Atypical Femoral Fractures: A Teaching Perspective

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Abstract

This article provides an overview of atypical femoral fractures with a highlight on their radiographic findings. Potent antiresorptive agents such as bisphosphonates or denosumab have been associated with the development of such fractures. However, at this time, a causal association has not been conclusively established. Atypical femoral fractures are insufficiency fractures, which frequently present with bone pain. Early identification of characteristic radiographic features and withdrawal of antiresorptive therapy may prevent the development of completed atypical femoral fractures.

Résumé

Cet article donne un aperçu des fractures fémorales atypiques en soulignant les observations radiographiques qui y sont liées. Les bisphosphonates et d’autres inhibiteurs de la résorption osseuse comme le dénosumab pourraient contribuer à l’occurrence de telles fractures. Cependant, en ce moment, aucune relation de cause à effet n’a été établie de manière concluante. Les fractures fémorales atypiques correspondent à des fractures par insuffisance, qui s’accompagnent fréquemment de douleur osseuse. L’identification précède d’éléments radiographiques caractéristiques et le retrait d’un traitement par des inhibiteurs de la résorption osseuse pourraient prévenir les fractures fémorales atypiques.

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Key Words: Atypical femoral fractures; Imaging; Bone scan; Computed tomography; Bisphosphonates

Clinical Context

Fragility fractures, particularly those that affect the proximal femur, are major features of untreated osteoporosis. However, in recent years, atypical femoral fracture (AFF) have been identified as a distinct fracture located along the femoral diaphysis from just distal to the lesser trochanter to just proximal to the supracondylar flare. Specifically excluded are fractures of the femoral neck, intertrochanteric fractures with spiral subtrochanteric extension, pathologic fractures associated with primary or secondary bone tumours, and periprosthetic fractures. To satisfy the American Society of Bone and Mineral Research 2013 criteria case definition of an AFF, at least 4 of the 5 major features listed below must be present. None of the minor features listed below are required but, when present, can support the diagnosis of an AFF [1,2]:

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Major features:

1. The fracture is associated with minimal or no trauma, as in a fall from standing height or less.
2. The fracture line originates at the lateral cortex and is substantially transverse in its orientation, although it may become oblique as it progresses medially across the femur (Figure 1).
3. Complete fractures extend through both cortices and may be associated with a medial spike; incomplete fractures involve only the lateral cortex (Figures 1-4).
4. The fracture is noncomminuted or minimally comminuted (Figures 1, 4).
5. Localized periosteal or endosteal thickening of the lateral cortex is present at the fracture site ("beaking" or "flaring") (Figures 1, 2, 4).

Minor features:

1. Generalized increase in cortical thickness of the femoral diaphysis.
2. Unilateral or bilateral prodromal symptoms, such as dull or aching pain in the groin or thigh.
3. Bilateral incomplete or complete femoral diaphyseal fractures.
4. Delayed fracture healing.

AFF are uncommon and account for approximately 1.1% of all femoral fractures [3]. Approximately 80% of AFF cases have occurred in the presence of aminobisphosphonate (ABP) drug therapy, although no such therapy had been used in approximately 20% of individuals with an AFF [4]. The risk of an AFF appears to decrease significantly after cessation of ABP therapy [4]. Although a causal role for ABP therapy has been suggested, a simple cause-and-effect relationship has not been proven. In addition, recently, AFFs have been reported in patients who received denosumab therapy. Again, a causal relationship has not been confirmed, and it is not clear at this time if the denosumab therapy contributed to the development of the AFF (Amgen, oral communication). It is important to recognize that, for patients on ABP therapy, the vast majority of fractures result from the underlying osteoporosis and not from its treatment. Antiresorptive therapy prevents far more fractures than might conceivably result from such treatment [2]. The number needed to harm with an aminobisphosphonate has been estimated at 1 in 2000 and with denosumab is estimated at 1 in 10,000 [2].

