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Dental care for a patient using bisphosphonate: Case report

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ABSTRACT

Introduction: Bisphosphonates (BPs) are currently the most relevant class of antiresorptive agents used in the treatment of bone pathologies, such as multiple myeloma, bone metastases, Paget's bone disease, osteogenesis imperfecta and osteoporosis. The mechanism of action of these drugs reduces the lifetime and function of osteoclasts, interfering with the bone remodeling process. In addition, they also promote inhibitory effects on inflammation mediators, which influence the bone repair process. Therefore, when used in association with dental surgical interventions, there is an increase in postoperative complications, since one of the steps for bone repair is remodeling, which is affected by bisphosphonates. The complications resulting from its use came to be called Osteonecrosis of the Jaws related to bisphosphonates. Objective: This paper aims to report the case of a female patient, 70 years old, with osteoporosis and systemic arterial hypertension, who uses sodium alendronate bisphosphonate (Osteoform®). The patient attended the Oral Surgery Clinic at Faculdade Paulo Picanço in need of extraction of the residual root of element 45, and underwent the surgical procedure. The procedure was performed under antibiotic coverage followed by laser therapy sessions. The patient was followed up for a period of 6 months, aiming to guarantee a good prognosis. Final considerations: Bisphosphonates (BFs) are first-choice drugs for various bone pathologies and their use is increasingly frequent. Preventive treatment plays a key role in reducing the chances of bisphosphonate-related Osteonecrosis of the Jaws (BMB). Currently, there are still no defined therapeutic dental protocols for the treatment of OMB, which emphasizes the importance of prevention as the best option in coping with this condition. Dental care prior to starting therapy with antiresorptive drugs is essential and should be an integral part of the treatment plan for patients who will use these drugs.

Keywords: Bisphosphonates, Osteonecrosis of the jaws, Oral surgery, Case report.

1 INTRODUCTION

Bisphosphonates (BFs) are synthetic analogues of the endogenous substance called pyrophosphate, which in the body has the function of naturally inhibiting bone resorption. While pyrophosphates have a P-O-P chemical structure, BFs have a P-C-P bond in their structure, providing characteristics that make them resistant to enzymatic hydrolysis, stable to heat, and most types of chemical reactants (Vasconcelos et al., 2023).

In the clinical dental context, the use of BFs is related to an increase in postoperative complications, especially in surgical procedures, such as tooth extractions and installation of osseointegrated implants. Both the medical and dental communities have been alerted to the growing problem since 2003. In 2004, the first series of reports on the new pathological entity called Bisphosphonate-Associated Osteonecrosis of the Jaws (OMB) was published in the scientific community (Marx et al., 2005; Ruggiero et al., 2014).

Although the first cases of OMB were reported in 2003, its pathogenesis is still poorly understood (Ruggiero et al., 2014). There are several hypotheses discussed in the literature on the development of OMB, including alterations in bone metabolism (remodeling and suppression of innate or acquired immunity), inhibition of angiogenesis, constant microtrauma, soft tissue toxicity of BFs, vitamin D deficiency, infection, and inflammation (Silva et al., 2017; Vasconcelos et al., 2023; Ruggiero et al., 2022). However, it is important to note that these hypotheses are still being investigated and there is no definitive consensus on the exact cause of OMB.

For the diagnosis of OMB, the patient needs to present three essential aspects: 1) history of previous or current treatment with bisphosphonates; 2) presence of exposed necrotic bone in the maxillofacial region, which does not heal within a period of eight weeks; 3) absence of previous exposure to radiotherapy in the jaws (Ruggiero et al., 2014). It is observed that BMO prefers occurring in the mandible (75%), followed by the maxilla (25%), and in both jaws in 4.5% of cases. Importantly, patients who use bisphosphonates intravenously seem to be more susceptible to the pathology compared to those who use them orally. In addition, there is a trend towards the occurrence of OMB in females (Ruggiero et al., 2022).

