Case Report / Olgu Sunumu

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Bilateral Bisphosphonate-related Atypical Femoral Neck Fracture in a Patient with Familial Mediterranean Fever: A Case Report

Ailevi Akdeniz Ateşi Hastasında Bilateral Bifosfonat-ilişkili Atipik Femur Boyun Kırığı: Olgu Sunumu

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Abstract

The authors present a rare case of bilateral bisphosphonate-related femoral neck fracture in a patient with Familial Mediterranean fever. Chronic subclinical inflammation that continues in the attack-free period is thought to cause osteopenia/osteoporosis. Locomotor system symptoms are frequently observed during the clinical course of the disease, and in the presence of hip pain in these patients, atypical femur fractures should be considered in addition to the hip involvement of the disease. Although bisphosphonate-related atypical femoral fractures are mostly seen in the diaphysis, atypical femoral neck fractures have also been defined recently, as in this case.
Keywords: Familial mediterranean fever, osteoporosis, atypical, femoral neck fracture, hip

Öz

Ataksız dönemde devam eden kronik subklinik inflamasyonun Ailevi Akdeniz ateşinde osteopeni/osteoporoza neden olduğu düşünülmektedir. Lokomotor sistem semptomları hastalığın klinik seyri sırasında sıklıkla gözlenmektedir ve bu hastalarda kalça ağrısı varlığında hastalığın kalça tutulumuna ek olarak atipik femur kırıkları da akla gelen nedenler arasında olmalıdır. Bifosfonat ilişkili atipik femur kırıkları daha çok diyafizde görülse de bu olguda olduğu gibi son yıllarda atipik femur boyun kırıkları da tanımlanmaya başlamıştır. Bu yazıda, kalça ağrısı ile başvuran bir Ailevi Akdeniz ateşi hastasında bilateral bifosfonatla ilişkili femur boyun kırığı saptanan nadir bir olgu sunulmuştur.
Anahtar kelimeler: Ailevi Akdeniz ateşi, osteoporoz, atipik, femur boyun kırığı, kalça

Introduction

Familial Mediterranean fever (FMF) is an autoinflammatory disease characterized by recurrent episodes of serositis and fever. FMF most commonly affects the populations originating from the Mediterranean region. Locomotor symptoms frequently occur during the clinical course of the disease. Hip involvement in FMF can be associated with protracted attacks of the disease itself or coexisting chronic inflammatory joint disease, especially spondyloarthropathies. In the case of hip pain in a FMF patient, although it is rare, the differential diagnoses of avascular necrosis and osteoporosis should also be kept in mind (1). It has been reported that there is an ongoing inflammatory activity in attack-free periods and chronic inflammation may lead to osteoporosis in FMF (2). Bisphosphonates are the first-line drugs for the prevention of fractures in osteoporosis. It is important to be aware of the side effects of bisphosphonates that are used for extended periods of time. Findings of atypical femoral fractures (AFF) may be overlooked in FMF patients receiving chronic bisphosphonate therapy. AFF are frequently reported as subtrochanteric and diaphyseal fractures, and cases of atypical femoral neck fractures are very rare in the literature. In this report, a case of bilateral atypical femoral neck fracture in a patient with known FMF presenting with hip pain is discussed in the light of the relevant literature.

Case Report

A 66-year-old female patient presented to the physical medicine and rehabilitation outpatient clinic with complaints of pain in the left hip and difficulty walking. She reported that hip pain increased gradually over a period of 1 month and worsened with

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weight bearing and walking. The patient had a history of FMF for 20 years and osteoporosis for 15 years. She had been using colchicine 2 g/day for FM, ibandronic acid 150 mg/month and calcium carbonate 1200 mg/day. According to the dual energy X-ray absorptiometry result of the patient, L1-4 T-score was -2,7 and non-operated femur neck T-score was -0,1. There was no history of trauma or fall, nor a history of smoking or alcohol use. On physical examination of the patient, internal rotation and flexion range of motion of the left hip were limited and painful. The FABER test was positive for the left hip and there was crepitation in the left knee. A plain radiograph was taken on the suspicion of avascular necrosis, which showed a suspicious fracture in the femoral neck. A computed tomography (CT) scan was planned for confirmation and a non-displaced fracture of the femoral neck of the left hip was detected (Figure 1). The orthopedics department was consulted, and subsequently was managed with internal fixation using a femoral neck system that includes a sliding screw and an anti-rotation bolt. It was learned that the patient had been using ibandronate treatment for 15 years which was eventually stopped. Post-op control radiographs of the patient also showed a suspicious fracture line in the right hip (Figure 2). The patient was referred to orthopedic rehabilitation for the left hip, and surgery for the right hip was scheduled 2 months later. Written informed consent was obtained from the patient prior to the drafting of the manuscript.

