

**Report**

# Atypical Femur Fractures: A Case Report and Literature Review

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**Abstract:** With the aging of the global population, osteoporosis has become a widespread phenomenon in the society. With the rapid increase of the number of osteoporotic fractures, a huge social and economic pressure has been caused. At the same time, it has attracted extensive attention. Bisphosphonates (BPs) can effectively prevent bone loss, improve bone density, and effectively reduce the incidence of osteoporotic fracture in the vertebral body and hip, which is the first choice for the treatment of osteoporosis. However, after tens of thousands of people take bisphosphonates for a long time, there are more and more reports of atypical femoral fractures (AFFs) caused by bisphosphonates, which cause the concerns of patients and doctors. The long-term use of bisphosphonates can promote the apoptosis of osteoclasts, inhibit the osteoclast's dissolution and absorption of bone trabecula, then reduce bone turnover, inhibit bone remodeling, lead to the accumulation of bone micro damage, and finally lead to fracture AFFs. We present an 83 year old woman who has been taking bisphosphonates for more than 10 years. The images indicate that there is nonunion in the middle and upper segments of both femurs. She was diagnosed as bilateral AFFs and was treated with plate and screw internal fixation for the left femur fracture and temporary conservative treatment for the right femur fracture. She was treated with anti infection, analgesia and circulation improvement after operation and the symptoms were relieved obviously and the effect was satisfactory. The case was reported as follows and reviews the related literature.

**Keywords:** Atypical Femoral Fractures, Bisphosphonates, Osteoporosis

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## 1. Introduction

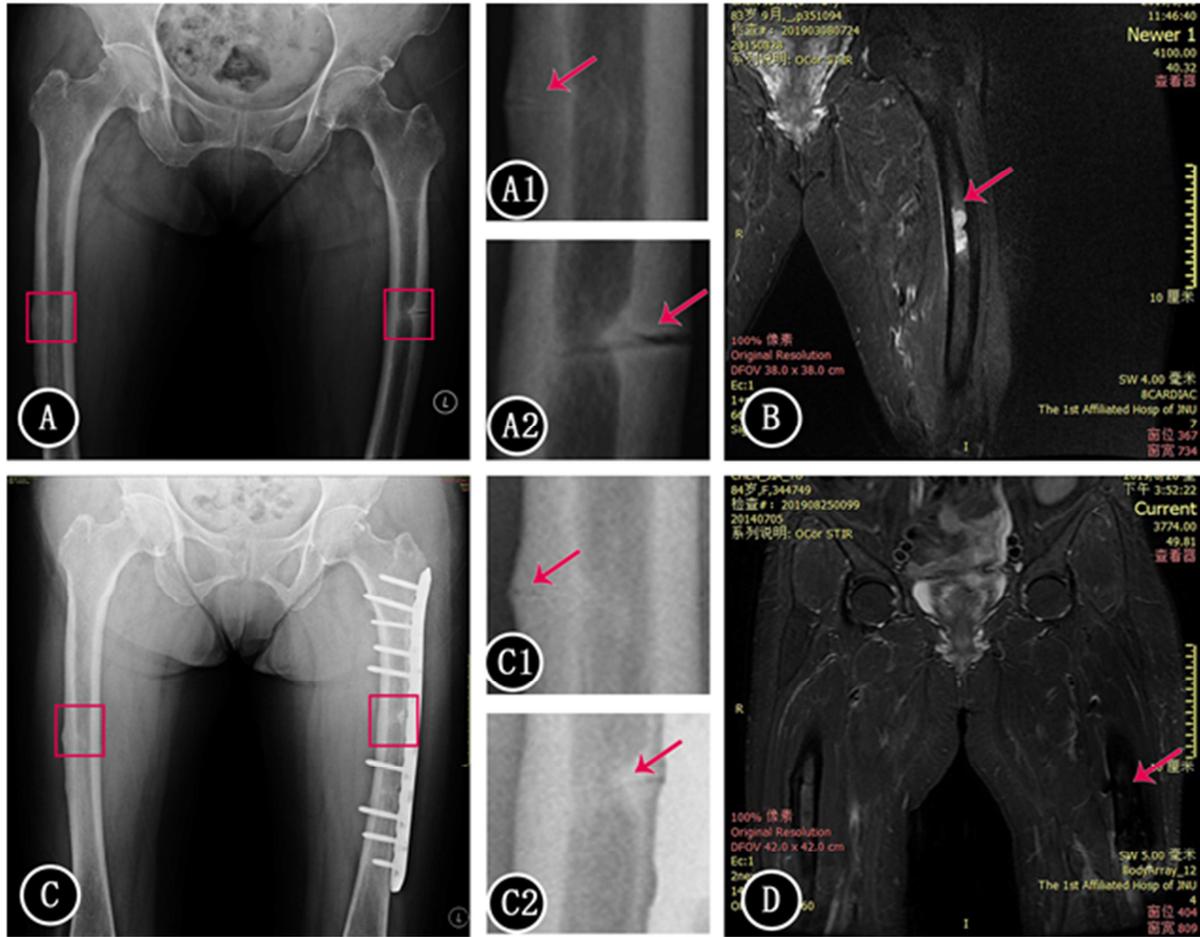
Since 2005, there have been articles reporting the cases of unusual brittle fracture in subtrochanteric and femoral shaft area of patients with osteoporosis after taking bisphosphonates for a long time, which has attracted great attention in the industry [1-3]. The American Society for bone and Mineral Research immediately established a special research group to study the pathogenesis, risk factors, epidemiology and how to manage such diseases [4-6]. This kind of fracture was named AFFs (atypical femur fractures) in 2010. In the second report of the American Society of bone and Mineral Research Group in 2014, it was defined as non-invasive or low traumatic fracture from the distal end of trochanter to the proximal end of condyle of femur. The diagnostic criteria were as follows: at least 4 of the following

