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Case Report

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Non-Invasive Laser Management of Stage 3 MRONJ (Medication-Related Osteonecrosis of the Jaws) in a Patient Undergoing Multidrug Therapy for Renal Metastatic Cell Carcinoma: A Literary Review and a Case Report

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Abstract

Background: This case report presents an instance of osteonecrosis of the jaw (ONJ) triggered by tooth extraction in a patient with metastatic renal cell carcinoma (RCC) undergoing multidrug treatment therapy. This was a 68-year-old man who presented in September 2023 to a private dental office complaining of severe pain that he had exposed bone in the alveolus of his left maxillary third molar 11 months following the extraction of the tooth root. **Methods:** The patient was treated for 4 months with various antibiotics and curettage to remove exposed bone with no improvement. The patient had received several courses of tyrosine kinase (TK) inhibitors, the Sunitinib® and Cabometix®, which were discontinued due to drug-related toxic effects and then Everolimus®, which was also discontinued due to pulmonary complications. A year earlier he had undergone antiresorptive therapy with the bisphosphonate Zolendronic® acid and then the human monoclonal antibody Denosumab®. A chronic non-healing extraction cavity's clinical and radiological picture was consistent with ONJ. **Results:** The CT scan showed a picture suggesting a focus on osteonecrosis. In contrast, the magnetic resonance imaging (MRI) scan showed evidence of ethmoidal-maxillary sinusopathy with the left maxillary sinus almost completely occupied by material fluid with fibrotic sprouts. The patient was treated for 4 months with various antibiotics and curettage to remove the exposed bone without improvement. After several oncology consultations, re- treatment with Sunitinib® was started. A few months later, the patient was referred to another dentist who suggested photobiostimulation therapy with a 980-nanometer diode laser and an ozone-based gel, which resulted in total healing. **Conclusions:** Mucosal lesions resolved with complete reconstitution of the oral tissue, accompanied by a progressive spontaneous expulsion of a bone sequestrum after topical ozone gel applications and photobiostimulation laser therapy. No toxicity was reported.

Keywords: Maxillary Osteonecrosis, Laser Therapy, Low-Level Dose Laser, Metastatic Renal Carcinoma, Dental Complications, Bisphosphonates, Antiangiogenic Drugs.

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INTRODUCTION

Osteonecrosis of the jaw (ONJ) is a well-recognized complication of drug therapies for bone metabolic disorders or cancer-related to the administration of antiresorptive (bisphosphonates and denosumab) and antiangiogenic drugs including renal cell carcinoma (RCC) [1-5]. In June 2014, the Special Committee of the American Association of Oral and Maxillofacial Surgeons (AAOMS) recommended a changing of the nomenclature in Medication-Related Osteonecrosis of the Jaw (MRONJ) describing criteria for its diagnoses: 1. Current or previous treatment with antiresorptive or antiangiogenic agents; 2. Exposed bone or bone that can be probed through an intraoral or extraoral fistula(e) in the maxillofacial region that has persisted for more than eight weeks; and 3. No history of radiation therapy to the jaws or obvious metastatic disease to the jaws [1].

This report presents an unusual case of MRONJ triggered by dental extraction in a RCC patient under multidrug therapy. This clinical issue is particularly relevant when planning a patient's treatment option. The AAOMS has suggested that, regardless of the stage of the disease, mobile bony sequestra should be removed without exposing uninvolved bone [1]. Antibacterial measures are therefore needed to support surgical treatment, including application of ozone [2], laser-assisted treatment [3], and long-term courses

of antibiotics.

