



Case Report

Atypical femoral fracture due to chronic use of bisphosphonates: case report[☆]



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ABSTRACT

The causal relationship between chronic use of bisphosphonates and occurrences of atypical femoral fractures has not yet been established. Nonetheless, it is known that their chronic use is more related to fractures with a pattern differing from that of classical osteoporotic fractures. Atypical fractures are still rare events and the benefit from using bisphosphonates remains greater for prevention and treatment of osteoporosis. There are few studies guiding the diagnosis and management of these fractures, thus making it difficult to achieve better results. In this report, we present the case of an elderly patient with an atypical femoral fracture that was managed in accordance with guidance from the American Society for Bone and Mineral Research.

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Fratura femoral atípica devida a uso crônico de bifosfonato. Relato de caso

RESUMO

A relação causal entre o uso crônico dos bifosfonatos e a ocorrência de fraturas femorais atípicas não tem sido ainda estabelecida. Todavia, sabe-se que o uso crônico dos bifosfonatos tem tido maior relação com fraturas com padrão diferente das clássicas fraturas osteoporóticas. Fraturas atípicas são ainda eventos raros e o benefício do uso dos bifosfonatos ainda é maior na prevenção e no tratamento da osteoporose. Pouco são os estudos que orientam o diagnóstico e a condução dessas fraturas, o que dificulta melhores resultados. Neste relato apresentamos caso de paciente da terceira idade com fratura femoral atípica conduzida segundo orientação da Sociedade Americana para Pesquisa Óssea e Mineral.

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Introduction

Bisphosphonates are today among the main types of medications prescribed worldwide for treating osteoporosis. Several studies have proven that they have an important role in reducing the incidence of vertebral and non-vertebral fractures when used for treating senile and postmenopausal osteoporosis.^{1,2} The indications for using these medications also extend to other metabolic diseases such as bone metastasis, Paget's disease and hypercalcemia.^{3,4} The action of bisphosphonates occurs through inhibition of the function of osteoclasts. This induces apoptosis of osteoclasts and gives rise to significant suppression of remodeling and consequent loss of bone balance.⁵ However, the use of these medications is not free from complications.

Several case series have already indicated that there is an association between atypical femoral fractures and prolonged use of bisphosphonates. These fractures differ from classical osteoporotic fractures in several respects, including the mechanism of action, location and fracture configuration.⁶⁻⁸ Although the American Society for Bone and Mineral Research (ASBMR) has published guidelines for evaluating and following up fractures that are considered atypical, little is known about this particular group of injuries.⁹ The aims of the present article were to present a case of atypical fracturing induced by chronic use of bisphosphonates and to review the characteristics, epidemiology, pathogenesis and treatment of such cases, so as to aid orthopedic surgeons in conducting similar cases.

Case report

The patient was a 90-year-old dark-skinned woman of weight 75 kg and height 1.50 m, who presented a painful condition of mechanical pattern in her right thigh that started in November 2013. Previously, she had been able to walk within her community. She suffered involution of her gait pattern as the painful condition intensified and became capable of walking only at home, with the help of a walking frame. She did not have any history of falls or any local traumatic factor. She was known to present systemic arterial hypertension, non-insulin-dependent diabetes mellitus, cardiopathy and osteoporosis, which were all being treated with drugs.

She sought the orthopedics and traumatology outpatient clinic of our service in February 2014, in order to have her complaint investigated. She had a history of a left-side proximal femoral fracture 6 years previously, which had been treated at our institution, without any complaint. She also reported that since then, she had been using calcium replacement and had kept on using bisphosphonates over the same period. She did not present any abnormality in the clinical examination, except for discomfort in her right lower limb, at thigh level when walking. Serial radiographs demonstrated normality and good evolution of the left-side fracture that had previously been treated, but with arching of the femoral cortical bone and sclerosis of the lateral wall in its middle third. In the light of these findings, magnetic resonance imaging of the thigh was requested. This showed the presence of incomplete fracturing of the posterolateral/lateral cortical bone with thickening

of the adjacent cortical bone and bone edema, in association with slight unilamellar periosteal thickening. Investigation of laboratory parameters did not show any associated metabolic abnormality (Fig. 1).

