

**Case Report**

# Stage 2 Medication Related Osteonecrosis of Jaws: Therapeutic Management: Actual Dilemma

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## Abstract

Medication-Related Osteonecrosis of Jaws (MRONJ) is a side effect of using antiresorptive and anti angiogenic drugs in oncologic and osteoporotic population. According to the literature, the frequency of MRONJ in the oncology patients receiving high doses of Intravenous Biphosphonates (IVBPs) is estimated at 1% to 15%.

While there is good agreement in term of diagnosis and staging system, treatment modality is still a subject of debate especially for stage 2 MRONJ, whether to choose a conservative surgical approach or an extended bone resection. We herein report a case of patient with MRONJ due to IVBPs, we discuss our therapeutic attitude in 2 stages of the disease (stage 2 and stage 3) and we analyze radiographic aspects than we propose a modification of MRONJ classification including radiographic findings and treatment modality.

**Keywords:** Medication-related osteonecrosis of jaws; Biphosphonates; Therapeutic management; Zoledronate

## Introduction

Medication Related Osteonecrosis of Jaws (MRONJ) occurs in patients who undergo treatment with antiresorptive agents as Biphosphonates (BPs), a class of drugs that modulate bone metabolism or antiangiogenics agents [1].

According to the American Association of Oral and Maxillofacial Surgeons (AAOMS), MRONJ can be classified into 4 pathological stages from 0 to 3 [2].

While there is a good author's agreement on the clinical diagnosis and staging criteria, there are still two controversial aspects: The need for radiological findings to precise the stage and the treatment modality particularly on stage 2 whether to choose a conservative surgical approach or an extended bone resection [3].

The aim of this paper was to discuss the therapeutic management of a case of MRONJ due to Intravenous (IV) BPs which was followed up at the military hospital of Tunis.

## Case Presentation

A 34 year old female was presented with 1cm of yellowish bone exposure in the extraction site of tooth n°15 with surrounding soft tissue inflammation after extraction of this tooth 2 months ago without any tendency to heal.

She has a history of breast cancer 2 years before treated with IVBPs (Zoledronic Acid), began from march 2015 and interrupted by

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her oncologist on October 2017 after the appearance of exposed bone with jaw pain exceeding the dental extraction.

She benefited of 18 perfusions of Zoledronic acid and she has no others pathologies, neither comorbidities factors.

CBCT showed mottled bone surrounding teeth n°14 and 16 without evidence of osteolysis. Stage 2 MRONJ associated to IVBPs was diagnosed (Figure 1). The patient refused the extend bone resection, so medical treatment (combination of 2 gr/day of Amoxicillin + 1.5 gr/day of Metronidazole) associated with conservative surgical management (minor debridement procedure to smooth sharp edges and reduce irritation to surrounding tissues) was done as recommended by the AAOMS. She was regularly controlled with persistence of bone exposure after 3 months. We missed the patient until she consulted after one year with pus discharge in the oral cavity and exacerbation of jaw pain.

Clinically, we founded an area of exposed bone much bigger than the first (2 cm), slight mobility of tooth n°14, pus discharge and inflammation of tissues surrounding the exposed bone. Medical treatment (combination of Amoxicillin/Clavulanic Acid 2 gr/day and 1.5 gr/day of Metronidazole) was amerced.

CBCT showed a bone sequestrum englobing teeth n°14 and 16 extending the floor of the right maxillary sinus. Stage 3 MRONJ due to IVBPs was diagnosed (Figure 2).

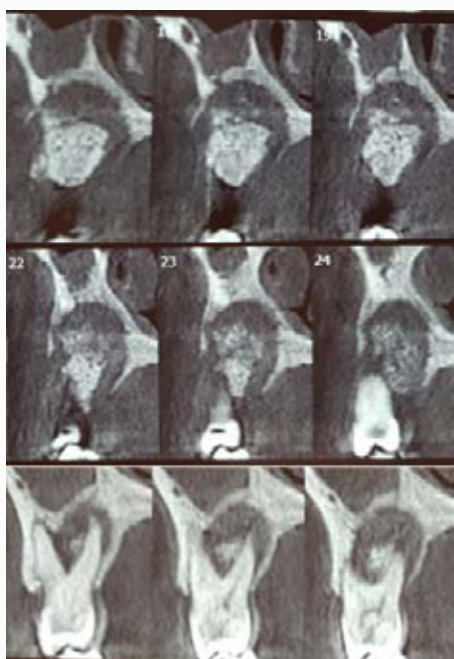
Extended bone resection, extraction of teeth n°14 and 16, filling material (Collagen) was used and a tension free closure under the same antibiotic therapy was done (Figure 3). No particularities were noted after one week. Cicatrisation was progressive with root exposure of tooth n°13 controlled regularly until epithelial cicatrization (Figure 4). A CBCT done 5 months later the surgery, showed no radiologic signs of recurrent osteonecrosis.

## Discussion

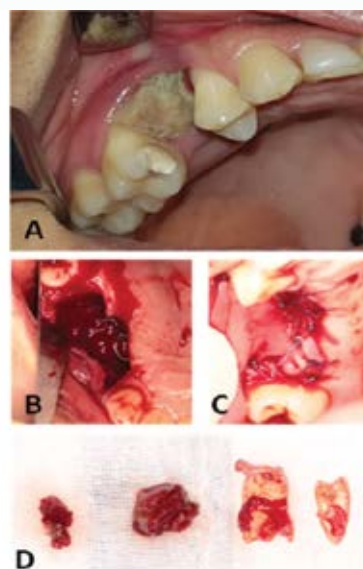
According to the literature, the frequency of MRONJ in oncology patients receiving oncology doses of IVBPs is estimated at 1% to 15% [4,5]. Several studies on MRONJ have been conducted since the first



**Figure 1:** A 34 year old female, who has treated with IVBPs (Zoledronic Acid) from March 2015 to October 2017 for breast cancer, consulted for bone exposure appeared 2 months after dental extraction of tooth n°15.  
 (A) Panoramic radiograph shows the affected area. The arrow indicates the region of osteonecrosis induced by IVBPs.  
 (B) CBCT shows a mottled bone surrounding teeth n°14 and 16 without evidence of osteolysis (Stage 2 MRONJ).



