

Case Report

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Osteonecrosis of the Jaw Related to Oral Bisphosphonate Treatment: A Clinical Case

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ABBREVIATIONS: ONJ: Osteonecrosis of the Jaw; AAOMS: American Association of Oral and Maxillofacial Surgeons.

INTRODUCTION

Bisphosphonates are inhibitors of osteoclastic activity and hence cause inhibition of bone resorption.¹⁻³ These drugs, which are synthetic analogy of natural pyrophosphate, have proven their effectiveness in the treatment of diverse metabolic bone diseases related to quantitative alterations, as is the case of osteoporosis,⁴⁻⁶ or qualitative ones, as in Paget's disease.⁷ The most common way for their administration is orally.⁵ These anti-resorptive drugs cause an increase of bone mineral density and a quick decrease of fracture risk.⁸⁻¹³ They are also effective in oncology patients (breast cancer, prostate cancer, lung cancer, and multiple myeloma, among others).¹⁴⁻¹⁹ Additionally, these medicines reduce the symptoms of bone pathology (bone pain, delay of the first new bone event, reduction in fracture appearance).^{4,17-19} They are normally administered intravenously. Bisphosphonates have anti-cancer effect alone or in combination with other chemotherapy treatments, as they maximize antineoplastic effects.²⁰ In pediatrics, they are used in the treatment of diseases related to abnormal calcinosis or ectopic bone formation, as is the case of osteogenesis imperfect.²¹⁻²³

Based on a total of 36 cases, Marx, et al. reported an adverse effect of the use of these drugs, which is called Osteonecrosis of the Jaw (ONJ).²⁴ Ruggiero, et al. further reported that of a total of 63 cases of patients with ONJ, 11.1% suffered originally from osteoporosis.²

Since then, numerous medical entities, scientific associations and expert committees have researched this adverse effect.²⁵⁻²⁸ It is known that it can appear spontaneously,¹⁶ with an estimated prevalence of 50% in the case of intravenously administered bisphosphonates and 30% in the case of oral administration.²⁹ On the other hand, it is usually associated with a trigger that invades the integrity of the bone tissue (e.g. tooth extractions, implants, periapical surgery³⁰⁻³⁶ or mucous tissue (e.g. rubbing of poorly adapted prosthesis, or taking dental impressions).^{37,38} There are factors inherent to the drug that can increase the risk of ONJ, such as bisphosphonate type, potency, or length of treatment. Usage of corticoids can also augment the risk of suffering from this complication. Additionally, there are factors inherent to the patient, such as

certain systemic pathologies, presence of dental inflammatory pathologies, or ageing.^{1,28-35,36,37-40}

Certain measures and attitudes exist that can decrease the incidence of this pathology. Referral to a dentist for an oral-dental check and elimination of focuses that can put the patients at risk is advised when they are about to receive this therapy, since this oral and maxillofacial complication decreases the patients' quality of life and involves an important health cost, as well as monetary expenditure for the patient.⁴¹⁻⁴⁶

A traumatic interventions are important in order to minimize the incidence of this dreaded effect in patients already undergoing treatment with bisphosphonates.^{37,46-48}

Once the injury is set, some experts think that the clinical expressions or symptoms of ONJ can improve by temporarily or permanently discontinuing the bisphosphonates medication. They advise conservative or minimally aggressive treatments combined with long-lasting antibiotic therapy.^{45,49-51}

It is desirable for specialists involved in administration of these therapies to count on studies designed with consensual, globally unified protocols that provide them with useful, validated information.

In this study, we present a case of ONJ in a patient undergoing oral bisphosphonates treatment.

CLINICAL CASE

A sixty-two-year-old woman undergoing oral bisphosphonate (Boniva®) treatment for osteoporosis for over 3 years. The patient attended a private clinic for right top canine extraction due to mobility. Six weeks later, she reported pain. During exploration, a gingival fistula with discharge (Figure 1) was observed, and therefore an intraoral radiography was performed (Figure 2).

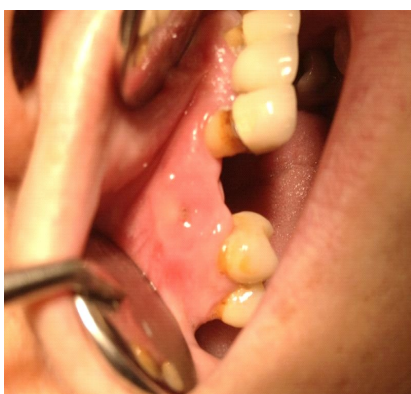


Figure 1: Image of intraoral injury. Gingival fistula can be observed.