The objective of this study is to report the case of a 70-year-old female patient with osteoporosis and systemic arterial hypertension who uses the bisphosphonate sodium alendronate (Osteoform®). The patient came to the Oral Surgery Clinic of Faculdade Paulo Picanço in need of extraction of the residual root of element 45, and underwent surgery. The procedure was performed under antibiotic coverage followed by laser therapy sessions. The patient was followed up for a period of 6 months to ensure a good prognosis.

2 METHODOLOGY

This is a qualitative and descriptive study, of the case report type, elaborated through anamnesis, medical and dental history, as well as photographs of the patient. This study was submitted to the Research Ethics Committee (REC), approved by the Research Ethics Committee of Faculdade Paulo Picanço, and conducted in accordance with the bioethical principles established by Resolution No. 466 of December 12, 2012 of the National Health Council. The patient consented and allowed the use of their images and information for this study, having signed the Free and Informed Consent Form (ICF) (Pereira et al., 2018). The theoretical basis was obtained by searching the scientific literature in the US National Library of Medicine (PubMed) and Scientific Electronic Library Online (SciELO) databases.

3 CASE REPORT

A 70-year-old female patient M.C.A.S., with leukoderma, came to the Oral Surgery Clinic of Faculdade Paulo Picanço with the need to perform the extraction of the residual root of element 45. During the anamnesis, the patient reported having systemic arterial hypertension and osteoporosis. In addition, the patient reported having been using the following drugs orally for more than 10 years: sodium alendronate (Osteoform®), calcium supplementation (Imecalcium®), simvastatin, and losartan potassium (Chart 1).

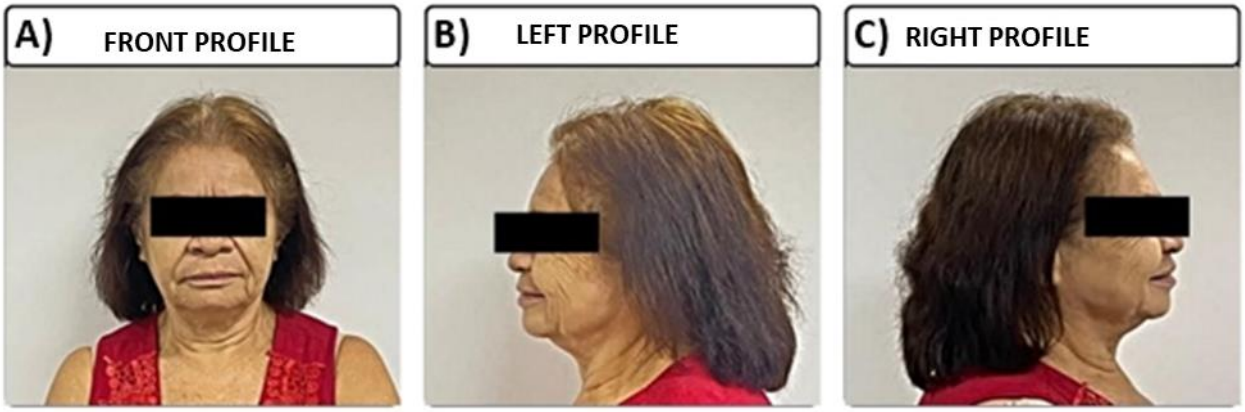
Chart 1 - Drugs used by the patient and their dosages.

DRUGS USED BY THE PATIENT		
DRUG	**DOSAGE**	**ROUTE OF ADMINISTRATION**
Sodium alendronate	70 mg/ without	Oral
Calcium Supplementation	500 mg + 400 UI / day	Oral
Simvastatin	20 mg/ day	Oral
Losartan Potassium	50 mg/ day	Oral

Source: Authors (2023).

