

Bisphosphonate-related atypical femoral fracture: a case report and literature review

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Abstract: Bisphosphonates (bisphosphonates, BPs) have been the gold standard for the treatment of osteoporosis (osteoporosis, O and P). However, long-term use of BPs is associated with a rare complication-atypical femoral fractures (atypical femoral fracture, AFF). The purpose of this article is to introduce a clinical case of incomplete atypical femoral fractures after long-term use of bisphosphonates for osteoporosis and review the relevant literature.

Keywords: bisphosphonates osteoporosis atypical femoral fractures

Since the early 1990s, BPs have been the mainstay of treatment for OP. BPs have been shown to be effective in preventing bone loss and reducing fractures in patients with osteoporosis^[1]. However, AFF may occur with long-term use of bisphosphonates. Although such complications are rare, but we still have to pay attention. In September 2021, we admitted a patient with incomplete AFF after long-term treatment with alendronate for OP. It is reported as follows.

1. Case reports

Patient Ixx, female, 66 years old, was admitted to hospital on September 22, 2021 mainly due to pain in her right thigh that worsened for one month and one day. The patient experienced pain in the upper right thigh when walking 1 month before admission, which can be relieved by rest. After treatment with Celebrex in the outer hospital, the patient improved. One day ago, he experienced increased pain in the right thigh when sitting and defecating, accompanied by limited movement of the right hip joint. He was hospitalized after outpatient treatment.

10 years' history of hypertension, with regular oral administration of Amlodipine Besylate Tablets, with stable blood pressure control; more than 10 years' history of hyperlipidemia, with regular oral administration of Atorvastatin Calcium Tablets; 10 years' history of osteoporosis, with long-term oral administration of Alendronate Sodium (Fosamax) 70mg/1 time/week (5 years since hospitalization). She had more than 20 years' history of lumbar disc herniation. Radiofrequency ablation of intervertebral disc was performed on December 23, 2019, and postoperative recovery was acceptable. No history of trauma.

Physical examination Junior College admission indicated painful claudication, no evident deformity of right lower extremity, tenderness in lateral side

of proximal right thigh, no palpable osseous sensation, limited movement of right hip joint due to pain, positive longitudinal percussion pain of right lower extremity, right “4” sign refused to be checked due to pain, negative for Thomas sign and Allis sign, normal blood supply and superficial sensation of right lower extremity.

radiographic examination: x-ray and ct indicated an incomplete subtrochanteric fracture of the right femur (**figure 1**).

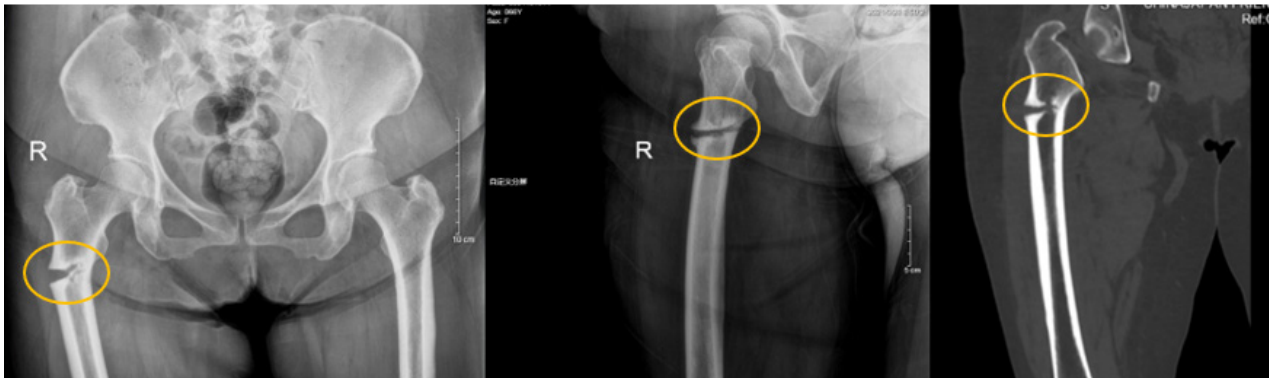


Figure 1. Preoperative X-ray CT showed incomplete subtrochanteric fracture of the right femur with outward angle

Primary Diagnosis: Incomplete atypical subtrochanteric fracture of right femur

Treatment: After admission, alendronate sodium was stopped, and after completing the relevant preoperative examination and preparation, the right femoral atypical fracture was treated with open reduction and intramedullary nail internal fixation + iliac bone graft under general anesthesia on September 29, 2021.

