

# Atypical femoral fractures

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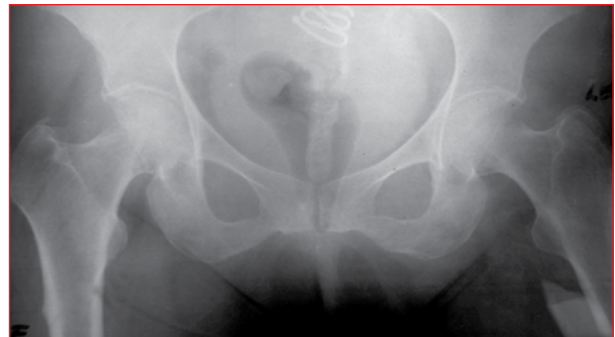
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## Introduction

A 73-year-old female patient with osteoporosis, who had been taking alendronate for over 15 years, sustained bilateral, atypical femoral fractures two years apart. There was evidence of a stress fracture preceding the current fracture, as seen in the X-rays performed two years prior. Subsequently, she was found to have primary hyperparathyroidism.

## Case report

A 73 year-old female patient was admitted to the orthogeriatrics unit at Helen Joseph Hospital in 2012 with a fracture of her right femur, following a fall from standing height. She was known to have severe osteoporosis, having sustained multiple previous fragility fractures involving her right distal radius, left olecranon and left proximal humerus. She had been admitted in 2010 with a low-trauma femur fracture on the opposite (left) side, and recalled that she had complained of right thigh pain at the time. Risk factors for osteoporosis included smoking, being of the female sex and of an older age. She had been taking oral alendronate continuously for the past 15 years, as well as vitamin D supplementation. At the time of her 2012 admission, her kidney function and thyroid-stimulating hormone levels were within the normal ranges. Her serum-corrected calcium was 2.39 mmol/l (2.05-2.56 mmol/l), her serum magnesium level 0.93 mmol/l (0.65-1.1 mmol/l), and serum phosphate level 1.03 mmol/l (0.80-1.40 mmol/l). Figures 1 and 2 show that the initial left femur fracture was transverse, non-comminuted and subtrochanteric, with an apparent thickening of the lateral cortex at the site of the fracture representing a periosteal reaction ("flaring"), and a medial spike that is characteristic of atypical femoral fractures.<sup>1,2</sup> Figures 1 and 3 show a lateral cortical ridge, indicating a stress fracture of the right femur, present at the time of the initial fracture in 2010. Subsequently, in 2012, she developed an atypical femoral fracture of her right femur at that site as well (Figure 4).



**Figure 1:** An antero-posterior pelvis X-ray performed in May 2010, showing the initial left atypical femoral fracture with subtrochanteric stress fracture (visible on the right)

The patient underwent successful surgical fixation of the fracture and recovered uneventfully. Oral bisphosphonate therapy was stopped and calcium and vitamin D supplementation continued. She was seen at a follow-up appointment one month after discharge, and was then found to have high corrected calcium levels of 2.77 mmol/l (2.05-2.56 mmol/l), with an associated high parathyroid hormone level of 8.7 pmol/l (1.2-8.5 pmol/l). Total 25-hydroxyvitamin D level at the time was 31.21 nmol/l. A parathyroid sestamibi scan localised a left inferior parathyroid adenoma. At the time of writing, she was awaiting surgical assessment for possible parathyroidectomy. The patient provided written informed consent to anonymous publication of her case details.

Parathyroid hormone can increase both the formation and resorption of bone, depending on whether or not it is administered intermittently or continuously. Intermittent administration causes a net increase in trabecular bone mass, with little net effect on cortical bone mass. In primary hyperparathyroidism, the continuously elevated parathyroid hormone has little impact on the trabecular bone and a decrease in the cortical bone.<sup>3</sup>

Atypical femoral fractures (AFFs) occur rarely. It is important to differentiate AFFs from other fractures of the femoral diaphysis, such as osteoporotic, malignant,

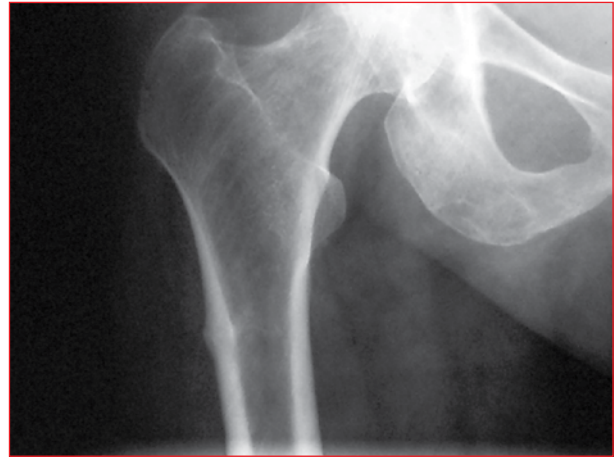


**Figure 2:** A closer view of the left atypical femoral fracture. It is transverse, non-comminuted, subtrochanteric, with an apparent thickening of the lateral cortex at the site of fracture representing a periosteal reaction ("flaring"), and a medial spike that is characteristic of atypical femoral fractures