**Figure 2:** Progression of the MRONJ from stage 2 to stage 3 one year after conservative debridement surgery. CBCT shows sequestrum formation engulfing teeth n°14 and 16 extending the floor of the right maxillary sinus with inflammatory reaction of the sinus mucosa.



**Figure 3:** Surgical management of stage 3 MRONJ. A) Clinical view before surgery. B) The cavity after removal of sequestrum and necrotic bone. C) Tension free closure. D) Sequestrum with teeth n° 14 and n°16.

description in 2003, but, the treatment strategy is still controversial without consensus particularly on stage 2 [3,6]. "Stage 2 MRONJ has been defined by the AAOMS when the following criteria were met: Exposed and necrotic bone or fistulae to the bone that was associated with infection, as evidenced by pain and erythema in the region of exposed bone, with or without pus discharge" [1]. According to the AAOMS, surgery is not recommended for stage 2 lesions and should only be performed for patients with stage 3 or stage 2 lesions refractory to conservative treatment [1,6].

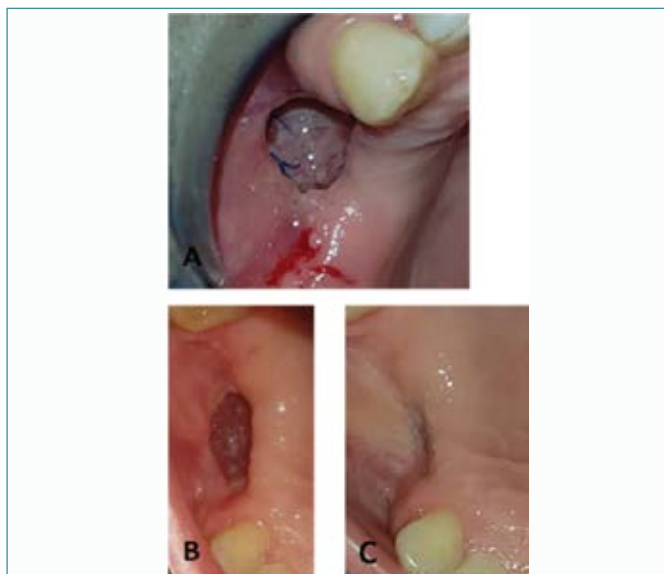
The recommended treatment for stage 2 MRONJ includes conservative therapy consisting of oral antibiotic plus antibacterial

mouth rinses, pain control and superficial debridement to relieve soft tissue irritation [7,8].

That was our first therapeutic attitude: minor debridement to smooth sharp edges and reduce inflammation surrounding the bone exposure associated with antibiotic therapy and mouth rinses with Chlorhexidine; however, no wound healing was noted 3 months and the lesion progressed from stage 2 to stage 3 with sequestrum formation after one year.

Resection surgery associated to antibiotic therapy, application of antiseptic gel (Periokin gel®) and filling material (Collagen) gave better results in term of healing and clinical benefit in shorter duration compared to conservative surgery.

According to the literature, surgical treatment has been shown effectiveness for both stage 2 and 3 MRONJ [6]. It improves



**Figure 4:** post-operative clinical follow-up. A) At two weeks after surgery. B) At 2 months postoperatively. C) At 5 months postoperatively: complete wound closure without recurrence of bone exposure.

early symptoms in the oral cavity and it has high success and low complication rates [1,9].

In our case we thought that if we opted for extended surgical resection from the beginning at stage 2, we avoided long term medical treatment and clinical symptoms specially that there is no medical contraindication for extended bone surgery.

We agree with Rugani et al. that necrotic bone may interfere with wound healing and prevent mucosal recovery in the affected sites that's why we thought that conservative surgery at stage 2 MRONJ may not give complete remission of the lesion [10]. To discern the limit between normal and necrotic bone, according to the literature, performing bone resection after fluorescence guided application based on the tetracycline absorption in bone administered before surgery is a beneficial option [6,11].

Indeed, recent data suggest including radiographic findings of disease as well as the radiographs extent of bone involvement to define more precisely the extent of the necrotic bone. Staging system proposed by the AAOMS should include both clinical and radiographic criteria [2].

Considering radiographs and the extent of bone involvement, stage 2 MRONJ can be subdivided on subtypes [2,12].

As Franco et al. we consider that most of the existing classifications are useful for diagnosis, but none of them offer a surgical orientation for the treating surgeon [10].

We reported the classification of Bagan et al. [12]. In which they have sub divided stage 2 on stage 2a and stage 2b. Herein, we propose this modification.

### Stage 2a

**Clinically:** Presence of exposed necrotic bone or oral fistula without exposure of necrotic bone.

**CBCT:** Localized bone changes. Medical treatment and conservative surgery (debridement surgery).

### Stage 2b

**Clinically:** Presence of exposed bone or oral fistula without exposure of necrotic bone.

**CBCT:** Extended bone alteration without current osteolysis. Medical treatment with extended bone surgery after fluorescence guided application [13].

### Conclusion

In conclusion, more studies are needed to make a conclusive differentiation between the effects of conservative surgery and extended bone resection including clinical and radiographic findings. Stage 2 MRONJ should be reconsidered in term of classification and treatment modality.

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