

SEGMENTAL BONE RESECTION ASSOCIATED WITH PHOTOBIOMODULATION AND PHOTODYNAMIC THERAPY IN THE TREATMENT OF DRUG-RELATED OSTEONECROSIS OF THE JAW: CASE REPORT AND LITERATURE REVIEW

**RESSECÇÃO ÓSSEA SEGMENTAR ASSOCIADA À FOTOBIOMODULAÇÃO E
TERAPIA FOTODINÂMICA NO TRATAMENTO DA OSTEONECROSE DA
MANDÍBULA INDUZIDA POR MEDICAMENTOS: RELATO DE CASO E REVISÃO
DA LITERATURA**

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TERAPIA FOTODINÁMICA EN EL TRATAMIENTO DE LA OSTEONECROSIS
MANDIBULAR INDUCIDA POR FÁRMACOS: REPORTE DE CASO Y REVISIÓN
DE LA LITERATURA**

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ABSTRACT

Medication-related osteonecrosis of the jaw (MRONJ) is a serious complication associated with the use of antiresorptive and/or antiangiogenic therapies, representing a significant therapeutic challenge. To report the successful management of an advanced case of MRONJ in the mandible using a multimodal therapeutic approach. A 56-year-old female patient with a history of breast cancer and bone metastasis, treated with zoledronic acid for four years. After tooth extraction, she developed bone exposure and purulent drainage. Treatment consisted of marginal bone resection of necrotic tissue, combined with intraoperative antimicrobial photodynamic therapy (aPDT) and postoperative photobiomodulation (PBMT) sessions. The patient presented satisfactory healing, was rehabilitated with a prosthesis, and, after 12 months of follow-up, showed no signs of recurrence. The combined approach of resective surgery with adjuvant photonic therapies (aPDT and PBMT) proved to be an effective strategy in resolving the condition, promoting the patient's rehabilitation and improving her quality of life

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Keywords: Bisphosphonate-Associated Osteonecrosis of the Jaw. Bisphosphonates. Zoledronic Acid. Laser Therapy. Photodynamic Therapy.

RESUMO

A osteonecrose dos maxilares relacionada a medicamentos (ONMR) é uma complicação grave associada ao uso de terapias antirreabsortivas e/ou antiangiogênicas, representando um desafio terapêutico significativo. Tem como objetivo relatar o manejo bem-sucedido de um caso avançado de ONMR na mandíbula utilizando uma abordagem terapêutica multimodal. Paciente do sexo feminino, 56 anos, com histórico de câncer de mama e metástase óssea, tratada com ácido zoledrônico por quatro anos. Após extração dentária, apresentou exposição óssea e drenagem purulenta. O tratamento consistiu em ressecção óssea marginal do tecido necrótico, combinada com terapia fotodinâmica antimicrobiana intraoperatória (aPDT) e sessões de fotobiomodulação pós-operatória (PBMT). A paciente apresentou cicatrização satisfatória, foi reabilitada com prótese e, após 12 meses de acompanhamento, sem sinais de recidiva. A abordagem combinada de cirurgia ressectiva com terapias fotônicas adjuvantes (aPDT e PBMT) mostrou-se uma estratégia eficaz na resolução do quadro, promovendo a reabilitação da paciente e melhorando sua qualidade de vida.

Palavras-chave: Osteonecrose da Arcada Osseodentária Associada a Difosfonatos. Bifosfonatos. Ácido Zoledrônico. Terapia a Laser. Terapia Fotodinâmica.

RESUMEN

La osteonecrosis mandibular asociada a fármacos (OMAF) es una complicación grave relacionada el uso de terapias antirresortivas y/o antiangiogénicas, lo que representa un importante desafío terapéutico. Presentar el tratamiento exitoso de un caso de OMAF avanzada en la mandíbula mediante un abordaje terapéutico multimodal. Paciente de 56 años con antecedentes de cáncer de mama y metástasis óseas, tratada con ácido zoledrónico durante cuatro años, presentó exposición ósea y drenaje purulento tras un traumatismo dental. El tratamiento consistió en la resección ósea marginal del tejido necrótico, combinada con terapia fotodinámica antimicrobiana intraoperatoria (TFDA) y sesiones postoperatorias de fotobiomodulación (FBM). La paciente presentó una cicatrización satisfactoria, se rehabilitó con prótesis y, tras 12 meses de seguimiento, no mostró signos de recidiva. El abordaje combinado de cirugía resectiva con terapias fotónicas adyuvantes (aPDT y PBMT) demostró ser una estrategia eficaz para resolver la afección, promover la rehabilitación del paciente y mejorar su calidad de vida.

