



Photodynamic Therapy and Photobiomodulation in the Treatment of Osteonecrosis: A Series of Cases

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Abstract

Introduction: This study reports five cases of osteonecrosis treated with photobiomodulation and antimicrobial photodynamic therapy (aPDT).

Methods: One patient had osteoradionecrosis, another had spontaneous osteonecrosis, and three had osteonecrosis associated with medication, all of which were smaller than 1 cm, with or without bone sequestration. aPDT sessions used 0.01% methylene blue followed by 9 J of red light and photobiomodulation sessions ranging from 1 to 3 Joules of red or infrared light. In one of the cases observed, osteoplasty was necessary to reduce exposed bone height.

Results: aPDT and photobiomodulation produced positive clinical responses, either alone or as adjuncts to minimally invasive procedures.

Conclusion: aPDT associated with photobiomodulation, removal of necrotic bone tissue, bone reduction, and antibiotic therapy proved to be effective in treating osteonecrosis described in the five cases reported.

Keywords: Photobiomodulation, Osteonecrosis, Antimicrobial photodynamic therapy

Introduction

Osteonecrosis of the jaws is associated with radiotherapy, bisphosphonates, and anti-angiogenic medications, presenting as persistent bone exposure, pain, fistulas, and tooth loss. The management of osteonecrosis of the jaws is complex and depends on the stage of the disease and the patient's systemic condition. Conservative approaches are preferred because they reduce the risk of surgical complications.¹⁻³

Conservative management typically involves antibiotics and hyperbaric oxygen therapy. Recently, the combination of antimicrobial photodynamic therapy (aPDT) and photobiomodulation (PBM) has shown promising results. aPDT uses a laser-activated photosensitizer to reduce the infectious load, while PBM stimulates tissue regeneration and modulates inflammation. This study presents clinical cases using this association as an effective and minimally invasive alternative in the treatment of osteonecrosis of the jaws.⁴⁻⁷ The treatment parameters used in all cases are summarized in Table 1.

This study aims to explore alternative therapies for the management of osteonecrosis, offering a minimally invasive and potentially effective therapeutic option.

Case 1

A 64-year-old male patient presented to the School

of Dentistry Clinic at the Christus University Center (Unichristus) with the main complaint of a non-healing area after tooth 34 had been extracted (Figure 1a). He had a history of chemotherapy and radiotherapy treatment for squamous cell carcinoma (SCC) in the jugal mucosa region in 2016; he underwent radiotherapy totaling 7,000cGy to the primary site and 4,600cGy to the cervical lymphatic drainage areas. On intraoral clinical examination, necrotic bone exposure was observed at the edge of the alveolar ridge on the right (Figure 1a). A computed tomography (CT) scan was performed to aid diagnosis, in which no area of bone sequestration was observed in the region.

The initial treatment proposed for the region of osteoradionecrosis was 3 sessions of antimicrobial Photodynamic Therapy (aPDT) using methylene blue gel 0.01% (Chimiolux) as a photosensitizer for 5 minutes and photobiomodulation with a laser (Therapy XT® - Diode laser, DMC, São Carlos, Brazil) with 9 J of red light (660 ± 10 nm; 100 mW) punctually on the exposed bone region once a week and photobiomodulation: 1 J red light (mucosa) and 3 J infrared (vestibular/lingual areas).

