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# Peri-implant Atypical Fractures Associated with Bisphosphonates: Should this Clinical Entity be Included in the Definition of Atypical Femoral Fracture? Case Report

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**Learning Point for the Article:**

Peri-implant atypical fractures associated with bisphosphonates should be considered as a possible variation of atypical femur fractures,since the presented cases suggest that the mechanical factors associated with the implants appear to be insufficient to explain such lesions.


## Abstract

**Introduction:** In recent years, growing evidence of the association between bisphosphonate use and incidence of atypical femoral fractures has emerged. Cases of peri-implant fractures associated with bisphosphonate use suggest the emergence of a new clinical entity because they are not currently covered by the definition of atypical femoral fracture.

**Case Report:** We present here two rare clinical cases treated in our hospital. Two women (68 and 76 years old) with peri-implant (cephalomedullary nail) fractures and history of prolonged bisphosphonate use (11 and 14 years). Both fractures occurred after minor trauma and showed an atypical fracture pattern. One of the patients underwent revision osteosynthesis and had a 12 months follow-up. The second patient was submitted to orthopedic treatment and had a 6months follow-up.

**Conclusion:** Although reports of periprosthetic fractures and peri-implant(plate and screws) have been published, references to peri-implant cephalomedullary nail fractures were not found in the literature. Here, we question if these fracture types should be included in the current definition of atypical femoral fracture, or form a new clinical entity.


**Keywords:** Peri-implant fracture, Bisphosphonate, Atypical femoral fracture.

## Introduction

The therapeutic effects of bisphosphonates result from its antiresorptive activity in the bone, which reduces the number of new osteoclasts, decreases osteoclasts activity, and stimulates apoptosis of this kind of cells, with consequent bone turnover reduction. Strong and prolonged inhibition deregulates the normal turnover of bone, inducing a bone remineralization process, which increases its rigidity, leading to "frozen bone," and microcrack accumulation, which may progress to fatigue fractures, in the absence of proper remodeling [1]. Despite these data, other studies showed increased bone stock and longer implant survival with bisphosphonate use after knee and hip arthroplasty [2,3]. Multiple publications have recently associated bisphosphonate use with the emergence of atypical subtrochanteric and shaft fractures of the femur. These are more common after continued use of this medication for 2 years, and up to a year after the last prescription [4,5,6]. Schilcher et al. [7] stated that the risk is higher in women and those using alendronate. However, this association was recognized only in 2014, in the Second Report of the American Society for Bone and Mineral Research Task Force, with obvious doubts regarding its strength and magnitude. Prolonged bisphosphonate use has been postulated to be associated with a relative increased risk, but the absolute risk is still low. In a latter

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**Figure 1:** Case 1 – ER episode

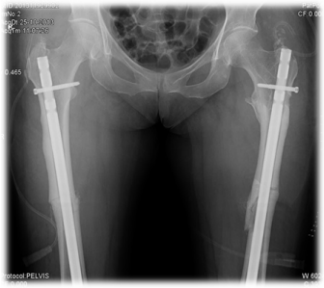

**Figure 2:** Case 1: After surgery (1)

study, periprosthetic and peri-implant fractures remain excluded from the definition of atypical femoral fracture.

## Materials and Methods

We present two clinical cases of patients treated in our department that showed peri-implant femoral fractures associated with long-term bisphosphonate (alendronate) use after low-energy trauma. The clinical and radiological study, treatment, follow-up, and complications are documented in this article.

## Result

### Case 1

We present a 68-year-old woman, with osteoporosis, treated with bisphosphonates for 11 years and a history of left subtrochanteric fracture 3 years ago, treated with short cephalomedullary nailing. She experienced sudden pain in the left thigh while walking around with subsequent fall from standing height with the trauma of the right hemibody. She presented in the emergency room withleft hip pain, not being able to walk and with no neurovascular alterations. The radiograph showed a bilateral atypical diaphyseal fracture in the femurs. In the previously intervened limb, the peri-implant fracture was located on the tip of the nail, immediately after the distal screw and with minimal comminution. Bilateral femoral cortical thickening was also evident (Fig. 1). The patient underwent long anterograde blocked bilateral nailing, which occurred without complications. Intake of alendronate, calcium and Vitamin D supplements was suspended(Fig. 2, 3). Subsequently, the

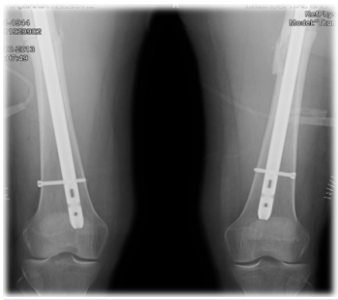

**Figure 3:** Case 1: After Surgery (2)

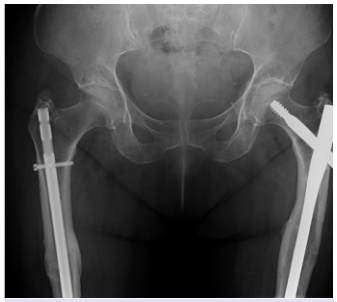

**Figure 4:** Case 2- First ER episode- no fracture

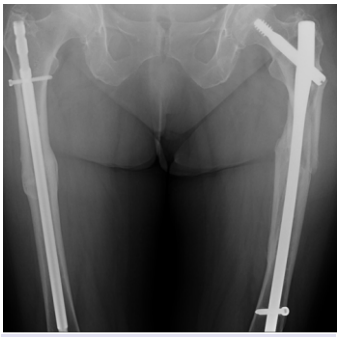

**Figure 5:** Case 2: Second ER episode (1)

**Figure 6:** Case 2: Second ER episode (2)

patient was followed up without complications. She was discharged after 1-year surveillance.

