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Case Report

Surgical Management of Stage-3 Osteonecrosis of the Jaw in a Patient with Rheumatoid Arthritis: A Case Report

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Abstract

Background: Medication-related osteonecrosis of the jaw (MRONJ) is an adverse reaction, characterized by the progressive destruction and necrosis of the jaw bone of patients treated with antiresorptive and antiangiogenic drugs, increasingly common in recent years. The propose of this study is to report surgical procedures in the treatment of third stage MRONJ. **Case Description:** A 68 years-old woman presented to the Oral and Maxillo-facial department at the University of Rome Tor Vergata in march 2021, complaining of pain and infection signs in the left side of the lower jaw. The Patient refers to be affected by rheumatoid arthritis treated for 18 months with Denosumab fl 60 mg every 6 months subcutaneously. In July 2020 undergoes tooth extraction in the third quadrant with no healing and persistence of pain refractory to medical therapy. After diagnosis of stage 3 MRONJ was performed a sequestrectomy, osteoplasty and suture by first intention. Clinical signs of pain, inflammation and oral infection have completely healed after the surgery intervention. **Conclusion:** The primary intent of surgical therapy of ONJ should not be palliative, but curative. Curative intent is the complete removal of the tissue macroscopically involved by the disease and the achievement of a healthy tissue that allows stable healing over time. Surgery will certainly be less invasive and will have a greater margin of success if the disease to be treated has a limited extent.

Background

Medication-related osteonecrosis of the jaws (MRONJ) is an adverse reaction, characterized by the progressive destruction and necrosis of the jaw bone of patients treated with antiresorptive and antiangiogenic drugs, in absence of a previous radiation treatment [1]. ONJ may also be the result of radiotherapy, chemotherapy and a complication of osteomyelitis [2]. Medications, such as Bisphosphonates and Denosumab, are used for the treatment of skeletal complications associated with bone metastases in oncological and osteometabolic diseases (osteoporosis, paget's disease and rheumatoid arthritis) [3]. Drug administration by Oral Subministration (OS) or injection (IN) shows great variability on bioavailability and incidence of the disease. Incidence varies from 1 to 9% in patients undergoing high drugs dose via IN and is approximately 0.10% in patients undergoing low doses via OS [4]. Risk factors for ONJ are systemic, related to the underlying disease, the type of drug and site of administration, and local, alveolar surgery and periodontal inflammatory diseases [5]. Diagnosis occurs through clinical signs as necrotic bone exposure, and radiographic signs as osteolytic area on Orthopantomogram (OPT) or Computed Tomography (CT) [6]. Prevention starts before drug treatment with antiresorptive or antiangiogenic drug. Any oral health problem must be addressed to minimize the appearance of inflammatory or infectious diseases of the oral cavity Treatment provides palliative medical therapy as antibiotics and analgesics in acute phase, and curative surgery variables depending on the severity of the injury [7]. We present here a patient treated with denosumab for Rheumatoid Arthritis (RA) that developed stage-3 ONJ after oral extraction.

Case Description



Figure 1: Pre-operative intraoral left lower jaw, the exposure of necrotic bone can be noted in corrdisponde of the post extraction sites.

A 68 years-old woman presented to the Oral and Maxillo-facial department at the University of Rome Tor Vergata in march 2021, complaining of pain and infection signs in the left side of the lower jaw. The Patient refers to be affected by rheumatoid arthritis (RA) treated for 18 months with Denosumab fl 60 mg every 6 months subcutaneously, methylpredniolone cp 4 mg a day and Tapentadol Hydrochloride cp 150 mg a day. She also was affected by Atrial Fibrillation treated with Bisoprolol cp 2,5 mg a day and panic attack treated with Hydrochloride Duloxetine cp 60 mg a day. In July 2020 the patient undergoes tooth extraction in the third quadrant. Since the patient came to our attention, she noted the persistence of symptoms with exposure of necrotic bone in correspondence with the post-extraction sites (Figure 1).

This symptomatology did not improve with topical and antibiotic therapy. After a clinical examination, the patient underwent a CT scan of the jaw which revealed an osteolytic area at the third quadrant level (Figure 2).

