

Bone scintigraphy depicts bilateral atypical femoral stress fractures with metachronous presentation, long before a complete fracture occurs

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Abstract

Atypical femoral fractures (AFF), although rare, are recognized more often during the last decade. They are located in the subtrochanteric region or the femoral shaft, may be bilateral, can evolve to complete fractures after bone overload or minimal trauma and have specific radiological features. The complete fractures have horizontal or slightly oblique configuration accompanied by a medial spike, are non-comminuted, and extend to both cortices. There is also generalized cortical thickening of femoral shaft. Newer evidence suggests that AFF are stress or insufficiency fractures, possibly associated with long-term use of bisphosphonates (BP). AFF can also occur in oncologic patients referred for bone scintigraphy and, in such a case, they should be differentiated from bone metastases. *We present here* a case with bilateral AFF with metachronous appearance in a female patient with a history of breast cancer and osteoporosis. The first AFF had been depicted on bone scintigraphy 3 years before a complete fracture occurred at this site, but the finding was overlooked. A second bone scan performed shortly after the fracture in order to exclude underlying bone metastases disclosed an additional unsuspected incomplete AFF in the contralateral femur, which was confirmed by radiography. *In conclusion*, oncologists should consider other causes of bone pain besides bone metastatic disease, and physicians interpreting whole body bone scans of oncologic patients should be aware of the entity of AFF, in order to avoid false positive results and provide early information about an impending complete AFF.

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Introduction

Cancer patients may suffer from other diseases also, that account for symptoms and findings in imaging studies which are unrelated to their cancer disease. Osteoporosis is common in elderly people, particularly females. It is a silent disease, until complicated by a bone fracture. Osteoporotic or insufficiency fractures usually occur in the vertebrae and the hip, either spontaneously during routine daily activities or following bone overload or minimal trauma. In oncologic patients these fractures are often difficult to differentiate from pathological fractures caused by underlying bone metastases. Osteoporotic fractures of the femoral diaphysis are uncommon. In addition to this unusual location, certain radiological and clinical features identify a unique entity of so-called "atypical" subtrochanteric or femoral fractures (AFF) [1]. Newer evidence suggests that AFF are actually stress or insufficiency fractures [2]. We present here a case of an AFF depicted on bone scintigraphy years before a complete fracture occurred at this site. Moreover, an additional unsuspected AFF in the contralateral femur was disclosed by a second bone scan performed in order to exclude bone metastases.

Case report

A 78 years old female was admitted to our hospital because of a right femoral shaft fracture that occurred after a fall from her own height (Fig. 1). The patient had a history of breast cancer diagnosed and treated 10 years earlier. There was no current evidence of cancer relapse. She also suffered from rheumatoid arthritis treated with anti-inflammatory drugs and occasionally corticosteroids, and osteoporosis treated with alendronate in the past, and subsequently with recombinant human parathyroid hormone (teriparatide) that was discontinued 2 years before admission. The patient also used proton pump inhibitors. The patient complained about long-lasting generalized bone pains, including worsening pain in both thighs during the last year. Because of the history of breast cancer concern was raised on the possibility of underlying bone metastases and a whole-body bone scan was performed. Apart from the fracture of the right femur, many other sites of increased

osteoblastic activity were demonstrated in the skeleton (Fig. 2). Abnormal findings in the shoulders, wrists and the right elbow could be attributed to rheumatoid arthritis. Focal lesions seen in the spine and some ribs bilaterally probably represented osteoporotic fractures, but metastatic bone disease could not be excluded. Interestingly, the scan also revealed a small focus of increased activity at the left mid femoral diaphysis. Plain X-ray film of the left femur revealed focal cortical thickening and a transverse radiolucent line across the lateral cortex, compatible with stress fracture (Fig. 3). In order to compare recent scintigraphic findings with those of previous studies, we retrieved from our archive a bone scan per-



Figure 1. Plain radiograph of the right femur in anterior-posterior view. The fracture is located in the femoral shaft, is non-comminuted, has a horizontal or short oblique orientation and is accompanied by a medial spike. Generalized cortical thickening of the femoral shaft is also noticed. These features are compatible with a complete AFF.

