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Maxillary osteonecrosis induced by antiresorptive medication (bisphosphonate) in a patient with multiple myeloma - Case report

Osteonecrose Maxilar Induzida por medicamento anti-reabsortivo (Bisfosfonato) em Paciente Portador de Mieloma Múltiplo – Relato de caso

Osteonecrosis maxilar inducida por medicación antirresortiva (bisfosfonatos) en un paciente con mieloma múltiple - Reporte de caso

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Abstract

Objective: to describe the clinical case of a patient with multiple myeloma, who developed maxillary osteonecrosis induced by anti-resorptive medication (bisphosphonate) submitted to

a conservative and surgical therapeutic approach and subsequent prosthetic rehabilitation. Patients and methods: the case report is presented based on a simple review of the literature and clinical experience for the diagnosis, clinical staging of the lesion, carrying out the excision of the necrotic bone, debridement, lesion control and making a obturator prosthesis. Results: Despite the difficulty offered by the pathological condition and continuous use of medication, the treatment employed was successful, restoring health and providing a better quality of life to the patient, which allowed the obturation prosthesis to be made in the 8-month postoperative period. Conclusion: The result obtained emphasizes the importance of knowledge of the staging of the lesion for the application of the treatment protocol, in addition to recognizing patients at risk for the practice of prevention in dental treatments.

Keywords: Osteonecrosis; Maxilla; Biphosphonate- associated osteonecrosis of the jaw.

Resumo

Objetivo: descrever o caso clínico de uma paciente portadora de mieloma múltiplo, a qual desenvolveu osteonecrose maxilar induzida por medicamento anti-reabsortivo (bisfosfonato) submetida à abordagem terapêutica conservadora e cirúrgica e posterior reabilitação protética. Pacientes e métodos: o relato do caso é apresentado com base em uma revisão simples da literatura e experiência clínica para o diagnóstico, estadiamento clínico da lesão, realização da exérese do osso necrótico, debridamento, controle da lesão e confecção de prótese obturadora. Resultados: Apesar da dificuldade oferecida pela condição patológica e uso contínuo da medicação, o tratamento empregado apresentou sucesso, restabelecendo a saúde e proporcionando maior qualidade de vida a paciente, o que permitiu a confecção da prótese obturadora no pós-operatório de 8 meses. Conclusão: O resultado obtido enfatiza a importância do conhecimento do estadiamento da lesão para aplicação do protocolo de tratamento, além de reconhecer os pacientes de risco para a prática da prevenção nos tratamentos odontológicos.

Palavras-chave: Osteonecrose; Maxila; Osteonecrose associada a bifosfonatos.

Resumen

Objetivo: describir el caso clínico de un paciente con mieloma múltiple, que desarrolló osteonecrosis maxilar inducida por medicación antirresortiva (bisfosfonatos) sometido a un abordaje terapéutico conservador y quirúrgico y posterior rehabilitación protésica. Pacientes y métodos: se presenta el caso clínico en base a una simple revisión de la literatura y experiencia clínica para el diagnóstico, estadificación clínica de la lesión, realización de la

exéresis del hueso necrótico, desbridamiento, control de la lesión y realización de una prótesis de obturación. Resultados: A pesar de la dificultad que ofrecía la condición patológica y el uso continuado de la medicación, el tratamiento empleado fue exitoso, devolviendo la salud y proporcionando una mejor calidad de vida al paciente, lo que permitió realizar la prótesis de obturación en el postoperatorio de 8 meses. Conclusión: El resultado obtenido enfatiza la importancia del conocimiento de la estadificación de la lesión para la aplicación del protocolo de tratamiento, además de reconocer a los pacientes en riesgo para la práctica de la prevención en los tratamientos dentales.

Palabras clave: Osteonecrosis; Maxilar; Osteonecrosis de los maxilares asociada a bifosfonatos**.**

1. Introduction

Biphosphonates are antiresorptive drugs wich belong to a class of drugs widely used in patients with osteoporosis, Paget's disease, metastatic cancer, multiple myeloma, in addition to reversing the hypercalcemia of the malignanci of tumors, promoting the apoptosis of the osteoclasts (Conte-Neto, Bastos, Spolidorio, Marcantonio & Marcantonio, 2012; Arantes, Silva, & Lazaretti-Castro, 2010; Griz, Bandeira, Assunção, & Bandeira, 2006; Fliefel, Tröltzsch, Kühnisch, Ehrenfeld, & Otto, 2015). It can be administered orally or intravenously, according to the patient's condition, suppressing activation and inducing osteoclast apoptosis. Thus, it helps prevent pathological fractures and other skeletal complications (Marx, Sawatari, Fortin, & Broumand 2005). The most commonly used are Zoledronate, Pamidronate, Alendronate e Ibandronate (Fliefel et al., 2015).

