Bisphosphonate-associated atypical subtrochanteric femur fractures in the older patient

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Abstract

Bisphosphonates, drug of choice in the treatment of osteoporosis have been associated with unusual skeletal side effects such as osteonecrosis of jaw and atypical femur fractures in recent years. We report two older patients with bisphosphonate associated atypical femur fracture from a South Australian tertiary care hospital and a brief discussion of potential diagnostic complexities in this patient population.

Bisphosphonates—considered as first-line therapy in treating patients with osteoporosis—have proven efficacy in the prevention of vertebral, hip and non-vertebral fractures. However, concerns have been raised regarding rarer side effects including atypical femur fractures, osteonecrosis of jaw, oesophageal cancer and atrial fibrillation.

Atypical subtrochanteric femur fractures have been reported with bisphosphonate treatment but these are rare and the aetiology remains unclear.

We report two older patients with atypical femur fracture admitted to our general teaching hospital in South Australia over a 3-year period, both on long-term bisphosphonates, and discuss the potential diagnostic challenges in this age group.

Case 1

A 68-year-old Caucasian lady presented with new onset right hip pain for 3 weeks. X-ray (Figure 1) revealed an incomplete transverse subtrochanteric fracture in the medial aspect that was treated with intramedullary nailing. She denied any fall prior to onset of hip pain and had no significant comorbidities. There was no evidence of cognitive impairment (MMSE=27/30) and investigations for secondary osteoporosis were negative. She was on long-term risedronate 35 mg weekly for 6 years with calcium/vitamin D based on previous bone density scans confirming osteoporosis with femur neck T score of -2.7. She underwent a DEXA scan that showed a vertebral T score of -1.2 and femur neck T score of -1.3. Specialist endocrinology input concurred with the likelihood of an atypical femur fracture associated with bisphosphonates. Bisphosphonates were ceased and strontium commenced, but prophylactic nailing on the left was declined by the patient prior to hospital discharge.
Case 2

A 73-year-old Caucasian lady presented with worsening yet unprovoked right hip pain for a month. Hip X-ray (Figure 2) confirmed right complete sub trochanteric fracture involving the inferior margins of the lesser trochanter and she underwent intramedullary nail insertion. Past medical history included cerebrovascular disease, atrial fibrillation, gastroesophageal reflux and hypertension.

Her usual medications included flecainide, candesartan, dothiepin, lercanidipine, esomeprazole, folic acid, frusemide, warfarin along with alendronate 70 mg weekly and calcium/vitamin D for 9 years following a fragility fracture of the radius. She reported good adherence with all medications and there was no evidence of cognitive impairment (MMSE – 26/30). Investigations for secondary osteoporosis were unremarkable.

A DEXA scan revealed a vertebral T-score of -1.6 and femur neck T-score of -0.9. Following discussion with the patient regarding alendronate and its possible association with atypical fractures, she was switched to strontium in hospital prior to discharge.

Figure 1. Hip and femur X-ray images illustrating relevant radiological major criteria

(1) Fracture located along the femur distal to the lesser trochanter to just proximal to the supracondylar flare.
(2) Associated with no or minimal trauma, as in a fall from a standing height or less.
(3) Transverse or short oblique configuration.
(4) Non comminuted nature.
(5) Complete fractures extend through both cortices and may be associated with a medial spike; incomplete fractures involve only the lateral cortex.
(6) Localised periosteal or endosteal thickening of the lateral cortex is present at the fracture site (“beaking” or “flaring”).
**Discussion**

The above cases highlight a rare but well described atypical fracture in elderly patients on bisphosphonates, usually for more than 5 years, which may be overlooked by busy clinicians.

Both our patients were on bisphosphonates for more than 5 years and fulfilled all the recent mandatory criteria proposed by the task group for atypical fractures. Most of the minor features supportive in diagnosis were also present in both cases. These include generalized increase in cortical thickness of the femoral diaphysis, unilateral or bilateral prodromal symptoms such as dull or aching pain in the groin or thigh, bilateral incomplete or complete femoral diaphysis fractures and delayed fracture healing.

Our second patient was on long-term esomeprazole which has been associated with an increased risk of atypical femur fractures when prescribed along with bisphosphonates. Proton pump inhibitors interfere with absorption of calcium and bisphosphonates thus affecting their anti-fracture efficacy and have been incriminated in osteoporotic fractures.

The time interval from the onset of pain and diagnosis of an atypical femoral fracture varies from 1 week to 2 years. Possible mechanisms involve reduced toughness due to accumulation of microdamage and lack of effective remodelling within the bone leading to failure in areas with high tensile force such as the subtrochanteric region.

Management strategies for these patients have included cessation of bisphosphonates, protected weight-bearing and prophylactic intramedullary rod insertion. Use of anabolic bone agents like teriparatide appear promising though not yet translated to standard clinical practice due to cost and license implications.

Intriguingly, not all atypical fractures are associated with bisphosphonate use or prolonged duration and it is unclear whether a drug holiday could definitely prevent the occurrence of these fractures. Moreover, the overall incidence and risk of osteoporotic fragility fracture in the elderly outweighs this relatively uncommon condition.

Association of age and atypical femur fracture is unclear. In one large case series by Girgis and colleagues, there was an increased likelihood (odds ratio= 3.6) of an atypical fracture in patients less than 65 years of age. A recent case control study by Erviti and colleagues showed that elderly women are at a higher risk for bisphosphonate-associated atypical fractures (adjusted odds ratio=4.3). Our local atypical fracture incidence rate in the above 65 year olds at 0.5% is lower than the current overall reported incidence of atypical fractures which is around 1% of all femur fractures.

We believe this may be due to underreporting as besides radiological diagnostic difficulty, a significant proportion of elderly patients with femur shaft fracture are not reviewed by an orthogeriatrician or metabolic bone disease specialist.

Diagnosis in the elderly with increasing prevalence of osteoporosis can be difficult. Atypical subtrochanteric fracture may be falsely classified as osteoporotic fragility
fracture and bisphosphonate treatment continued exposing them to a higher fracture risk.

Also in the elderly, cognitive impairment and delirium may make it difficult to elicit a thorough history leading to the fracture masking the true clinical diagnosis. Moreover elderly patients with a higher falls risk due to comorbidities may actually sustain a fall secondary to thigh pain leading to a wrong diagnosis of osteoporotic fracture unless a complete and detailed history leading to the fall is elicited.

Thus in older patients, a much higher index of suspicion is required to recognise bisphosphonate associated atypical fractures with important implications for clinical practice.

Greater awareness of this condition would help optimise clinical management and minimise risk of further debilitating fractures in vulnerable older patients.

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