UZUN DÖNEM BİFOSFONAT KULLANIMINA BAĞLI EŞZAMANLI BİLATERAL FEMUR SUBTROKANTERİK KIRIK İLE BAŞVURAN HASTA

Concurrent Bilateral Subtrochanteric Femoral Fracture Related with Long-Term Bisphosponate Usage

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Geliş tarihi/Received: 17.10.2019
Kabul tarihi/Accepted: 08.12.2019
DOI: 10.16919/bozoktip.634012

Bozok Tıp Derg 2020;10(2):241-44
Bozok Med J 2020;10(2):241-44

ÖZET

Bifosfonatlar osteoporoz tedavisinde yaygın olarak kulanılmaktadır. Bifosfonatların etki mekanizması, kemik rezorpsiyonu supresyonudur. Uzun dönem bifosfonat kullanımında ise son yıllarda gittikçe artan sayıda atipik femur kırıkları bildirilmektedir.

Biz, 60 yaşında, metastatik meme karsinomu tanılı, uzun süreli bifosfonat kullanımına bağlı eşzamanlı bilateral femur subtrokanterik kırık ile başvuran postmenapozal kadın hastada, klinik presentasyon, tanı konulması, tedavi ve takibini yayınlıyoruz.

Her iki kırık hattından frozen gönderildi, frozen inceleme sonucunda, tümöral dokuya rastlanmadı. Hastanın aynı seansta sağ kalçasına proksimal femoral çivi, sol kalçasına femur proksimal anatomik plak uygulandı. Her iki alt ekstremitesine tam yük vererek yürüyebildiği, kalça eklem hareketlerinde istirahat ve egzersizle ağrı olmadığı görüldü.

Anahtar kelimeler : *Bifosfonat; osteoporoz; femur kırığı*

ABSTRACT

Bisphosphonates are widely used in the treatment of osteoporosis. Bisphosphonates act via suppression of bone resorption. Growing numbers of atypical femur fractures have been reported in the use of long-term bisphosphonates in recent years.

In this case report, we present clinical presentation, diagnosis, and treatment as well as follow-up of a 60-year-old postmenopausal female patient who had metastatic breast carcinoma, with bilateral femoral subtrochanteric fracture associated with long-term use of bisphosphonates.

Frozen species were sent from both fracture lines, as a result of the frozen examination, no tumoral tissue was found. Proximal femoral nail to right hiccup and femur proximal anatomical plaque to left hiccup were applied in the same session. The patient was able to walk with full load on both lower extremities, and there was no ain in the hip joint movements in the rest and exercise.

Keywords: *Bisphosphonate; osteoporosis; femoral fracture*

Bu vaka raporu, 26. Ulusal Ortopedi ve Travmatoloji Kongresinde poster sunum olarak sunulmuştur.

Bozok Tıp Derg 2020;10(2):241-44
Bozok Med J 2020;10(2):241-44

INTRODUCTION

In the treatment of osteoporosis, bisphosphonates are widely used. The mechanism of pharmacological action of bisphosphonates that they bind to the hydroxyapatite crystals in the bone and enhance bone mineral densities in the short-term follow-up(1).

When current literature is reviewed, case reports or case series about atypical femur fractures associated with long-term use of bisphosphonates have been reported(2-5). More rarely, bilateral femoral fractures occurred at different times have also been observed.(2,5).
We present a concurrent, bilateral atypical femur fracture in a postmenopausal female patient using long-term alendronate.

CASE REPORT

60-year-old female patient was diagnosed with left breast invasive ductal carcinoma in 2006, no distant metastasis was detected at the time of diagnosis on the date of diagnosis, modified radical mastectomy was performed by general surgery, and following mastectomy, chemotherapy was started. The patient was asked if data concerning the case could be submitted for publication, and he consented.

Ibandronate (50 mg/day) treatment together with calcium and vitamin D were initiated with postmenopausal osteoporosis diagnosis in 2009.
The patient who suffered from generalized pain was screened periodically. In January 2009, whole body bone scintigraphy and thoracic vertebra, MRI showed Th5, Th6, and Th8 vertebra metastasis, and palliative radiotherapy was performed.

Radiotherapy was applied to the hips due to bilateral femoral neck metastasis In July 2011, and to the lumbar region due to L4 vertebra metastasis in May 2012. In between april 2013 and 2014, it was assumed that the disease was stable in follow-up examinations. The patient did not come to control until 2016.In March 2016, the patient admitted to the orthopedic clinic with bilateral hip pain and pain while stepping full strenght increasing for the last two years.

The limitation of motion and deformity in the bilateral hip joint were present on her examination. There was no history of trauma.There was no pathological movement proximal to both femurs. Direct radiography, MRI, and WBBS were evaluated. In WBBS, bilateral trochanter minor involvement was detected. Bilateral subtrochanteric pathologic fracture were detected on X-ray and MRI(figure 1, figure 2). It was learned that the patient continued to ibandronate treatment without interruption for 8 years and that they did not take calcium and vitamin D preparations regularly.