Operation: the patient supine position, installation of lower limb traction frame, limb rotation, adduction position. The surgical field is disinfected regular iodine and alcohol, and sterile towels, medium sheets and holes are spread. Operative area with sterile surgical film. First, take a straight incision about 4cm long at the proximal end of the right greater trochanter, cut through the skin, subcutaneous and deep fascia, blunt separation of gluteus medius, palpable the apex of the greater trochanter, and the needle was pierced into the medullary cavity, and the hardened band at the fracture end affected the insertion of the guide needle. Therefore, a 6cm long lateral incision was made at the fracture site to expose the fracture end, and the fracture end was seen as a transverse incomplete fracture, angularly outward, and severe bone sclerosis at the fracture end. Due to the obvious angular deformity of the fracture end, which affects the implantation of intramedullary nail, the medial cortical bone shall be truncated to change the incomplete fracture into a complete fracture, the broken end shall be reduced to correct the angular deformity, the guide pin shall be inserted at the top point of the large trochanter under the maintenance of reduction, the 9-11 reamed drill shall be repeatedly reamed to open up the hardened medullary cavity under direct vision, and then the fracture end of the fracture with the scraper, and the scraper,

and the scraper, and the hardened bone. The fluoroscopy shows that the fracture is opposite to the line. The proximal intramedullary nail (240mm long) was inserted by free hand. Adjust the position under X-ray, repeatedly drive in under fluoroscopy, so that the proximal nail is located in the middle and lower 1/3 of the femoral neck, the lateral position is located in the middle and rear, the proximal end of the medulla is opened, and the proximal anti-rotation blade is located. Guide the installation of the distal locking pin. The anterior superior iliac spine was exposed, the periosteum was cut and dissected, and the iliac bone was taken, and the bone was crushed into fine particles for bone grafting at the fracture end. Check the fracture end reduction and internal fixation position satisfaction, flushing, layer by layer suture of each incision, sterile dressing.

Postoperative treatment: Cefazolin sodium for prevention of infection, flurbiprofen axetil for analgesia, rivaroxaban for prevention of thrombosis, calcium carbonate, vitamin D and other drugs, regular wound dressing, guidance of limb functional exercise, early limb to avoid weight-bearing. Before discharge (1 week after operation), review X-ray (**Figure 2**), and outpatient review in the first month, third month, sixth month, and tenth month after discharge (**Figures 3, 4, 5, and 6**). Patients with postoperative 10 months fracture healed smoothly.



Figure 2. X-ray 1 week after operation



Figure 3. X-ray after 1 month



Figure 4. X-ray in March after operation



Figure 5. The bone connection of the fracture end can be seen on the X-ray 6 months after operation.



Figure 6. X-ray visible fracture fracture end osseous healing in 10 months after operation

2 Discussion and literature review

AFF is the 1 rare fracture that occurs in the subtrochanteric or diaphyseal region of the femur. This fracture was first reported by Odvina CV et al. ^[2] in 2005, arguing that it may be the 1 potential complication after long-term use of alendronate. Since then, more and more studies have shown that long-term use of BPs may lead to AFF. In 2010, the American Association for Bone and Mineral Research (American Society for Bone and Mineral Research, ASBMR) first developed diagnostic criteria for AFF based on its characteristics ^[3]. Subsequently,

ASBMR updated the diagnostic criteria for AFF again in the second report in 2014 ^[4]. (Table 1)

Table 1. Revised diagnostic criteria for AFF 2013 by the ASBMR Working Group

Standard
MUST STANDARDS
The fracture must be located in the area of the femoral shaft between the distal end of the small trochanter and the proximal end of the supracondylar
Main criteria (at least 4)
Fractures are low-energy injuries caused by non-traumatic or minor trauma (e. g., falls not higher than standing height)
The fracture line originates from the lateral cortex and is essentially transverse or short oblique
Incomplete fractures involve the lateral cortex, while complete fractures extend to the bilateral cortex and may be accompanied by medial protrusions
Non-comminuted or micro-comminuted fractures
Localized “beak” periosteum or endosteal thickening in the lateral cortex of the fracture site
Secondary criteria (not required, but may be relevant to the occurrence of AFF)
Extensive thickening of the cortical bone of the femoral shaft
Unilateral or bilateral prodromal symptoms, such as dull pain or soreness in the groin or thigh
Bilateral complete or incomplete femoral shaft fractures
Delayed healing of fractures

ASBMR: American Association for the Study of Bone and Mineral; AFF: Atypical Femoral Fractures

Femoral neck fractures, intertrochanteric fractures with subtrochanteric spiral extension, periprosthetic fractures, and pathological fractures associated with primary or metastatic bone tumors and other bone diseases (e. g., Paget’s disease, fibrous dysplasia) are excluded.