After three weeks, minimal surgical intervention was considered to lower the necrotic bone in order to facilitate the union of mucosal tissues. Laboratory tests (prothrombin time (PT), activated partial thromboplastin time (APTT), and complete blood count) were obtained

Table 1. Summary of Treatment Parameters for All Cases

Case	aPDT Protocol	PBM Protocol	Sessions	Antibiotics	Surgical Adjuncts
1	-Photosensitizer: 0.01% methylene blue (5 min); -Laser: 660±10nm, 100 mW - 9J applied directly to exposed bone	- 1J red (mucosa) - 3J infrared (vestibular/lingual)	- aPDT: 7 - PBM: 5	-Amoxicillin 500mg, 1 day before+7 days after (total 8 days)	Bone reduction with a spherical diamond bur
2	Same aPDT protocol as Case 1	- 1J red (mucosa)	- aPDT: 2 - PBM: 1	None	Removal of bone sequestrum (spicule)
3	Same aPDT protocol as above	- 2J infrared on surgical area (post-debridement)	- aPDT: 3 sessions (1 initial +2 after osteoplasty) - PBM: 1	- Amoxicillin 875mg+Clavulanate 125mg for 15 days	Bone reduction with a spherical diamond bur
4	-Laser: 660nm (red) / 808nm (infrared) Protocol combined with PBM over 14 weeks	- 808nm infrared - 2–4J/point	- 28 combined aPDT + PBM sessions over 14 weeks	- Clindamycin 300mg, 3x/ day for 7 days	Debridement of non-resistant sequestrum after 28 sessions
5	1 session of aPDT (methylene blue+light; same general protocol)	- 2J infrared around lesion edges (weekly, 4 sessions) - Post-op: 2J red on mucosa	- aPDT: 1 - PBM: 4 pre-debridement+1 post-op	- Clindamycin 300mg every 8h for 7 days	Debridement of non-resistant necrotic bone (after 6th session)

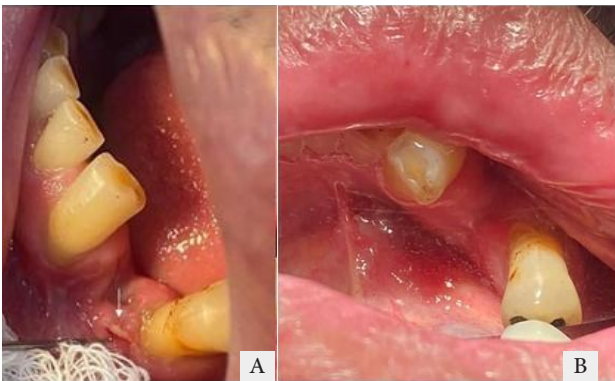


Figure 1. Intraoral photos. **A.** Arrow: Region of exposure of a necrotic lesion on the region of the lower premolars. **B.** Healed region after the antimicrobial photodynamic therapy (aPDT) and photobiomodulation protocols after 3 months of treatment

prior to the procedure, and they were within the normal range. The prescribed pharmacological regimen was antibiotic coverage with oral administration of amoxicillin (500mg) for 8 days, in which the patient was instructed to start the protocol by taking 1 tablet 1 day before the procedure and continue taking it for the following 7 days. After preparation, standard antisepsis with 2% chlorhexidine was performed (extraoral) and bone reduction was performed with a spherical diamond tip followed by the application of the already established aPDT protocol.

Over the next four weeks, the aPDT and photobiomodulation protocols continued as previously planned. The patient returned with complete remission of the lesion and total healing of the mucosa (Figure 1b). A total of 7 sessions of aPDT and 5 sessions of photobiomodulation were carried out.

Case 2

A 36-year-old female patient with no history of radiotherapy treatment reported no use of medication, alcohol, or tobacco. She presented with a non-healing extraction site at tooth 45 (Figure 2a). An intra-oral examination was conducted, imaging tests were ordered, and aPDT was initiated thereafter, using the same protocol