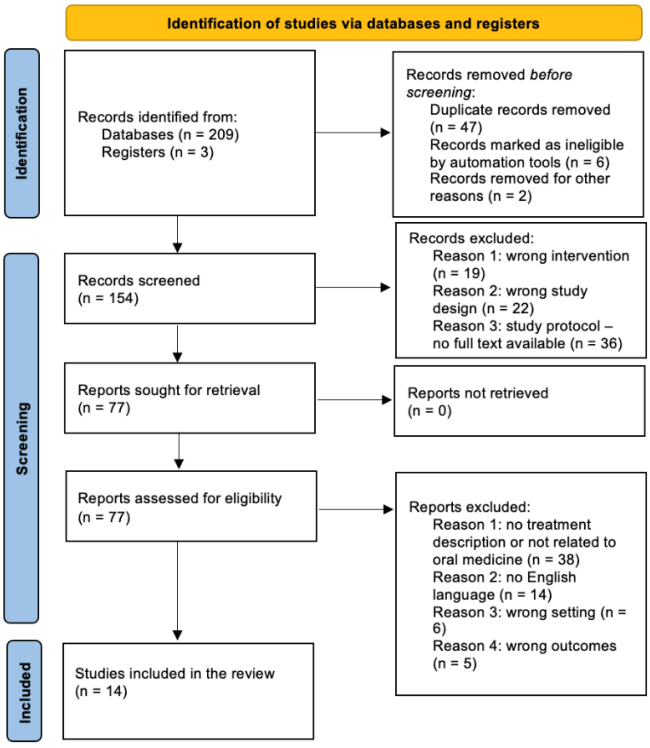
The dental literature does not provide guidelines for the treatment process in the case of MRONJ. Even if a recent literature review supported the use of laser-assisted treatment to manage and treat MRONJ evaluating the effectiveness of laser therapy [4]. It included only 10 studies reporting type of laser device, and with different approaches (low-level laser therapy, laser-assisted surgery, laser-assisted treatment plus platelet-rich plasma) [4]. This article intends to fill a gap in the literature by reviewing the effectiveness of photobiomodulation (PBM) using a diode laser. It also presents a previously tested method that has proven successful in managing post-extraction complications involving bone sequestration.

MATERIALS AND METHODS

According to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Table 1), an electronic search in MEDLINE (PubMed), the Cochrane Library, Scopus (Elsevier), and Web of Science (Thomson Reuters) databases up to January 2025 was performed to identify all potentially eligible articles regarding laser-assisted management of MRONJ patients. The eligibility criteria included human studies, randomized controlled trials (RCTs), prospective or retrospective cohort studies, case-control studies, cross-sectional studies, and also case report studies. These studies should present and describe the treatment plan, in which diode laser has been used to provide Low-Level Laser Therapy (LLLT) as a monotherapy or as an adjunctive device to the treatment protocol of MRONJ lesions. All the papers were in English.

Initially, published articles were reviewed based on their titles and abstracts. The following data were extracted: authors and year, study design, number of patients, case-related factor of the MJORN lesion, treatment performed, parameters of the diode laser and its time of application, follow-up and clinical findings. A table summarizing all this data was created, and the results provide an overview of the extracted information.

Table 1: PRISMA Flowchart of the research



RESULTS

This literature review analyzes findings from 14 studies summarized in a comprehensive table that highlights the most significant aspects for comparison. The research is limited to the last 15 years to ensure the literature is up-to-date. It includes three retrospective studies [5-7]; two prospective studies [8,9]; one pilot study [10]; two case series [11,12]; and six case reports [13-18]. Initially, the aim was to focus specifically on the use of diode laser as a monotherapy for the treatment of Medication-Related Osteonecrosis of the Jaw (MRONJ) patients. However, due to a limited number of papers, the scope was expanded to include studies that utilized the diode laser for Photobiomodulation (PBM) as an adjunctive therapy. Only two studies investigated the diode laser as a monotherapy in treating MRONJ lesions [8,17], while one retrospective study reported findings that included it alongside medication therapy 6. Two additional retrospective studies compared the medication plus PBM treatment to other therapeutic approaches [7,9]. All other included studies described PBM therapy in association with conventional surgery [5,7,11,18] minimally invasive surgery with burs [10,13], Er:YAG [12,15,16] or a piezotome [9,12,14]. The final sample comprised 473 patients, with bisphosphonate medication being the primary causative factor for both oncologic and non-oncologic reasons.

The table 2 reports all findings, focusing on the treatment options available to clinicians, their corresponding PBM parameters, and the timing of application.

The parameters for photobiomodulation therapy with the diode laser are detailed in a specific column of the table. Most studies utilized continuous mode (seven out of ten), while only one study used a super pulsed wave mode. In two studies [9,18], the diode laser employed three different wavelengths, with biostimulation applied using both continuous and super-pulsed modes. The average power level, expressed in Watts, was 1 (±3)W, excluding two studies that did not specify this information [15,17].

Additionally, data on timing and the number of sessions have been reported in a specific column. Unfortunately, no standardized protocol exists; all authors suggested different approaches. However, it is evident that all employed the device during short recall sessions in the initial days or weeks of the wound healing period, gradually extending the recall intervals over time until the end of follow-up. One case series [19], was found in the initial literature search but was excluded because it did not involve MRONJ lesions. This study investigated the adjunctive application of antimicrobial photodynamic therapy for the prevention of medication-related osteonecrosis of the jaw following dentoalveolar surgery. The sample consisted of 11 non-oncologic osteoporotic patients undergoing treatment with non-intravenous antiresorptive agents, requiring tooth extractions and/or implant removal. Photodynamic therapy was performed using a 100 mW diode laser with a wavelength of 660 ± 10 nm, with weekly applications of low-level laser therapy for a total of six weeks. Recall visits were scheduled weekly for the first two months and monthly thereafter for up to six months. No intraoperative complications were observed, and the immediate postoperative period was generally uneventful, except for mild pain; any ecchymosis resolved spontaneously. Healing occurred without complications, and no clinical or radiological signs of MRONJ were observed at the latest follow-up visit [19].

