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Case Report

Untreated Atypical Left Femoral Shaft Fracture: A Case Report of Its Complication

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Abstract

Background: Bisphosphonate therapy is used to manage osteoporosis and decrease the risk of vertebral and hip fractures. These drugs act by suppressing osteoclast activity by inducing the inhibition of bone resorption and increasing bone mineral density. It has been shown that long-term use of bisphosphonate is correlated to a higher incidence of atypical femoral fractures.

Case report: This is a case report of an 81-year-old female, on bisphosphonate therapy for 12 years and with chronic left thigh pain for two and a half years who developed an incomplete atypical left femur fracture. What's special about this case is that the fracture was ignored and then progressed after three months into a complete displaced spiral fracture that required surgical fixation.

Conclusion: The benefits of bisphosphonate treatment in preventing osteoporotic fractures outweigh the risk of the occurrence of these atypical fractures. Orthopedic surgeons as well as primary care physicians must keep atypical fractures in their differential diagnosis in patients presenting with prodromal symptoms and who are on long-term bisphosphonate therapy

Keywords: Atypical femoral fracture, bisphosphonate usage, complications, osteoporosis, elderly trauma

Introduction

Bisphosphonate has been widely used over the past 50 years in clinical practice and has shown effectiveness in the management of osteoporosis as well as in decreasing vertebral and hip risk fractures [1,2]. These drugs suppress osteoclast activity, inducing the inhibition of bone resorption and increasing bone mineral density [2,3].

Controversial studies have been emerging regarding the safety of bisphosphonate therapy and the possible side effects [4]. It has been shown that bisphosphonate therapy was associated with jaw osteonecrosis, atrial fibrillation, subtrochanteric fractures, and cancer of the esophagus [2] as well as atypical femur fractures [5–7].

Atypical femoral fractures are also called bisphosphonate-associated fractures or insufficiency fractures [1]. They are stress fractures that originate in the lateral part of the femoral shaft after minimal to no trauma [1]. Since 2006, several case reports of bisphosphonate-associated atypical femur fractures started to come into sight [8,9]. Several criteria both minor and major that help defines this type of fracture were established by the American Society for Bone and Mineral Research [7]. They are located distal to the lesser trochanter and proximal to the supracondylar flare, and four out of five major features should be present for diagnosis [7] (Table 1). Minor features such as the presence of prodromal symptoms are also related to atypical fractures of the femur but they are not necessary for the diagnosis [7]. When it comes to treatment, these fractures are usually managed surgically when complete using an intramedullary rod and medically when incomplete using anabolic medications such as teriparatide and by suspending bisphosphonates [1]. Sometimes surgical management can also be used as a prophylactic treatment in case of incomplete fracture [1].

In this case, the fracture was not treated and this led to a more complicated injury and management. To our knowledge, this is the first case reporting a complication of an untreated bisphosphonate-associated fracture.

Case Presentation

We present the case of an 81-year-old Middle-Eastern woman, known to have hypertension, hypothyroidism, and osteoporosis for which she took bisphosphonate therapy for a total of 12 years. The patient took risedronate 35mg once weekly for 10 years and then switched it to ibandronate 150 mg once monthly. The patient had undergone right total knee replacement for osteoarthritis four years ago.

She initially presented to our clinic for left thigh pain that has been present for two and a half years prior to the presentation. Left thigh pain was dull, non-radiating, atraumatic, and not alleviated or exacerbated by rest and activity respectively. Plain radiographs of the pelvis and left femur were done initially, not showing any bony abnormalities. This was followed with a Magnetic Resonance Imaging (MRI) of the left hip that showed focal thickening in the lateral cortex of the proximal shaft of the left femur 10 centimeter (cm) distal to the lesser trochanter with underlying focal intense bone marrow edema, along with surrounding periosteal thickening and mainly involving the lateral femoral cortex. The MRI findings were suggestive of a bisphosphonate-induced stress fracture of the left femur (Figure 1).

The patient was advised to stop the medication and to undergo a blood workup for any underlying secondary cause of her presentation, including metabolic and oncologic tests. She was also given the option of a conservative non-weight bearing protocol or to undergo a prophylactic surgical fixation of the left femur. The patient agreed on stopping bisphosphonate but did not comply with the non-weight-bearing regimen and refused to do blood workups, or undergo any surgical procedure due to financial and travel issues, and the patient was lost to follow-up.