The incidence of AFF is very low, many times lower than that of hip, vertebral or other osteoporotic fractures. For example, the number of AFF is about 3 to 5 out of every 1000 hip fractures. There is consistent evidence from radiological studies that the incidence of AFF increases with the duration of BPs treatment, especially after 5 years ^[5]. According to a previous large US cohort study ^[6], the incidence of AFF in patients using BPs for less than two years was 1.8/100,000 per year, while the incidence in patients using BPs for 8 to 9.9 years was 113/100,000 per year.

Due to long-term use of BPs and other anti-resorptive agents, excessive inhibition of bone remodeling and natural repair ability decreased, leading to secondary calcification and micro-damage, weakened bone is the main feature of AFF ^[7, 8]. Neviaser AS and other ^[9] scholars believe that AFF and the associated prodromal pain are due to long-term administration of BPs excessively inhibiting bone transformation, resulting in abnormal bone remodeling and eventually stress fracture. In addition, the mechanical theory is supported by several scientific studies ^[10- 12] that these atypical fractures are associated with an abnormal distribution of stresses in the lateral cortical region of the femur. Severyns M ^[13], through biomechanical studies, believes that changes in the mechanical axis of the lower limb will affect the stress distribution at the femoral shaft, thereby increasing the risk of AFF. Axial deformation of inversion is particularly prone to AFF.

Regarding the treatment of AFF, all patients diagnosed with AFF should

stop using BPS and start taking calcium and vitamin D supplements []. It has been observed that the risk of AFF decreases by 70% per year [] once the use of BPS is stopped.

As with complete AFF, the standard surgical treatment for incomplete AFF is intramedullary nailing ^[16]. However, in some cases, the anterior femoral arch is so severe that intramedullary nail insertion is difficult. In this case, it can be treated by intramedullary nail combined with osteotomy. Sato S ^[17] and others have achieved satisfactory results in the treatment of severe arcuate incomplete AFF through intramedullary nail and osteotomy. Hopf JC et al. ^[18] suggest that AFF can usually be treated with traditional intramedullary nails, but must be used according to the morphology of the femur. Umut Canbek and others ^[19] in the treatment of atypical femoral fractures with intramedullary nailing, it was found that patients treated with open surgery had similar healing and complication rates as those treated with closed surgery, but the radiographic healing time is shorter, because open surgery can handle the sclerotic bone at the broken end of the fracture well. It is conducive to fracture healing.

In this case, open surgery was used to clean up the hardened bone at the broken end of the fracture, open up the medullary cavity, turn the incomplete fracture into a complete fracture to correct the angular deformity, reset the broken end of the fracture, fix it with intramedullary nail, and implant bone from the iliac bone to promote fracture healing. The broken end of the bone healed smoothly in October after the operation.

AFF fracture healing is more complex than typical diaphyseal or subtrochanteric fractures ^[20, 21]. The most commonly reported complications in patients with AFF are nonunion, delayed healing, and endophytic ^[22]. Therefore, in addition to surgical treatment, the key to the treatment of AFF is to restore bone turnover. Giving teriparatide (teriparatide, TPTD), a drug that promotes osteoblast proliferation and bone metabolism, may contribute to fracture healing ^[23] in patients with AFF. 2023 1 Meta-analysis ^[24] Conclusion AFF after TPTD treatment is beneficial to fracture healing, reduce delayed healing and non-union rate, shorten fracture healing time. From the European Association of Calcific Organizations ^[25] conclusion, TPTD can be used as an adjunct to promote fracture healing, can also be used as a treatment for AFF as the 1 option, and recommended for AFF patients for a period of two years of TPTD treatment.

3. Summary

AFF is the 1 complication of OP patients receiving BPS treatment for a long time. Its incidence rate is low. It is diagnosed according to the updated diagnostic criteria of ASBMR in 2014. At present, the more recognized treatment methods are: stopping bisphosphonate drug treatment, performing surgical fixation (mostly intramedullary nail) according to fracture type and femoral morphology, supplementing sufficient calcium and vitamin D, and recommending two-year

teriparatide treatment.