Given these factors and the symptomatic condition, a surgical approach was indicated. There was discussion regarding the best fixation method: intramedullary fixation using a cephalomedullary nail or fixation using a plate. In this specific case, an initial attempt was made to use an intramedullary nail, but because of diaphyseal arching and the risk of worsening the existing fracture, it was decided to place a locked plate as a bridge.

Today, the patient presents 4 months of postoperative evolution, with involution of the symptomatic condition and improvement of the gait pattern, and without any complaints. She already presents radiological indications of fracture consolidation (Fig. 2). Because of the history of a previous proximal femoral fracture and the atypical fracture induced by bisphosphonates (high risk of new fractures), it was decided to maintain the supplementation of calcium and vitamin D, withdraw the use of bisphosphonates and start the patient on denosumab.

Discussion

Because of the lack of criteria for defining atypical femoral fractures, the ASBMR has established major and minor conditions for diagnosing these fractures. The presence of the major conditions is fundamental for designating the fracture as atypical and distinguishing it from osteoporotic fractures, while the minor conditions may be associated with atypical fractures but are not fundamental (Table 1).⁹ Atypical femoral fractures have been correlated with several factors, including Asian ancestry, bilateral fractures, indicative signs and symptoms, chronic use of corticosteroids and proton pump inhibitors, vitamin D deficiency and presence of diabetes mellitus and rheumatoid arthritis.^{7,8} The ASBMR has estimated that the accumulated incidence of atypical fractures is 0.9 to 78 cases per 100,000 individuals per year. The increase each year is two cases per 100,000 after 2 years

Table 1 – Major and minor conditions for diagnosing atypical femoral fractures.

Major conditions	Minor conditions
<ul style="list-style-type: none"> - Absence of any traumatic conditions - Femoral fracture in any diaphyseal location: from below the lesser trochanter to proximal to the supracondylar region - Transverse or short oblique fracture - Non-comminutive fracture - Medial spoke in complete fractures; fractures that involve only the lateral cortical bone in incomplete cases 	<ul style="list-style-type: none"> - Periosteal thickening in the lateral cortical bone - Indicative symptoms - Comorbidities in association with the use of medications that predispose toward fractures - Association with bilateral fracture and/or symptoms

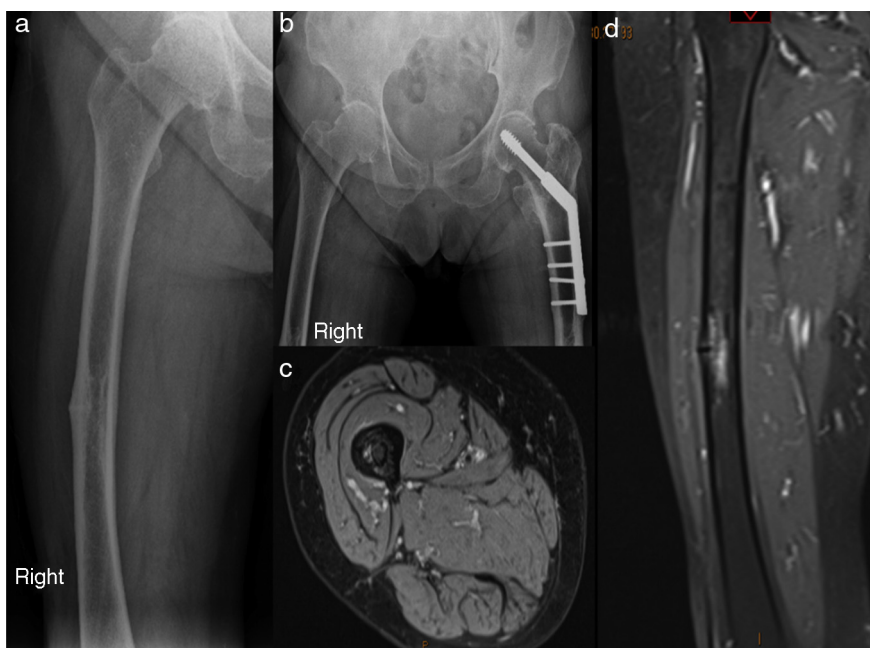


Fig. 1 – Preoperative radiological evaluation. (a, b) Radiographic images showing area of sclerosis in the middle third and synthesis material from previous femoral fracture and (c, d) magnetic resonance imaging slices showing area of incomplete fracture in the posterolateral cortical bone, with permeating edema.