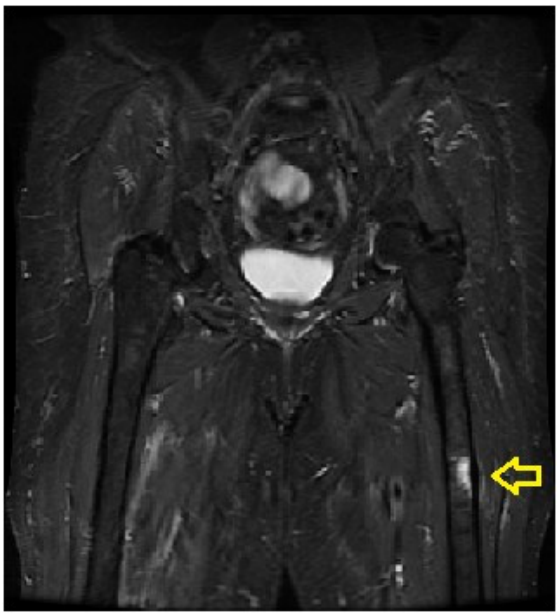

Figure 1: Coronal cut of a pelvis MRI (STIR sequence) showing at the level of the left femur, 10 cm distal to the lesser trochanter, focal thickening of the lateral cortex with underlying bone marrow edema (yellow arrow) with features and location suggestive of a fracture associated with bisphosphonate intake.

Three months later, the patient presented to the emergency department with severe pain in her left thigh after falling from a standing height. She reported hearing a snap in her left thigh while standing and immediately felt severe left thigh pain and fell on her left side.

An X-ray of both femurs was done in the emergency department and they showed a spiral complex fracture of the mid-femoral shaft of the left femur (Figure 2).

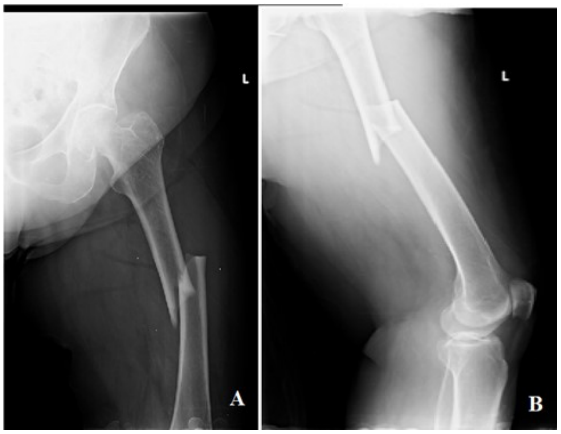

Figure 2: Plain radiographs of the left femur (A) Antero-posterior view showing a midshaft spiral fracture with displacement and (B) lateral view further showing the fracture pattern.

A pelvis Computed Tomography (CT) scan was also done to rule out a left femoral neck fracture and showed a spiral fracture of the left mid-femoral diaphysis with prominent posterior displacement of the distal fragment (Figure 3).

The patient underwent the next day surgical fixation of the fracture with intramedullary nailing with two distal and two proximal locking screws. During surgery, the fracture was found to be segmental with a butterfly fragment non-displaced distally, which wasn't apparent on imaging. The surgery was performed under spinal anesthesia, with no intra-operative complications.

The patient was discharged two days postoperatively in stable condition.

Serial weekly followed by monthly follow-ups were reassuring with patient muscle preserving physical therapy sessions compliance, and stable regular radiological follow-ups. She remained on a non-weight-bearing physical therapy regimen until fracture healing, which was three months post-operatively in her case, where clinical and radiologic signs of healing were evident (Figure 4).

The patient is currently on full-weight ambulation with significant improvement and returns to previous daily activities.

Discussion

The incidence of atypical fractures of the femur is around 5,9 per 100000 patient years [7]. The chronic use of bisphosphonate is correlated to a higher incidence of these fractures [5–7,10,11], especially after three to five years of use [11,12]. The patient had been taking bisphosphonate for 12 years when she started to have prodromal symptoms of left thigh pain around two and a half years prior to the fall. Bisphosphonate accumulates in the mineral phase of the long bone containing hydroxyapatite, promotes osteoclasts apoptosis, and results in the suppression of bone turnover [13,14]. As a result, the bone cannot repair microdamage after a strain and microcracks may start to appear leading to weakness in bone