Figure 1. CT of the left femur shows fissural linear fracture line that causes discontinuity in the cortex in the superior section at the level of the femoral neck
CT: Computed tomography

Discussion

FMF is an autosomal recessive disorder that mainly affects Jewish, Turkish, and Arab populations. In FMF patients, differential diagnoses of seronegative spondyloarthropathy, osteoporosis, arthritis and rarely avascular necrosis of the femoral head should be considered in the presence of hip pain (3-5).

Negative balance of bone turnover occurs in the course of chronic inflammatory diseases. Proinflammatory cytokines (IL-1, IL-6, TNF-α, receptor activator of NF-κB (RANK), RANK ligand, and osteoprotegerin) play a role in the etiopathogenesis of osteoporosis (6). Yildirim et al. (7) reported that patients with FMF had lower lumbar spine, femoral neck and femur total bone mineral density than healthy subjects. Bisphosphonates are the first-line drugs for fracture prevention in osteoporosis. However, recent studies reported that long-term use of bisphosphonates may be associated with low-energy subtrochanteric and femoral shaft fractures (8,9). The most commonly implicated agent in this regard has been alendronate. As in our case, cases of AFF in patients using ibandronate are very rare in the literature.

A revised definition of AFF was proposed by the American Bone and Mineral Research Association in 2013. Accordingly, AFF were defined as femoral diaphysis fractures between the distal part of the lesser trochanter and the proximal supracondylar region and meeting at least four of the five core criteria (10). Atypical femoral neck fractures are defined as linear incomplete fractures in the lateral cortex of the femoral neck in patients with long-term bisphosphonate treatment without a history of repetitive stress or trauma (11). In the guidelines, femoral neck and intertrochanteric fractures are excluded from the AFF case definition. However, in recent years, cases related to atypical femoral neck fractures have emerged in the literature and started to be considered as a new variant of AFF (11-13).

Radiologically, it appears that these fractures may cause cortical thickening and periosteal reaction and they start from the lateral cortex with transverse-oblique orientation. The stress fracture line is obscured unless a near-perfect radiographic projection is obtained. The fracture line is best detected by CT imaging. In their study, Neviaser et al. (14) examined 70 low-energy subtrochanteric femoral fractures, and 3 blinded orthopedic surgeons evaluated radiographs separately. A characteristic fracture pattern (simple, transverse, or short-oblique pattern in areas of cortical thickening with a unicortical beak) was

Figure 2. Suspicious fracture line in the right hip on post-op control pelvis AP X-ray
AP: Anteroposterior

associated mostly with bisphosphonates (76%) and has been even reported specifically for alendronate (98%) (14).

The incidence of AFF has been reported to range between 1/100,000 and 5/10,000 in various studies, but it has been shown that the incidence increases with longer duration of bisphosphonate use. As in this case report, it is predicted that about 25% of the cases may also develop fractures in the contralateral femur, and therefore, it is advised to investigate the contralateral femurs of the patients in terms of the presence of incomplete AFF (15).

In this case, we believe that the etiology of bilateral femoral fracture was the ongoing inflammation and osteoporosis in FMF and a double hit of long-term bisphosphonate treatment.

It is important to raise awareness among clinicians of the potential for atypical fractures in patients using long-term, high-dose bisphosphonates. There is a need to find a balance between the increased risk of fractures and the benefits of these drugs. Protocols have been established for the dosage and duration of the bisphosphonate treatment, and timing of the drug holiday. As a proactive measure, it is crucial to monitor the patients in accordance with these protocols and to question the duration and doses of the patients' medication in every follow-up visit. If a patient has a complete or incomplete insufficiency fracture while using bisphosphonates, actions to be taken require additional consideration.

Ethics

Informed Consent: Written informed consent was obtained from the patient prior to the drafting of the manuscript.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: S.B., B.D.K., Concept: S.B., B.D.K., Design: S.B., B.D.K., Data Collection or Processing: S.B., B.D.K., Analysis or Interpretation: S.B., B.D.K., Literature Search: S.B., B.D.K., Writing: S.B., B.D.K.

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