebral fractures, did not show an improvement in the rate of non-spine fractures or that of vertebral fractures as detected by morphometry.

In addition to that, a number of case reports and case series raised concern about a small increase in fracture risk. These atypical fractures are usually non-traumatic and are preceded by a prodomome of pain at the thigh for a few weeks. Radiologically, they are located at the subtrochanteric area or the proximal femoral shaft, are transverse or short oblique fractures, and the femurs are described to have thickeged cortices. These fractures are usually bilateral, either simultaneously or sequentially.

Although these fractures can occur in individuals who never had bisphosphonates therapy, the incidence is estimated to be more than 15 times higher in those exposed to this therapy for prolonged periods. The suggested mechanism of these fractures is accumulation of microfractures that are not repaired with normal bone turn-over because of bisphosphonates inhibition of osteoclasts. With time, these predispose to stress fractures that probably coincide with onset of prodomal pain and subsequently lead to a full fracture.

Some studies however argue against the relationship of these atypical fractures with bisphosphonates. Based on a review of the Danish registry, 'atypical' fractures sharg the epidemiology and treatment response of classical hip fractures. Moreover, in a secondary analysis of patients in three large randomised studies, there was no significant increase in risk of fractures associated with bisphosphonate use. However, among other limitations, and as highlighted by the authors, most patients in these trials received bisphosphonates for less than 5 years and some received low doses. Because of the rarity of atypical fractures, the American Society of Bone and Mineral Research recommended creation of diagnostic and procedural codes for these fractures. It also suggested an international registry should be established to support further research in this area.

It is important to emphasise that the overall risk of developing fractures secondary to bisphosphonates therapy is negligible when compared to the risk of fractures resulting from untreated osteoporosis. Physicians should not be discouraged from using bisphosphonates. It is suggested however, particularly in low risk patients, that bisphosphonates are held after 3 to 5 years of therapy as long as BMD is stable and no fractures occur. Low risk patients include those with no incident fractures, T-score > 2.0 and no other major risk factors. Physicians are also advised to be alert to symptoms of thigh and groin pain and consider early investigations like bone scans or MRI to identify these fractures at an early stage.

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Figure 1: Pelvic X-rays at time of prodomal pain (1a) and following the atraumatic fracture (1b).
References


Comments:

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