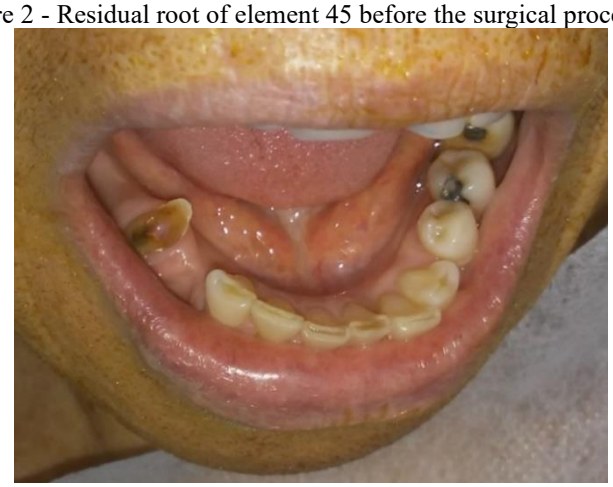
Extraoral physical examination showed no relevant alterations, as shown in Figure 1. During the intraoral physical examination (Figure 2), the real need for tooth extraction was identified. In addition, a panoramic X-ray was requested (Figure 3), which revealed tooth absences and carious lesions in some elements of the arch.

Figure 1 - Extraoral physical examination; (A) Front view, (B) Left profile view, (C) Right profile view.



Source: Authors (2023).

Figure 2 - Residual root of element 45 before the surgical procedure.



Source: Authors (2023).

Figure 3 - Preoperative panoramic radiograph.

Source: Authors (2023).

As evidenced by the panoramic radiography, it is possible to observe the presence of the residual root of element 45, which was treated endodontically. In addition, multiple dental absences,

restorations, and alterations compatible with carious lesions were identified in some elements of the arch.

To perform the extraction, antibiotic coverage with clindamycin of 300 mg every 8 hours was prescribed, starting one day before the surgical procedure, and continuing for 14 days after the procedure. The choice of clindamycin in this case is due to its rapid diffusion into bone tissue (Lima et al., 2014).

A conservative surgical approach was planned and executed to minimize possible injuries and, consequently, reduce the risks of infection of the oral cavity. For anesthesia, the anesthetic articaine 4% with epinephrine 1:100,000 was used using the supraperiosteal infiltrative terminal technique. Articaine was chosen due to its greater diffusion capacity in bone tissue compared to other local anesthetics, due to its chemical properties (Aragão et al., 2016).

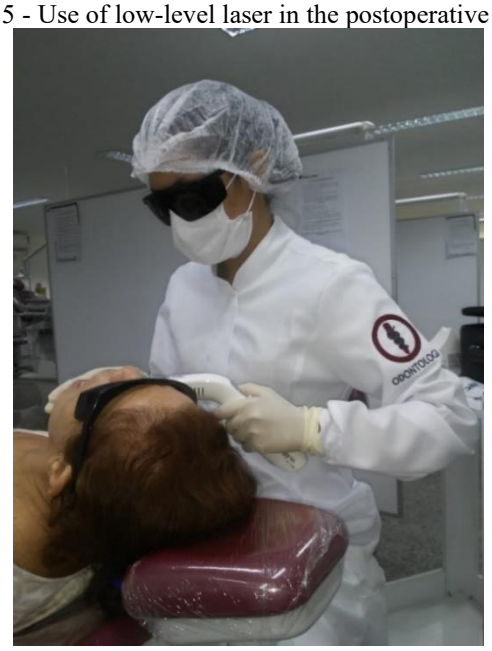
For excision, the second technique was initially used, using the Seldin No. 2 lever with wedge action, followed by the first technique, with the use of forceps No. 65 for dental avulsion. The synthesis was performed with a simple interrupted suture using 4-0 nylon thread, as illustrated in Figure 4. After surgery, low-level laser therapy was used immediately, following the protocol of 808 nm ± 10 nm, 6 J/cm², infrared, in the alveolar region.