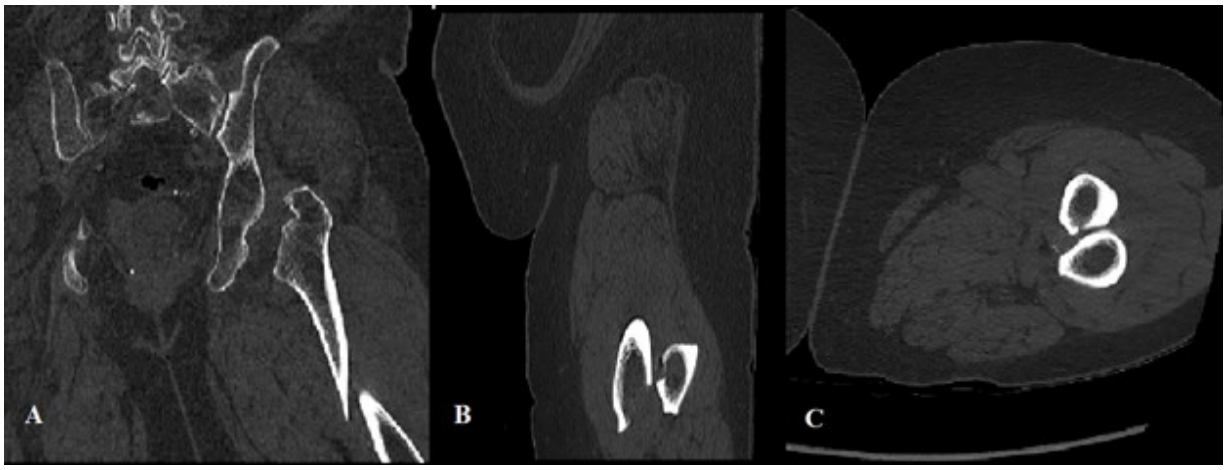

Figure 3: A pelvis CT scan in the (A) coronal, (B) sagittal and (C) axial views showing a spiral fracture of the left mid femoral diaphysis with prominent posterior displacement of the distal fragment.

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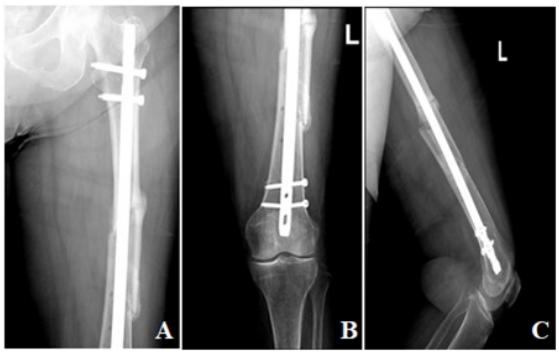

Figure 4: Radiographs of the left femur in the (A, B) Antero-posterior and (C) lateral views done 3 months post operatively showing the intramedullary nail in place stabilizing a healing fracture. A callus is noted with adequate alignment.

strength [10,14,15]. The prolonged usage of bisphosphonate can cause a higher suppression of bone turnover and thus an increase in skeletal fragility and fractures in patients may result [3,6,16].

The presence of prodromal pain and the radiographic imaging showing cortical thickening as seen in the above-described patient should prompt immediate medical attention as these are predictable findings of atypical femoral fractures [10]. Although the patient had the radiographic signs of a bisphosphonate-associated atypical femoral fracture prior to the fall, she ignored it and came back to the emergency department three months later showing a complete spiral fracture of the left mid-femoral diaphysis. When symptoms are present but plain radiographs are normal, further imaging techniques should be used, such as computed tomography or even magnetic resonance imaging because the latter is more specific and sensitive to marrow edema [17,18].

Treatment with bisphosphonate must be discontinued when the patients are diagnosed with an atypical femoral fracture [16,19]. The rate of atypical femur fractures decreases with time once bisphosphonate therapy is discontinued [5,11,20]. In the literature, it is recommended, after 3 to 5 years of treatment with bisphosphonates to have a drug holiday depending on the drug and this discontinuation should last 1 to 3 years while evaluating bone resorption markers [20].

Non-operative management such as using teriparatide, partial weight bearing, or prophylactic surgical fixation when the fracture is incomplete can be implemented but the latter is recommended especially in patients who are experiencing prodromal pain since the incomplete atypical fractures will naturally progress to complete fractures [19,21]. A quantitative bone health assessment along with Vitamin D, parathyroid functions, and calcium levels should also be monitored in these fractures [7,22–24]. When the fracture is complete, Intramedullary nailing is recommended when compared to other fixation techniques because it showed the lowest rate of failure [1]. Early surgical intervention prevents not only the progression to a complete femoral

shaft fracture but also post-operative delayed union, non-union, and implant failure [20]. Selective estrogen receptor modulators can be an alternative to bisphosphonate and patients should be also on calcium and vitamin D supplementation if it is already not in their treatment [19].

