



CASE REPORT

Surgical management in patients with bisphosphonate-related osteonecrosis of the jaw: four cases

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ABSTRACT

Bisphosphonates, which have been introduced into medicine in the early 1990's, is now being used successfully for treatment of primary osteolytic bone diseases such as metastatic diseases, multiple myeloma, paget disease, hypercalcemia in malignancies and management of pain occurring in these bone pathologies. Their half-life in circulation is very short, but they can stay for years in bone tissue. On the other hand, reports about bisphosphonate-related osteonecrosis of the jaw has been increasingly published recently. In this case report, bisphosphonate-related osteonecrosis of the jaw and treatment modalities has been evaluated in four cases.

INTRODUCTION

Bisphosphonates (BPs) have been widely used in medicine as anti-resorptive agents owing to their anti-osteoclastic action.¹ Patients treated with BPs may develop osteonecrosis of the jaw bone after minor local trauma including dental procedures, recently labelled as bisphosphonate-related osteonecrosis of jaw (BRONJ). BPs impair bone turnover leading to compromised bone healing which may result in the exposure of necrotic bone in the oral cavity frequently following tooth extraction or trauma of the

oral mucosa.² The first case of osteonecrosis after BP was reported by Marx and Stern in 2002.³ The definition was made as non-healing open bone wound on the jaw bones during more than eight weeks' period in patients who had oral or intravenous BPs but never had radiotherapy.³ Invasive procedures as tooth extraction, periodontal operations, implant surgery, oral surgical operations can also lead to osteonecrosis.⁴ There are many studies discussing the etiology and treatment of BRONJ in medical literature,⁵⁻⁹ but it appears that

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there are so many aspects to be researched. The aim of this case report was to evaluate the surgical treatment procedures in patients with BRONJ.

CASE REPORT

Case 1

48-year-old woman presented 18 months after tooth extractions with empty painful socket lower right first molar (Figure 1a). Because of the breast cancer, the patient had been treated with zoledronic acid (Zometa, Novartis) once a month for 4 years. Conventional radiological examination displayed persistent pockets with no signs of bony regeneration (Figure 1b). After a short phase of follow-up together with routine conservative treatment, there was neither evidence for acute inflammation nor signs of spontaneous regeneration. Surgical procedure was performed and bony sequester was removed and shaped to a smooth contour with primary flap closure (Figure 1c,d). Post-operative antibiotic therapy was administered (amoxicillin 1 g per os and metronidazole 500 mg per os) for 1 week. Histologic examination of a collected biopsy confirmed the diagnosis of (BRONJ). The 12-month follow-up showed

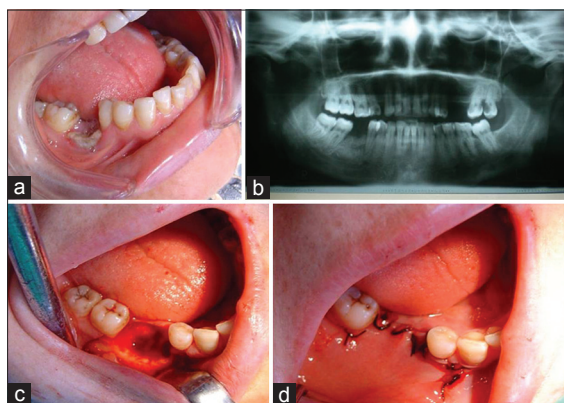


Figure 1. (a) Bone necrosis of the right mandible. (b) Radiographic view of the osteonecrosis. (c,d) Post-surgical view of the right mandible.

no progression of disease, and confirmed a stable mucosal coverage.

Case 2

54-year-old man who consulted our clinic complaints of severe pain and bone exposure in the upper right molar area because of the non-fitting removable maxillary denture (Figure 2a). He had received long-term treatment with zoledronic acid (Zometa, Novartis) to manage bone metastases due to prostate cancer. Surgical procedure was performed under local anesthesia, the infected bone region of the maxillary right premolar-molar area was resected (Figure 2b,c). Preventative antibiotics (amoxicillin 1 g per os and metronidazole 500 mg per os) were started. Six months postoperatively, the healed mucosa was observed (Figure 2d). The patient was educated in efficient oral hygiene and clinical follow-up took place every year.

Case 3

63-year-old man was referred to our department with pain and necrotic bone exposure in the left mandibular molar area, after tooth extraction (Figure 3a,b). He

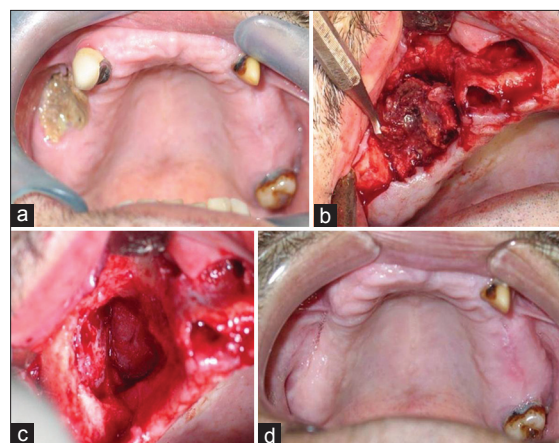


Figure 2. (a) Necrotic bone area of the right maxilla. (b,c) Surgical treatment with removal of the bone sequestrum. (d) Post-surgical view of the healing area.