pathological, peri-prosthetic and major trauma-related fractures. The American Society for Bone and Mineral Research (ABMR) consensus criteria for the radiological features of the case definition have recently been amended.<sup>2</sup> These fractures occur with minimal force, but are often preceded by a painful prodrome. Sometimes X-ray changes consistent with a stress fracture may be visible before frank displacement occurs. They are characterised by an unusual X-ray appearance in the circumstances of a low-trauma injury (as described in the case report above), or even by spontaneous occurrence, as well as by a high incidence of bilaterality and delayed healing. Because of frequent bilateral involvement, the contralateral femur should undergo imaging. If a stress fracture is seen, then prophylactic surgical fixation is recommended, although conservative management can be considered in certain situations.<sup>2</sup>

The pathophysiology of AFFs is thought to be owing to over-suppression of bone turnover, with an accumulation of microcracks due to the adynamic bone that has lost the ability to repair. These microcracks propagate and weaken the bony area, leading to eventual complete fracture. The subtrochanteric region of the femur, usually one of the strongest parts of the femur, becomes vulnerable as it is the site of maximal bending force.<sup>1</sup>

An increased risk of AFFs is associated with specific diseases and drug exposure, as well as particular lower limb geometry. Once the diagnosis has been made,



**Figure 3:** A closer view of the lateral cortical ridge, indicating a stress fracture of the right femur



**Figure 4:** An antero-posterior pelvis X-ray taken in September 2012, showing the subsequent atypical fracture occurring at the site of the stress fracture on the right femur

such associations should be sought. Importantly, AFFs have also occurred in patients with no apparent risk factors.<sup>2</sup>

Atypical femoral fractures occur more often in patients on bisphosphonate therapy. A longer duration of treatment increases the risk. A cohort study carried out in the USA reported an incidence of 1.78/100 000/year in patients exposed to bisphosphonates for 0.1-1.9 years, which increased to 113.1/100 000/year in patients exposed for 8-8.9 years.<sup>4</sup> Stopping bisphosphonate therapy reduces the subsequent risk.<sup>5</sup> The relative risk in patients on long-term bisphosphonates varies between studies, but is high, ranging from 2.11-128, and increases with increasing duration of therapy. However, the absolute risk remains extremely low at 3.2-50/100 000 patient-years. Other associations that have been reported are glucocorticoid therapy, denosumab, proton-pump inhibitors, low vitamin D levels, rheumatoid arthritis, being of the Asian race and type 2 diabetes mellitus.<sup>2</sup> To our knowledge, atypical femur fractures fulfilling ABMR consensus criteria such as these have not been reported in association with primary hyperparathyroidism, although this may be because of under-reporting. The case definition for these fractures was only formalised in 2009, and prior studies

may have reported fractures as “proximal femoral”, without differentiating this important subcategory. Epidemiological research, using International Classification of Diseases codes, has shown a high proportion of incorrectly coded fractures.<sup>2</sup>

We postulate that primary hyperparathyroidism predisposed our patient to develop fractures. We also postulate that long-term bisphosphonate therapy contributed to the development of atypical femoral fractures since the radiological features of thickening of the lateral cortex were not consistent with bone changes because of the hyperparathyroidism alone. Our case demonstrates that patients with hip fractures require follow-up to ascertain the cause and facilitate management of their bone disease.

Bisphosphonates are extremely safe, with proven efficacy over four years at reducing the risk of vertebral and non-vertebral fractures in women with osteoporosis. The risk of atypical femoral fractures is low, compared to the risk of hip fractures in untreated osteoporosis. For example, 300 hip fractures are expected in 10 000 high-risk patients/year. Bisphosphonate therapy reduces the number of hip fractures by preventing 108 hip fractures over five years of treatment, with only 3-6 subtrochanteric fractures gained.<sup>6</sup> Therefore, the benefit of bisphosphonate therapy greatly outweighs the risk in patients with osteoporosis. Bisphosphonates have lasting effects on bone mineral density and bone markers after treatment has ceased.<sup>7</sup> Given the paucity of data, in particular on nonvertebral fracture reduction beyond four years, as well as the recognition of rare, but important, adverse events associated with prolonged therapy, concern has been generated regarding long-term uninterrupted use of these agents. The current National Osteoporosis Foundation of South Africa guideline recommends that after five years of bisphosphonate treatment, a drug holiday should be considered. Switching to alternative drugs, such as strontium ranelate or teriparatide, is recommended for high-risk patients.<sup>8</sup>

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