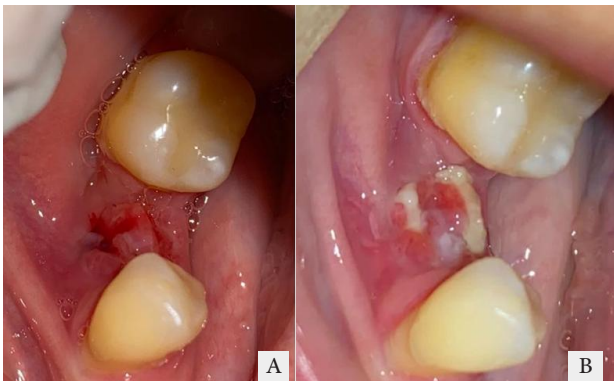


Figure 2. Intraoral photos. **A.** Region of the patient's main complaint with the presence of necrotic bone exposure observed during the first dental appointment. **B.** Region of controlled osteonecrosis and area of healing mucosa

as in case 1. Persistent inflammatory signs were noted in the following week, so the protocol with aPDT was repeated and a sequestered bone spicule was removed. In the following week, the infection regressed, and then PBM was applied with 1J red per point on the alveolar mucosa. After a week, the patient returned, showing complete healing of the alveolar ridge and remission of the bone necrosis (Figure 2b). In total, 2 sessions of aPDT and 1 session of photobiomodulation were carried out with an interval of 1 week between each protocol.

Case 3

A 55-year-old male patient presented with pain when eating in the molar region. Anamnesis revealed that the patient had Multiple Myeloma and was treated with 9 cycles of Cyclophosphamide 50 mg+Thalidomide 100 mg+Dexamethasone in 2017. He subsequently underwent a bone marrow transplant and received Cyclophosphamide 540 mg+Bortezomib 2.7 mg (17 doses) until 2021.

During the intraoral clinical examination, bone exposure was observed in the region of tooth 47 (Figure 3a). Imaging examinations were requested, and aPDT was performed at the first appointment,

following the same protocol as in this study (Figure 3b). In the following two weeks, the bone was lowered with a spherical diamond tip under saline irrigation, followed by the same protocol with aPDT and antibiotic coverage with Amoxicillin 875 mg + Potassium Clavulanate 125 mg for 15 days (Figure 3c). After 7 days, the patient returned and underwent a photobiomodulation session, with complete closure of the surgical wound, and 2 J infrared was then applied to the area described (Figure 3d).

Case 4

A 71-year-old male patient with multiple myeloma who had been receiving zoledronic acid for more than two years presented to the Unichristus School of Dentistry Clinic with severe mandibular pain and an area of bone exposure that had been evolving for the past two months. Clinical examination revealed areas of mandibular torus in the anterior and posterior lingual region and a 2cm, well-circumscribed bone exposure, surrounded by erythema, edema, and purulent drainage compatible with drug-related osteonecrosis (Figure 4a,b).

Clindamycin 300 mg (3x/day for 7 days) and mouthwash with 0.12% chlorhexidine were prescribed. The oncologist suspended the use of Zoledronic acid, and imaging tests and a blood count were ordered. After seven days, CT imaging revealed hyperdense areas in the mandible without clear signs of necrosis. A total of 28 aPDT and

PBM sessions were administered over 14 weeks using a 808-nm laser (Laser Therapy XT-DMC, 100mW, 606nm red/ 808nm infrared) with therapeutic energy ranging from 2-4 J/point.

One month after treatment began, there was a significant improvement in edema, pain, erythema and drainage of purulent secretion. A CT scan was carried out in which a hyperdense area was observed, accompanied by a small hypodense line just below, separating the necrotic bone from the healthy tissue (bone sequestration). Two months after the start of treatment, a new CT scan was carried out which showed a hypodense area below the hyperdense area, showing an almost complete separation between necrotic tissue and healthy bone tissue (Figure 4c,d).

After 28 sessions, the non-resistant bone sequestration was debrided, with neoformed epithelial tissue and satisfactory healing (Figure 5).

Case 5

A 55-year-old male patient presented to the Unichristus School of Dentistry Clinic, reporting pain in his mandible. During anamnesis, he reported a diagnosis of osteoporosis and the use of Zoledronic Acid. Clinical examination revealed a lesion in the mandibular torus region with erythematous borders, a hardened consistency, and a grayish-white color, suggesting mandibular osteonecrosis (Figure 6a).



