

BILATERAL SIMULTANEOUS ATYPICAL FEMORAL PERIPROSTHETIC FRACTURE. A CASE REPORT AND REVIEW OF THE LITERATURE

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ABSTRACT

Atypical femoral fracture is one of the many complications after the long-term use of bisphosphonates. Long-term use of bisphosphonates (BPs) has been associated with a specific type of tensile-side femoral stress fracture known as Atypical Femoral Fracture (AFF). The American Society for Bone and Mineral Research has officially excluded periprosthetic femoral fractures (PFFs) from the definition of atypical femoral fractures (AFFs). However, several case reports correlate prolonged BP use with the occurrence of a type of PFF with an atypical pattern (atypical PFF, APFF). The aim of the present study is to report a case of bilateral APFF after prolonged BP use. A 77-year-old female with a history of long-term bisphosphonate use (over 15 years) and a total bilateral hip replacement 7 and 8 years ago, after minimal domestic trauma, reported a bilateral periprosthetic femoral fracture. Investigative results (Rx, histological examination biopsy) allowed us to classify these fractures as atypical. This case is consistent with the definition of bisphosphonate-related atypical femoral fracture around a well-fixed, total hip replacement. These findings challenge the current definition of atypical femoral fractures that excludes peri-prosthetic fractures.

KEYWORDS: *atypical femoral fracture, bisphosphonate, osteoporosis, bone, bone remodeling*

INTRODUCTION

Worldwide, osteoporosis causes more than 8.9 million fractures annually, resulting in an osteoporosis fracture every 3 seconds (1). Across Europe in 2019 (European Union, plus Switzerland & UK), 32 million individuals aged >50 are estimated to have osteoporosis, equivalent to 5.6% of the total European population aged >50, or approximately 25.5 million women (22.1% of women aged >50) and 6.5 million men (6.6% of men aged >50) (2).

Bisphosphonates are widely used in the treatment of osteoporosis to reduce fractures because they affect bone metabolism (3) and can cause necrosis of the jaws (4). Because of their long retention time in bone and uncommon side

effects, questions have been raised about the optimal duration of therapy. Prolonged bisphosphonate use has been related to the suppressing bone turnover, minimizing bone remodeling, and reducing bone healing capacity. This process will probably result in a frozen bone that is unable to repair the microcracks that may arise in the femoral shaft and could evolve into both incomplete and complete AFF. In fact, several retrospective studies have also suggested an association between bisphosphonate use and atypical femur fractures, although the results from larger observational studies are discordant (5, 6).

In a 2010 report from an international task force appointed by the American Society of Bone and Mineral Research to review this issue, major and minor criteria for atypical fractures were defined but did not include atypical periprosthetic femoral fractures (APFFs) (7).

Atypical femoral fractures usually occur at the subtrochanteric region or proximal to the mid-shaft of the femur because of high regional tensile stress. They are characterized by uni-cortical thickening (especially lateral) and transverse or short-oblique fracture patterns.

Because of the rarity of cases and limited awareness of this condition, to date, there are far fewer APFF studies than those on AFFs and typical periprosthetic femoral fractures (PFFs)

CASE REPORT

In November 2022, a 77-year-old woman presented with severe bilateral pain in both legs after minor trauma at home. She had been in treatment for over 15 years with bisphosphonates. In 2015 and 2016, she had undergone sequential bilateral Total Hip Arthroplasty for advanced osteoarthritis. Radiographs showed a Vancouver type-B1 periprosthetic fracture of both femurs (Fig. 1).

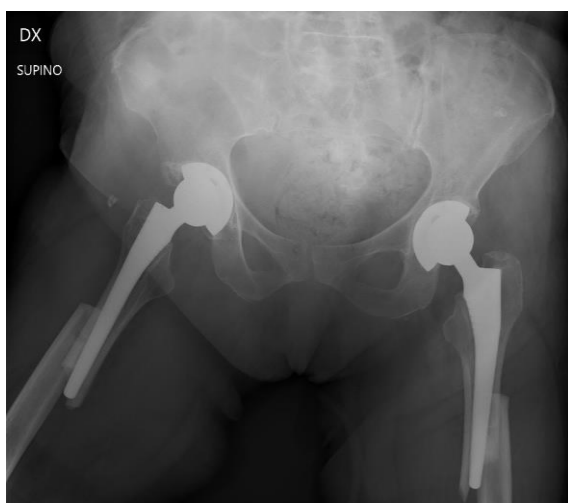


Fig. 1. Vancouver type-B1 periprosthetic fracture of both femurs.

A thickened femoral cortex or a ‘beak sign’ was noted bilaterally. The fractures were configured as an ‘inverted square root’, and the femoral stems were well fixed. Preoperatively, a laboratory workup was performed, including calcium, 25-OH vitamin D, bone alkaline phosphatase, and parathyroid hormone (PTH) levels.

Our patient underwent revision surgery involving the replacement of the femoral component with a revision of the long stem through an extended trochanteric osteotomy approach. At first, the procedure was performed only on one femur, after two days, the other side was operated on to allow for some recovery time between the two surgeries. A lateral approach to the hip, following the previous incision, was extended down to the knee. During the surgery, we could appreciate thickening of the cortex (Fig. 2).



Fig. 2. *Thickening of the femoral cortex.*

The fracture site was debrided, and a histological sample was taken. A revised long stem was then implanted (Fig. 3).



