Subtrochanteric femoral stress fracture with features of atypical femoral fracture in patient with Paget’s disease: a case report

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Summary

Atypical femoral fracture (AFF) has been widely issued since the American Society for Bone and Mineral Research (ASBMR) taskforce stated a possible association with long-term use of bisphosphonate in 2010. ASBMR taskforce recommended to include Paget’s disease as one of variables to investigate the AFF in 2010. On the other hand, the ASBMR taskforce in 2014 excluded Paget’s disease in the definition of AFF. Still, any rationale has been barely documented about this change. We described the rationale by reporting an 85-year-old man who had a subtrochanteric fracture with features of atypical femoral fracture which turned out to be Paget’s disease of bone in the pathology.

KEY WORDS: atypical femoral fracture; Paget’s disease.

Introduction

Atypical femoral fracture (AFF) was widely reported as a potential complication of long-term bisphosphonate therapy, even though bisphosphonate treatment was accepted as a safe and efficient treatment of osteoporosis (1-4). The incidence of AFF in patients treated with bisphosphonates ranged from 55 to 100 per 100,000 person-years (5-8). AFF was mostly due to low energy trauma and had radiologic features of insufficiency fracture. The ASBMR Task Force has defined the five major radiologic features for AFF since 2010 (9, 10). First, the fracture was not associated with trauma. Second, the fracture was a complete transverse fracture. Third, the complete fracture extended through both cortices and may be associated with a medial spike. Fourth, the fracture was non-comminuted. Fifth, fracture located in subtrochanteric and diaphyseal area of the femur.

Paget’s disease impairs bone metabolism by increasing bone resorption and formation, and causes pain, fractures, and deformity (e.g. bowing of the long bones). The incidence of PDB is estimated to be 1 to 2% in Caucasians older than 55 years, but the incidence is very rare in Asian populations (11).

Historically, Paget’s disease was excluded as miscellaneous bone disease in revised definition established by 2014 ASBMR taskforce (10), while it was included in the definition of AFF in 2010 ASBMR taskforce report (9).

We report a case of a subtrochanteric fracture that occurred in patients with Paget’s disease that fulfills the major criteria defined by the second ASBMR Task Force report for an AFF and that was not associated with use of bisphosphonate. In addition, we reviewed the rationale why Paget’s disease has been excluded in the recent definition of AFF established by 2014 ASBMR taskforce.

Case report

An 85-yea-old man visited our emergency room with right severe hip/groin pain. He was community dwelling ambulatory with cane. After having a minor fall from standing height in the morning, he could not walk. He heard that he had a geographic osteolytic and osteosclerotic region of pelvic bone as well as subtrochanteric femoral fracture in the initial radiographs at another hospital. Having a suspicion of malignant tumor involvement, the primary physician referred the patient to our tertiary referral hospital.

Upon thorough history taking, the patient had never had pain around his right hip or right thigh, neither taken bisphosphonate therapy. In plain radiography, subtrochanteric femoral fracture was shown (Figure 1) and diffuse irregular cortical and trabecular bone thickening from femoral head to diaphyseal area of right femur was distinctly recognized compared to that of left one. The fracture was a complete transverse fracture through both cortices without comminution at subtrochanteric area of the femur, which fulfilled all major features of AFF established by ASBMR taskforce. The magnetic resonance imaging (MRI) showed neither metastatic nor tumorous lesion, but just fat marrow signal intensity between the thickened coarse trabeculation from femoral head to diaphyseal area (Figure 2). Therefore, Paget’s disease of right femur with subtrochanteric femoral fracture was suspected. Serum alkaline phosphatase (115, normal range 30-115 IU/L) and bone specific alkaline phosphatase (20.3 ug/L, normal range <20.1 ug/L) were around the upper limit of the normal range. Parathyroid hormone (37.9, normal range 15-65 pg/ml) was within normal range. C-telopeptide was 0.886 ng/ml, and osteocalcin was 28.4 ng/ml. His dual energy X-ray absorptiometry (DXA) scan showed T-score of 0.6 and 1.4 in femoral neck and total femur in left hip.
Closed reduction and internal fixation with intramedullary nailing was performed, and a biopsy was conducted. Biopsy turned out to be Paget's disease of bone, resembling jigsaw puzzle with prominent irregular cement lines (Figure 3). Patients took 5 mg of intravenous zoledronate (Aclasta; Novartis AG, Basel, Switzerland) intravenously.

