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Letter to the Editor

OSTEONECROSIS OF THE MANDIBLE ASSOCIATED WITH ZOLEDRONATE THERAPY

F. Fiori[1] and A. Romano[2]

[1]Independent Researcher, Portici Napoli, Italy;
[2]Independent Researcher, Marano di Napoli, Italy

Correspondence to:
Antonio Romano, DDS
Multidisciplinary Department of Medical-Surgical and Dental Specialties,
University of Campania Luigi Vanvitelli,
Naples, Italy
e-mail: doctorantonioromano@gmail.com

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INTRODUCTION

Bisphosphonates are synthetic compounds that mimic the structure of a naturally occurring substance called inorganic pyrophosphate (1). They have a high affinity for hydroxyapatite, the mineral component of bone tissue, and bind to regions of bone with high turnover (2); this allows them to effectively inhibit the activity of osteoclasts, which are the cells responsible for breaking down and resorbing bone tissue (3). As a result, bisphosphonates can be used to treat various bone disorders by preventing bone resorption at the molecular, cellular, and tissue level (4). The standard of care for treating osteopenia and osteoporosis, as well as Paget's disease and Osteogenesis imperfecta, still involves oral bisphosphonates (5). Additionally, intravenous bisphosphonates such as pamidronate (Aredia) and zoledronic acid (Zometa) are also used for these conditions (6).

Multiple myeloma and metastatic bone lesions are commonly treated with pamidronate and zoledronic acid, effectively preventing skeletal complications like pathologic fractures and hypercalcemia of malignancy (7). The action of bisphosphonates involves several mechanisms, such as inhibiting the differentiation of osteoclast precursors, promoting apoptosis of osteoclasts, and stimulating the release of osteoclastic inhibitory factors to osteoblasts (8). Additionally, these compounds can interfere with cellular metabolism by resembling adenosine triphosphate (ATP), disrupting cellular processes and further reducing osteoclast activity (9).

While bisphosphonates offer various therapeutic benefits, a notable complication that can arise in some patients receiving these drugs is bisphosphonate-related osteoradionecrosis of the jaws (BRONJ) (10). This condition, first identified and reported by Marx in 2003 (11), can have significant consequences for affected individuals. The onset of symptoms in BRONJ can be unpredictable, making it difficult for clinicians to diagnose and manage the condition promptly (12). This

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variability in presentation often means that the disease is only identified once it has become symptomatic, posing a challenge for effective diagnosis and management (13). The following report describes a case of BRONJ involving the lower maxilla in a patient suffering from multiple myeloma.

CASE REPORT

A 74-year-old female patient reported pain and swelling in the left lower jaw that has been present for several weeks.

The patient's medical history reveals that she has a history of diabetes, hypertension, and kidney failure, in addition to the previous history of multiple myeloma and treatment with intravenous zoledronate for two years. Upon local examination, it was observed that the patient had partial edentulism and alveolar mucosal dehiscence in the left body of the mandible. In addition, there was evidence of an exposed bone section that appeared yellowish-white in colour close to the posterior mandibular region, next to the roots of the first left lower molar (Fig. 1).

The orthopantomogram revealed the presence of diffuse osteolytic lesions and erosion on the left side of the mandible, affecting both the buccal and lingual cortical plates (Fig. 2). The size of the exposed bone gradually expanded, and the area became increasingly more sensitive to pain. The first-line conservative measures, comprising administration of chlorhexidine 0.2% mouthwash and oral antibiotics, resulted in a reduction of pain but failed to bring about resolution of the denuded bone.

Considering the progressive nature of the BRONJ, surgical intervention of sequestrectomy was subsequently planned. Using a large round burr and saline irrigation, the necrotic maxillary alveolus was excised until healthy, actively bleeding bone was achieved. Subsequently, a biopsy was performed to affirm the bone's vitality and exclude any malignancy. One year later, the patient reported discomfort, swelling, and pain, prompting the need for further clinical evaluation. Cone beam computed tomography revealed loss of integrity and diffused erosion of the lingual cortical bone. (Fig. 3).