Fig. 3. *Postoperative X-ray.*

Intraoperative specimens were fixed in 4% formaldehyde, decalcified for 48 hours, and paraffin embedded. Tissue blocks were cut in 4 μ m thick sections and stained with hematoxylin-eosin. The sample collected showed tissue characterized by marginal areas of necrotic bone with irregular borders, surrounded by active osteoclasts and lamellar bone with empty lacunae. The intertrabecular spaces were focally fibrotic, with scattered multinucleated osteoclast-like cells. In proximity to the rim of the fracture, some areas of bone remodeling were evident (Fig. 4).

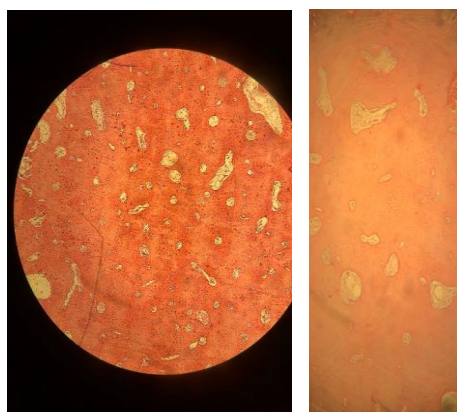


Fig. 4. *Scattered multinucleated osteoclast-like cells.*

Postoperatively, the patient maintained partial weight ambulation for 8 weeks and then advanced to full weight-bearing. In this case, calcium or vitamin D supplementation was not required. She regained the ability to walk without pain and any gait aid.



Fig. 5. Post-operative X-rays (right and left).

DISCUSSION

Epidemiology and diagnosis

As mentioned above, PFF is currently excluded from the definition of AFF based on the ASBMR task force reports (7, 8). According to the literature, there is a significant correlation between the use of bisphosphonates and atypical femoral fracture, particularly when the therapy is prolonged (> 5 years) (9, 10). These fractures currently represent a rare event; it is plausible that with the increase in annual performed THAs and the expanding indication for bisphosphonates use, the number of PFFs and, subsequently, APFFs could rise. It is crucial to diagnose an APFF, given that evidence supports a different type of approach and treatment for these patients.

In order to do that, an adequate collection of anamnestic data, with special attention to prior and current medications, is fundamental. It's also useful to investigate the mechanism of injury and possible occurrence of prodromal symptoms. An appropriate and early diagnosis of an APFF could also improve their outcomes. In fact, their treatment was more challenging, and their outcomes were worse than typical PFF because of the high rate of delayed healing, non-union, and fixation failure (11, 12).

Histological findings

The bilateral occurrence and delayed fracture healing support the hypothesis of an intrinsic bone deficiency over local stress factors. As different studies point out, bisphosphonates could lead to the formation of brittle hypermineralized bone that can suffer from low-impact stress. Indeed, drugs that decrease remodeling (i.e., antiresorptives) have been found to prevent bone healing through this mechanism. In a biopsy study by Miller and McCarthy (13), AFF patients had evidence of lower bone remodelling than expected, the rate increased with withdrawal of bisphosphonate therapy and commencement of teriparatide treatment.

Treatment strategies

Regarding treatment strategy, APFFs show poor fracture healing potential and require special attention. The management of atypical fractures is a big challenge, and the outcome is much poorer than that of typical fractures because of the delayed healing process, poor bone consolidation, difficulty of fracture fixation and high mortality rate (14, 15). Moreover, APFF union times were significantly longer than traditional AFF times (12). Indeed, fractures that were surgically treated took double the average time to union than those conservatively treated (16). Publications suggest that whenever identified, APFFs should be approached in a multidisciplinary way (16). Based on the radiographical pattern of the fracture, it is advisable to choose a surgical or conservative treatment: incomplete APFFs could benefit from both types, whereas complete ones require a surgical approach. Conservative treatment consists in avoiding weight bearing, in addition to medical management.

From a surgical point of view, treatment options for APFFs consist of fixation or revision. The choice between these approaches depends on different factors, as well as the surgeon's preference. Fixation consists of MIPO, a long-locked plate with or without cerclages, and structural graft. Adding a structural graft, granting the required construct stiffness and osteoconductive support for bone healing, provides both a mechanical and biological advantage. Otherwise, a more aggressive surgical approach could consist of a revision to a long stem. Medical management is based on clinical experience and a few uncontrolled studies (7, 8). Available options advocated by experts include the withdrawal of antiresorptive therapy, calcium, vitamin D supplementation, and consideration of anabolic therapy. In the USA, currently, the most utilized anabolic drug for osteoporosis is teriparatide, a protein consisting of the first 34 amino acids of

parathyroid hormone. There have been reports of some cases of healing following a daily subcutaneous injection of teriparatide in incomplete AFFs (13).

CONCLUSIONS

Accurate identification and diagnosis of APFFs are crucial for management planning and, eventually, the outcome. To this purpose, a precise medical anamnesis recollection of traumatic events and/or stressors is needed. It is also advisable to obtain a full laboratory workup, including calcium levels, 25-OH vitamin D, bone alkaline phosphatase, and parathyroid hormone (PTH) levels, since evidence has shown that, for these patients, oral supplementation or adjustment of blood levels could improve the outcome. Moreover, individualized preoperative planning is important, also considering the option of conservative treatment for incomplete APFFs to reduce union time.

Furthermore, it has been shown to be beneficial to withdraw, where present, the antiresorptive therapy to restore the potential for bone remodeling and, therefore, strength. New research is also pointing forward to the use of anabolic drugs, of which teriparatide is the most widely known and used. Longer follow-ups of these patients would be useful in studying long-term outcomes.

Unfortunately, due to the rare occurrence of APFFs and the lack of consensus on their classification and treatment, further studies are definitely needed in order to define the optimal management option for this type of fracture. In this context, we hope to contribute with the presentation of this case report to the characterization of these clinical presentations and the deepening of our knowledge in this field.

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