

Mandibular Osteonecrosis After Biphosphanates Therapy: An Atypical Clinical Presentation: A Case Report and Literature Review

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Abstract

Introduction : Osteonecrosis is a complication of long-term treatment with bisphosphonates (BP) occurring mainly in patients treated for bone metastases or multiple myeloma. However, a few rare cases have been observed during osteoporosis treatment. The mandible is the preferential location of this disease.

Presentation of the cases : We report the case of a 56-year-old patient treated for osteoporosis for 6 years with oral bisphosphonates who consulted for cutaneous-oral fistulas of the chin region. The imagery showed osteo-condensing and fistulated foci related to mandibular Osteonecrosis. After discontinuing bisphosphonates, the patient was put on long-term antibiotic and corticosteroid therapy and received hyperbaric oxygen therapy. The evolution after 5 months was favorable.

Discussion : During mastication, the maxillae are subjected to everyday stress that stimulates remodeling activity leading to greater incorporation of biphosphonates, promoting bone necrosis. The clinical presentation of the disease can range from a poorly healing socket after tooth extraction to massive jaw necrosis. Faced with this relatively rare but disabling and difficult-to-treat condition, it is essential to identify patients at risk and apply preventive measures.

Conclusion : Given the lack of objective data regarding the precise incidence, pathogenesis, and treatment of this complication, there is an urgent need for controlled studies to improve the management of these patients and ensure the best possible quality of life.

Keywords : AAOMS, Biphosphanates, Case report, Osteonecrosis.

Introduction

Osteonecrosis is a complication of long-term treatment with bisphosphonates (BP) occurring mainly in patients treated for bone metastases or multiple myeloma. However, a few rare cases have been

observed during osteoporosis treatment. Given the particularity of our study, which reports the case of a severe advanced form in a patient followed for osteoporosis under treatment with oral bisphosphonates.

Case report

We report the case of a 56-year-old female patient followed for osteoporosis for 6 years on oral biphosphonates (Alendronate), who consulted for pain in front of the mandible and dental mobility associated with dental avulsions for 1 year, with an evolution marked by the appearance of two superinfected skin fistulas in the mental and submental regions; stage 3 according to the classification proposed by the American Association of Oral and Maxillofacial Surgeons (AAOMS) (Table 1), (Figure 1).

An extension workup was performed, including an orthopantomogram, and a Denta-Scan showed osteo-condensing and fistulized foci related to mandibular Osteonecrosis. (Figure 2) After discontinuing bisphosphonates, the patient was put on long-term antibiotic therapy, corticosteroid therapy, mouthwash with chlorhexidine, and hyperbaric oxygen therapy. The evolution after 5 months was favorable.

Table 1: 2014 AAOMS Classification and Proposed Treatment Strategies

Stage	Description	Management
At risk	Asymptomatic patients with no apparent necrotic bone who have been treated with IV or oral antiresorptive or antiangiogenic drugs	- No treatment indicated - Patient education - See dentist regularly
Stage 0	- Non-specific symptoms or clinical/radiographic findings suggesting bone necrosis - No evidence of exposed necrotic bone, but sinus tract or fistula may be present	- Antibacterial mouth wash - Pain medication and antibiotics, if symptomatic* - Patient education
Stage 1	- No evidence of pain/infection - Exposed necrotic bone	- Antibacterial mouth wash - Follow-up every 3–4 months - Patient education
Stage 2	- Pain and/or infection - Exposed and necrotic bone or a fistula that probes to bone	- Antibacterial mouth wash - Pain medication and antibiotics* - Debridement - Patient education
Stage 3	- Exposed and necrotic bone or fistulas that probe to bone with evidence of infection and at least 1 of the following: - exposed necrotic bone extending beyond the region of alveolar bone - pathologic fracture - extraoral fistula - oral antral or oral nasal communication - and/or osteolysis extending to the inferior border of the mandible or sinus floor	- Antibacterial mouth wash - Pain medication and antibiotics* - Debridement - Patient education