All considered papers reported a follow-up period of no less than six months, with the longest follow-up extending to two years in two studies [13,16], which continued to monitor patients even after the healing period had concluded. Regarding outcomes, all papers reported complete healing or a reduction in the severity of lesions. A common clinical finding was immediate pain relief, sometimes noted just after the first PBM session, along with an overall improved quality of life. The most frequently reported adverse event in this literature review was the recurrence of lesions, noted in only four studies with more than ten

patients [6,8,10,12]. One reported recurrence occurred after nine months of follow-up12, suggesting a need for a longer follow-up period in future clinical studies.

PBM, whether used as a standalone or adjunct treatment, is effective for the preventive or therapeutic management of MRONJ [20]. However, establishing a standardized and replicable protocol remains inconclusive due to a high risk of bias in most studies. Nonetheless, it is possible to extrapolate the PBM dosimetry from two studies that closely align with the WALT recommendations parameters [20].

CASE REPORT

Medical History

In February 2011 a 57-year-old man had been diagnosed with right renal carcinoma.

The patient provided both oral and written informed consent for treatment.

The patient underwent a radical right nephrectomy, resulting in a histological diagnosis of clear renal cell carcinoma, Fuhrman grade 3, infiltrating. In November 2012, due to pulmonary recurrence, the patient underwent left pulmonary metastasectomy surgery followed by an active surveillance program.

In October 2016, a thorax-abdomen CT scan showed secondary localizations at the level of the right renal loggia, the rectus muscle of the left abdomen, and a lymph node in the left inguinal location for which he started monthly cycles of systemic first-line treatment with a tyrosine kinase (TK) inhibitor having antiangiogenic activity (vascular endothelial growth factor-VEGF), the Sunitinib (Sutent®). (Table 3)

In 2018, a new CT scan showed, at the lateral profile of the quadratus muscle of the loins, a tissue thickening of approximately 11 mm in transverse diameter, suggestive of small focal recurrence of disease, for which he underwent stereo-ablative IGRT (Image Guided radiotherapy) treatment on the location at the level of the lateral profile of the right quadratus muscle of the loins. In January 2020, following the onset of pain and functional limitation of the right upper limb, he underwent a CT scan of the shoulder and right humerus which showed a secondary localization to the head and upper third of the right humerus for which he was initially treated with stereotactic radiotherapy without improving. Thus, resection of the proximal right humerus and reconstruction with an inverted prosthesis of the right shoulder was performed at Orthopedic Clinica of Padova, Italy

A further CT scan in May 2020 showed bone progression in the right femur, so treatment with Sunitinib® was discontinued and a systemic second-line treatment with Nivolumab (OPDIVO®) was administered for eight months.

This drug is indicated as monotherapy for the treatment of advanced renal cell carcinoma after prior therapy in adults. The patient received stereotactic radiotherapy at the level of the right ilio-pubic spine followed by preventive nailing surgery of the right femur after embolization of the lesion at the Orthopedic Clinica of Padova.

Throughout this period, the hematochemical examinations did not show any particular changes, except for slight anemia (11.7 g/dl in the blood count) and mild thrombocytopenia (platelet (PLT) counts of 91×10^9/L). The RCP (reactive C protein) was always within limits.

Between January 2021 and March 2023, the patient underwent antiresorptive treatment first with a bisphosphonate Zolendronic acid (Zometa®) and later with a human monoclonal antibody (IgG2) directed against RANKL (receptor activator of nuclear factor kappa B), the Denosumab (Xgeva®). At the same time, due to disease progression at the bone level, the patient was started on a third-line systemic treatment with another TK inhibitor with anti-angiogenic activity, the Cabometyx (Cabozantinib®), started at the standard dose of 60 mg per day, then reduced to 40 mg per day due to asthenia, general malaise, lack of appetite and weight loss (86 Kg), and further to 20 mg per day. Based on oncological counseling, the patient suspended the Cabometix®. This resulted in the worsening of the abdominal chest CT scan and the appearance of new lesions especially in the liver. The patient then underwent treatment with Everolimus (Afinitor®), an inhibitor of mTOR, which however he had to discontinue because of the onset of noninfectious interstitial pneumonia.