main characteristics were met: (1) no trauma or slight trauma caused fracture, such as standing position or more Low fall; (2) the fracture line originates from the lateral cortex, and its direction is basically transverse, which may become inclined when passing through the femoral shaft; (3) complete fracture, the fracture line passes through the bilateral cortex, and may appear the "peak" of the medial cortex; incomplete fracture only involves the lateral cortex; (4) non comminuted or slightly comminuted fracture; (5) thickening of the lateral cortex at the fracture site, with periosteal reaction. Secondary features (not necessary): extensive thickening of the bone cortex of the femoral shaft; unilateral or bilateral prodromal symptoms, such as tonic or sore pain in the groin or thigh; bilateral incomplete or complete fracture of the femoral shaft; delayed union of the fracture [7-9]. A typical case of atypical femur fractures was reported as follows.

## 2. Case Report

The female patient, 83 years old, had pain in the left thigh without obvious inducement one month ago, increased significantly when standing, walking and turning over activities, and could be relieved by lying down rest. The

patient had bone mineral density examination more than 10 years ago, and was diagnosed with "osteoporosis". She took 70mg once a week alendronate tablets orally. She took the medicine regularly for more than 10 years, without special discomfort, and did not have regular bone mineral density examination.



**Figure 1.** Treatment and follow-up of the patient. A and B, preoperative X-ray films showed the local discontinuity of bone cortex could be seen in the middle and upper segments of both femurs, and the two transverse transparent shadows could be seen, with no displacement of the broken end (Red box and red arrow) and MRI showed that the high signal intensity was not uniform on Stir weighted MRI (red arrow); C and D, 6 months postoperatively, X-ray of femur showed that the fracture healed with callus formation and the high signal at fracture site has disappeared on MRI.

After the patient was admitted to the hospital, the relevant examination was completed. X-ray showed that the local discontinuity of bone cortex could be seen in the middle and upper segments of both femurs, and the two transverse transparent shadows could be seen, with no displacement of the broken end. MRI showed that the low signal intensity was not uniform on T1 weighted MRI. According to the patient's history, symptoms, physical signs and auxiliary examination, it was diagnosed as bilateral atypical femoral fractures (AFFs). Then, the patient was asked to stop taking alendronate tablets, and to take calcium tablets and vitamin D orally instead. Open reduction, plate and screw internal fixation were performed for the left middle and upper femur fracture. During the operation, there was a transverse fracture line on the lateral side of the middle and upper part of the left femur. The circular fracture line had exceeded the central axis of the femoral shaft from the outside to the inside until the medullary cavity. The

fracture width was about 1.5mm. After removing the surrounding soft tissue, select the appropriate length of steel plate for screw fixation. Although there was nonunion in the middle and upper right femur of the patient, X-ray showed that the fracture line did not penetrate the lateral bone cortex, and there was no pain in the right thigh, so we temporarily gave conservative treatment (Figure 1 A and B). After the operation, the incision healed well (Figure 1 C and D), the pain symptoms were alleviated obviously, the patients were mainly asked to lie in bed, and the weight-bearing of both legs was avoided. After incision healing and suture removal, the patient is advised to use a walker to limit weight-bearing walking and use Teriparatide. After discharge, the patient insists on using tripartide injection, 2.6  $\mu$  l IM once a day. Half a year after the operation, the reexamination showed that the bilateral fractures had basically healed.

### 3. Discussion

According to diagnostic criteria: our case almost meets all the main characteristics, no history of trauma, fracture line from lateral cortex horizontally, incomplete fracture, only through the lateral cortex, located under the femoral trochanter, no comminution, periosteal reaction in the lateral cortex, secondary characteristics are extensive thickening of the bone cortex, unilateral prodromal pain, bilateral nonunion. Based on our case history of long-term use of bisphosphonates combined with symptoms and auxiliary examination, we diagnosed as AFFs.