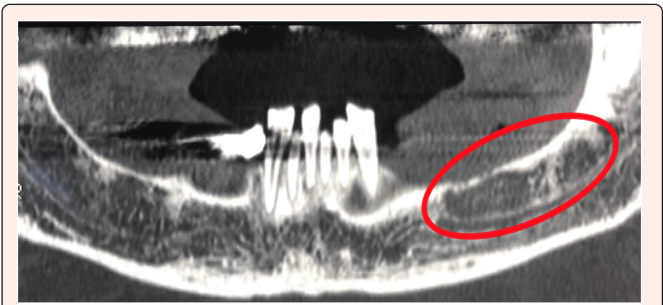


Figure 2: Pre-operative lower jaw CT show osteolytic area in correspondance of III quadrant.

The diagnosis was third stage MRONJ according to the American Association of Oral and Maxillofacial Surgeons criteria [7]. The surgery treatment proposed involved sequestrectomy, alveolar curettage and surface osteoplasty, performed under general anesthesia. Patient's written informed consent has been obtained. The patient underwent drug therapy lasting 7 days, from the day before the surgery to 6 days. The pharmacological therapy proposed, according to the Italian Oral and Maxillo-Facial Society (SICMF- Società Italiana di Chirurgia Orale e Maxillo Facciale) [8], was Amoxicillin cp 1000 mg every 8 hours and metronitrazole cp 500 mg every 8 hour. We also recommend the use of chlorhexidine 0,12% mouthwash 3 times a day from 10 days previously to 10 days after surgery. During the surgery we raised a full-thickness muco-periosteal flap extended to reveal the entire area of bone necrosis and over the disease-free margins (Figure 3).

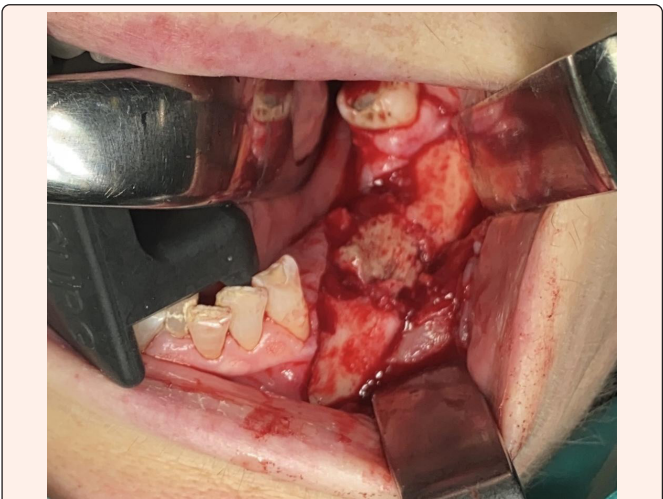


Figure 3: mucoperiosteal flap, it should be extended enough to reveal the entire area of necrotic bone and healthy bone margins.

The bone sequestration was subsequently eliminated. The resection of the affected bone was extended horizontally and inferiorly to achieve healthy, bleeding bone (Figure 4).

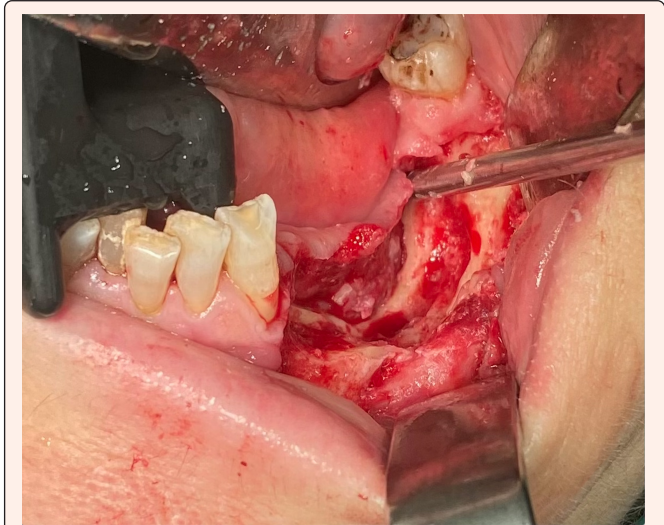


Figure 4: sequestrectomy and jaw bone resection, an osteoplasty of the adjacent bone surface it is necessary to eliminate possible residual asperities and to allow closure for primary intention of the defect.