of use of bisphosphonates and this rises to 78 per 1,000,000 every year after 8 years of use of this medication.⁹

Several pathogenic mechanisms that explain the relationship between chronic use of bisphosphonates and atypical femoral fractures have been studied. Chronic use is responsible for the deleterious effect on bone quality, because this inhibits bone remodeling at cell level. Although increased remodeling predisposes toward bone fragility, this effect

also contributes toward an accumulation of architectural damage, reduction of the heterogeneity of the cell matrix, increased glycation of the final products and losses through remodeling.^{1,2,7-9} After a condition of atypical femoral fracture has been diagnosed, use of bisphosphonates should be halted. The idea of vitamin D and calcium supplementation should be evaluated; introduction of bone anabolic agents should be considered (denosumab or teriparatide); laboratory

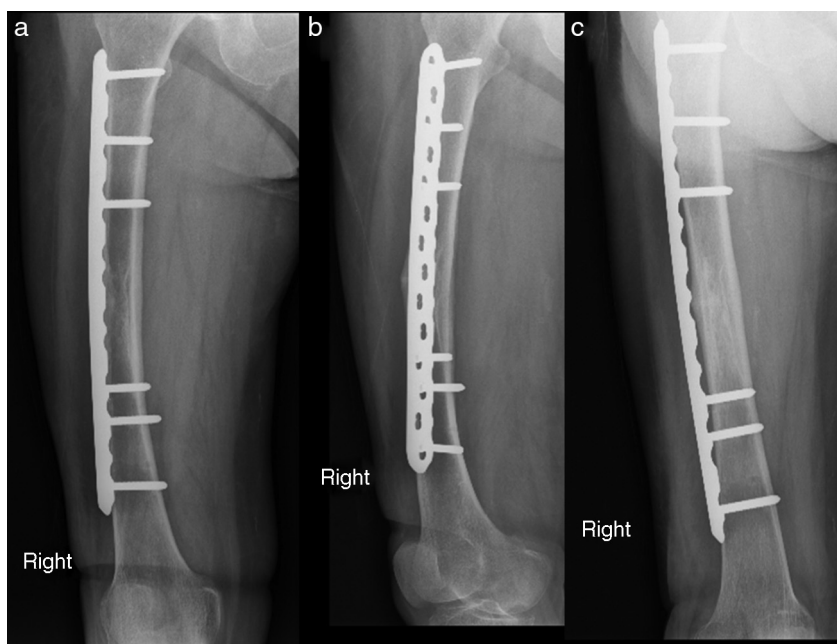


Fig. 2 – Late-stage postoperative radiological evaluation (3 months) showing consolidation in anteroposterior (AP) view (a) and oblique view (b, c).

tests should be used to identify any existence of predisposing metabolic conditions; the contralateral side should be evaluated, given that the risk of bilaterality is 28–44.2%; and lastly, the best fixation method should be evaluated.^{8,9} No controlled studies comparing fixation with plates and screws in relation to intramedullary fixation have been conducted, although the latter has the theoretical benefit of presenting consolidation through endochondral repair. Therefore, there is a certain degree of preference for using nails for treating atypical femoral fractures.⁸⁻¹⁰ Despite all the care that is taken today, and the better knowledge available, the prognosis for these fractures is still poor, with descriptions of the need to repeat the procedure in up to 44% of the cases in some studies. The time taken for consolidation to be achieved that has been described in the literature ranges from 12 to 60 months.

The screening for evaluating bone abnormalities in all patients receiving bisphosphonates is inadequate because of the low incidence rate of these fractures and because radiological abnormalities are often unidentifiable. Nevertheless, in view of the presence of pain of mechanical pattern in patients who make chronic use of bisphosphonates, careful assessment needs to be made using serial radiological imaging, scintigraphy and magnetic resonance imaging, in order to institute early diagnosis and treatment.^{5,8-10} Because many questions relating to atypical femoral fractures still do not have answers, further studies aiming toward better histomorphometric and bone biomechanical evaluations and the relationship of these fractures to certain medications are fundamental. Moreover, discussion toward creating a national register of atypical femoral fractures will ensure better understanding and discussion of these cases.

Conflicts of interest

The authors declare no conflicts of interest.

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