Osteonecrosis of the jaws induced by antiresorptive drugs is a complication characterized by previous use of the drug, intraoral or extraoral bone exposure for more than eight weeks, with or without cutaneous fistula (Ruggiero et al., 2014). Clinically, the disease can manifest spontaneously or due to an invasive surgical procedure, such as tooth extraction, periodontal surgery or installation of dental implants. Furthermore, maxillofacial trauma, infection and poor hygiene are predisposing factors to the development of the disease (Kos, Kuebler, Luczak, & Engelke, 2010).

The staging of this condition can be classified in stage 0: without clinical evidence of necrotic bone, but with clinical inespecifics findings, radiogrphic changes and simptoms; stage 1: necrotic bone exposure or fistulas that probe to bone in assimptomatic patients or without evidence of infection; stage 2: necrotic bone exposure or fistulas that probe to bone

associated with infection, as evidenced by pain, erythema in the exposure region, with or without pus dreinage; stage 3: necrotic bone exposed or fistulas that probe to bone in patients with pain, infection and at least one of the following items (exposure and bone necrosis beyond alveolar region, resulting in pathologic fracture, extraoral fistula, oroantral communication, or osteolysis that extends to mandibular base or maxillary sinus floor (Ruggiero et al., 2014).

Treatment of multiple myeloma whit biphosphonates, aiming to inhibit the osteoclastic activitie and reduce the skeletal repercussion of the disease, limits its evolution, pain, pathological fractures and associated hypercalcemias. Consequently, the morbidity becomes reduced. However, in these cases, the development of osteonecrosis of the jaws indiced by bisphosphonates has already been described in the literature, with rates of 46% (Krstevska et al., 2015).

Therefore, this article presents an approach for the treatment of osteonecrosis in the maxilla as a consequence of the use of bisphosphonate in the treatment of multiple myeloma.

2. Methods

This case repot is presented based on a simple literature review with the descriptors (Osteonecrosis; Maxilla, Biphosphonate- Associated Osteonecrosis of the jaw) in Pubmed, Web of Science, and Embase, and included references until 20 years, similar to Conte-Neto et al. (2011). For this conduction, the Ethics Committee was no needed, but the informed consent was signed by the patient.

3. Case Report

A 82-year-old female patient was referred to the Oral and Maxillofacial Surgery team to evaluation of a lesion in right maxila with one year of progression. Patient reported having received two monthly 4 mg Zoledronate infusions, and afterwards, a monthly infusion up to the sixth month. In addition, she reported use of Meloxicam, Thalidomide and Prednisone.

Oroscopy, showed 4 mm necrotic bone exposure in right maxila, region that supported a poorly adapted total prosthesis (Figure 1). It was also observed an oroantral communication, fetid odor, mouth opening limitation and pain during palpation. The previous incisional biopsy report revealed bone infiltration with plasmocytic cells, suggesting multiple myeloma.

Laboratorial exam presented no changes. Panoramic radiography evidenced area of bone sequestration evolving right maxila with pathological fracture (Figure 2).

Figure 1. Initial aspect of necrotic bone tissue exposure and oroantral communication.

Source: Authors.

Figure 2. Panoramic radiography, showing the region of bone sequestration in the right maxilla, with pathological fracture.

Source: Authors.

Weekly irrigation with 0.12% chlorhexidine, and maintenance of mouthwash twice a day with 15 ml were proposed. After two weeks, the surgery to removal of necrotic bone was performed, with lesion debridement, ostectomy and cleavage until complete removal (Figure

3)**.** Samples were send to histopathological analysis (Figure 4), which later confirmed necrotic bone, favoring the conclusive diagnosis of maxillary osteonecrosis induced by biphosphonate. Compatible with stage 3. After debridement, the simptoms of pain and fetid odor were eliminated, providing better social interaction and quality of life.

Figure 3. Clinical aspect after debridement, ostectomy and necrotic bone cleavage.

Source: Authors.

Figure 4. Necrotic bone sample sent for histopathological analysis.

Source: Authors.

After eight months of postoperative with satisfactory healing (Figure 5), an obturator

prosthesis was made, aiming improve chewing and reduce food retention in oroantral comunication (Figure 6). After the prosthesis installation, patient maintained bimontly follow-up to for local evaluation and hygiene. Currently, with two year of follow-up, patient is recovered from her inicial debilitation and the oroantral communication is in excellent condition (Figure 7). The patient remains on Thalidomide therapy with daily doses to treatment of multiple myeloma.