Palabras clave: Osteonecrosis de los Maxilares Asociada a Difosfonatos. Difosfonatos. Ácido Zoledrónico. Terapia Láser. Terapia Fotodinámica.



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INTRODUCTION

Medication-related osteonecrosis of the jaw (MRONJ) is one of the most severe oral complications associated with prolonged use of antiresorptive agents, such as bisphosphonates (BPs) and denosumab, and/or antiangiogenic agents. First described by Marx (2003) in users of intravenous bisphosphonates (IV BPs), it is currently defined by the American Association of Oral and Maxillofacial Surgeons (2022), as an area of exposed or probeable bone through an intraoral or extraoral fistula that persists for more than eight weeks in patients with no history of radiotherapy in the head and neck region. The definition includes cases associated with other agents, such as denosumab and antiangiogenic drugs.

The clinical relevance of MRONJ is particularly pronounced in the oncology population. Patients undergoing treatment for bone metastases with intravenous zoledronic acid, for example, are at significantly higher risk. The prevalence of MRONJ varies according to the drug, route of administration, cumulative dose, and presence of triggering factors, such as tooth extractions and periodontal infections. Cancer patients using IV zoledronic acid are at significantly higher risk (0.5–4.6%) compared to users of oral BPs (<0.21%) (Ruggiero et al., 2022; Shibuya et al., 2023).

The pathogenesis is multifactorial and complex, based on the suppression of bone remodeling by osteoclast apoptosis and profound impairment of angiogenesis, which makes the jaws particularly vulnerable. Local triggering factors, such as tooth extractions or trauma from prostheses, disrupt the integrity of the mucosa and, in bone with compromised repair capacity, initiate a vicious cycle of necrosis and secondary infection that perpetuates the lesion (Kawahara et al., 2023).

The pathophysiological mechanism involves inhibition of bone remodeling by osteoclast apoptosis, impaired angiogenesis, accumulated microfractures, and secondary infection. Local factors (prosthetic trauma, periodontitis) and systemic factors (diabetes, corticosteroid therapy, chemotherapy) contribute to the pathogenesis (Araújo et al., 2024; Migliorati et al., 2022).

Consequently, treating advanced stages of MRONJ is challenging, and surgical resection of necrotic bone is often necessary. However, surgical intervention in biologically compromised tissue can have unpredictable results. In this context, the search for adjuvant therapies that can modulate the local microenvironment and optimize tissue repair has become a frontier in clinical research. Among the new approaches, photobiomodulation (PBMT) and antimicrobial photodynamic therapy (aPDT) have emerged as promising strategies, promoting analgesia,

neovascularization, tissue repair, and microbial control (Ruggiero et al., 2022; Marx, 2003)

PBMT acts by stimulating mitochondrial activity, promoting neovascularization and healing, as well as promoting analgesia, while aPDT offers potent localized microbial control without the need for long-term systemic antibiotic therapy. Given the synergistic potential of these technologies, the objective of this study is to present the management of an advanced case of MRONJ, detailing the multimodal approach that combined surgical resection with aPDT and PBMT, and to discuss its results in light of current scientific evidence (Araújo et al., 2024; Maria et al., 2023).