Pathogenesis

The pathogenesis of an AFF is not well understood at this time. Bisphosphonates decrease bone remodelling. One hypothesis is that this may lead to accumulation of microdamage and the formation of a stress fracture similar to the fractures seen in athletes or military recruits, which results from repetitive trauma [5]. Because ABPs accumulate on fracture surfaces and make the fracture surface resistant to resorption and repair, microcracks may propagate through the bone and lead to the development of an AFF. Bisphosphonates affect bone mineralization density distribution [5]. Microcrack propagation may be facilitated by increased homogeneity in bone mineral and ultimately leads to an AFF [6,7]. With an increase in the mineralization of the bone, the toughness of the bone is decreased, and this may also contribute to the development of new microcracks [8-10]. Acute traumatic fractures of long bones heal by endochondral ossification, and bisphosphonates have not been shown to affect the healing of long-bone fractures. However, stress fractures heal by bone remodelling and the healing of a stress fracture may be delayed or prevented with bisphosphonate therapy [11-13]. Bone histomorphometry has been evaluated with individuals on long-term bisphosphonate therapy. Markedly suppressed bone formation and a decreased osteoblast surface were noted in patients treated with alendronate for 3-8 years and who had developed spontaneous nonvertebral fractures [14]. A decrease in trabecular connectivity and decreased osteoid on trabecular surfaces with a lack of tetracycline labeling on bone biopsy specimens also was...
noted by other investigators [15]. Evidence of decreased bone remodelling also has been reported in 15 patients treated with bisphosphonates for 2-10 years [15]. Other investigators have noted an increase in the osteoclast number on biopsy without evidence of hypermineralized bone in the presence of decreased bone formation [16].

Imaging Findings

The imaging findings evolve with the stage of the disease and are best considered in that context, as presented in Table 1.

There is no justification for obtaining femoral radiographs of patients who are asymptomatic and on ABP [17,18]. However, such patients often have dual-energy x-ray absorptiometry examinations and astute observers have noted that early changes may be detected on dual-energy x-ray absorptiometry examinations seen as focal cortical thickening or “beaking,” as described above. However, some focal cortical thickening may be a scar from stress reaction and may be inactive; these individuals usually have negative bone scans. The US Food and Drug Administration recently approved a scan mode and software program for bone densitometers that specifically evaluate features of AFFs.
Figure 3. A 76-year-old woman with osteoporosis had been on various bisphosphonates for many years. Back and left hip pain prompted radiographs (A), showing an ill-defined lucency and minimal cortical thickening in the lateral left subtrochanteric femur (arrowhead). Bone scan planar (B) and single-photon emission computed tomography/computed tomography (SPECT/CT) (C, coronal and axial slices from SPECT [upper] and CT [lower]), 4 months later showed intense uptake at the site in the left femur (arrowheads) but also moderate uptake in the same location in the right femur (arrows), in keeping with bilateral atypical femoral fractures. This diagnosis led, 6 weeks later, to prophylactic bilateral intramedullary nail fixation (D) to prevent completion of the fractures.

Figure 4. A 58-year-old woman was on bisphosphonates for 10 years because of increased fracture risk, which resulted from long-term steroid use for rheumatoid arthritis. She underwent a bone scan (A) because of left foot pain, which revealed a focus of uptake in the lateral cortex of the right femur (arrowhead). This led to a radiograph (B) and computed tomography (C), which demonstrated mild cortical thickening (arrowheads) and a subtle horizontal lucency (arrows), in keeping with an atypical femoral fracture (AFF). In response to minor trauma 2 years later, she completed the fracture (D). One year later, she underwent a bone scan (E) because she had developed left thigh pain. In addition to intense uptake at the fracture site in the right femur (which had been internally fixated), there now was a focus in the lateral cortex of the left femur (arrowhead), in keeping with an AFF. She proceeded to prophylactic intramedullary nail placement on the left. A subsequent radiograph (F) also demonstrates the AFF (arrowhead).
Table 1