Figure 4 - Transoperative; (A) Extraction, (B) Alveoli after extraction, (C) Suture performed.

Source: Authors (2023).

Low-level laser therapy (Laser DMC Therapy EC) was used at the surgical site immediately after the procedure, and treatment was continued in subsequent sessions over three weeks. The application protocol consisted of a weekly session with infrared laser: 808 nm ± 10 nm, 6 J/cm², applied intraorally, as illustrated in Figure 5. In addition, the patient was prescribed nimesulide 100 mg, dipyrone sodium 500 mg, and chlorhexidine digluconate 0.12%. Antibiotic coverage with clindamycin 300 mg was maintained for 14 days.

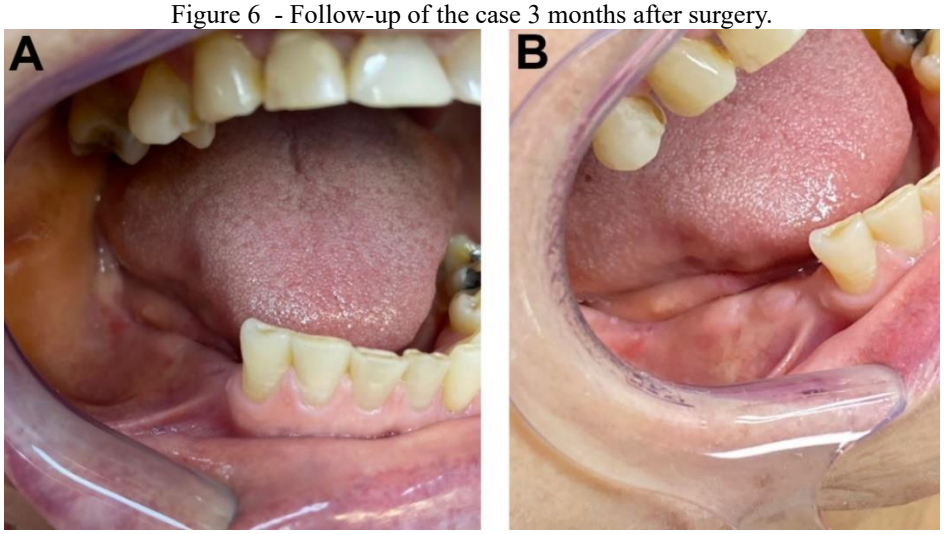
Figure 5 - Use of low-level laser in the postoperative period.



Source: Authors (2023).

After a 30-day follow-up since the procedure, no changes were observed in the surgical site repair process. After 3 months, the patient returned for a new clinical evaluation, and the repair of the surgical site was satisfactory, as illustrated in Figure 6.

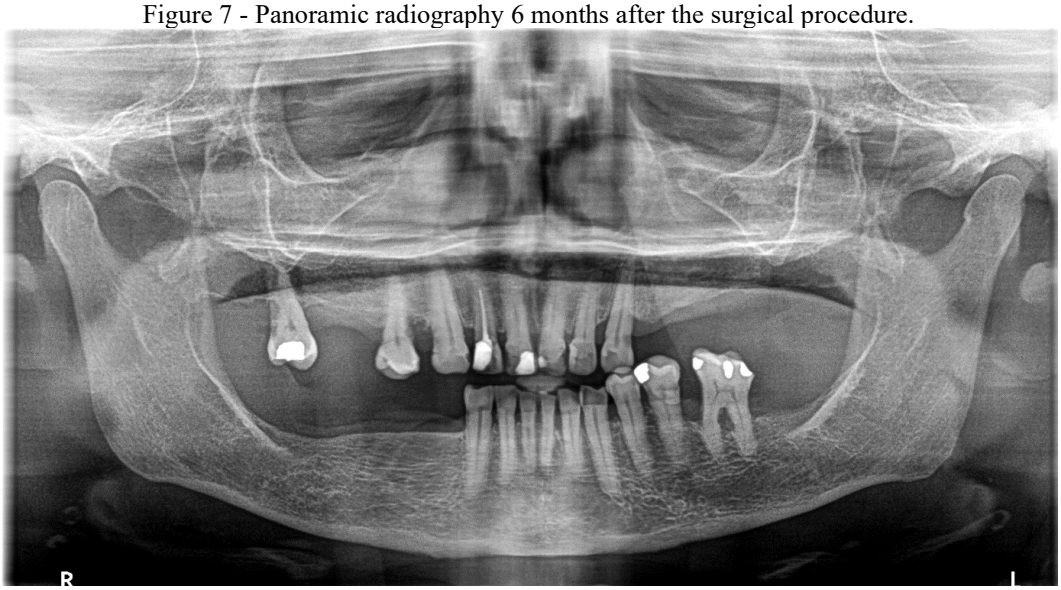
Figure 6 - Follow-up of the case 3 months after surgery.