Analgesic (Paracetamol 650 mg) and antibiotic (Amoxicillin/Clavulanic acid 1000 mg/125 mg, 2 pills every 12 hours) treatment was established for 15 days, combined with home mouthwash using chlorhexidine 0.12%.^{37,52-53} An appointment was set for clinical assessment.



Figure 2: Radiologic image of the number 13 post-extraction socket. Osteolytic lesion can be observed.

After 8 weeks of persistent symptoms, a case of post-extraction ONJ was confirmed, American Association of Oral and Maxillofacial Surgeons (AAOMS) 2006.^{15,28,54-56} The same conservative treatment was maintained for 15 more days, her prescription doctor was advised to withdraw the bisphosphonate medication and another appointment was made for a new control check.³⁷ Finally, it was decided to remove the falling necrotic tissue by surgical sequestrectomy,^{1,53} performed with the use of local anaesthesia. The underlying bone was not operated on except for a slight curettage (Figure 3).

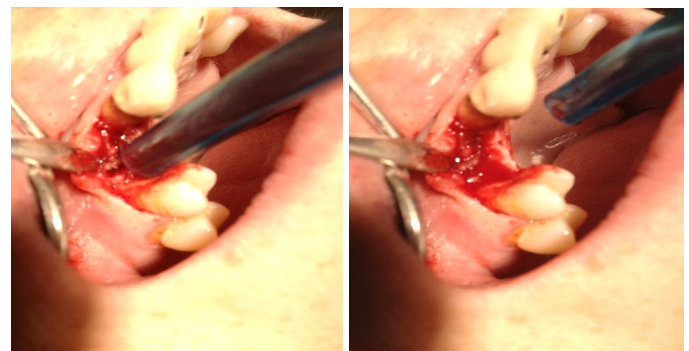


Figure 3: Surgical treatment: Sequestrectomy. Removal of necrotic bone.

It was a case of ONJ at clinical stage II, according the American Association of Oral and Maxillofacial Surgeons (AAOMS) classification.^{2,57} The case evolved favourably, and with complete resolution.

DISCUSSION

Patients attending dental consultations with previous records of undergoing or having undergone oral bisphosphonates treatment (for postmenopausal, glucocorticoid, or male osteoporosis) are becoming more frequent.^{3,8,9,58,59,60,61}

The incidence of ONJ derived from oral bisphosphonates is lower than in the case of intravenous administering. Additionally, existing literature describes the extent and severity of these injuries to be less significant in the case of orally administered bisphosphonates, having a more favourable evolution and frequently ending in healing, in contrast to the more arduous evolution of lesions associated with intravenous therapy.^{1,3,29,37,62,63}

Marx et al recommend suspending bisphosphonates treatment for at least two months previous to an intervention. This attempts to normalize the rate of bone turnover, owing to the inhibitory effect of the osteoclasts and a vascular necrosis (anti-angiogenic effect).^{24,43,45} However some authors⁴⁴ disagree since the bisphosphonate remains embedded in the bone tissue for long periods of time (up to 12 years), and others consider that a critical concentration is necessary for this oral-jaw complication to occur.⁶⁴

ONJ is a clinical entity related to: an alteration of the blood supply, an inhibition of the osteoblastogenesis, and the apoptosis of osteocytes. All the above result in a vascular necrosis of the bone tissue and frequently in super infection and bacterial colonization as well.^{37,64,65} Strains of the genus *Actinomyces* have been found (specifically *A. naeslundii*, *A. israelii*).⁶⁶

Overall, in order to stabilize the symptoms some authors propose a conservative treatment of the lesions, continued long-lasting antibiotic therapy, and discontinuation of bisphosphonates when possible.^{49,51-52} Other authors propose the application of plasma rich in growth factors as an alternative therapy in order to stimulate the angiogenesis and repair of the local bone tissue.⁶⁷⁻⁶⁹

Decisions should be made by a complete multidisciplinary team (oral and maxillofacial surgeon, oncologist, and rheumatologist) on the basis of the current clinical stage according to the AAOMS.^{51,70}

CONCLUSIONS

Informing the pharmacovigilance service is important in these clinical cases in order to know the real incidence of these lesions.

It is imperative to refer to the dentist all patients that are going to be treated with bisphosphonates, whether orally or intravenously, in order to eliminate possible risk factors to subsequently suffer ONJ.

CONFLICTS OF INTEREST

The authors state that they have no conflicts of interest.

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