Clinical findings and radiographic features of AFF

<table>
<thead>
<tr>
<th>Clinical findings</th>
<th>Imaging findings</th>
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<tbody>
<tr>
<td>1. Clinical and radiologic normality</td>
<td>No disease; diffuse femoral cortical thickening has been associated with the</td>
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<td>diagnosis of AFF but minimal disease may be hard to recognize, and no criteria</td>
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<td>exist to define the dimensions of the normal width of the femoral cortex or</td>
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<td>if this is even a precursor of AFF.</td>
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<td>2. Thigh pain or disease recognized incidentally either on radiographs or dual-energy x-ray absorptiometry (DXA) examination</td>
<td>Although the natural history of untreated AFFs has understandably not been</td>
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<td>studied with imaging, the following outlines a plausible sequence: (a) at first,</td>
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<td>microcracks in bone may be asymptomatic, and imaging may be normal; (b) as</td>
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<td>the process evolves, thigh pain may result, and the radionuclide bone scan</td>
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<td>may show focal radiotracer concentration at the site of injury and/or repair,</td>
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<td>typically, the lateral aspect of the femur (Figures 1–4); (c) an additional</td>
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<td>manifestation that is visible on radiographs may be a focal cortical thickening</td>
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<td></td>
<td>on the periosteal or endosteal surfaces of the lateral cortex</td>
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<td>(Figures 1, 2–4); (d) with increasing thigh pain, an incomplete fracture line</td>
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<td>can be seen on plain radiograph (&quot;beaking&quot;) or computed tomography scan</td>
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<td>(Figure 4) (Ref. 19); The process can be bilateral, even when only 1 side is</td>
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<td></td>
<td>symptomatic.</td>
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<td>3. Fracture</td>
<td>Catastrophic skeletal failure after minimal trauma or even spontaneously;</td>
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<td>fractures extend through both cortices and may be associated with a medial</td>
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<td>spike; defining features are a mostly transverse fracture line with no or</td>
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<td>minimal comminution (Figures 1, 4).</td>
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AFF = atypical femoral fracture; DXA = dual-energy x-ray absorptiometry.

Clinical Management

Prevention

Patients being treated with ABP are often being considered for a “drug holiday” after 5 years of use, particularly if their bone mineral density has significantly increased on treatment and their fracture risk is not high. Treatment with ABP in patients with a low 10-year fracture risk should be avoided because the risk-benefit ratio is not in favor of therapy.

Treatment of Incomplete Fractures

Incomplete fractures recognized clinically or on imaging are treated by discontinuation of the bisphosphonate or denosumab therapy and decreasing weight-bearing activities. Previously, most patients also had immediate internal fixation of the fracture, but, over time, a more conservative approach has been adopted that includes radiologic monitoring and/or switching to an anabolic agent such as teriparatide. Internal fixation is reserved for cases that progress, with persistent debilitating pain, or where there are features of incipient fracture [1]. There have been no clinical trials to afford an evidentiary basis for guiding the therapy choice in this context. What has become apparent is that the risk of an AFF decreases after the ABP is withdrawn. The reduction in the risk of an AFF has been observed to be approximately 70% in the year after cessation of ABP therapy [4]. It has been surmised that this may be due to a compounding effect of the ABP. We know from long experience that methylene diphosphonate (labelled with technetium 99m) localizes in active stress fractures. ABPs and methylene diphosphonate have similar actions. Thus, the ABP may preferentially be deposited at the site of the stress fracture and may impair the reparative process, which allows the stress fracture to progress.

Treatment of a Complete AFF

The care of a fracture is a surgical issue. However, it is important to recognize that, although the complete fracture may be unilateral, the process is often bilateral. Clinical and radiologic attention to the contralateral limb is mandatory.

Radiographic Management of an Incomplete AFF

An incomplete AFF, defined by the presence of a lucent cleft on plain radiographs or computed tomography scans or a positive bone scan, requires immediate attention. The clinician should be advised of the need to proceed with further imaging and assess both femurs with plain radiographs. Also, the attending physician should be alerted to the presence of an incomplete AFF and the possible association of this fracture with ABP or denosumab therapy.

Conclusion

AFFs represent another facet of the radiology of osteoporosis. However, they are rare and their detection requires vigilance as early detection and intervention may well prevent a complete AFF. It is essential for the radiologist to alert the referring physician to the presence of radiographic features of an AFF and to know the possible association with antiresorptive therapy, including ABP and denosumab use. Appropriate further investigation and management is recommended, particularly in view of the risk of a bilateral process. It also is important to recognize that antiresorptive therapy prevents many more fractures than it may contribute to and the risk-benefit ratio of antiresorptive therapy needs to be carefully considered in each individual.

References