Source: Authors (2023).

After 6 months, a new panoramic X-ray was requested to evaluate the bone repair process. After analysis of the imaging test, no changes were observed in the healing process (Figure 7).

Figure 7 - Panoramic radiography 6 months after the surgical procedure.



Source: Authors (2023).

4 DISCUSSION

The etiopathogenesis of OMB remains unknown. Several studies, both in animals and humans, suggest that antiresorptive medications such as bisphosphonates (BFs), associated with inflammation or infection, may be responsible for the induction of OMB (Gridelli, 2007). An increase in the life expectancy of the population is observed, which consequently leads to an increase in the number of elderly patients with bone pathologies such as osteoporosis and cancer. As a result, the number of patients benefiting from this BF therapy also increases (Damasceno et al., 2022; Gridelli, 2007).

Undoubtedly, there is a need for a greater understanding of the mechanisms of action of BFs and their potential risk factors. Data suggest that the risk of OMB is considerably higher in the group of malignancies than in the group of osteoporosis. Regardless of the indications for therapy, the duration of antiresorptive use is a risk factor (Pereira et al., 2022; Ruggiero et al., 2022). Recent estimates demonstrate that the risk of OMB among osteoporosis patients exposed to BFs after tooth extraction ranges from 0% to 0.15%, while for cancer patients exposed to bisphosphonates, the risk of developing OMB after tooth extraction ranges between 1.6% to 14.8% (Ruggiero et al., 2022).

It is now known that more invasive dental procedures have a strong correlation with the prevalence of OMB. In this sense, tooth extraction is considered the main procedure associated with the development of this condition. Periodontal disease, due to its highly inflammatory nature, is also a significant risk factor for BMO. In addition, ill-fitting prostheses are considered risk factors. In addition, concomitant use of BFs and corticosteroids is related to a higher risk of OMB (Ruggiero et al., 2022). It is important to highlight that the duration of BF use is directly related to the increased risk of OMB (Dorigan et al., 2021; Barasch et al., 2011).

OMB has a varied clinical appearance and can manifest asymptomatically for weeks, months, and even years. However, necrotic bone exposure may also occur, associated with pain and suppuration

(Carneiro et al., 2020; Mourão et al., 2013). Several signs and symptoms precede its clinical manifestations, such as pain, erythema, ulceration, edema in the adjacent mucosa, and tooth mobility (Vasconcelos et al., 2023; Monte et al., 2023). Most of the time, the diagnosis of BMO is made by means of clinical-radiographic analysis. The stages of clinical presentation of this pathology are divided based on symptomatology and image analysis (Ruggiero et al., 2022; Meneguini et al., 2017), as shown in Chart 2.

