Cukurova Medical Journal
ÇUKUROVA ÜNİVERSİTESİ TIP FAKÜLTESİ

Cukurova Med J 2024;49(1):235-238
DOI: 10.17826/cumj. 1353368

LETTER TO THE EDITOR

Long-term bisphosphonates use and atypical femoral fracture

Uzun süreli bisfosfonat kullanımı ve atipik femur kırığı

Gaukhar Bakhtiyarova[1], Mehtap Tınazlı[1], Deniz Aydın[1]

[1]Near East University, Nicosia, Cyprus

To the Editor,

Osteoporosis is a systemic skeletal disorder characterized by low bone mass and microarchitectural deterioration, increasing the risk of fractures[1]. As the global incidence of osteoporosis rises, it has become a pressing concern for healthcare professionals. Long-term use of bisphosphonates (BPs), commonly prescribed for osteoporosis, has been associated with atypical femur fractures (AFFs). While AFFs are relatively rare, they are a serious concern due to their potential complications[2].

We present a 72-year-old female with a history of hypertension, hypothyroidism, and osteoporosis presented with right hip pain. She had been on alendronate therapy for 18 years and had a previous left femur fracture attributed to alendronate use. Bone Mineral Densitometry (BMD) scans have shown improvements in bone density over time. She was admitted to the Emergency Department with right hip pain. No acute pathological conditions were detected in the examination performed in the emergency department. After the patient was first examined by the emergency medicine specialist, a joint X-ray was taken in two directions, the knee was compared with the foot (bidirectional) and a femur X-ray was taken in two directions (right AP + lat). The patient was admitted to the orthopedic ward for surgery. As we mentioned before she had a history of known hypertension, hypothyroidism, and osteoporosis and she had no previous history of cancer, tobacco and alcohol use. Daily used medicines included; Atenolol 50mg tb 1x1, Valsartan 80mg tb 1x1, Levothyroxine 75mcg tb 1x1, Naproxen sodium 500mg fort tab, Esomeprazole 40mg tb 1x1, Calcimax-D3 1000mg/880IU tb and Alendronate for the previous 18 years. She had a left femur fracture (due to Alendronate use) and underwent surgery 6 years ago. During this time, the patient had Bone Mineral Densitometry (BMD) performed in 2014, 2017 and 2023y (Table 1).

Physical examination: height – 155cm, weight – 75kg. She was hemodynamically stable, with no fever. She had tenderness in the middle of the right thigh. Knee and hip movements were comfortable. Systemic examination was normal. Laboratory and radiological examinations: CBC – Hb 11.5 g/dL, Ca – 7.9mg/dL, vit d 25(OH) – 30.5ng/mL, TSH – 4.31 uIU/mL, fT3 -2.0 pg/mL, fT4 – 1.08ng/mL, creatinine – 0.95mg/dL, urea – 32 mg/dL, AST/ALT – 20/15U/L, ALP – 53U/L, Na- 145mmol/L, K - 4.5mmol/L. As can be seen in the preop X-ray images taken in the emergency room, there was no fracture in the femoral bone, but osteoporotic thickening and decreased bone density (marked with arrows) indicating a high risk of fracture IMN (intramedullary nailing) surgery was also performed for pain and as a prevantative action for possible femoral fracture by supporting the bone from the inside (fig 1,2).

Address for Correspondence: Gaukhar Bakhtiyarova, Department of İnternal Medicine, Near East University, School of Medicine, Nicosia, Cyprus E-mail: gypocrat@mail.ru
Received: 31.08.2023Accepted: 11.11.2023

Table 1. Progression of bone mineral density over time

T-score	2014	2017	2023
Height - 155cm, Weight - 75 kg			
Femur neck	-2.78	-2.96	Due to the presence of metals in the bilateral hips. the length of the femur could not be withdrawn.
Trochanter	-2.28	-2.43	
Wards Trigon	-3.37	-3.49	
AP Spine			
L2	-0.68	-0.78	-1.5
L3	-1.35	-1.50	- 0.9
L4	-0.81	-0.92	-0.5
L2-L4	-1.01	-1.14	-0.4

