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Clinical case

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Bilateral atypical femoral fractures caused by long-term use of bisphosphonate treatment in postmenopausal osteoporosis

Fracturas femorales atípicas bilaterales causadas por uso prolongado de tratamiento con bifosfonato en osteoporosis postmenopáusica

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ABSTRACT. This paper presents two cases of bilateral atypical femoral fractures in postmenopausal women who underwent prolonged bisphosphonate therapy for osteoporosis. Both patients, aged 83 and 76, experienced fractures after long-term bisphosphonate treatment, highlighting concerns about suppressed bone turnover. Each case was treated with intramedullary nailing, and bisphosphonates were discontinued in favor of alternative therapies. These cases underscore the risks of atypical femoral fractures linked to extended bisphosphonate use, emphasizing the need for careful patient monitoring and further research to optimize osteoporosis treatment strategies and prevent such complications.

Keywords: osteoporosis, bisphosphonates, atypical femoral fracture, osteoporotic fracture, intramedullary nailing.

RESUMEN. Este artículo presenta dos casos de fracturas femorales atípicas bilaterales en mujeres posmenopáusicas con tratamiento prolongado con bifosfonatos para la osteoporosis. Ambas pacientes, de 83 y 76 años, sufrieron fracturas tras un tratamiento prolongado con bifosfonatos, lo que pone de manifiesto la preocupación que suscita la supresión del recambio óseo. En ambos casos, la reducción de las fracturas fue mediante colocación de clavos intramedulares y se suspendió el tratamiento con bifosfonatos cambiando el manejo por terapias alternativas. Estos casos dan relevancia a los riesgos de fracturas femorales atípicas relacionadas con el uso prolongado de bifosfonatos, y subrayan la necesidad de un seguimiento cuidadoso de los pacientes y de más investigación para optimizar las estrategias de tratamiento de la osteoporosis y prevenir tales complicaciones.

Palabras clave: osteoporosis, bifosfonatos, fractura femoral atípica, fractura osteoporótica, clavo intramedular.

Introduction

Osteoporosis has been defined as low bone mass that slowly affects the healthy architecture of the bone, increasing its fragility and making it more susceptible to fragility fractures.[1]

For the assessment of bone quality, Bone Mineral Density (BMD) has been the most valuable tool; according to the World Health Organization (WHO), osteoporosis is diagnosed with a BMD score that is 2.5 standard deviations (SD) or more below compared to the average

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score for healthy women. Another diagnostic criterion is the presence of fragility fractures without other diseases predisposing to bone fragility.[2,3]

One of the most common treatments for osteoporosis is bisphosphonates (BISPHs), derivatives of inorganic pyrophosphate which inhibit bone resorption by targeting osteoclasts, leading to increased bone mineral accretion and reduced bone turnover.[4,5] However, concerns have arisen regarding the remodeling processes, essential for bone growth, as they may cause bone deformity or disrupt the normal mineralization process.[6] These mechanisms impair the healing of naturally occurring bone microcracks and elevate the risk of fractures.[7]

In the literature, there is a strong correlation between BISPHs treatment duration and Atypical Femoral Fractures. The incidence in the first year of alendronate use is 2 per 100,000 patients per year of treatment, increasing to 25 per 100,000 patients per year after 3-5 years of treatment and to 130 per 100,000 patient-years with more than eight years of treatment.[8]

Typical hip fractures often occur in the femoral neck and intertrochanteric regions, and fractures resulting from suppressed bone turnover have been described as atypical and affect primarily the subtrochanteric femur, infrequently affected by osteoporotic fractures.[9]

The purpose of this paper is to present two cases of bilateral atypical femoral fractures in postmenopausal women treated for osteoporosis with bisphosphonates and discuss their treatment.

