

## MRONJ: Stage 3, the Best Moment to Develop Surgery Techniques

Eduardo Rey<sup>1\*</sup>, Rodriguez Genta<sup>2</sup> and Picardo Silvana Noemi<sup>3</sup>

<sup>1</sup>President of the National Academy of Dentistry; Consultant to the National Academy of Medicine; Former Professor of Oral and Maxillofacial Surgery I and II School of Dentistry University of Buenos Aires, Argentina

<sup>2</sup>Head of Practical Works Chair in Oral and Maxillofacial Surgery II School of Dentistry University of Buenos Aires, Argentina

<sup>3</sup>Head of Practical Works Chair in Oral and Maxillofacial Surgery II School of Dentistry University of Buenos Aires and Department of Dentistry Favalaro Foundation University Hospital, Argentina

\***Corresponding author:** Eduardo Rey, President of the National Academy of Dentistry; Consultant to the National Academy of Medicine; Former Professor of Oral and Maxillofacial Surgery I and II School of Dentistry University of Buenos Aires, Argentina

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### Abstract

Antiresorptives (bisphosphonates: BPs, denosumab: DS) induce a marked inhibition of bone resorption. Low concentrations are used to treat osteoporosis (OP) or other metabolic bone diseases including osteopenia. Besides, high concentrations are primarily used as an effective treatment in the management of cancer-related disorders, including hypercalcemia of malignant and skeletal-related events associated with bone metastases. MRONJ (Medication Related Osteonecrosis of the Jaw) is one of the most serious therapy complications with such drugs. In this regard, although the pathogenesis of MRONJ is not understood yet, several papers suggest that antiresorptives may play a role in its development [1].

According to the American Association of Oral and Maxillofacial Surgeons (AAOMS, 2014), MRONJ is defined as exposed or necrotic bone in the maxillofacial region that has persisted for more than 8 weeks in association with

current or previous BPs or DS therapy and with a lack of head and neck radiotherapy. AAOMS divided the MRONJ into 4 stages from 0 to 3, according to the clinical and radiological aspect of the osteonecrotic lesion: stage 0: Osteonecrotic lesion without sign-pathognomonic evidence of osteonecrosis: stage 1: osteonecrotic lesion with clinical signs and absence of clinical symptoms; Stage 2: Osteonecrotic lesion with sign and evident clinical symptoms; Stage 3: Osteonecrotic lesion with signs and evident symptoms that involve noble structures: pathological fractures, anesthesia of the lower dental nerve, oral-nasal communication, oral-sinus communication, skin fistulas [2].

The most important drug-risk factors for developing MRONJ appear to be the potency of the drug, its cumulative dose and the local-risk factors related to several dento-alveolar interventions [3].

### Keywords

Antiresorptives (AR); Bisphosphonates (BPs); Denosumab (DS); Medication Related Osteonecrosis of the Jaw (MRONJ)

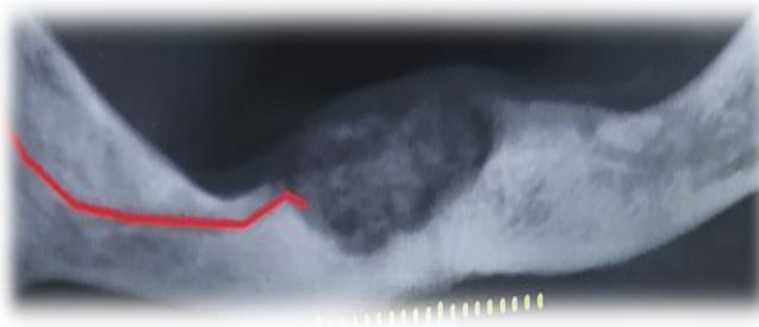
## Clinical Cases

### Osteoporotic patient

Male patient, 72 years old, from Buenos Aires (Argentina), osteoporotic, hypertensive, under treatment with Ibandronate 150 mg / m/ 9 years. With a history of four implants remove because of peri-implantitis: 44; 42; 32; 34 two years before the consultation (Figure1,2).

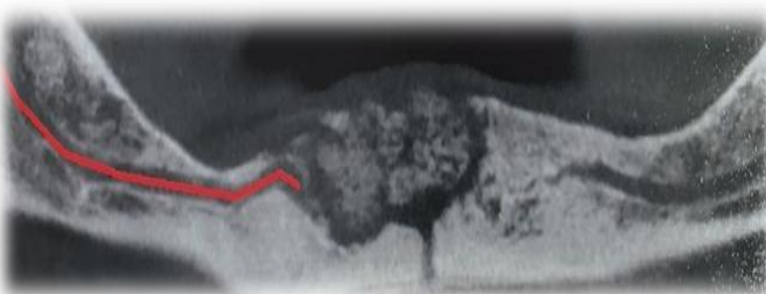


**Figure 1:** Clinical appearance of osteoporotic patient stage 2: MRONJ with history of four implants remove because of peri-implantitis: 44; 42; 32; 34.



**Figure 2:** Tomography appearance of osteoporotic patient stage 2: MRONJ with history of four implants remove because of peri-implantitis: 44; 42; 32; 34.

Bone curettage, each 2 weeks with the aim of achieving remission of the necrotic lesion. The patient had presented pathological fracture. Diagnosis of certainty: MRONJ clinical stage 3. The patient reported that he had used his lower complete prosthesis with ball attached system and a complete denture since MRONJ manifested himself. Clinical doctor requested an inter-consultation, since he had a frank fracture in his body mass.