In this case report, the patient stopped bisphosphonate therapy but disregarded her incomplete fracture and refused prophylactic surgical intervention. The patient described initially presented with many of the major criteria for the diagnosis of a bisphosphonate-induced femoral fracture including fracture occurring without any trauma, transverse fracture with the fracture line emanating from the lateral cortex, incomplete involving only the lateral cortex with associated endosteal thickening at the lateral cortex. The incomplete fracture developed within three months duration into a complete, spiral-displaced fracture that required a more complicated surgical fixation with a higher risk of postoperative complications.

Moreover, since some atypical femoral fractures occur bilaterally [4], a plain radiograph of the contralateral femur should be ordered in patients with a complete fracture to be able to prevent a further fracture on the contralateral side [19,25].

Conclusion

Although cases of bisphosphonate-associated atypical femoral fractures have been emerging, there were no reports about the consequences of disregarding this injury. The dramatic benefits of bisphosphonate treatment in preventing osteoporotic fractures outweigh the risk of occurrence of these atypical fractures. However, orthopedic surgeons as well as primary care physicians must keep atypical fractures in their differential diagnosis in patients presenting with prodromal symptoms and who are on long-term bisphosphonate therapy. A proper early diagnosis of these atypical fractures is of utmost importance and a drug holiday alongside a prophylactic surgical fixation allows for the appropriate management and prevents many complications such as progression of an incomplete to a complete fracture, delayed healing, and non-union with surgical revision. Non-operative management should first consist of discontinuing bisphosphonate and considering calcium and vitamin D supplementation. Teriparatide therapy is a possible alternative to a bisphosphonate. Finally, imaging of the contralateral femur is also necessary since atypical femoral fractures are usually bilateral.

References

1. Tile L, Cheung AM. Atypical femur fractures: current understanding and approach to management. Ther Adv Musculoskelet Dis. 2020;12:1759720X20916983. PMID: 32913448. https://doi.org/10.1177/1759720x20916983

2. Reid IR. Bisphosphonates in the treatment of osteoporosis: a review of their contribution and controversies. Skeletal Radiol. 2011;40(9):1191-1196. PMID: 21847749.

3. Ma S, Goh EL, Jin A, et al. Long-term effects of bisphosphonate therapy: perforations, microcracks and mechanical properties. Sci Rep. 2017;7:43399. PMID: 28262693. https://doi.org/10.1038/srep4339

4. Maalouly J, Aouad D, Feghali M, Habib C, El-Rassi G. Bilateral Atypical Femoral Fractures after Prolonged Bisphosphonate Therapy: A Case Report and New Approach to the Management of Iatrogenic Fractures. Glob J Med Res. 2019;19(2):21-26. https://doi.org/10.34257/gjmrhvol19is2pg21

5. Adler RA, El-Hajj Fuleihan G, Bauer DC, et al. Managing Osteoporosis in Patients on Long-Term Bisphosphonate Treatment: Report of a Task Force of the American Society for Bone and Mineral Research [published correction appears in J Bone Miner Res. 2016 Oct;31(10):1910]. J Bone Miner Res. 2016;31(1):16-35. PMID: 26350171. https://doi.org/10.1002/jbmr.2708

6. 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 [published correction appears in J Bone Miner Res. 2011 Aug;26(8):1987]. J Bone Miner Res. 2010;25(11):2267-2294. PMID: 20842676. https://doi.org/10.1002/jbmr.253

7. Shane E, Burr D, Abrahamsen B, 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):1-23. PMID: 23712442. https://doi.org/10.1002/jbmr.1998

8. Lovy AJ, Patterson D, Skeeles L, et al. Atraumatic segmental atypical femur fracture secondary to bisphosphonate use: A case report. J Clin Orthop Trauma. 2017;8(Suppl 1):S67-S71. PMID: 28878545. https://doi.org/10.1016%2Fj.jcot.2017.03.005

9. Gopal GK, Tam KL, Krishnan SP, Maddern IL. Bisphosphonate-associated atypical subtrochanteric femur fractures in the older patient. N Z Med J. 2014;127(1389):81-85. PMID: 24548959

10. Bhadada SK, Sridhar S, Muthukrishnan J, et al. Predictors of atypical femoral fractures during long term bisphosphonate therapy: a case series & review of literature. Indian J Med Res. 2014;140(1):46-54. PMID: 25222777.