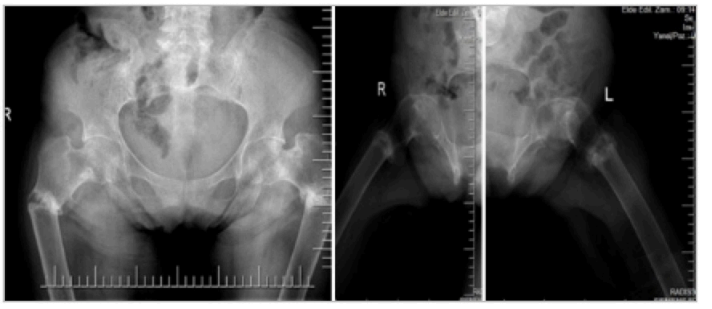

Figure 1a, b, c : Antero-posterior / lateral direct charts at the time of the patient's application.

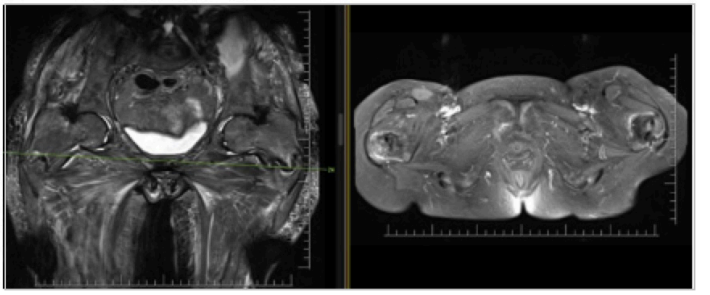

Figure 2a, b: Coronal t2 sequence and axial t1 contrast-enhanced MRI images at the time of admission of the patient.

Hemoglobin (Hb), platelet, white blood cell counts, serum parathormone (PTH), calcium (Ca), 25-hydroxylamine D, osteocalcin, and urinary Ca values were found to be at normal levels in the laboratory examinations. No pathology was found in the analysis of acute phase reactants including erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and also in protein electrophoresis.
The patient was evaluated with a multidisciplinary approach including orthopedics, radiology, medical oncology and pathology departments.

The findings of the WBBS were insufficient in the distinction of metastasis /malaise fracture. There was no finding supporting the presence of tumoral lesions such as mass lesion appearance, bone destruction, soft tissue component in X-ray and MRI. Also these examinations showed the presence of atypical fracture in the subtrochanteric region which is the most common fracture localization due to the use of bisphosphonate. On the grounds, patient who had history of long-term bisphosphates usage was diagnosed asconcurrent, bilateral, atypic femoral subtrochanteric fracture associated with long-term use of bisphosphonates

The patient was placedin the supine position. After proper staining and sterile covering, both hipswere incised, and the fracture line was reached, and macroscopic examination did not show any tumor tissue.
Frozen species were sent from both fracture lines, as a result of the frozen examination, no tumoral tissue was found. After taking sufficient amount of biopsy material from both fracture lines, proximal femoral nail to right hiccup and femur proximal anatomical plaque to left hiccup were applied in the same session.
On the first postoperative day, the patient was walked by applying a complete load to the right lower extremity and a partial load to the left lower extremity.
The patient was discharged on the second postoperative day. She did not come to the post-operative periodic follow-up visits . Histopathological examination of the biopsy species which was examined with all serial sections, revealed no material of any tumoral tissue or any specific pathology.

The patient admitted at postoperative 6 months. Orthopedic evaluation was performed. The patient was able to walk with full load on both lower extremities, and there was no pain in the hip joint movements in the rest and exercise.

DISCUSSION

Osteoporosis is a common health problem in the elderly population. It is described as a low-density bone disease and these micro-architectural defects constitutes a risk of fracture of the bone (6).

In postmenopausal period, the protective effect of estrogen on bones diminishes with the decreasing amount of estrogen. Bisphosphonates improve bone destruction in short-term follow-up and are the first treatment choice to be considered in the current treatment of osteoporosis (7).

As well as apostmenopausal osteoporosis treatment, bisphosphonates are used as antiresorptive agents in patients with extensive bone metastases (8,9). In our patient, there was also a history of bone metastases related to breast cancer.
When the adverse effects of bisphosphonates are evaluated, in addition to gastrointestinal effects such as nausea and dyspepsia, muscle pain, osteonecrosis of the mandible and cardiac effects such as atrial fibrillation can be observed (10).

Apart from these effects, atypical femur fractures (proximal femur - femur shaft) due to long-term use of bisphosphonates have been reported in the current literature. These fractures are often seen as a single fracture, and more rarely, bilaterally. These cases are usually present with a fracture in the opposite extremity followed by a recurrent admission (2-5). In our case, bilateral fracture was present at the time of admission.
Alendronate, risedronate, ibandronate and zoledronate are the most common bisphosphonates (11). Alendronate is an FDA approved drug and has

been used in the treatment of osteoporosisfor a long time. Atypical fractures related to alendronate have been reported in the literature. In our case, the bisphosphonate that the patient used, was alendronate.