The therapeutic approach was based on administering amoxicillin + clavulanic ac 1gr x 2 /day, metronidazole 1000 mg/day for 15 days, and oral chlorhexidine (0.12%) rinses three times a day. Intravenous Zoledronate was stopped. Spontaneous bone sequestration eventually occurred a few months later, followed by the mandibular bone's stable and painless mucosal coverage. At follow-up after one year, the patient was disease-free (Fig. 4).

DISCUSSION

There are several possible causes of swelling in the jaws.

Fig. 1. *Exposed bone section that appeared yellowish-white in color close to the posterior mandibular region, next to the roots of the first left lower molar.*

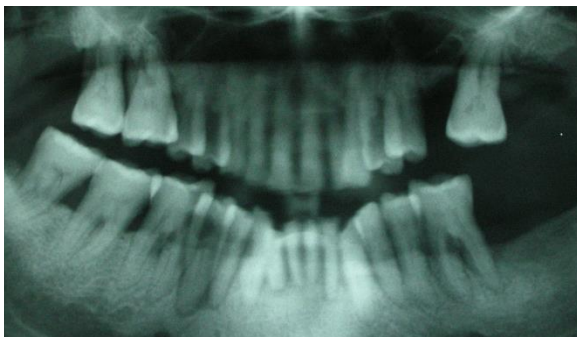

Fig. 2. *The orthopantomogram revealed the presence of diffuse osteolytic lesions on the left side of the mandible.*

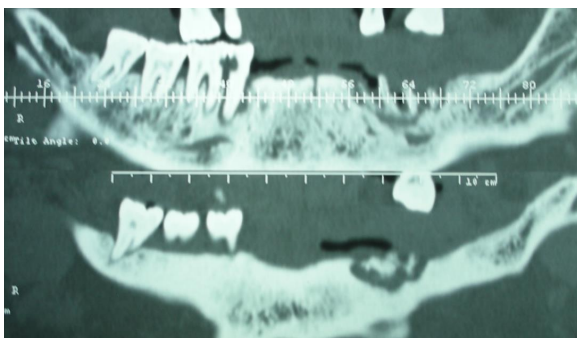

Fig. 3. *Cone beam computed tomography after one year.*

Fig. 4. *Follow-up after one year.*

An infection in the jaw can cause swelling, pain, and tenderness due to poor oral hygiene, dental caries, or a periodontal abscess (14). Furthermore, disorders of the salivary glands, such as sialadenitis or sialolithiasis, can cause swelling in the jaw (15). Benign or malignant tumors and cysts can develop in the jaw and lead to swelling (16). Also, swelling and tenderness may occur in patients with temporomandibular joint (TMJ) disorders (17). Lastly, a fracture, an injury, or other trauma to the jaw can cause swelling (18).

In the abovementioned case, the patient's medical history reveals a 2-year treatment course of intravenously administered bisphosphonates, specifically zoledronic acid, after diagnosing multiple myeloma. The patient presented with clinical symptoms of swelling and exposed non-vital bone in the left alveolar region. This presentation is consistent with the possibility of jaw osteonecrosis, a rare but known complication associated with the long-term use of bisphosphonates.

An oral-maxillofacial surgeon first reported osteonecrosis of the maxilla and mandible as a complication of intravenous bisphosphonate treatment in 2003 (11). Following this, osteonecrosis of the jaw was also reported in patients taking oral bisphosphonates for osteoporosis (19). Since then, the number of reported cases of BRONJ has increased, but the estimated incidence varies considerably from less than 1% to 18.6% (20). The drug's potency, administration route, and therapy duration are determining factors, with zoledronate (Zometa) having the highest reported incidence and the oral forms having a relatively low incidence (21). Both dental and oncological practitioners must possess a thorough awareness of the significant risk of developing osteonecrosis of the jaw (ONJ) in patients who are receiving bisphosphonate therapy (22).

Hence, the reported case re-affirms that dental and oncological professionals must exercise caution when treating patients receiving BPs and provide appropriate education and monitoring to minimize the risk of ONJ development.

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