**Figure 3:** Tomography pathological fracture jaw in osteoporotic patient Stage 3 MRONJ.

Antiseptic washes were started with 0.12% Chlorhexidine, 10% Povidoneiodo and 0.05% Rifamycin, alternating them monthly in order to produce the reflux of the inflammatory content, opportunely accompanied with antibiotic therapy: Amoxicillin 500 mg + clavulanic acid 125 mg each 8 hours for 7 days, talking with the treating doctor, accompanying your two systemic clinical exacerbations (lymphadenopathy, fever, tumor).

The clinical lesion of MRONJ was treated with titanium fixation and had been removed necrotic bone sequestration, reconfirming its diagnosis with the support of the Laboratory of Pathological Anatomy. His soft tissues were impossible to recovered, necrotic bone returns surrounded fixation screws in osteosynthesis plates presenting recurrences clinical and / or radiological MRONJ lesions in four months. Prosthetic rehabilitation was indicated indeed on the lesion in order to improve his occlusion.

### Oncology Patient

Male patient, resident in CABA, 69 years, history of kidney AC: malignant pulmonary and liver hypercalcemia, under treatment with DENOSUMAB 60mg / ml /20 days, with previous prescription of Zoledronic acid 4mg / 1 month (Figure 4).

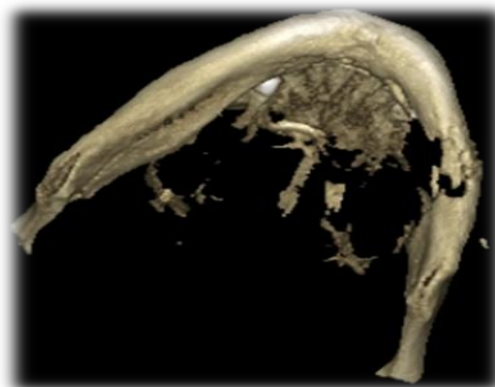


**Figure 4:** Clinical Stage 2 in oncology patient showing MRONJ.

He was presented with panoramic X-ray showing a radiolucent image, painless, suppurating without systemic compromise with frank over contaminated bone exposure. Injury that started after tooth extraction 37 with 6 months of evolution corresponding MRONJ stage 2, with pathological stimulation with the Lower Dental Nerve despite its proximity and pathological jaw fracture because of excessive surgery toilets. Necrotic bone expanded because of surgery manipulation was few weeks later and nowadays corresponding MRONJ stage 3 (Figure 5,6).



**Figure 5:** Panoramic X ray showing Stage 3 MRONJ in oncology patient.



**Figure 6:** Tridimensional Tomography reconstruction showing Stage 3 MRONJ in oncology patient.

Antiseptic washes were started with 0.12% Chlorhexidine 10% Povidoneiodo and 0.05% Rifamycin, alternating them monthly in order to produce the reflux of the inflammatory content, opportunely accompanied by antibiotic therapy: ciprofloxacin 500 mg every 12 hours for 7 days, indicated in consultation with the oncologist. After the first exacerbation, the patient exfoliated a bone fragment that was sent to the Laboratory of Pathological Anatomy, to reconfirm the correct diagnosis. Spontaneous total exfoliation of the MRONJ lesion was achieved in two years, under antiseptic treatment and timely antibiotic follow-up at times of clinical exacerbation. There was presence of neuronal injury and wound closure and necrotic bone exposure, therefore pathological fracture jaw: clinical Stage 3 MRONJ. A referral was made for his prosthetic rehabilitation since during the process of expulsion of the necrosis and patient was operated with titanium osteosynthesis and necrosis surround fixation plates presenting recurrences clinical and or radiological MRONJ lesions approximately eight months' recurrences.

## Discussion

In the case of MRONJ, its fundamental characteristic is positioned in the biochemical particularity of the pharmacokinetic expression of antiresorptive drugs, reversibly (DS) or irreversibly (BPs) inhibiting the functionality of the osteoclast [4]. Therefore, the consideration of invading bone tissue as little as possible and performing resective therapies in cases of systemic infectious spread follows, since its long-term resolution would not be effective because the drug (BPs) has frank accumulation at a distance, a characteristic used by treating doctors and it would not have clinical relevance to suggest its suspension [5]. But some clinical evaluation depends on therapies which patients were submitted in relation with previous resective surgeries that's perhaps had not been developed opportunity in case osteoporotic patient presented in this publication who his resected therapy made him developed changing clinical stage 2 to irreversible stage-3 [6].

Given the aforementioned, both osteoporotic and oncological pathologies require the accumulation of the drug due to the need to use antiresorptive protocols that present higher relative potencies, such as the case of treatment in oncological patients [7].

Therefore, always the best clinical therapy referring pathological fractures, indeed osteoporotic and oncology patients is the osteosynthesis with plates fixation in spite of the fact surgeons knows MRONJ is going to relapse (recidivar??) in case necrotic bone is going to surround plates fixation and expanddrug necrosis volumetrically due to bone accumulation of BPs or DS time later [8].

## Conclusion

From the results found and from those published in the bibliography, it appears that the interaction between health professionals is essential since the prevention of MRONJ is better than the treatment. In this sense, prior dental evaluation of patients is recommended, in order to carry out dental interventions before establishing chronic treatment with antiresorptive drugs [9].

These findings, according to literature reports, suggest that BPs and DS are the very low bony renewal capacity may contribute to pathogenesis of MRONJ. Although most of the cases were developed in oncological patients, as demonstrated in the present study, it could also be identified in osteoporotic patients who were operated on surgically removed developing new focuses of bone necrosis in irreversible stage 3 MRONJ, also be carefully followed by preventive oral care before beginning antiresorptive treatment[10].

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