Figure 1: Image of the patient showing cutaneous-oral fistulas

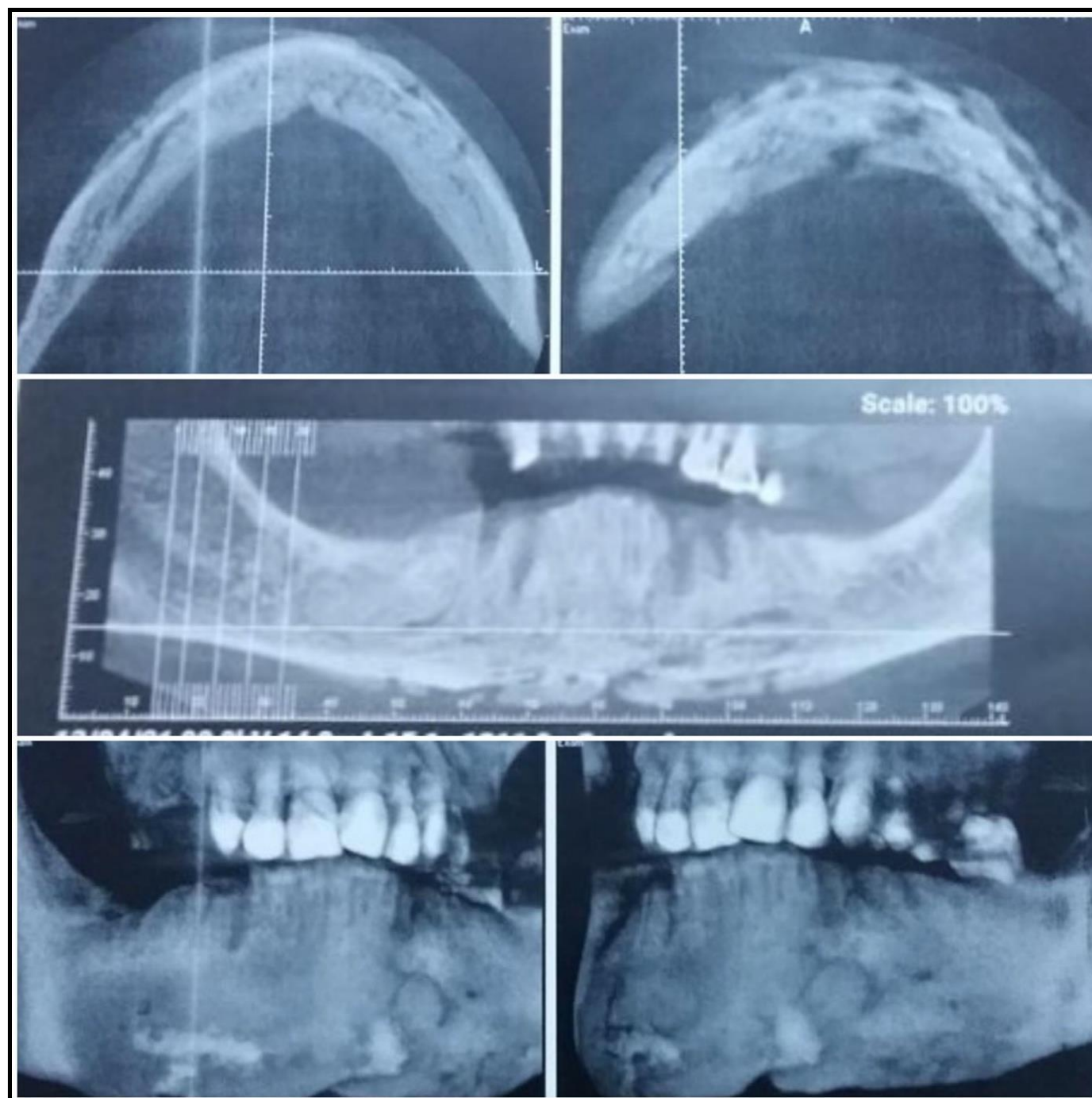


Figure 2: Scannographic images showing mandibular osteonecrosis with foci of bone lysis.

Discussion

BPs are synthetic analogs of pyrophosphates with a strong affinity for hydroxyapatite crystals.

A distinction is therefore made between first-generation bisphosphonates containing no nitrogen (etidronate, clodronate), first-generation amine derivatives (Alendronate, Pamidronate), and new-generation amine derivatives (zoledronic acid, risedronate) where the nitrogen is located on a heterocycle [1].

They are widely used in the symptomatic treatment of bone metastases and pathologies characterized by a deregulation of bone turnover, such as osteoporosis and Paget's disease.

Resorbed bisphosphonates bind to bone at sites of active metabolisms, such as the maxillomandibular region, under constant pressure and trauma, where they reach their therapeutic concentration [2,3]. These molecules inhibit hydroxyapatite crystals' dissolution and decrease bone remodeling and turnover [4,5]. During the bone resorption phase, PBs are internalized by osteoclasts and lead to their dysfunction.

Maxillomandibular osteonecrosis (MMO) is characterized by an area of exposed bone in the maxillofacial region that does not heal within 8 weeks of appropriate care in patients who have received or are

receiving PB and have not been treated with maxillofacial radiotherapy [6].

The most important risk factors are the dose and duration of exposure, especially if it is longer than 2 years, and the type of BP. The injectable form and the amino derivatives have higher toxicity. Therefore, most osteonecrosis is described on Zoledronate, reaching more than 10% of treated patients. Next, we find patients treated with Pamidronate, followed by Zoledronate, then Pamidronate, and lastly, Alendronate. One in ten necrosis would be due to oral bisphosphonate for osteoporosis [7-9].

The location is mandibular in 2/3 of cases. A previous extraction is demonstrated in 60 to 77% of cases¹. The average onset of bone necrosis after dental treatment is 6.6 months. The symptomatology is not specific, ranging from a poorly healing socket after dental extraction to massive jaw necrosis [10]. Complementary examinations to assess the severity, extension, and follow-up are primarily orthopantomogram and CT scan or Denta-Scan.

The treatment of these bone necroses is unsatisfactory. Local debridement maneuvers result in more significant denudation of the treated area. In addition, since the entire bone is affected, it is difficult to resect the affected area macroscopically with healthy margins, as

in osteoradionecrosis resections. Cover flaps lead to significant fistulas. Hyperbaric oxygen therapy does not improve the situation. Therefore, we are limited to chlorhexidine-based mouthwashes, antibiotics in case of superinfection, and painkillers on demand.

Conclusion

Given the lack of objective data regarding the precise incidence, pathogenesis, and treatment of this complication, more controlled studies are needed to improve the management of these patients and ensure the best possible quality of life.

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Removing bone spurs that injure the surrounding tissues is performed for the patient's comfort. Discontinuation of bisphosphonates is without effect since their bone half-life is estimated to be more than 10 years [9].

Informed consent: The patient has given free and informed consent.

Conflicts of interest: The authors declare no conflicts of interest.

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