In view of this, an oncology consultation re-prescribed the first-line treatment with the Sunitinib® which he still continues. In September 2024, a new CBCT scan showed signs of stability in the absence of new injuries. The report stated: "*ipodense material, with soft tissue density, in the right frontal sinus only. Similar material in the left frontal sinus and ethmoidal cells, particularly on the right".* No signs of ONJ were found in the left maxillary bone.

Dental History

At the end of October 2022, the patient underwent a dental examination for a crushed left maxillary third molar with subsequent single-root pulpotomy surgery and extraction of residual root element (maxillary molar #2.8). About three months later, in January 2023, the patient reported intense pain in the left maxillary jaw that was unresponsive to common pain therapies, including NSAIDs but excluding opiates, and was diagnosed with osteonecrosis of the left jaw. The CT scan report from June 2023 revealed the following: In the recent extraction of tooth element 2.8, there is continuous resolution of the floor of the left maxillary sinus, with a maximum extension in the coronal plane of about 5 mm. There is complete involvement of the maxillary sinus, along with diffuse inhomogeneity of the trabecular bone structure of the alveolar process of the adjacent maxillary bone, extending anteriorly to element 2.7 for approximately 14 mm. Bone resorption is more pronounced on the buccal side, accompanied by a focal interruption of the cortical profile on the palatal side. The finding suggests a focus of left maxillary osteonecrosis. (Figure 1 and 2). The MRI confirmed the CT report: "*evidence of signs of ethmoid-maxillary sinusopathy with marginal involvement of left frontal sinus and involvement of related osteo-meatal complexes with major finding at left maxillary sinus, almost completely occupied materially fluid with fibrotic shoots*".

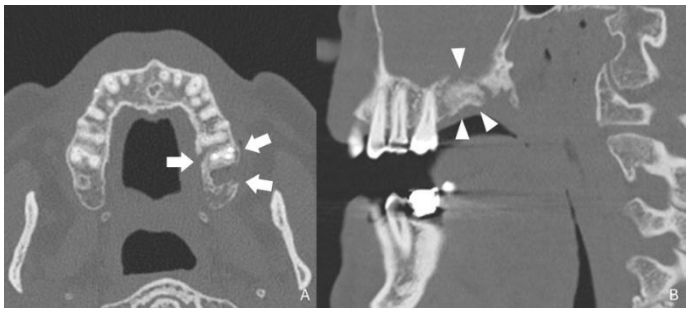


Figure 1: Axial computed tomographic image (A) and sagittal reformatted reconstruction (B) showing osteolytic change (arrows in A) with destruction of the left maxilla and a bony sequestrum (arrowheads in B), findings consistent with osteonecrosis

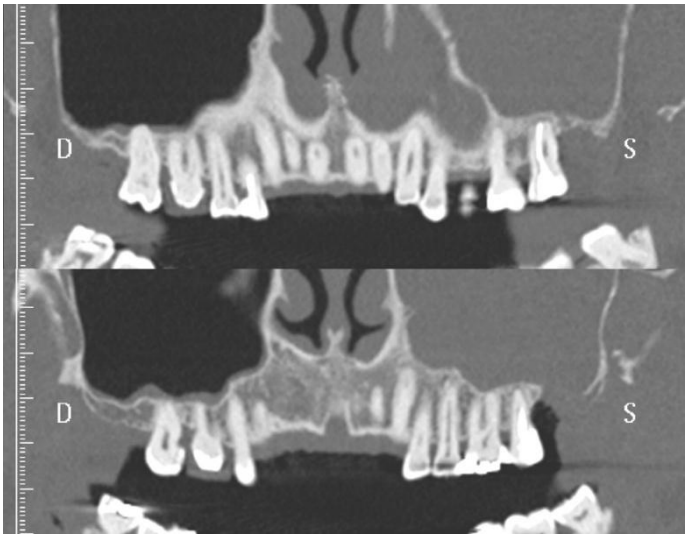


Figure 2: Panorex views derived from a Dentascan examination of the patient in June 2023, showing destruction of the left maxillary sinus floor and complete lumen opacification, suggestive of odontogenic sinusitis

Upon the dentist's prescription, the patient underwent repeated antibiotics and monthly bone curettage without experiencing any clinical improvement. A maxillofacial surgeon advised the patient to undergo surgery to remove ONJs, but he chose not to proceed with it.

In August 2023, after a private consultation with a laser therapy dental expert and nearly 11 months post tooth extraction, the patient underwent low-level laser therapy accompanied by multiple courses of antibiotics using amoxicillin-clavulanate. (1g x 3/day) and metronidazole, 750 mg x 3/day every three weeks according to protocol of Vescovi [3], resulting in clinical improvements, thereby reducing soft tissue inflammation and pain symptoms.