Figure 3. Intraoral photos. **A.** Region of the patient's main complaint with exposure of a necrotic bone lesion in the lingual region of the lower molars. **B.** Application of photosensitizing agent methylene blue gel at 0.01% concentration (Chimilux) for 5 minutes. **C.** Bone debridement with spherical diamond drill. **D.** Healed area of osteonecrosis



Figure 4. **A.** Bone exposure measuring approximately 2 centimeters, well circumscribed, with a slightly erythematous area around it, with drainage of purulent and yellowish secretion, with a clinical diagnosis compatible with Bisphosphonate-Induced Mandibular Osteonecrosis. **B.** Computed Tomography (CT) scan in axial section, before treatment, showing hyperdense areas throughout the mandible. It is not possible to delineate the bone necrosis observed clinically. **C, D.** After two months of conservative treatment, a new CT scan was carried out, showing a hypodense area below a hyperdense area, indicating almost complete separation between necrotic tissue and healthy bone tissue.

After imaging tests, clindamycin 300 mg was prescribed every 8 hours for 7 days. Four sessions of PBM were carried out each week, with an infrared laser used at an energy of 2 J around the edges of the necrotic lesion and one session of aPDT.

By the sixth session, inflammatory signs had resolved and the necrotic tissue had detached, allowing surgical debridement without resistance (Figure 6b). After seven days, the surgical area was completely closed, with mild erythema still present. At this stage, an additional session of red laser photobiomodulation (2 J per point) was performed. The treatment resulted in re-epithelialization, closure of bone exposure, and pain improvement (Figure 6C).

Discussion

The diagnosis of OM is complex, and diagnosis requires the integration of clinical, imaging and medical findings. To this end, it is common for osteonecrosis findings to be observed by professionals in ulcerative stages, accompanied by pain, which are often associated with secondary infections, including bone sequestration or fractures⁸. In these cases, it was possible to observe the common complaint of a lesion that did not heal, whether due to traumatic factors (exodontia) or spontaneous factors, which is common in the management of radiotherapy patients.

The present case series demonstrates favorable clinical responses to conservative management of osteonecrosis using photobiomodulation (PBM) and antimicrobial

photodynamic therapy (aPDT), either alone or as adjuncts to minimally invasive procedures. Although osteonecrosis of the jaws remains a challenging condition, especially in patients receiving antiresorptive or antiangiogenic agents, conservative protocols have gained importance as first-line strategies for early stages of the disease^{1,8}.

PBM has positive effects in the treatment of various oral pathologies and conditions, such as mucositis, trismus, paresthesia, and neuralgia, and recent research shows that it also promotes tissue repair through biomodulatory effects that include enhanced angiogenesis, reduced inflammation, modulation of pain, and stimulation of osteoblastic activity. These cellular effects have been associated with improved healing in MRONJ and ORN lesions across multiple clinical reports and systematic reviews.^{9,10,11} In the present cases, PBM contributed to notable reductions in pain, edema, and inflammatory signs, supporting published evidence and reinforcing its role as a non-invasive therapeutic option.

aPDT provides complementary benefits by reducing the local microbial load through the activation of a photosensitizer and the production of reactive oxygen species. This mechanism allows broad-spectrum antimicrobial action without inducing bacterial resistance¹². Prior clinical and experimental studies have demonstrated that aPDT can enhance alveolar repair and prevent the progression of osteonecrosis in patients and animal models^{13,14}. In our cases, aPDT assisted in infection control, facilitating granulation tissue formation and mucosal coverage.

The combined use of PBM and aPDT appears to offer synergistic advantages by pairing microbial reduction with biostimulation. Reports suggest improved mucosal healing, symptom reduction, and overall clinical stability when these modalities are incorporated into conservative protocols for MRONJ and ORN^{1,13}. The present findings are consistent with this evidence, as patients receiving the combined approach showed progressive lesion resolution with minimal morbidity.