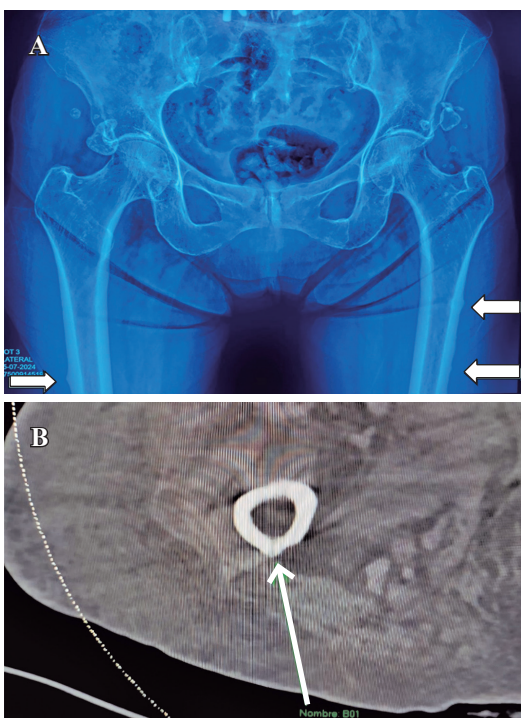

Figure 1: A) Antero-posterior pelvis X-ray showing cortical thickening and atypical cortical fractures in the subtrochanteric area of the femur. **B)** Axial CT image of the left leg showing the atypical fracture.

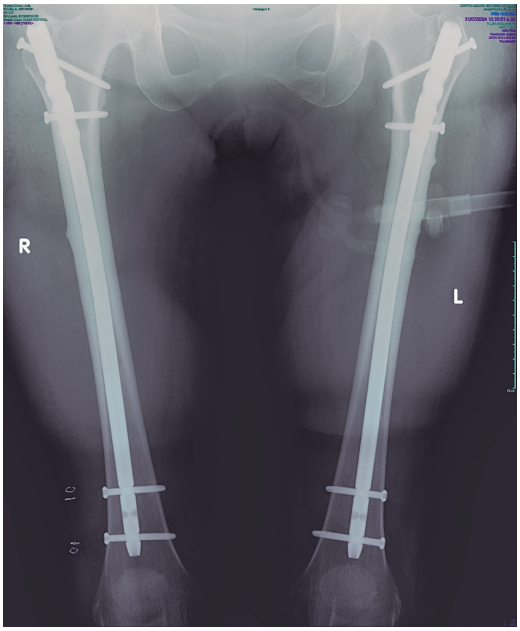

Figure 2: Surgical fracture repair with intramedullary nailing.

Case presentation

Case1

An 83-year-old female with a 10-year history of bisphosphonate treatment for osteoporosis (alendronic acid, 70 mg presentation), came to the orthopedic consult after feeling leg pain. Normal movement, with limitation and instability, while standing up. An X-ray and CT scan of the pelvis were obtained. *Figure 1* shows the thickening of the bone cortex, with the presence of atypical incomplete bilateral fractures in the subtrochanteric femur. After a complete assessment, the patient underwent surgical treatment with intramedullary nailing *(Figure 2)*, and thromboprophylaxis with Apixaban 2.5 mg every 12 hours for 28 days was indicated.

After the procedure, bisphosphonate therapy was suspended and replaced with romosozumab, vitamin D, and calcium supplementation. Physical rehabilitation was also prescribed, aiming for gait rehabilitation and full range of motion.

Case 2

A 76-year-old female patient used alendronate for four consecutive years, switching afterward to zoledronic acid and using it for five more years, making it a total of nine years of BISPH use. She arrived at the emergency room after experiencing a spontaneous fracture of the left femur while taking a walk *(Figure 3)*, leading to a fall from her height. The clinical examination and radiographs demonstrated a left Atypical Femur Fracture (AFF). Upon further observation, an incomplete fracture was found in the right femur *(Figure*

4). She underwent a first surgical intervention, and two days later, a second one; intramedullary nailing was performed in both femurs *(Figure 5)*. A lumbar spine dual-energy X-ray absorptiometry (DEXA) was performed, which reported a T Score of −0.9, spine TBS of 1.382, left femoral neck T-score of −1.5, and right femoral neck T-score of −1.7, leading to an osteopenia diagnosis.