A diode laser (980 nm, Wiser 2, Doctor Smile, Lambda S.p.A.,Vi, Italy) in Photo-biostimulation mode was utilized once a week for three months and once a month for the following six months, with the following parameters: Power: 0.3 Watt; mode: CW Fluence 10 J/cm2; frequency 20 Hz; time: 3 for 1 with twice-weekly appointments (Figure 3) associated with scrupulous home hygiene using medicated gauze (Digital Brush, Enacare, Micerium, Avegno, Ge, Italy) with scrubbing motion (roll technique), interdental brush (Interdental Brush, Enacare, Micerium, Avegno (Ge) Italy), and single tufted toothbrush (CS 708 IMPLANT BRUSH CURAPROX©, SWISS PREMIUM ORAL CARE) to better reach the distal surface of the left maxillary second molar. Over the following months, the situation continued to improve; symptoms were gradually reduced, pain was no longer present, and the macroscopic appearance of the lesion showed signs of clear improvement (Figure 4).

Figure 3: Photo biostimulation with 980-nanometer diode laser to promote and optimize healing (Wiser 3, Doctor Smile, Lambda S.p.A.,Vi, Italy)

Figure 4: Macroscopic appearance of osteonecrosis lesion in the left palatal-maxillary site

In April 2024, a significant but fairly mobile bone sequestration of approximately 15 mm by 15 mm was gently removed under anesthesia using atraumatic tweezers (Figure 5).

Figure 5: Significant and bulky bone sequestration of about 15 mm on each side following removal with atraumatic tweezers from the palatal aspect of the left maxillary retromolar area

The authors sought to accelerate healing of the resulting wound (Figure 6) with photo biostimulation sessions at least once a week, also associated with the application of an ozone-based gel (Figure 7) (Ozosan Gel® dental line Bioactiva srl, Vicenza Italy), maintained at a temperature of "below 6°C", for a second intention wound-healing of inflammatory muco-osteonecrosis conditions of the oral cavity. Six-month follow-up clinical healing aspect (Figure 8). Complete wound closure (Figure 8) of the lesion evident in Figures 3 and 4, and the current clinical outcome is satisfactory for both patient and clinician.

A radiographic follow-up conducted one year after the last one confirms near-complete resolution of the left maxillary sinusitis with restoration of the thin bony sinus floor. (Figure 9).

Figure 6: Clinical aspect of the residual wound following osteonecrosis fragment removal

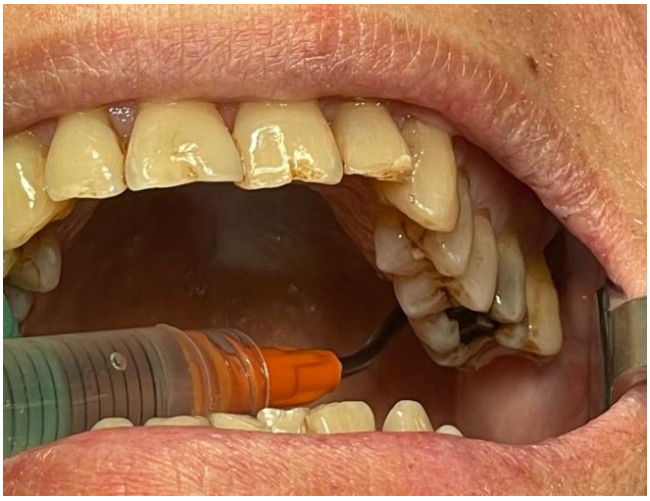


Figure 7: Pure ozone was kept in a refrigerator until use was applied to create a thermal shock, which assisted its biological effect (Ozosan Gel® dental line Bioactiva srl, Vicenza Italy)

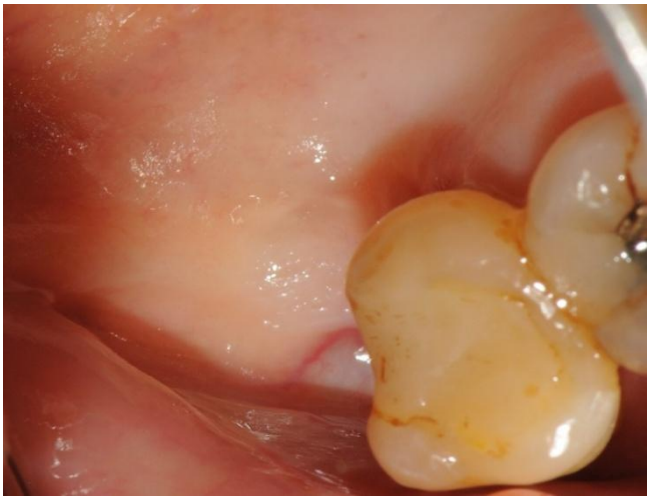


Figure 8: Clinical healing aspect of the same site as in Figures 2 and 4. Complete wound closure is observed at six-month follow-up

