



## Atypical Bilateral Femur Fractures in a Long-Term Bisphosphonate Therapy: A Case Report

Roberto Valentini\*, Alessandro Moghnie, Veronica Scamacca, Marcellino Martino, Silvia Perin and Luigi Murena

*Orthopedic Clinic, University of Trieste, Scienze Mediche Chirurgiche e Salute, Italy*

### Abstract

Atypical Femur Fractures (AFF) are associated with Bisphosphonate Osteoporosis Therapy. Bisphosphonate therapy is widely used as the Gold-Standard Therapy for Osteoporosis: it increases bone density and reduce the risk of vertebral, non-vertebral and hip fractures. However, long-term alendronic acid administration can causes severely suppressed bone turnover and finally non-traumatic stress fractures. Here we present a case of Non-Traumatic stress fractures of bilateral femoral shafts in a Long-Term Alendronic Acid Therapy.

**Keywords:** Atypical bilateral femur fractures; Long term bisphosphonate therapy

### Case Report

A 76-year-old postmenopausal woman presented to E.R. department with a 4 months history of bilateral pain at the thigh and the patient had to walk using a crutch [1,2]. The patient had a small trauma on the left side: at the beginning it was performed only left leg X-Rays that revealed a displaced fracture in mid-thigh (Figure 1).

Patient was on Alendronic Acid 70 mg once a week for postmenopausal osteoporosis for more than 5 years.

On first physical examination, there was a severe bilateral pain in mid-thigh: it was performed a X-Ray of right femur showing a lateral cortex thickening and a transverse fracture line of the mid-thigh (Figure 2).

The patient used vitamin D supplies but vitamin D (25-OH) blood level was very low.

The patient was referred to Orthopaedic Surgery and underwent the closed reduction and internal fixation with IMHS (Intra Medullary Hip Screw) to both femoral shafts (Figures 3 and 4). Surgery outcome was good with no complications. The patient was kept under observation with 25-hydroxycholecalciferol (Calcifediol) supplementation. The clinic follow-up was based on periodic examinations and 1-3-6-12 months postoperative X-Rays (Figures 5-10).

The patient was discharged ambulating using two crutches with no pain. Active hip flexion 90 degrees and passive 100 degrees.

### Discussion

AFF can occur in patients treated with long-term alendronate therapy [3]. The incidence of these kind of fractures is estimated in 78 cases per 100,000 patients taking oral bisphosphonates [4] for more than 5 years [5,6].

The half-life of bisphosphonate is more than 10 years and it exerts its effects even after cessation of therapy [4].

The ability of bone to remodel may be impaired by long term administration of bisphosphonate because it induces prolonged suppression of bone turnover, accumulation of micro-damage and it compromises the bone strength and leads to insufficiency stress fracture [7], but the AFF pathogenetic mechanism has not been defined yet.

The American Society for Bone and Mineral Research (ASBMR) task force suggested several possibile pathogenic mechanisms [7]:



Figure 1: Left leg X-Ray.

1. Alteration of the normal pattern of collagen cross-linking.
2. Micro-damage accumulation.
3. Increased mineralization.
4. Reduced heterogeneity of mineralization.
5. Variation in bone turnover rate.

\*Corresponding author: Dr. Roberto Valentini, Aggregated Professor, Orthopedic Clinic, University of Trieste, Scienze Mediche Chirurgiche e Salute, Trieste, 34100, Italy, Tel: 003-90403994054; E-mail: [rvalentini@units.it](mailto:rvalentini@units.it)

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Figure 2: X-Ray of right femur.



Figure 5: Fracture at 1 month post-op..



Figure 3: X-ray of femoral shafts.



Figure 6: Fracture at 1 month post-op..



Figure 4: X-ray of femoral shafts.



Figure 7: Fracture at 6 month post-op.



Figure 8: Fracture at 6 month post-op.

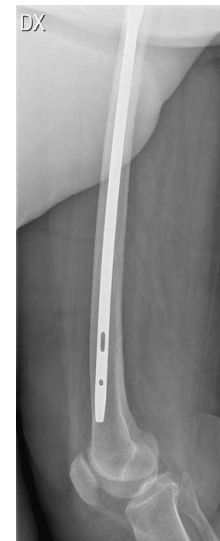


Figure 10: Fracture at 6 month post-op.



Figure 9: Fracture at 6 month post-op.

1. Generalized increase in cortical thickness of the femoral diaphysis.
2. Unilateral or bilateral prodromal symptoms, such as dull or aching pain in the groin or thigh.
3. Bilateral incomplete or complete femoral diaphysis fracture.
4. Delayed healing.

We can diagnose AFF if major criteria exist.

Pain, typically sharp, well-localized to the mid or upper thigh, for several weeks to months prior to the fracture are prodromal clinical features. As described by Rizzoli et al. [8] fractures occur with minimal or no trauma and Giusti et al. [3] reported about 40% of these fracture occurred with no trauma history. When a patient has such a kind of features in a long-term alendronate therapy the first exam to perform is bilateral radiographs of the femur looking for stress reaction and then if necessary MRI.

The clinical features of these fractures are prodromal pain, typically sharp, well-localized to the mid or upper thigh, for several weeks to months prior to the fracture [3]. As described by Rizzoli et al. [8] fractures occur with minimal or no trauma and Giusti et al. [3] reported about 40% of these fracture occurred with no trauma history. Therefore, critical evaluation of patients on long-term bisphosphonate therapy presenting with pain in the thigh is required. Routine bilateral radiographs of the femur looking for stress reaction is required and if necessary, advanced imaging such as bone scan or magnetic resonance imaging should be considered. Silverman and Christiansen [1] proposed the concept of a “drug holiday”, based on evidence of sustained protection from increased bone turnover and fracture in patients who had received bisphosphonate therapy 5 or more years.

## Conclusion

In conclusion, we suggest discontinuation of long-term bisphosphonate therapy after 4-5 years in patient with osteoporosis and, in case of thigh pain, we ask for X-Rays in order to confirm the diagnosis of AFF. The orthopedic surgical therapy can be closed reduction and internal fixation. Orthopedic follow-up is based on periodic clinical examinations and 1-3-6-12 months postoperative X-Rays.

6. Reduced vascularity and anti-angiogenic effect.

The ASBMR set major and minor diagnosis criteria.

The major criteria are:

1. The fracture is associated with no or minimal trauma, as in a fall from standing height or less.
2. The fracture line originates at the lateral cortex and is substantially transverse in its orientation, although it may become oblique as it progresses medially across the femur.
3. Complete fractures extend through both cortices and may be associated with a medial spike, whereas incomplete fractures involve only the lateral cortex.
4. The fracture is un-comminuted or minimally comminuted.
5. Localized periosteal or endosteal thickening of the lateral cortex is present at the fracture site (“breaking” or “flaring”).

The minor criteria are:

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