

Mandibular Osteonecrosis after Biphosphanates Therapy: An Atypical Clinical Presentation: Case Report and literature Review

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Abstract

Introduction:

Osteonecrosis is a complication of long-term treatment with biphosphanates (BP) occurring mainly in patients treated for bone metastases or multiple myeloma. However, a few rare cases have been observed during per 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 biphosphanates who consulted for cutaneous-oral fistulas of the chin region. The imagery showed osteo-condensing and fistulated foci related to mandibular osteonecrosis. After discontinuation of biphosphanates, the patient was put on long-term antibiotic therapy, corticosteroid therapy and received hyperbaric oxygen therapy. The evolution after 5 months was favorable.

Discussion:

During mastication, the maxillae are subjected to regular stress that stimulates remodeling activity leading to greater incorporation of biphosphanates, promoting bone necrosis. The clinical presentation of the disease can range from a poorly healing socket after tooth extraction to massive necrosis of the jaw. Faced with this rather rare but disabling and difficult to treat condition, it is important 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 biphosphanates (BP) occurring mainly in patients treated for bone metastases or multiple myeloma. However, a few rare cases have been observed during per 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 biphosphanates.

Case report:

We report the case of a 56-year-old female patient followed for osteoporosis for 6 years on oral biphosphanates (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).



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

Stage	Description	Management
At risk	<ul style="list-style-type: none"> Asymptomatic patients with no apparent necrotic bone who have been treated with IV or oral antiresorptive or antiangiogenic drugs 	<ul style="list-style-type: none"> No treatment indicated Patient education See dentist regularly
Stage 0	<ul style="list-style-type: none"> Non-specific symptoms or clinical/radiographic findings suggesting bone necrosis No evidence of exposed necrotic bone, but sinus tract or fistula may be present 	<ul style="list-style-type: none"> Antibacterial mouth wash Pain medication and antibiotics, if symptomatic* Patient education
Stage 1	<ul style="list-style-type: none"> No evidence of pain/infection Exposed necrotic bone 	<ul style="list-style-type: none"> Antibacterial mouth wash Follow-up every 3-4 months Patient education
Stage 2	<ul style="list-style-type: none"> Pain and/or infection Exposed and necrotic bone or a fistula that probes to bone 	<ul style="list-style-type: none"> Antibacterial mouth wash Pain medication and antibiotics* Debridement Patient education
Stage 3	<ul style="list-style-type: none"> Exposed and necrotic bone or fistulas that probe to bone with evidence of infection and at least 1 of the following: <ol style="list-style-type: none"> 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 	<ul style="list-style-type: none"> Antibacterial mouth wash Pain medication and antibiotics* Debridement Patient education

Table 1 : 2014 AAOMS Classification and Proposed Treatment Strategies

An extension workup was performed including an orthopantomogram, and a Denta-Scan showed osteo-condensing and fistulized foci related to mandibular osteonecrosis. **(Figure 2)**

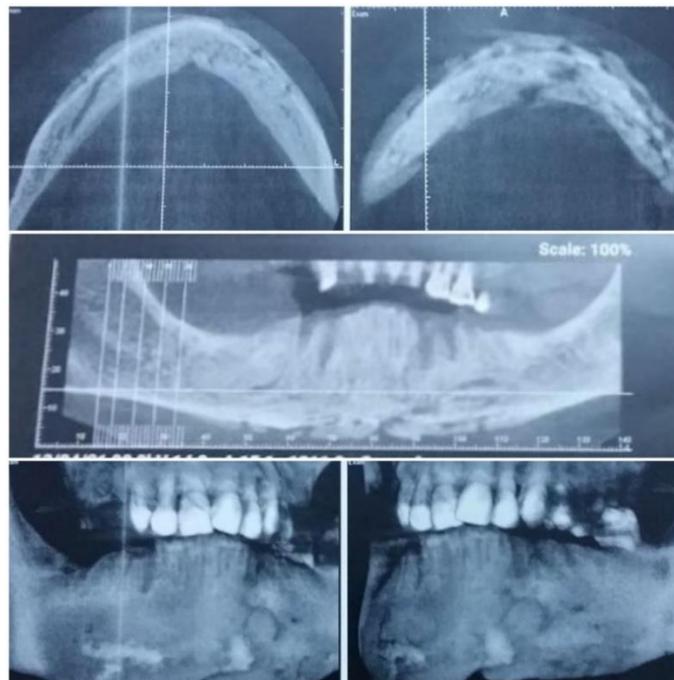


Figure 2: Scannographic images showing mandibular osteonecrosis with foci of bone lysis.

After discontinuation of 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.

Discussion:

BPs are synthetic analogues 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 metabolism, such as the maxillo-mandibular region, which is under constant pressure and trauma, where they reach their therapeutic concentration [2,3]. These molecules inhibit the dissolution of hydroxyapatite crystals and induce a decrease in bone remodeling and turnover [4,5]. During the bone resorption phase, PBs are internalized by osteoclasts and lead to their dysfunction.

Maxillo-mandibular 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 a higher toxicity. The majority of osteonecrosis is therefore 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 cases. The average time of onset of bone necrosis after dental treatment is 6.6 months. The symptomatology is not very specific, ranging from a poorly healing socket after dental extraction to massive necrosis of the jaw [10]. Complementary examinations performed 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 a 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 is the case in

osteonecrosis resections. Cover flaps lead to significant fistulas. Hyperbaric oxygen therapy does not improve the situation. We are therefore limited to the use of chlorhexidine-based mouthwashes, antibiotics in case of superinfection and painkillers on demand. The removal of 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].

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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