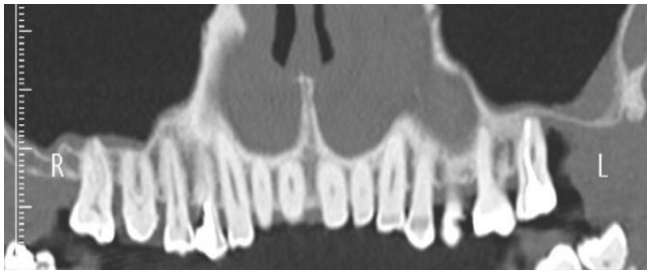


Figure 9: Comparative Panorex view versus Figure 2, derived from a Dentascan examination after treatment; note the near-complete resolution of the left maxillary sinusitis with restoration of the thin bony floor of the sinus

DISCUSSION

Two classes of drugs are implicated in the etiopathogenesis of drug-related MRONJ: drugs with predominantly antiresorptive activity, such as bisphosphonates (particularly aminobiphosphonates), and Denosumab and drugs VEGFR-TK inhibitors with predominantly anti-angiogenic activity, such as Sutent® Sorafenib®, Cabometix® and mTOR inhibitors Everolimus® and Temsirolimus® [21].

Patients receiving concomitant treatment with VEGFR-TK inhibitors and bone resorption inhibitors have a five to ten times higher risk for the development of MRONJ compared to patients treated with bone resorption inhibitors alone [21,22].

The patient studied was a patient with RCC who had been exposed over time to several lines of TK and mTOR inhibitors and antiresorptive drugs that have contributed to the ONJ likely associated with inhibition of the vascular endothelial growth factor (VEGF) pathway, which involved inhibition of angiogenesis and hindering local host defense mechanisms [23]. However, the oral trigger of bone necrosis appeared after tooth root extraction. Concomitant risk factors include tooth extractions (in about 60% of cases), invasive dental surgery during the course of anti-resorptive therapy and duration of the therapy [24]. Patients previously exposed to bisphosphonates and TK inhibitors may experience MRONJ, especially after oral surgical interventions [20,22]. It is likely that healing was achieved by Laser-Assisted Management photo-biostimodulation sessions associated with the application of an ozone-based gel. As shown in previous studies [3,25], in addition to having a bactericidal action, the laser has a 'biostimulating action", which accelerates soft tissue and bone healing compared with conventional treatments. Low-level laser therapy (LLLT) is a logical additional option, as it has been recognized effective for the management of chemotherapy and/or radiotherapy-induced mucositis [26]. LLLT irradiation has anti-inflammatory actions and thus can help to control pain, as well as biostimulating properties with favorable actions on bacterial control and wound healing [26]. Ozone has antimicrobial and wound-healing properties. The O_3 could induce tissue repair by cleansing the osteonecrotic lesions, and leading to mucosal healing [24]. Ozone therapy in the management of bone necrosis or in extractive sites during and after oral surgery in patients treated with BPs may stimulate cell proliferation and soft tissue healing [3].

Several types of ozone products have been explored in the literature, yielding varying degrees of success [27-30]. The specific material utilized in this clinical case must be stored in a refrigerator at a consistent temperature until application [31,32]. By leveraging the thermal shock effect it can induce in tissues, this ozone product retains considerable amounts of ozone for an extended period, provided it is thermally stabilized. This stabilization is crucial for maximizing its efficacy in therapeutic applications. Evidence to date suggests that health care providers can lower the risk further by dental evaluations and care prior to initiating antiresorptive therapies and by monitoring dental health during and after treatment [21,33].