The bone spurs were rounded and finally the soft tissues were sutured by primary intention to obtain a tension-free closure (Figure 5).



Figure 5: Primary intention surgical closure is necessary to allow perfect healing of the defect.

Several authors reported better results with larger resections than with limited surgery or conservative therapy [9].

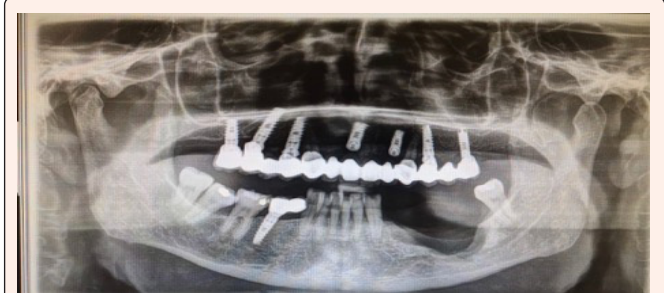


Figure 6: 6 months follow up OPT show the healing of the bone margins of the difect.



One week after the surgery, we removed the sutures. The patient returned for weekly follow-up visits during the first month and then once a month for the next 5 months. After 6 months from the surgery and Orthopantomogram X-Ray was carried out which demonstrated the resolution of the case (Figure 6). Clinical signs of pain, inflammation and oral infection have completely healed.

Conclusion

ONJ associated with drug treatment, most often referred to in the more recent literature as Medication-Related Osteonecrosis of the Jaw (MRONJ) can affect patients' quality of life [10]. The first recommendations discouraged surgical treatment to solve the problems related to ONJ. Conservative therapy was adopted continuously up to a possible progression of the disease with worsening of the clinical case. Many reports demonstrate the success and resolution of ONJ cases with surgery [11]. The primary intent of surgical therapy of ONJ should not be palliative, but curative. Curative intent is the complete removal of the tissue macroscopically involved by the disease and the achievement of a healthy tissue that allows stable healing over time. Surgery will certainly be less invasive and will have a greater margin of success if the disease to be treated has a limited extent [12]. Therefore reserving surgery for the most advanced stages of the disease as claimed up to now is no longer a desirable choice [13]. Healthy tissue surrounding the lesion must be identified with a good safety margin for complete removal of the pathological bone tissue. In current clinical practice, the surgeon is able to identify the real extent of the pathological tissue before surgery, through the use of radiological methods, but an intraoperative assessment of the lesion margins is essential. The assessment of bone bleeding is still the most widely used means for the intraoperative identification of surgical margins in MRONJ [14]. Undoubtedly, in order to recognize initial forms of MRONJ, the need for an accurate radiological evaluation is increasingly evident. CT [15] allows a detailed study of the bone, identifying osteolytic lesions, bone sequestrae and changes in density, while MRI allows to identify the degree of involvement of adjacent soft tissues [16]. An important aspect in ONJ therapy, which still does not have a clear answer, is understanding the time that must pass after a treatment to consider a patient effectively cured. The stability over time of the effects of a treatment is the essential requirement that allows to evaluate the degree of effectiveness, especially for surgical therapies. Some studies show that most clinical relapses of the disease occur within 6 months but a significant number of relapses are also revealed in the following 6 months and in any case within the year, whatever the surgical therapy adopted [14]. There are different surgical techniques to treat ONJ, but in the absence of shared and standardized surgical protocols it is impossible to compare their effectiveness and results [17]. In conclusion, osteonecrosis treatment varies according to the severity of the lesion and the patient's underlying pathology. Therefore the sooner necrosis is diagnosed, the sooner it is treated and the less invasive the treatment will be.

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