Antibiotics were used selectively when acute infection was present or surgical manipulation was anticipated. Although they may help reduce bacterial burden and control acute inflammatory episodes, their role is supportive rather than definitive, and their benefits appear



Figure 5. The patient returned seven days after debridement and satisfactory healing was observed. The patient is being followed up without recurrence, pain or mandibular discomfort.

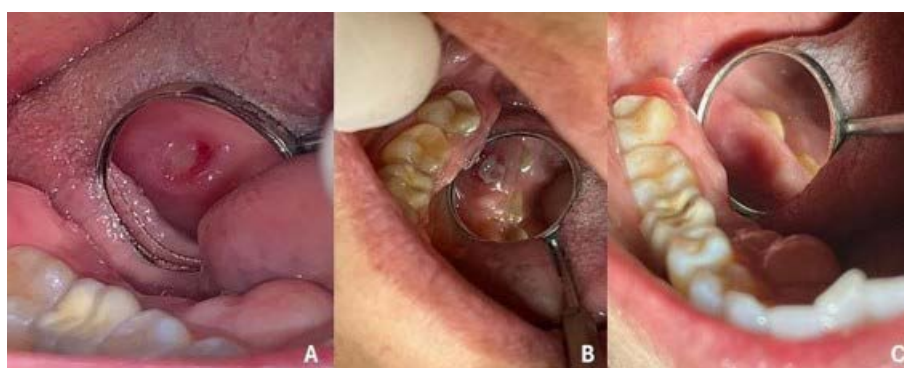


Figure 6. Intraoral photos. **A.** Lesion in the mandibular torus region with erythematous borders, hardened consistency and grayish-white color. **B.** Detachable necrotic area for surgical debridement. **C.** Surgical area completely closed after 7 days of surgical debridement

enhanced when integrated with adjunctive modalities such as PBM and aPDT^{7,13}.

There was no difference in efficacy between the use of red or infrared wavelengths, and methylene blue was chosen as an alternative photosensitizer.¹² The use of methylene blue as a photosensitizer in the five cases is based on safety and is used in aPDT for infections with a wide variety.¹⁵

The scientific literature presents a diversity of protocols for the treatment of osteonecrosis using photobiomodulation (PBM) and antimicrobial photodynamic therapy (aPDT), reflecting the lack of a definitive consensus on the ideal application parameters⁶. Several studies use a dosage of between 2 and 4J of infrared light for photobiomodulation in bone tissue and 1 to 3J of red light in the mucosal region. For aPDT, the protocol varies between 6 and 9J. This variability highlights the need for individualized approaches, adapted to the particularities of each patient and the specificity of the lesion.

Even if surgical treatment is the modality of choice for treating ONM, the use of aPDT and PBM should be considered since their effects can contribute to patient recovery and reduce recurrences at the surgical site. Overall, this case series highlights the usefulness of conservative, minimally invasive therapies for managing osteonecrosis of the jaws and suggests that PBM and aPDT can contribute to clinically meaningful improvements when applied in a structured protocol^{11,16,17}.

Limitations

This case series has limitations, including the small sample size, absence of a control group, heterogeneity among cases, and lack of standardized outcome measures. In addition, variations in treatment parameters may limit reproducibility. Further controlled studies with standardized protocols are needed.

Conclusion

The adjuvant use of aPDT, Photobiomodulation, bone sequestration removal, bone debulking, and antibiotics was successful in treating osteonecrosis in the five cases reported, elucidating that non-invasive therapies can effectively manage necrotic lesions.

Authors' Contribution

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Validation: Thinali Sousa Dantas.
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Writing—Review & Editing: Thinali Sousa Dantas.

Competing Interests

The authors have no conflict of interest.

Ethical Approval

This study was approved by the Human Research Ethics Committee under protocol number 7.112.041. Written informed consent was obtained from all patients.

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