Table 2: Summary of the characteristics and results of the included studies

Author and year	Study design	Sample size	Cause-factor of MRONJ	Treatment	Laser parameters	Timing of application	Follow-up	Results	Adverse effects
Scoletta et al. 2010	Prospective study	20 p	Biphosphonates: (15 oncologic, 5 non-oncologic)	PBM	GaAs diode laser 904nm: 200mW, SPW mode (50kHz), 28.4 J/cm^2, 0.4 W/cm^2	10 laser irradiation sessions over 20 days: four sessions in the first week, three sessions in the second week, and three in the last week	8 mo	Symptoms remained stable in 17 p, and the size of lesions remained stable in 16 p, two failures	During the follow-up period, three patients developed new lesions with pus, two patients had new fistulas, and two patients reported halitosis
Martins et al. 2012	Retrospective study	22 p	Biphosphonates: (22 oncologic)	CS+Med+ PBM	Indium-gallium-aluminum-phosphide (InGaAlP) diode laser 660 nm: 40mW, 6 J/cm^2, 6 s, 0.24 J	Laser irradiation started at the first visit and continued daily until mucosal healing was observed	6 mo	Sixteen (72%) of patients exhibited complete response after 6-months of follow-up	NA
Altay et al. 2012	Case series	11 p	Biphosphonates: (11 oncologic)	CS+Med+ PBM	GaAlAs diode laser 808 nm continuous wave, 0.5 W, 5 J/cm^2, 120-sec tot	1, 3, 5, 7, and 10 post-operative days	8-25 mo	An uneventful healing was achieved in seven patients. Gradual relief of previously recorded symptoms notably evident after postoperative day 3 was recorded for the patient.	Because of the broad extent of the lesions and inadequate bony support, failure of primary closure and consequent secondary healing was observed in four patients.
Merigo et al. 2018	Case series	21 p	Biphosphonates: (11 oncologic, 9 non-oncologic)	Piezosurgery+ Er:YAG+PRP+ PBM	Diode laser 808 nm: 1 W of power in continuous mode for 1 minute for 5 times (TF:21231 J/cm2)	First session after suture; subsequent ones 2 times/ week until completely closed surgical wound.	9.6 mo	Complete recovery was observed in 20 out of 21 patients (95.23%)	One patient (Stage 3) showed a recurrence after 9 months
Favia et al. 2018	Retrospective study	106 p	Biphosphonates: (95 oncologic, 36 non-oncologic)	Med+PBM	Diode laser 800 ± 10 nm, at the power of 0.5–1 W	NA	18 mo	In all stage I and II patients and 86.5% of stage III, lesions completely healed, and there was no evidence of MRONJ persistence or recurrence.	Only 13.5% of stage III lesions did not heal but rather underwent a reduction in staging
Tenore et al. 2020	Retrospective study	34 p	Biphosphonates: (34 oncologic)	13 p: CS+L-PRF+PBM 8 p: Med+CS 13 p: Med+ PBM	Multidiodic laser (650, 810, 980 nm): 0.6 W, time of 15 min, frequency 30 kHz, and total energy of 577.4 J.	Two sessions per week for four weeks (total of eight sessions)	6 mo	At six months follow-up, complete healing was recorded in 22 patients (64.7%), clinical improvement in 7 patients (20.6%)	Recurrence in 5 patients (14.7%)
Nica et al. 2021	Prospective study	241 p (“at risk” p= 84 STAGE 0= 49	Biphosphonates (143 non-oncologic patients; 98 oncologic)	STAGE 0= Med+PBM STAGE 1, 2 and 3= Med+ preoperative PBM+ Piezosurgery	InGaAsP Diode laser 940 nm: 100 mW, power density 157.4 W/cm2 , in continuous mode, 40 s on each side, energy 8 J per each session, energy density 3.937 J/cm2	During the 7 consecutive days, followed by other 6 sessions distributed in the following 2 weeks	6 mo	Pain reduction and a decrease in mucosal inflammation for all STAGE 0 patients. The percentage of complete healing of patients in stage 1, 2 and 3 was 91,66% (while for 7,4% a downscaling to stage 1 was obtained)	NA