Chart 2 - Clinical Stages of Osteonecrosis of the Jaws Associated with the Use of Bisphosphonates

STAGE	CLINICAL CHARACTERISTICS
PATIENT AT RISK	Asymptomatic, but the patient is being treated with oral or intravenous BF's
STAGE 0	No clinical evidence of necrotic bone. However, the patient presents with nonspecific symptoms or radiographic findings, e.g. Toothache without odontogenic cause, bone resorption not associated with periodontal disease; Periodontal fistula not associated with pulp necrosis.
STAGE 1	Exposure of necrotic bone in patients, but without clinical evidence of infection
STAGE 2	Exposure of necrotic bone in patients with painful symptoms and clinical evidence of infection
STAGE 3	Exposure of necrotic bone in patients with painful symptoms, infection and presence of at least one of the following symptoms: 1) exposure of necrotic bone that extends beyond the alveolar region, resulting in pathological fracture; 2) Extraoral fistula; 3) Oroantral or oronasal communication; 4) Osteolysis that extends to the lower edge of the mandible or floor of the sinus.

Source: Adapted from Vasconcelos et al. (2023).

The American Association of Oral and Maxillofacial Surgeons (AAOMS) has proposed a protocol of therapeutic management strategies, in which there are therapeutic measures for each stage of OMB. As the stage of the disease progresses, treatment modalities become more aggressive. However, there is no consensus in the literature on which treatment modality is more effective, ranging from conservative approaches, such as the use of antimicrobial agents, hyperbaric oxygen therapy, laser therapy, superficial debridement, to more radical approaches, such as en bloc bone resections, which are performed only in stage 3 of OMB (Ruggiero et al., 2014; Ruggiero et al., 2022), as shown in Table 3.

Chart 3 - Therapeutic management strategies of the American Association of Oral and Maxillofacial Surgeons.

THERAPEUTIC MANAGEMENT STRATEGIES	
STAGE 0	The recommended treatment should be symptomatic only, including the use of medications for chronic pain and the use of antibiotics when necessary
STAGE 1	The use of antiseptic mouthwashes, such as the use of 0.12% chlorhexidine, and periodic clinical monitoring are recommended.
STAGE 2	Irrigation with antiseptics and antibiotic therapy with penicillin derivatives are effective; however, refractory or resistant cases may require prolonged use of antibiotics and even intravenous antibiotic therapy.
STAGE 3	Surgical resection is reserved for patients at this stage

Source: Adapted from Ruggiero et al. (2022).

It is important to emphasize preventive management strategies such as dental visits prior to the initiation of antiresorptive therapies. Preventive management strategies include surgical procedures prior to the start of therapy, an adjustment of the oral environment, along with oral hygiene instruction and regular visits to the dentist (Almeida et al., 2021; Fernandes et al., 2022). After the initiation of antiresorptive therapy, surgical procedures should be planned to cause minimal trauma, including the surgical technique employed, choice of instruments, and antimicrobial prescription (Ruggiero et al., 2022).

A conservative therapeutic management strategy that has been gaining ground in postoperative follow-up is low-level laser therapy, as this modality is capable of modulating cell metabolism and improving wound healing and reducing pain. The biostimulant effects of laser irradiation expand the organic matrix of bone and elevate the mitotic index of osteoblasts, increasing their proliferation and differentiation. Because of this, there is an increase in the amount of differentiated osteoblastic cells, also increasing their activity, thus accelerating the process of bone neoformation (Weber et al., 2016).

5 FINAL THOUGHTS

Bisphosphonates (BFs) are often chosen as first-line drugs to treat various bone diseases and their use is becoming increasingly common. Preventive treatment plays a key role in reducing the chances of developing osteonecrosis of the jaws. Currently, there are still no well-defined therapeutic dental protocols for the treatment of OMB, which reinforces the importance of prevention as the best approach to address this condition. It is critical that patients who will start therapies with antiresorptive drugs undergo prior dental care as part of the treatment plan. In addition, further studies are needed to better understand the etiopathogenesis of OMB, with the aim of reducing its occurrence and establishing defined treatment protocols to deal with this condition.

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