AP: anteroposterior ,L: lomber

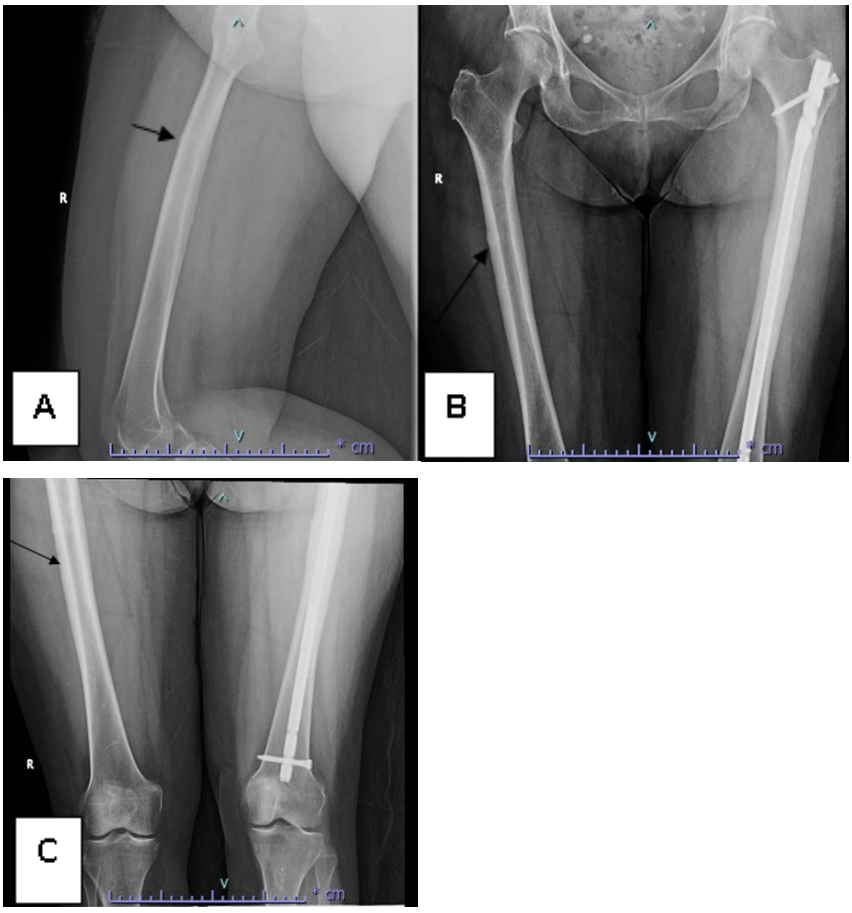

Figure 1 (A-C). Preop Osteoporotic thickening appearance of the right femur bone and areas with a high probability of fracture (marked with arrows) and Postop view of the Left femur (in the past).

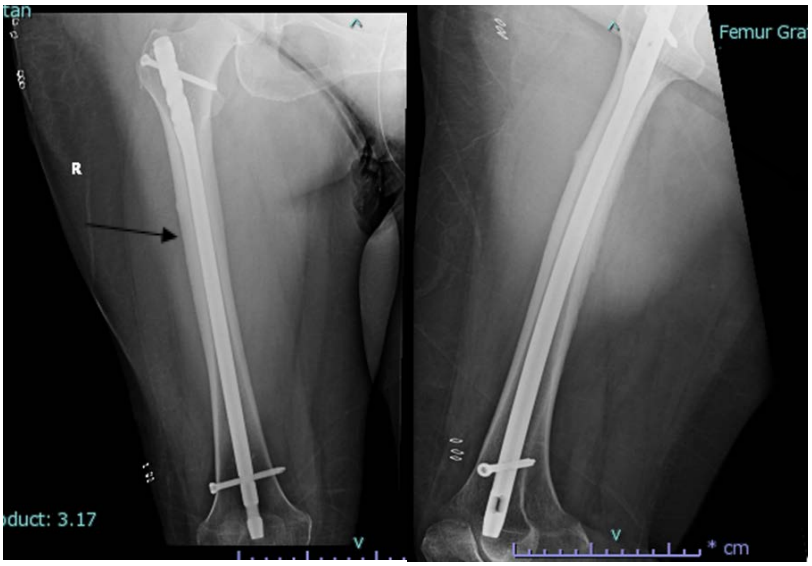

Figure 2. Right femoral bone: postop images. The region with a high risk of fracture is shown with arrows. Prevention of fracture by performing IMN.

Surgery was recommended to prevent pathological fracture, and the patient was taken into surgery after being evaluated preoperatively. The patient underwentclosed IMN surgery, which was completed successfully without any problems confirmed by performing scopy controls. In the postoperative period, the patient did not experience any problems. The patient was mobilized, discharged and followed in outpatients.

The patient came for control 2 months after the operation. Alendronate was stopped according to the control examination, and the laboratory results were as follows: CBC –Hb 13.9g/dL, Hct-46%, ALP 93 U/L, Calcium – 9.8mg/dL, Magnesium 1.9mg/dL and 25(Oh) vitamin D – 31,6 and BMD results. Denosumab treatment was started subcutaneous every 6 months, and BMD and blood tests were planned for every 6 months, with her outpatient follow-up.