Discussion

Historically, ASBMR taskforce recommended that Paget's disease should be included in future study for AFF in 2010 reporting (9). Paget's disease and fibrous dysplasia were excluded as miscellaneous bone disease to define AFF in 2014 ASBMR taskforce report (10), while it was included in the definition of AFF in 2010 ASBMR taskforce report (9). There was a case report describing AFF that occurred in patient with Paget's disease between 2010 and 2014 (12). In 2011, Kilcoyne and Heffernan (12) reported a subtrochanteric fracture in a 78-year-old man who had a 16-year history of alendronate use to treat Paget's disease. The patient complained of gradually increasing left groin pain, with a linear radiolucency and beaking in the lateral cortex of bilateral subtrochanteric area on a radiograph. After low energy trauma

Figure 1 - Hip anteroposterior radiograph shows right subtrochanteric femoral fracture with diffuse trabeculation on proximal femur compared to left femur.

Figure 2 - Magnetic resonance imaging of thigh with T2 weighted image shows diffuse irregular cortical and subchondral bone thickening.

Figure 3 - Microscopy shows jigsaw puzzle pattern with prominent irregular cement lines.
(fall from standing), the patient suffered a complete transverse fracture at the site of the previously identified radiolucency. Authors believed that patients with Paget’s disease may be predisposed to AFF and in whom the relationship with AFF may be overlooked. They raised an issue whether the insufficiency fractures in patient with Paget’s disease are related to the bisphosphonate treatment rather than the disease itself (12).

Because patients with Paget disease are commonly treated with long-term bisphosphonate treatment (13), some Authors included patients with Paget disease to estimate the incidence of AFF in patients on bisphosphonate (14). However, subtrochanteric transverse insufficiency fractures (which may be complete or incomplete) are well-documented complications of Paget’s disease in the femur and typically begin on its lateral aspect (15, 16). Although fractures in patients with Paget’s disease showed usually stress fracture, its pathophysiology might be distinctively apart from bisphosphonate-associated insufficiency fracture (17). Stress fracture in Paget’s disease is caused by the disorganized bone remodeling due to excessive breakdown (osteoclast) and formation (osteoblast) of bone, while bisphosphonate-associated insufficiency fracture is caused by severely suppressed bone turnover due to decreased activity of osteoclast (9, 10).

ASBMR taskforce recommended that bisphosphonate should be discontinued in patients with AFF, because patients with AFF were considered as severely suppressed bone turnover status (9, 10, 18, 19). On the other hand, the stress fractures in patients with Paget’s disease may heal in response to bisphosphonate treatment (17, 20). Moreover, in terms of treatment for severely suppressed bone turnover, teriparatide, anabolic agent, may be used for treatment of AFF (21-23). However, teriparatide should be prohibited in patients with Paget’s disease, because there might be malignant transformation from Paget’s disease, one of precancerous lesion (24). Conventionally, Paget’s disease of bone has been treated with oral bisphosphonate. Recently, intravenous bisphosphonate with higher potency has been introduced to treat osteoporosis by decrease of osteoclast activity (25, 26). We administered intravenous zolendronic acid to manage Paget’s disease.

Although the stress fracture in Paget’s disease fulfilled all five major features of AFF established by ASBMR taskforce, Paget’s disease should be excluded in the definition of AFF, because different pathophysiology (severely suppressed bone turnover status) and treatment between both disease entities. These may be the rationale why Paget’s disease was excluded in the definition of AFF by 2014 ASBMR taskforce.

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References


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