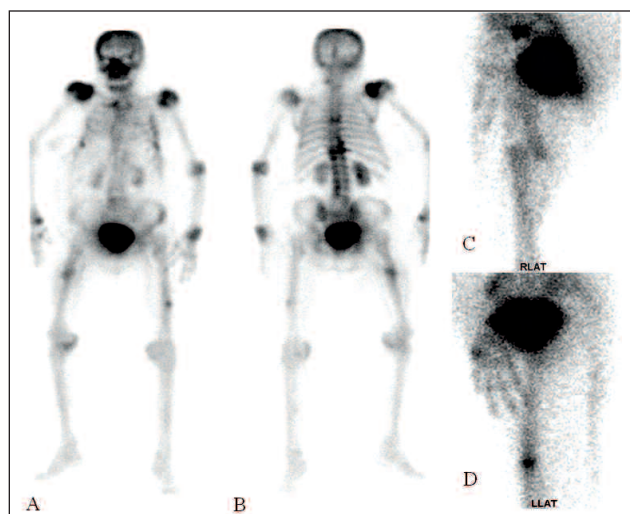


Figure 2. Bone scan performed shortly after the occurrence the right femoral fracture, in order to exclude underlying bone metastases. A: Anterior view, B: posterior view of the whole-body scan, C: right lateral spot view of the right femur and D: left lateral spot view of the left femur: Scan findings are detailed in the text.

formed 3 years earlier (Fig. 4). Images of the two bone scans were similar, except for the fracture of the right femur and the aforementioned “hot” spot at the lateral cortex of the left femoral shaft. A careful inspection of the earlier scan revealed a focus of slightly increased activity in the right femur (pointed by an arrow on Fig. 4), at the site where a complete fracture subsequently occurred, which had been overlooked and was unnoticed in the report. Taking into consideration the history of osteoporosis, the radiographic images and the findings of the two bone scans performed 3 years apart, bilateral AFF were suspected. Metastatic bone disease was considered unlikely. Surgical endoprosthetic restoration of the right femoral fracture was performed. Histology of the material obtained during surgery confirmed the absence of malignancy. There was concern about the lesion of the left femur because of the increased risk of a second complete fracture. Prophylactic nailing was recommended, but the patient denied the procedure. Alternatively, instructions for avoidance of leg weight bearing were given, teriparatide was prescribed and an appointment after a few months was scheduled. However, the patient was lost from further follow-up.

Discussion

Atypical subtrochanteric and femoral shaft fractures are rare, with reported incidence of approximately 30 cases per 100,000 person-years [3]. It seems that their incidence is increasing over the last decade, but the absolute number of cases still remains very low [4]. Atypical femoral fractures are distinguished from ordinary femoral fractures by the presence of certain radiological and clinical characteristics. These features have been previously defined and recently updated by a Task Force of the American Society for Bone and Mineral Research [1, 2]. The AFF have been associated with long-term use of BP [5-9], but are also encountered in BP-naïve patients [10]. In a recent study the prevalence of BP use among patients with AFF was reported to be significantly

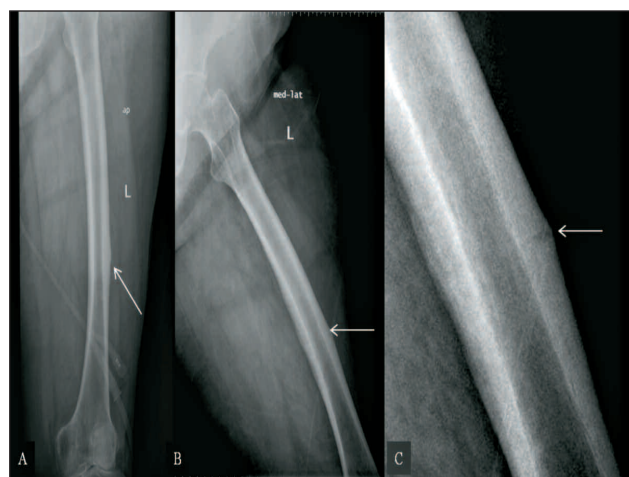


Figure 3. Plain X-rays films of the left femur A: in anterior-posterior view, B: medial-lateral view, and C: zoomed medial-lateral view. Arrows point at the site of the lesion. A fine radiolucent line is observed in the middle of focal cortical thickening at the lateral cortex, along with mild periosteal reaction. These features are compatible with a stress AFF.