The patient was hemodynamically stable and had tenderness in the right thigh[3]. Imaging revealed osteoporotic thickening, decreased bone density, and a high risk of fracture[4]. Surgical intervention was recommended, and the patient underwent IMN surgery to prevent fracture and support bone structure[5].

After surgery, the patient's condition improved and she was discharged outpatient. Follow-up included discontinuation of alendronate, initiation of Denosumab treatment[6] and planned regular BMD and blood tests[7].

AFFs are rare but serious complications associated with long-term BP use, often occurring in the subtrochanteric or femoral diaphysis regions. They differ from typical osteoporotic fractures in terms of clinical features and radiological characteristics[2]. Prolonged BP use can improve BMD but predispose patients to microdamage accumulation, increasing the risk of AFFs. Therefore, treatment strategies need to be carefully considered. Bisphosphonates should be discontinued in patients with AFFs[8].

Medical alternatives like Raloxifene or Teriparatide may be considered[9]. Surgical intervention with IMN is recommended[5]. Denosumab treatment and other treatments as like a monoclonal antibody, can improve BMD and is a viable option[6].

Atypical femur fractures are serious complications of long-term bisphosphonate use[3]. Early detection, discontinuation of bisphosphonates, and appropriate management, including surgical intervention and medical alternatives, are crucial[5]. Healthcareproviders should be vigilant in monitoring patients on long-

term bisphosphonate therapy to prevent AFFs and improve their quality of life[10].

Author Contributions: Concept/Design :GB, MT, DA;Data acquisition: GB, MT, DA;Data analysis and interpretation: GB, MT, DA;Drafting manuscript: GB, MT, DA;Critical revision of manuscript: GB, MT,Final approval and accountability: GB, MT, DA;Technical or material support: GB, MT, Supervision: GB, MT, DA;Securing funding (if available): n/a.
Ethical Approval: Ethics Committee approval is not required as it is a case report. Informed consent has been received from the patient.
Peer-review: Editorial review.
Conflict of Interest: Authors declared no conflict of interest.
Financial Disclosure: Authors declared no financial support

REFERENCES

1. Kanis JA, Cooper C, Rizzoli R, Reginster JY; Scientific Advisory Board of the European Society for Clinical and Economic Aspects of Osteoporosis (ESCEO) and the Committees of Scientific Advisors and National Societies of the International Osteoporosis Foundation (IOF). European guidance for the diagnosis and management of osteoporosis in postmenopausal women. Osteoporos Int. 2019;30:3-44.
2. Shane E, Burr D, Abrahamsen B, Adler RA, Brown TD, Cheung AM et al. Atypical subtrochanteric and diaphyseal femoral fractures: second report of a task force of the American Society for Bone and Mineral Research. J Bone Miner Res. 2014;29:1-23.
3. Meier RP, Perneger TV, Stern R, Rizzoli R, Peter RE. Increasing occurrence of atypical femoral fractures associated with bisphosphonate use. Arch Intern Med. 2012;172:930–6.
4. Kang JS, Won YY, Kim JO, Min BW, Lee KH, Park KK et al. Atypical femoral fractures after anti-osteoporotic medication: a Korean multicenter study. Int Orthop. 2014;38:1247-53.
5. Shane E, Burr D, Ebeling PR et al. Atypical subtrochanteric and diaphyseal femoral fractures: Report of a task force of the American Society for Bone and Mineral Research. J Bone Miner Res. 2010;25:2267-94.
6. Moen MD, Keam SJ. Denosumab: a review of its use in the treatment of postmenopausal osteoporosis. Drugs Aging. 2011;28:63-82.
7. Aspenberg P, Genant HK, Johansson T, Nino AJ, See K et al. Teriparatide for acceleration of fracture repair in humans: a prospective, randomized, double-blind study of 102 postmenopausal women with distal radial fractures. J Bone Mineral Res. 2010;25:404-14.
8. Sayed-Noor AS, Sjödén GO. Case reports: two femoral insufficiency fractures after long-term alendronate therapy. Clin Orthop Relat Res. 2009;467:1921-6.
9. Black DM, Geiger EJ, Eastell R et al. Atypical femur fracture risk versus fragility fracture prevention with bisphosphonates. N Engl J Med. 2020;383:743–53.
10. Hwang S, Seo M, Lim D, Choi MS, Park JW, Nam K. Bilateral atypical femoral fractures after bisphosphonate treatment for osteoporosis: a literature review. J Clin Med. 2023;12:1038.