References

- [1] Khosla S, Bilezikian JP, Dempster DW, et al. Benefits and risks of bisphosphonate therapy for osteoporosis [J]. *J Clin Endocrinol Metab*, 2012, 97 (7): 2272-2282.
- [2] Odvina CV, Zerwekh JE, Rao DS, et al. Severely suppressed bone turnover: a potential complication of alendronate therapy[J]. *J Clin Endocrinol Metab*, 2005, 90(3):1294-1301.
- [3] 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]. *J Bone Miner Res.*, 2010, 25(11): 2267-2294.
- [4] 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]. *J Bone Miner Res.*, 2014, 29(1):1-23.
- [5] Black DM, Abrahamsen B, Bouxsein ML, et al. Atypical Femur Fractures: Review of Epidemiology, Relationship to Bisphosphonates, Prevention, and Clinical Management[J]. *Endocr Rev*, 2019, 40(2):333-368.
- [6] Dell RM, Adams AL, Greene DF, et al. Incidence of atypical nontraumatic diaphyseal fractures of the femur[J]. *J Bone Miner Res.*, 2012, 27(12):2544-2550.
- [7] Lim SJ, Yeo I, Yoon PW, et al. Incidence, risk factors, and fracture healing of atypical femoral fractures: a multicenter case-control study[J]. *Osteoporos Int*, 2018, 29(11):2427-2435.
- [8] Kang JS, Won YY, Kim JO, et al. Atypical femoral fractures after anti-osteoporotic medication: a Korean multicenter study[J]. *Int Orthop*, 2014, 38(6):1247-1253.
- [9] Neviaser AS, Lane JM, Lenart BA, et al. Low-energy femoral shaft fractures associated with alendronate use[J]. *J Orthop Trauma*, 2008, 22(5):346-350.
- [10] Oh Y, Wakabayashi Y, Kurosa Y, et al. Potential pathogenic mechanism for stress fractures of the bowed femoral shaft in the elderly: Mechanical analysis by the CT-based finite element method[J]. *Injury*, 2014, 45(11):1764-1771.
- [11] Haider IT, Schneider P, Michalski A, et al. Influence of geometry on proximal femoral shaft strains: Implications for atypical femoral fracture[J]. *Bone*, 2018, 110:295-303.
- [12] Hagen JE, Miller AN, Ott SM, et al. Association of atypical femoral fractures with bisphosphonate use by patients with varus hip geometry[J]. *J Bone Joint Surg Am*, 2014, 96(22):1905-1909.
- [13] Severyns M, Belaid D, Aubert K, et al. Biomechanical analysis of the correlation between mid-shaft atypical femoral fracture (AFF) and axial varus deformation[J]. *J Orthop Surg Res*, 2022, 17(1):165.
- [14] Toro G, Ojeda-Thies C, Calabro G, et al. Management of atypical femoral fracture: a scoping review and comprehensive algorithm [J]. *MBC Musculoskelet Disord*. 2016, 17:227.
- [15] Schilcher J, Koeppen V, Aspenberg P, et al. Risk of atypical femoral fracture during and after bisphosphonate use[J]. *Acta Orthop*. 2015, 86(1):100-107.
- [16] Schneider PS, Wall M, Brown JP, et al. Atypical femur fractures: a survey of current practices in orthopedic surgery[J]. *Osteoporos Int*, 2017, 28:3271-3276.
- [17] Sato S, Kitamura D, Murase S, et al. Incomplete Atypical Femoral Fracture With Severe Bowing Treated by Intramedullary Nail and Corrective Osteotomy[J]. *Cureus*, 2023, 15(4): e38175.
- [18] Hopf JC, Rommens PM, Drees P, et al. Atypical femoral fracture : Pitfalls in surgical treatment[J]. *Unfallchirurgie (Heidelb)*, 2023, 126(1):72-76.
- [19] Canbek U, Akgun U, Aydogan NH. Efficacy of bone-end intervention on fracture healing in bisphosphonate-related atypical femoral fractures[J]. *Orthop Traumatol Surg Res*. 2020, 106(1):77-83.
- [20] Giusti A, Hamdy NA, Papapoulos SE. Atypical fractures of the femur and bisphosphonate therapy: A systematic review of case/case series studies[J]. *Bone*, 2010, 47(2):169-180.
- [21] 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]. *J Bone Miner Res*, 2014, 29(1):1-23.

- [22] Grasko JM, Herrmann RP, Vasikaran SD. Recurrent low-energy femoral shaft fractures and osteonecrosis of the jaw in a case of multiple myeloma treated with bisphosphonates[J]. J Oral Maxillofac Surg, 2009,67 (3) : 645-649.
- [23] Oh YK, Moon NH, Shin WC. Management of Osteoporosis Medication after Osteoporotic Fracture[J]. Hip Pelvis ,2022,34(4):191-202.
- [24] Byun SE, Lee KJ, Shin WC,et al. The effect of teriparatide on fracture healing after atypical femoral fracture: A systematic review and meta-analysis[J]. Osteoporos Int, 2023 Aug,34(8):1323-1334.
- [25] Van de Laarschot DM, McKenna MJ, Abrahamsen B, et al. Medical Management of Patients After Atypical Femur Fractures: a Systematic Review and Recommendations From the European Calcified Tissue Society[J]. J Clin Endocrinol Metab ,2020,105(5):1682-1699.