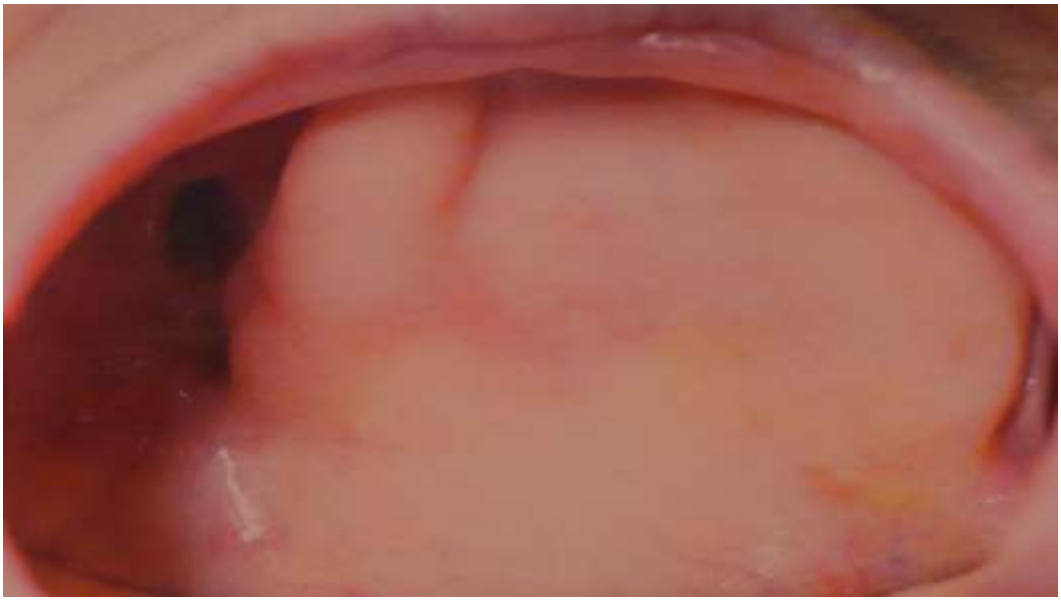
Figure 5. Postoperative clinical appearance at 8 months, showing satisfactory healing.

Source: Authors.

Figure 6. Obturator prosthesis designed to optimize masticatory function and limit food retention in the region of oroantral communication.

Source: Authors.

Figure 7. Satisfactory clinical appearance at 2 years postoperatively.



Source: Authors.

4. Discussion

Most cases of biphosphonate induced osteonecrosis is associated with treatment of a malignancy condition, particularly the multiple myeloma (Fliefel et al., 2015; Wang, Kaban, Strewler, Raje, & Troulis, 2007) however, it is seen more frequently in the mandible (Fliefel et al., 2015; Ruggiero, Mehrotra, Rosenberg, & Engroff, 2004) although this case has developed in maxilla. Conditions as osteoporosis, breast cancer and prostate cancer are frequently encountered (Escobedo et al., 2020). In the present case, the 4 mg Zoledronate therapy in mothly doses during six months, for treatment of her base disease, was enough to development of osteonecrosis, once this medicine is among the most potent antiresorptives, due to the presence of nitrogen in its heterocyclic ring (Russel, Watts, Ebetino & Rogers, 2008), in addition to the intravenous administration route being strongly associated with the development of this condition. Conversely, the intravenous route of administration appears to have little influence on the development of the condition (Escobedo et al., 2020; Guazo et al., 2017)

The use of corticosteroids, chemotherapy, and Thalidomide, associated with biphosphonate therapy, denotes a fator of potential systemic risk for development of osteonecrosis (Wang, Goodger, & Pogrel, 2003; Zervas et al., 2006). In this way, therapy with Prednisone, Meloxicam, and Thalidomide, may have increased the patient propensity for complication. Although development of osteonecrosis can occur spontaneously, or in cases

of surgical procedures, extensive use of corticosteroid, which can contribute to delaying healing and consequently, resulting in osteonecrosis, intense soft tissue trauma with local pain, and irritation due to prosthetic maladjustment proved to be a delicate fator wich should receive atention to avoid complications, such as the one presented (Ruggiero et al., 2014; Wang et al., 2003). Control of disease progression in most cases is obtained with antibiotictherapy, pain control, mouth rinse with mouthwash, as chlorhexidine 0.12%, in addition to debridement sessions until complete removal (Ruggiero et al., 2014). In this case, the inicial conservative treatment was followed by debridement and ostectomy in short sessions, following the proposed protocol, once radiographically the bone sequestration had no insertion.

Cases of maxillary osteonecrosis require addicional care, once the resection of necrotic bone can result in extensive oroantral communication, making it necessary to make a permanent obturator prosthesis (Marx, 2009) similar to the case presented, in wich after advanced stage of healing the prosthesis was made aiming to optimize chewing and reducing local food retention.

Interruption of bisphosphonate therapy, in patients who will be submitted to debridement and resection, has no evidence of presenting only benefits and should be discussed with the oncologista of the case (Curi et al., 2011). In this way, in some therapeutic protocols, the use of biphosphonate is not interrupted, obtaining, however, success in osteonecrosis treatment (Curi et al., 2011). Furthermore, are necessary clarify the success rates, in long term, of surgical and conservative treatments. As a way to prevent or reduce the incidence of osteonecrosis of the jaws induced by bisphosphonates, it is necessary to apply preventive measures, studying the dental condition risk factors and possible forms of treatment, avoiding invasive procedures in patients at risk (Ruggiero et al., 2014).

5. Conclusion

Management of patients using biphosphonates, in daily clinic, must be attentive, with amusing anamnesis, wich allows to conduct prevention in risky patients. Once the disease is installed, knowledge of the staging of the lesion for application of the treatment protocol is essential to obtain success, as presented.

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