CASE REPORTS

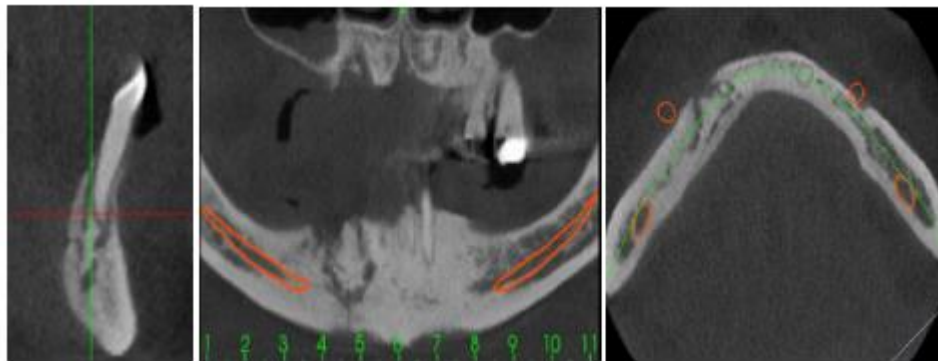
Patient R.C.S.M., female, 56 years old, attended the dental office complaining of pain and bone exposure in the right hemimandible. During the anamnesis, she reported having breast cancer that was treated surgically and with chemotherapy sessions, which, however, progressed to bone metastases. She underwent treatment with zoledronic acid, which began in 2011, with monthly doses administered over a period of four years. After extraction of tooth 44, the patient developed bone exposure in the right hemimandible comprising the region corresponding to teeth 44, 45, 46, and 47 with purulent drainage.

Figure 1. Bone exposure with purulent drainage and absence of healing in the region of 44 to 47 after extraction of tooth 44.



Source: Authors

Figure 2. Tomographic section showing the area of bone sequestration in the right hemimandible.

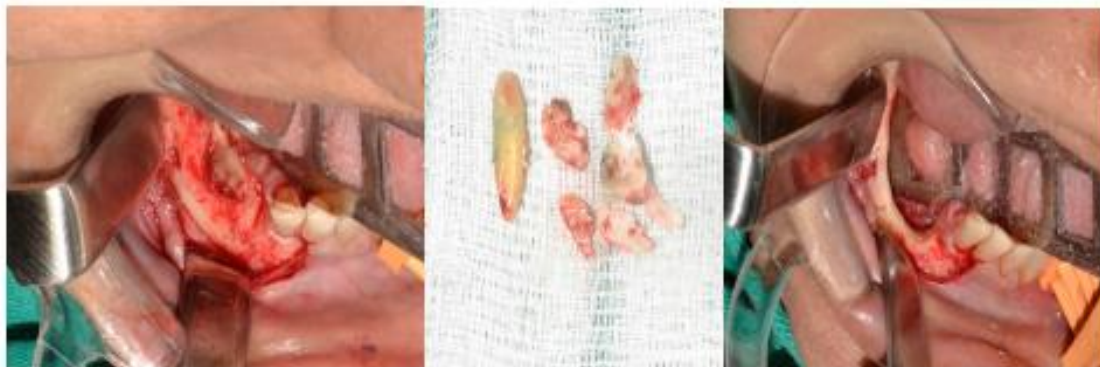


Source: Authors

According to the report, the patient underwent hyperbaric oxygen therapy, completing 60 sessions after bone exposure. Initially, an incisional biopsy was performed, with histopathological results showing the presence of avascular bone tissue, consistent with bone necrosis.

After initial care, surgical treatment was planned with marginal resection for excision of the necrotic bone tissue associated with intraoperative photodynamic therapy activated with methylene blue and postoperative laser therapy using a DMC Whitening laser device, with daily sessions for two weeks, comprising 12 sessions.

Figure 3. Marginal resection of the affected area, exposing the necrotic bone.



Source: Authors

Figure 4. Photodynamic therapy (PDT) with intraoperatively activated methylene blue for infection control.



Source: Authors

After clinical examination with satisfactory healing and clinical conditions of mucogingival tissue compatible with normal characteristics, rehabilitation was performed with a removable partial denture (30 days) and absence of clinical symptoms, remaining without remission of symptoms for one year after surgical intervention.

Figure 5. A: Clinical appearance of satisfactory healing after 30 days. B: Patient rehabilitated with removable partial denture.