higher (78%) than controls (10%), but the absolute risk was small when compared to the beneficial effects of the drug. After BP withdrawal, the risk diminished by 70% per year [9]. Hypothetically, the reduction of bone remodeling induced by BP allows the accumulation of microcracks over time, leading to stress fractures at certain sites of the skeleton [5, 11]. However, a significant BP-AFF correlation has not been substantiated in other trials [12, 13] and the issue is still debated [11]. Other medication, such as corticosteroids, denosumab, estrogen, raloxifene, calcitonin, proton pump inhibitors and comorbid conditions like cancer, diabetes, rheumatoid arthritis, vitamin D deficiency and hypophosphatasia are implicated in AFF [1, 2]. Fracture repair by intramedullar full-length nails to protect the entire femur is the preferred method of treatment for complete AFF. The contralateral femur must be evaluated by radiography, scintigraphy or MRI to exclude bilateral involvement [14]. For incomplete fractures accompanied by pain, prophylactic nail fixation is recommended [15]. In the absence of symptoms, conservative therapy may be considered during which weight bearing should be limited and vigorous activity avoided. The patients have to be reevaluated at regular intervals with imaging studies to test for AFF healing or progression. Potent antiresorptive agents should be discontinued. Vitamin D deficiency should be appropriately treated. The benefits of BP in patients at medium or high risk of ordinary osteoporotic fractures outweigh the potential hazards of AFF development. However, alternative treatment for osteoporosis could be considered after long-term BP therapy [1, 2]. A few reports suggest a beneficial effect of teriparatide in healing AFF [16], but concrete clinical evidence is lacking.

Our case satisfied all major and most of minor features required for the definition of AFF [1, 2]. More specifically, both fractures occurred distal to the lesser trochanter and proximal to the supracondylar flare; the complete fracture on the right was associated with minimal trauma, had slightly oblique configuration accompanied by a medial

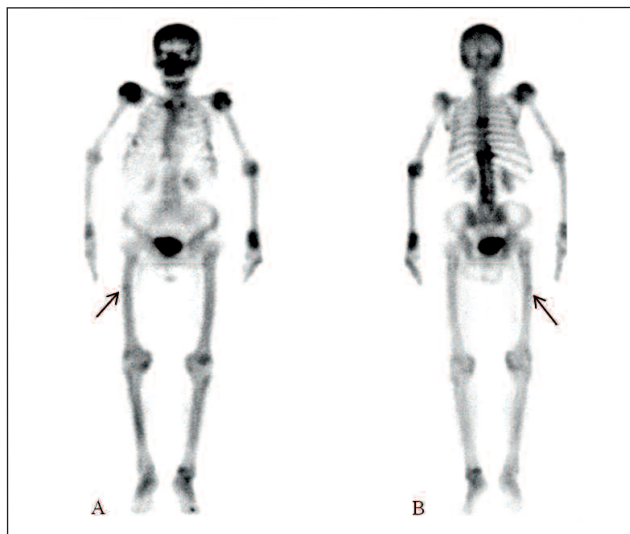


Figure 4. A: Anterior and B: posterior views of a whole-body bone scan performed 3 years earlier. Arrows point to a focus of slightly increased osteoblastic activity in the right femur, at the site where a complete fracture occurred later.

spike, was non-comminuted and extended to both cortices; the incomplete fracture on the left affected only the lateral cortex and mild periosteal reaction was present. Also, generalized cortical thickening was evident in both femoral shafts, the focal lesions were bilateral (with metachronous presentation) and the patient mentioned prodromal symptoms in both thighs, which is reported in literature as a common feature of AFF [11]. Our patient had used BP for long time and occasionally corticosteroids in the past, but she had discontinued this medication years before the occurrence of the fracture. She currently received proton pump inhibitors which are also possibly related to AFF [1]. Furthermore, our patients had additional risk factors as mentioned above. Of note, signs of an incipient stress AFF were evident on bone scintigraphy 3 years before the development of complete fracture. Bone scintigraphy is a sensitive method that can depict AFF early enough. Although SPET/CT was not used in our patient, this technique probably can identify such lesions even earlier.

In conclusion, the case presented here illustrates the scintigraphic and radiologic appearance of complete and incomplete AFF. Moreover, it aims at drawing the attention of oncologists, radiologists and nuclear medicine physicians to this uncommon clinical entity when encounter oncologic patients with focal findings in the femoral shaft. Stress lesions identified on bone scintigraphy may precede complete AFF for years and should be differentiated from bone metastases. If measures are taken early, the deleterious effects of a complete fracture can be prevented.

The authors declare that they have no conflicts of interest.

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