Recently, in a in-vitro study of atypical fractures related with alendronate use, researchers suggested that fractures associated with bisphosphates occured in the long term (6-10 years) use of these drugs (12). Based on the studies about this side-effect, cessation of alendronat etreatment after 5 years,is recommended (3). In our case, the patient used alendronate for 7 years.

Insufficiency fractureshave some characteristic features including cortical thickening in the fracture site, and a transverse fracture pattern (3).

In the treatment of bisphosphonate-related fractures, conservative approach doesn't provide a precisetreatment, and surgical fixation is recommended.

Prophylactic fixation is also recommended for atypical femoral insufficiency fracture. In a study on bisphosphates related fractures,the symptoms of the majority of patients followed conservatively, showed progression at a mean of 10 months and surgery was required (12,13).

In this case, we performed bilateral surgical treatment and determined that treatment was adequate in follow-up visits.

Atypical femoral fractures can be treated with plaque fixation or intramedullary nailing, but intramedullary nailing is technically challenging due to cortical thickening (4,14-16). We performed plaque fixation on one side and intramedullary proximal femoral nailing on the other. This treatment was well toleratedby the patient.

CONCLUSION

Bisphosphonate-related femoral insufficiency fractures with use are seen unilaterally but rarely bilaterally at different times as well as bilaterally at the same time.In patients presenting with pathologic fracture,even if there was a history of long-termbisphosphonateuse, other causes of pathological fracture must be excluded before a bisphosphonate-related fracture can be diagnosed.

REFERENCES

1- Tonino RP, Meunier PJ, Emkey R, Rodriguez-Portales JA, Menkes CJ, Wasnich RD, et al. Skeletal benefits of alendronate: 7-year treatment of postmenopausal osteoporotic women. J Clin Endocrinol Metab 2000;85:3109-15.

2- Çakmak S, Mahiroğulları M, Keklikçi K, Sarı E. Bilateral low-energy sequential femoral shaft fractures in patients on long-term bisphosphonate therapy. Acta Orthop Traumatol Turc 2013;47(3):162-72

3- Atik OŞ, Suluova F, Görmeli G, Yıldırım A. Insufficiency femoral fractures in patients undergoing prolonged alendronate therapy . Eklem Hastalık Cerrahisi. 2010;21(1):56-9

4- Ataoğlu B, Kaptan AY, Eren TK, Yapar AE. Atypical femoral fracture following zoledronic acid treatment. Eklem Hastalık Cerrahisi 2016;27(1):54-7.

5- Ustabaşıoğlu F, Çağlar NS; Akın T, Ayşar Ö, Aytekin E. Uzun Dönem Bifosfonat Kullanım Sonrası Bilateral Femur Diafiz Kırığı: Olgu Sunumu Türk Osteoporoz Dergisi 2012;18: 92-4.

6- Consensus development conference: diagnosis, prophylaxis, and treatment of osteoporosis. Am J Med 1993;94:646-50.

7- Fleisch H. Bisphosphonates: mechanisms of action. Endocr Rev 1998;19:80-100.

8- Yılmaz S, Atalay İB, Öztürk R, Güngör BŞ. The Evaluation of the Surgical and Functional Results of the Tumor Resection Prosthesis in Proximal Femur Malignant Bone Tumors. Acta Oncol Tur. 2019; 52(2): 250-5. DOI: 10.5505/aot.2019.62134

9- Toğral G, Arıkan M, Aktaş E, Öztürk R, Güven O, Eksioğlu F. Surgical management of bone metastases from urological malignancies: an analysis of 70 cases. Acta Orthop Traumatol Turc. 2015;49(6):634-40

10- Schubert M, Klatte I, Linek W, Müller B, Döring K, Eckelt U, et al. The Saxon bisphosphonate register - therapy and prevention of bisphosphonate-related osteonecrosis of the jaws. Oral Oncol 2012 ;48:349-54.

11- Boonen S, Laan RF, Barton IP, Watts NB. Effect of osteoporosis treatments on risk of non-vertebral fractures: review and meta-analysis of intention-to-treat studies. Osteoporos Int. 2005;16:1291–8.

12- Bala Y, Depalle B, Farlay D, Douillard T, Meille S, Follet H, et al. Bone micromechanical properties are compromised during long-term alendronate therapy independently of mineralization. J Bone Miner Res 2012;27:825-34.

13- Banffy MB, Vrahas MS, Ready JE, Abraham JA. Nonoperative versus prophylactic treatment of bisphosphonateassociated femoral stress fractures. Clin Orthop Relat Res 2011;469:2028-34.

14- Akdeniz H, Atalay İB, Kaya V, Özanlağan E, Toğral G. Surgery and Functional Results of Pathological Fractures of Long Bones of Lower Extremities in Malignant Tumors.

15- Ulucaköy C. Primer Benign Kemik Tümörleri Güncel Tanısal Yaklaşımlar Ve Tedavi Prensipleri. 1. baskı. Ortopedi ve Travmatoloji. Akademi Kitabevi, Ankara. 2013;9-13

16- Öztürk R, Arıkan ŞM. Comparison of locking plate and cephalomedullary nailing in unstable proximal femur fractures. J Clin Anal Med 2018;9(1): 18-22 DOI:10.4328/JCAM.5250