Source: Authors

RESULT AND DISCUSSION

Medication-related osteonecrosis of the jaw (MRONJ) is a difficult complication to manage, especially in cancer patients undergoing prolonged intravenous bisphosphonate regimens. Although initially described more than two decades ago, its pathophysiology is still not completely understood, which justifies the multiplicity of therapeutic strategies (Pandolfi et al., 2023; Shibuya et al., 2023). In the present case, the patient had a history of zoledronic acid use for four years, a risk factor already established in the literature. Studies show that the risk of ONJ

is proportional to the duration of exposure and the cumulative dose of bisphosphonates, especially in the cancer population, where the dose is higher and the frequency of administration is more intense (Yamashita et al., 2023).

The treatment of choice in advanced cases remains controversial. An individualized approach is recommended, which may range from conservative therapies, such as antibiotic therapy and infection control, to segmental resections in refractory cases (AAOMS, 2022). In this report, the surgical option was associated with adjuvant therapies with growing evidence: photobiomodulation (PBMT) and antimicrobial photodynamic therapy (aPDT).

The current literature has highlighted the benefits of PBMT in MRONJ. The biostimulating effects of low-intensity laser are related to mitochondrial activation, increased ATP synthesis, and stimulation of neovascularization, promoting healing and bone repair (Araújo et al., 2024; Huang et al., 2023). In addition, there are reports of improved analgesia and reduced local inflammation, which are fundamental aspects for the patient's quality of life (Kawahara et al., 2023). The success of our clinical case reinforces this evidence, since the daily application of PBMT in the postoperative period contributed directly to satisfactory tissue healing and the absence of pain.

A aPDT, in turn, combines a photosensitizer, such as methylene blue, with the action of light at a specific wavelength, resulting in the production of reactive oxygen species capable of promoting microbial lysis (Migliorati et al., 2022). Considering that secondary infection plays a central role in the perpetuation of bone necrosis, aPDT has shown promise, especially as an adjunct to surgical treatment (Pandolfi et al., 2023). The use of aPDT during surgery, as demonstrated in this case, ensures control of the bacterial load before flap closure, minimizing the risk of failure.

Recent studies reinforce that the combination of surgical resection and photonic therapies enhances results, reducing recurrence rates and accelerating the repair process (De Oliveira et al. 2022; Gonçalves et al., 2024). In the reported case, the absence of recurrence after 12 months of follow-up corroborates this evidence, suggesting that the integration of surgery, PBMT, and aPDT can be considered an effective alternative for advanced cases of MRONJ. Another relevant aspect is the impact on functional and aesthetic rehabilitation. After satisfactory healing, the patient was able to be rehabilitated with a removable partial denture, recovering masticatory function and aesthetics. This outcome emphasizes the importance of multimodal protocols that not only control the disease but also restore quality of life.

Therefore, the experience presented, in line with the current literature, reinforces that PBMT and aPDT should be considered as adjuvants in clinical protocols for ONJ, especially in advanced stages undergoing surgical resection. Nevertheless, there is a need for randomized clinical trials with a larger number of patients and long-term follow-up to consolidate the role of these therapies in the management of osteonecrosis of the jaws.

CONCLUSION

This case study demonstrates that the integration of surgical approaches and photonic therapies may be a promising strategy for the treatment of medication-related osteonecrosis of the jaw, especially in refractory and advanced cases. Marginal resection of necrotic bone tissue, combined with infectious control of antimicrobial photodynamic therapy (aPDT) and biostimulation of photobiomodulation (PBMT), resulted in complete healing and no recurrence at 12 months.

The results presented suggest that the synergy between surgical debridement and the use of lasers acts not only in controlling the disease but also in optimizing the tissue repair process, a constant challenge in the management of MRONJ. The patient's successful prosthetic rehabilitation reinforces the importance of multimodal protocols aimed at complete restoration of function and quality of life.

Although a case report does not replace evidence from clinical trials, the experience described here offers a valuable contribution to the literature, validating the use of photonic therapies as effective adjuvants. It is hoped that this report will stimulate prospective studies with larger sample sizes and longer follow-up periods in order to consolidate the role of aPDT and PBMT as pillars in the treatment of MRONJ.

CONFLICT OF INTEREST

We declare that the manuscript has not been submitted elsewhere for publication and that there are no conflicts of interest to disclose. We also confirm that all authors have made substantial contributions to the research and preparation of the manuscript, and that all necessary permissions have been obtained for the use of patient data and/or images.

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