		STAGE 1, 2 and 3= 108)							
Author and year	Study design	Sample size	Cause-factor of MRONJ	Treatment	Laser parameters	Timing of application	Follow-up	Results	Adverse effects
Valente and Andreana 2018	Case report	1 p	Biphosphonates (oncologic patient)	Minimally invasive single-flap surgery + Med + PBM	Diode-laser 810 nm: 0.8 W in continuous pulse energy mode	4 weekly consecutive biostimulations (starting one week after surgery and repeating once every 7 days)	24 mo	Good radiographic and clinical results already evident at 9 months	No adverse effects
Sánchez Ramíre et al. 2024	Case report	1 p	Biphosphonates (non-oncologic patient)	Piezosurgery+Med + PBM	Diode laser 808nm: 40,64J/cm2: 1W	Daily laser sessions until day 3, then twice a week for four weeks	60 days	At day 30, complete wound healing, after 60 days, the CT scan showed hyperdense cancellous bone with well-formed cortical and no alterations	No adverse effects
Romeo et al. 2011	Pilot study	12 p	Biphosphonates: (11 oncologic, 1 non-oncologic)	Regularization of sharp necrotic exposed bone surfaces+ Med+ PBM	GaAs double diode laser 650 and 904–910 nm: continuous mode 100 mW + super-pulsed emission mode 50 kHz, peak power 45W, average power 500 mW, pulse duration 200 ns	A total of nine cycles: every 3 days for 2 weeks	6 mo	Reduced pain. One patient had complete mucosal healing after the spontaneous removal of a small bony sequestrum; for three patients, sequestrum removal was not spontaneous but by the operator. The remaining eight patients showed clinical improvement and partial mucosal closure.	One of the patients presented a single new lesion during the follow-up period
Porcaro et al. 2015	Case report	1 p	Biphosphonates (oncologic patient)	Med+ Er:YAG + PBM	Diode laser 890nm: continuous mode	Three cycles of 1 minute were repeated once a week until complete healing was observed (23 cycles of biostimulation)	12 mo	lesion regression from stage 3 to stage 1 and nearly complete healing without symptoms and suppuration.	No adverse effects
Fornaini et al. 2017	Case report	1 p	Biphosphonates (oncologic patient	Er::YAG+ PRP+ PBM	Diode laser 808 nm: 1 W in continuous mode, 1 minute for 5 times, (TF: 21231 J/cm2)	First irradiation after the suturing; subsequent ones 2 times/week until suture removal and completely closed wound	2 ys	Complete healing of the MRONJ	No adverse effects and no recurrence
Monteiro et al. 2021	Case report	1 p	Antineoplasic multi-target drug (oncologic patient)	PBM	Diode laser 635 nm: in a continuous mode for 25 seconds,10 J/ cm2	5 sessions during 5 consecutive weeks (one session per week)	6 mo	Immediate relief after the first session; complete mucosa healing after 1 month, bone integrity confirmed on radiographs.	No recurrence
Da Guarda et al. 2012	Case report	1 p	Biphosphonates (oncologic patient	Curettage of bone+ Med+ PBM	GaAlAs diode laser 860 nm: 70 mW; continuous wave; 4.2 J/cm2	every 48 hours for 10 days (a total of five treatment sessions)	12 mo	After 7 days, good healing results, without evidence of complications until the 30th day of follow-up.	No complications and no recurrence

Abbreviations:
p: patient
PBM: Photobiomodulation
CS: Conventional surgery
L-PRF: Leukocyte- and platelet-rich fibrin
PRP: platelet-rich plasma
TF: theoretical fluence
Med: Antimicrobial mouth rinses and antibiotic medication
NA: not assessed

Parameters	*Value/ characteristics*
Wavelength	
Operating mode	
Power	W
Beam spot size at target	
Duration (per cm^2)	
Energy per point	J
Radiant exposure	J/cm^2
Area irradiated	cm^2
Application technique	Contact/noncontact mode and the distance
Number and frequency of treatments	

Table 3: Shows the drugs, dosage, and duration of intake over time

Target agent 1st line-therapy	**Duration of 1st line-therapy (months) and response**	**Target agent 2nd line therapy**	**Duration of 2nd line therapy (months) and response**	**Target agent Third line therapy**	**Duration of Third-line therapy (months) and response**	**Target agent Fourth-line therapy**	**Duration of fourth-line therapy (months) and response**	**Re-challenge**
Sunitinib * (Sutent ®)	26 (April 2016 - March 2019) PR	Nivolumab^ (Opdivo ®)	8 months (May 2020- December 2020) PR	Cabozantb^^ (Cabometix®) antiresorptive treatment#	23 (January 2021-March 2023) BR	Everolimus§ (Afinitor ®)	6 April 2023-Sept 2023 BR	Sunitinib (Sutent ®) October 2023 - present

* cyclic doses of 37.8 mg once daily for 2 weeks followed by 1 week off ; ^ dose of 480 mg g1q28 every 4 weeks, ^^ standard dose of 60 mg per day, then reduced to 40 mg; § 10 mg once daily; PR = partial response, BR = bad response;
#Zolendronic acid (Zometa ®) administered intravenously at a single monthly dosage of 4 mg and then Denosumab (Xgeva ®) administered as single subcutaneous injection at a dose of 120 mg once every 4 weeks

CONCLUSION

Patient's satisfactory standard of home care and dedicated maintenance, combined with an ozone-based gel application and with adjunctive repeated diode laser photo biostimulation therapy, successfully promoted relevant second intention wound-healing, yielded significant clinical and CBCT improvements at an observation period of 8 months. The clinical outcomes of this case report might be relevant in managing MRONJ.

Conflicts of Interest

The author reports no conflicts of interest.

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