11. Black DM, Geiger EJ, Eastell R, et al. Atypical Femur Fracture Risk versus Fragility Fracture Prevention with Bisphosphonates. N Engl J Med. 2020;383(8):743-753. PMID: 32813950. https://doi.org/10.1056/nejmoa1916525

12. Khow KS, Shibu P, Yu SC, Chehade MJ, Visvanathan R. Epidemiology and Postoperative Outcomes of Atypical Femoral Fractures in Older Adults: A Systematic Review. J Nutr Health Aging. 2017;21(1):83-91. PMID: 27999854. https://doi.org/10.1007/s12603-015-0652-3

13. Odvina CV, Levy S, Rao S, Zerwekh JE, Rao DS. Unusual mid-shaft fractures during long-term bisphosphonate therapy. Clin Endocrinol (Oxf). 2010;72(2):161-168. PMID: 19302584. https://doi.org/10.1111/j.1365-2265.2009.03581.x

14. Phillips HK, Harrison SJ, Akrawi H, Sidhom SA. Retrospective review of patients with atypical bisphosphonate related proximal femoral fractures. Injury. 2017;48(6):1159-1164. PMID: 28410753. https://doi.org/10.1016/j.injury.2017.03.025

15. Visekruna M, Wilson D, McKiernan FE. Severely suppressed bone turnover and atypical skeletal fragility. J Clin Endocrinol Metab. 2008;93(8):2948-2952. https://doi.org/10.1210/jc.2007-2803

16. Odvina CV, Zerwekh JE, Rao DS, Maalouf N, Gottschalk FA, Pak CY. Severely suppressed bone turnover: a potential complication of alendronate therapy. J Clin Endocrinol Metab. 2005;90(3):1294-1301. PMID: 15598694. https://doi.org/10.1210/jc.2004-0952

17. Anagnostis P, Stevenson JC. Bisphosphonate drug holidays--when, why and for how long?. Climacteric. 2015;18 Suppl 2:32-38. PMID: 26507608. https://doi.org/10.3109/13697137.2015.1099092

18. Tins BJ, Garton M, Cassar-Pullicino VN, Tyrrell PN, Lalam R, Singh J. Stress fracture of the pelvis and lower limbs including atypical femoral fractures-a review. Insights Imaging. 2015;6(1):97-110. PMID: 25448537. https://doi.org/10.1007/s13244-014-0371-z

19. Black DM, Abrahamsen B, Bouxsein ML, Einhorn T, Napoli N. Atypical Femur Fractures: Review of Epidemiology, Relationship to Bisphosphonates, Prevention, and Clinical Management. Endocr Rev. 2019;40(2):333-368. PMID: 30169557. https://doi.org/10.1210/er.2018-00001

20. Koh A, Guerado E, Giannoudis PV.

Atypical femoral fractures related to bisphosphonate treatment: issues and controversies related to their surgical management. Bone Joint J. 2017;99-B(3):295-302. PMID: 28249967. https://doi.org/10.1302/0301-620x.99b3.bjj-2016-0276.r2

21. Ha YC, Cho MR, Park KH, Kim SY, Koo KH. Is surgery necessary for femoral insufficiency fractures after long-term bisphosphonate therapy?. Clin Orthop Relat Res. 2010;468(12):3393-3398. PMID: 20865463. https://doi.org/10.1007/s11999-010-1583-2

22. Tang BM, Eslick GD, Nowson C, Smith C, Bensoussan A. Use of calcium or calcium in combination with vitamin D supplementation to prevent fractures and bone loss in people aged 50 years and older: a meta-analysis [published correction appears in Lancet. 2012 Sep 1;380(9844):806]. Lancet. 2007;370(9588):657-666. PMID: 17720017. https://doi.org/10.1016/s0140-6736(07)61342-7

23. Bischoff-Ferrari HA, Willett WC, Wong JB, Giovannucci E, Dietrich T, Dawson-Hughes B. Fracture prevention with vitamin D supplementation: a meta-analysis of randomized controlled trials. JAMA. 2005;293(18):2257-2264. PMID: 15886381. https://doi.org/10.1001/jama.293.18.2257

24. Blood T, Feller RJ, Cohen E, Born CT, Hayda R. Atypical Fractures of the Femur: Evaluation and Treatment. JBJS Rev. 2015;3(3):e1. PMID: 27490887. https://doi.org/10.2106/jbjs.rvw.n.00062

25. Capeci CM, Tejwani NC. Bilateral low-energy simultaneous or sequential femoral fractures in patients on long-term alendronate therapy. J Bone Joint Surg Am. 2009;91(11):2556-2561. https://doi.org/10.2106/jbjs.h.01774