### Case 2

We present a 76-year-old woman, with a history of bisphosphonate intake for 14 years, a subtrochanteric fracture of the left femur 10 years prior treated with long cephalomedullary nailing. The patient, who had intermittent pain in the left thigh while walking in the past few weeks, went to the emergency service after a low energy fall with left hip injury and pain aggravation. Nonetheless, the radiographic study did not display any injury (Fig. 4). She returned after 3 days because pain persisted, and the X-ray showed an atypical

**Table 1: ASBMR Task Force 2013 Revised Case Definition of AFFs**

| |
|---|
| Major features[a] |
| The fracture is associated with minimal or no trauma, as in a fall from a standing height or less |
| 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 |
| Complete fractures extend through both cortices and may be associated with a medial spike; incomplete fractures involve only the lateral cortex |
| The fracture is non comminuted or minimally comminuted |
| Localized periosteal or endosteal thickening of the lateral cortex is present at the fracture site ("beaking" or "flaring") |
| Minor features |
| Generalized increase in cortical thickness of the femoral diaphyses |
| Unilateral or bilateral prodromal symptoms such as dull or aching pain in the groin or thigh |
| Bilateral incomplete or complete femoral diaphysis fractures |
| Delayed fracture healing |
| ASBMR: American Society for Bone and Mineral Research, AFF: Atypical femur fracture. (a) Excludesfractures of the femoral neck, intertrochanteric fractures with spiral subtrochanteric extension, periprosthetic fractures, and pathological fractures associated with primary or metastatic bone tumors and miscellaneous bone diseases (e.g., Paget's disease and fibrous dysplasia) |

**Figure 7:** Case 2 – 6 weeks later

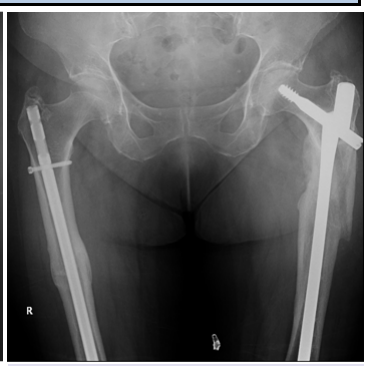

**Figure 8:** Case 2: 3 months and 1 week later (1)


**Figure 9:** Case 2 -3 months and 1 week later (2)

peri-implant femoral shaft fracture, without nail fracture, after new imaging examinations were performed (Fig. 5, 6). Conservative treatment was chosen, together with no weight bearing, walking with crutches and analgesics. The patient reported clinical improvement during follow-up, 6 weeks after. Nonetheless, radiographically, she displayed failure of osteosynthesis material with cephalomedullary nail fracture, but with bone callus formation (Fig. 7). Maintenance of an expectant attitude and close monitoring during consultation were chosen(Fig. 8, 9). Currently, the patient walks and remains asymptomatic, with consolidation without fracture displacement after 6 months.

## Discussion

The American Society for Bone and Mineral Research defines atypical subtrochanteric or diaphyseal fracture of the femur as those that meet four of the five major criteria and without mandatory compliance to minor criteria, as shown in Table 1 [8]. As we can see among the exceptions, periprosthetic fractures are excluded from this definition. No references are found for other metallic implants. The only study that we found in our research addressing the existence of fractures associated with osteosynthesis implants only refers to plates and screws. This is a series of 11 atypical fractures in patients treated with a system of plates and screws. We may be dealing with a new clinical entity called peri-implant fracture associated with bisphosphonates. They consider that the atypical fractures may also occur in arthroplasties and constructs with plates and screws. Intramedullary implants are not considered in this publication [9]. The existence of other confounding factors, such as stress shielding, decrease of the blood supply in the cortical bone adjacent to the plate, and changes of stiffness in the tips of the plates should be studied to assess the degree of influence of bisphosphonates in this fracture type. The use of intramedullary implants would seem to reduce external mechanic factors because they offer a more homogenous distribution of forces of stress than osteosynthesis with plate and screws. Case 2 is a paradigmatic example of what we consider to be a peri-implant fracture associated with bisphosphonates. This patient with prodromal pain, who after low-energy trauma, develops an atypical fracture in a bone with stigmata from prolonged bisphosphonate use. The location is unusual (middle third of the nail) and apparently more protected from mechanical stress factors. No similar case was found in the literature. The bilateral trend among these fractures and the delay in consolidation suggest intrinsic alterations in the bone morphology beyond local mechanical stress factors. Atypical femoral fractures tend to be located more often in the lateral cortical subtrochanteric where the tension forces are higher [10]. Vascularization of this femoral region is less developed compared with others, notably in the intertrochanteric portion, which may decrease bone regeneration ability. The implants concentrate stress within their proximal and distal limits, altering anatomical tension forces and turning plaque bone joints into weak points, subjecting these assembly boundary areas to greater tension forces, thus causing successive microlesions in an altered bone without the usual regeneration power. Lee et al. [9] proposed the use of long intramedullary implants to solve this problem.

## Conclusion

This study continues a growing trend for publication of cases of atypical peri-implant and periprosthetic fractures associated with long-term bisphosphonate use. We did not find cases of similar characteristics in the literature, and there is no established association between these drugs and the described lesions. Further biomechanical studies are also needed. However, we believe that this study provides pertinent information to understand these lesions from a physiopathological point of view, and acknowledges this as a probable new clinical entity, resulting from the consequence of medical activity in contemporary society.

### Clinical Message

Bisphosphonate use should be managed carefully because it might deregulate the normal turnover of bone leading to fatigue fractures, in the absence of proper remodeling. We suggest that these changes could affect the implant survival and new strategies should be created to improve our knowledge on the biomechanical and physiological factors that affect this kind of patients.

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