The patient progressed favorably; she was prescribed physical therapy and began using a walker. BISPH therapy was immediately suspended and replaced with Teriparatide, calcium supplements, and vitamin D. Due to clinical improvement, the patient was discharged from the Orthopedics Unit.

Figure 3:

Atypical femoral fracture in the subtrochanteric region of a 76-year-old female patient.

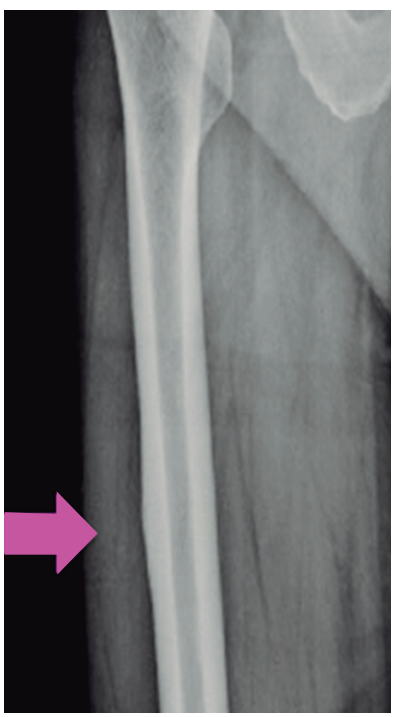

Figure 4:

Incomplete atypical fracture of the right femur.

Figure 5: Intramedullary nailing of both femurs as treatment of atypical fractures.

Discussion

There is an ongoing discussion regarding the long-term effects of the BISPHs-based therapy in osteoporotic patients. Oral and intravenous (IV) BISPHs have maintained their position as the most commonly used anti-resorptive agents. Prolonged use of these agents may lead to several adverse effects, such as AFF and jaw osteonecrosis.[10] Clarita V et al., suggest that BISPH treatment in a clinical environment is responsible for a condition known as severely suppressed bone turnover, which is one of the most notable risk factors for osteoporotic fractures.[11] In the cases presented in this report, both patients presented a long-term treatment with BISPHs.

The main concern among physicians nowadays is the presence of AFF, initially characterized by cortical thickening, cortical deformity, and microcracks caused by high levels of collagen cross-linking that reduces bone toughness and its ability to absorb energy.[12] Transverse fractures are due to low-energy events or even atraumatic events, as in the case of both patients presented.[13]

As performed in both cases, various studies recommend intramedullary nailing as the first-line treatment for complete fractures. Hwang S et al., in their literature review, affirm that intramedullary nails are favored because they can be helpful in difficult-to-heal fractures by allowing the formation of an endochondral

callus.[8] Also, they should be offered as a prophylactic treatment to patients with intractable pain and routinary radiographic imaging should be obtained aiming for the recognition of asymptomatic fractures.[14]

The use of Teriparatide has been suggested since these patients presented AFF due to long-term BISPHs-based therapy. A systemic review and meta-analysis by Nayak and Greenspan concluded that a discontinuation of the BISPHs is recommended in women that has not presented low hip BMD scores after three to five years of treatment, but for the ones that show low hip BMD, the continuation of the treatment may be beneficial. We acknowledge that a treatment washout is an appropriate approach to avoid complications, BMD does not equate to bone quality.

Prolonged use of BISPHs has proven to be a risk factor in AFF incidence.[15]

After considering many aspects of the literature about atypical femoral fractures due to prolonged use of BISPHs, we suggest that further investigation is needed to better understand which treatment should be offered to osteoporotic patients. Also, a screening tool that predicts the outcome of patients with BISPHs treatment could be helpful to avoid atypical fractures and prevent their progression.

In conclusion, atypical femoral fractures represent a risk of complete subtrochanteric fracture in osteoporotic women, a full assessment of the patient on BISPH treatment should be performed, and in the pertinent cases, it should be discontinued.

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