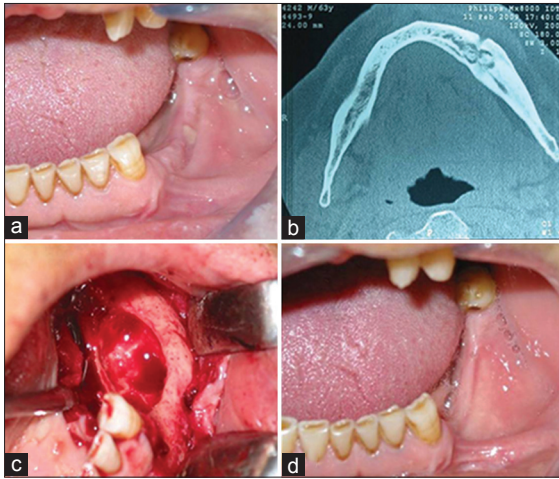


Figure 3. (a) Non-healing mucosa of the left mandible. (b) Radiographic view. (c) Surgical resection. (d) Healing mucosa after the surgery.

had been diagnosed with prostate cancer and treated with zoledronic acid (Zometa, Novartis) once a month for 4 years. After 3 months drug holiday period, operation was performed under local anesthesia, necrotic bone area was removed (Figure 3c,d). Histologic examination confirmed the diagnosis of BRONJ. Antibiotic therapy was started (amoxicillin 1 g per os and metronidazole 500 mg per os). Efficient oral hygiene and clinical follow-up was advised to the patient.

Case 4

52 year-old man was referred our clinic who was receiving BP for bone metastasis of prostate cancer with a history of approximately five months ago left lower second molar extraction and a physical examination finding of with unhealing necrotic bone (Figure 4a). Clinical and radiological examination showed non-healing extraction socket (Figure 4b). Operation was performed under local anesthesia. Surgical debridement was performed, necrotic bone was removed (Figure 4b,c). Wound closure was indicated, including superficial contouring of the alveolar ridge using rotating burs, and

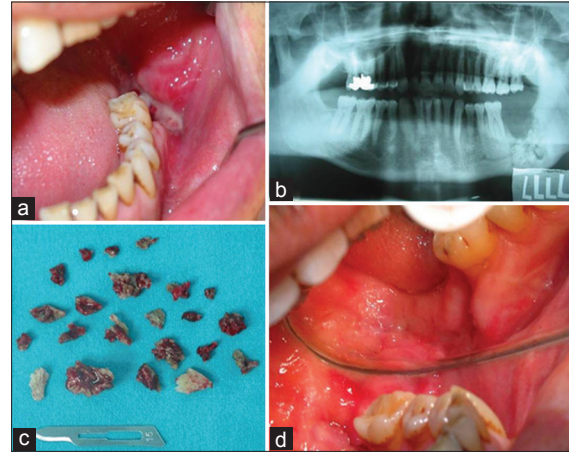


Figure 4. (a) Bone necrosis of the left posterior mandible. (b) Radiographic view. (c) Removed necrotic bone. (d) Post-surgical view.

subsequent dense and tensionless soft tissue closure was made with a vestibular mucosal flap (Figure 4d). Medical treatment with antibiotics (amoxicillin 1 g per os and metronidazole 500 mg per os) was started and continued for 15 days. Mouth washes with chlorhexidine were also prescribed.

DISCUSSION

BP therapy can be a key component of a patient's chemotherapy regimen. Use of BPs is on the rise and the beneficial effects of alleviating bone pain associated with an array of disorders are clear.¹⁰ According to the oncologist, the patients interrupted the BPs therapy before or after the first oral evaluation and before surgical treatment, actually, because of the long half-life of BPs and the lack of evidence on discontinuation of BP therapy once osteonecrosis develops or before invasive dental procedures, the patients continue the BP therapy.¹¹ The dentist must educate the patient preparing to undergo any chemotherapy regimen about the possible dental side effects of BP and take the necessary preventive measures to keep potential side effects to a minimum.¹² The role of hyperbaric oxygen therapy is still unclear but some benefits of this treatment have recently been described

in association with discontinuation of BP therapy and conventional therapy (medical or/and surgical).¹³ Surgical treatment, in accordance to the American Association of Oral and Maxillofacial Surgeons (AAOMS) Position Paper, is reserved to patients affected by Stage III of BRONJ even if in the last version a superficial debridement is indicated to relieve soft tissue irritation also in the Stage II (lesions being unresponsive to antibiotic treatment).¹⁴ Aggressive surgical treatment may occasionally results in even larger areas of exposed and painful infected bone. Surgical debridement or resection in combination with antibiotic therapy may offer long-term palliation with resolution of acute infection and pain. Mobile segments of bony sequestrum should be removed without exposing unaffected bone.^{7,12} Moreover, ozone therapy and laser applications (Low Level Laser Therapy - LLLT) have been also reported in the literature for the treatment of BRONJ.¹⁵⁻¹⁸ However it must be recognized that interindividual variability, gender, age, physical activity, and seasonal and circadian variation exist that can result in difficulty in interpreting the treatment and more research is needed.

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