At present, the pathogenesis of AFFs has not been fully elucidated, but most scholars believe that it is closely related to the inhibition of bone turnover and the weakening of bone remodeling function caused by long-term use of bisphosphonates [9]. Bone remodeling is a dynamic process of bone absorption and formation. BPs can inhibit osteoclast mediated bone absorption, reduce the situation of bone loss, inhibit the further decline of bone microstructure and decrease the risk of fracture. However, with the long-term use of BPs, bone formation will decrease with the inhibition of bone absorption, and bone remodeling will be seriously inhibited, which may be indirectly caused by the decrease of NF KB ligand receptor activator [10-12].

AFFs has the characteristics of stress fracture: the local cortex of the fracture site is thickened. ASBMR believes that it is a special stress fracture or incomplete fracture that develops continuously [11, 13]. The healing of the stress fracture is achieved through the targeted bone remodeling of the injured site through the apoptosis mechanism of bone cells. In this process, through the increase of NF KB ligand receptor activator, a repair signal is sent to increase the formation of osteoblasts [14, 15]. Osteoclasts are responsible for the reabsorption of fracture to remove the damage, and then through the formation of osteoblasts to replace the absorption of bone Complete the fracture repair. Under the premise that the long-term bone remodeling function is severely inhibited, the fatigue damage of bone initially appears in the form of microcracks in the cortex of bone, which can not be repaired in time. As time goes on, microcracks continue to gather and coagulate, and when they accumulate to the critical size, they will appear clinical fractures and fractures [10, 16, 17]. At the same time, the half-life of bisphosphonates in vivo is 10 years or longer. Long-term use of bisphosphonates seriously inhibits bone turnover, resulting in delayed or non healing of AFFs. According to the statistical analysis of the healing time of 22 AFFs patients by Cemil kayali, the average healing time was 7.4 months, and 5 patients had nonunion [16]. S. J. Lim counted 225 patients with AFFs, and the rate of delayed or nonunion was 18.2% [18].

At present, there is a consensus on the treatment of incomplete or complete AFFs that the strong anti absorption drugs should be stopped and calcium and vitamin D should be supplemented properly. It is reported that the risk of AFFs can be reduced by 70% when BPs is stopped for one year [16]. ASBMR recommendation: for incomplete fractures with

prodromal pain, it is recommended to use reconstruction nail for fixation. If there is only slight pain or no prodromal pain, it is feasible to carry out experimental conservative treatment (using crutches and walking aids to limit the load), limit the load, avoid strenuous activities, and review MRI regularly until no bone edema or increased activity is found on bone scanning. After 2-3 months, if there is no significant improvement in symptoms or no significant reduction in MRI edema, it is strongly recommended to carry out surgical treatment. At present, the conservative treatment of AFFs is still controversial, and the incidence of re fracture is high. Banffy reported in the literature that six patients had undergone conservative treatment, 5 of which developed into complete, and Cemil kayali reported that four patients developed into complete AFFs after conservative treatment [2, 16, 18].

At present, fixation technology of incomplete or complete AFFs can be roughly divided into intramedullary device (intramedullary nail, intramedullary needle) and extramedullary device (plate screw). Most surgeons tend to use intramedullary nail device. Because of its special biomechanical characteristics, it can span the whole length of the femur longitudinally, protect the whole femur, bear the gravity, and theoretically reduce the risk of fracture in the future [2]. The special feature of our case is that the patient has nonunion on on both sides and prodromal pain on the left side, which is a typical incomplete AFFs. We chose plate and screw internal fixation; there is no prodromal pain and other clinical symptoms on the right side, but X-ray indicates extensive thickening of the lateral cortex, local stress fracture line and periosteal reaction, so we chose experimental conservative treatment for the right side, active after operation The results showed that the fracture line on the left side was basically healed, and the pain symptoms disappeared completely. The fracture line on the right side was also basically healed, and the bilateral recovery was good.

There are many references that the use of special cases of pethidine can promote the healing of AFFs, but there are also many references that teriparatide has no effect on AFFs, and AFFs is not an indication of teriparatide [2]. The function of teriparatide stimulating bone formation and bone resorption may promote the healing of some AFFs patients, but there is no theoretical support at present. The difference of its clinical effect needs further study. In this case, the patient insisted on the use of teriparatide after operation, and the fracture healed well 5 months after operation. It can not be excluded that teriparatide played a positive role in the healing process of this patient.

### 4. Conclusion

AFFs is a rare disease with a very low incidence, which is closely related to long-term use of bisphosphonates. Short-term use of bisphosphonates can effectively prevent osteoporotic fractures. Short-term use of bisphosphonates yield is far greater than any risk. For patients with long-term use of bisphosphonates, we should be alert to the occurrence

of AFFs, inform patients of relevant complications before use, strengthen patients' awareness of prodromal pain, take bilateral X-ray examination in time for patients suspected of AFFs, and out of use bisphosphonates in time. The effective prevention and management of AFFs need further observation and research.

## Conflict of Interests

All the authors do not have any possible conflicts of interest.

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