



# Antimicrobial Photodynamic Therapy for the Treatment of Alveolar Osteitis in a Patient With Acute Lymphoid Leukemia: A Case Report

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## Abstract

**Introduction:** Acute lymphoid leukemia (ALL) is a malignant disease, the prognosis of which depends on the age of the patient and the treatment. The aim of this article was to report the treatment of this rare and interesting case of alveolar osteitis with antimicrobial photodynamic therapy (aPDT) in a patient with ALL that was resolved efficiently and quickly.

**Case Presentation:** A 33-year-old male diagnosed with ALL attended the public service, complaining of pain in the region of tooth 48, without function. Extraction was performed, and the patient returned for postoperative follow-up, complaining of severe pain in the area of the alveolus. Clinical examination revealed osteitis. The alveolus was treated using aPDT with 0.005% methylene blue photosensitizer, followed by the application of a low-level red laser at a wavelength of 660 nm (321 J/cm<sup>2</sup> – site). After 15 days, soft tissue closure was observed and complete filling of the alveolus was observed radiographically with a 7-month follow-up.

**Conclusion:** The authors suggest that aPDT can be an effective treatment of alveolar osteitis in a patient with ALL.

**Keywords:** Antimicrobial photodynamic therapy, Acute lymphoid leukemia, Alveolar osteitis

## Introduction

Acute lymphoid leukemia (ALL) is a pediatric malignancy that has a good prognosis and a high cure rate. It can also occur in adults, although less frequently, and the prognosis is less favorable, with frequent relapses. There are several factors responsible for the poor prognosis of ALL in adults, including comorbidities, low adherence to treatment and a higher frequency of high-risk genomic subgroups.<sup>1</sup>

Alveolar osteitis (alveolitis) is one of the most common complications after the extraction of permanent teeth and usually presents as an open wound with clot degradation, delayed healing and severe pain. Treatment is aimed at relieving pain and promoting the healing of exposed bone by palliative means.<sup>2</sup>

In dentistry, low-level laser therapy (LLLT) has been used predominantly as photobiomodulation therapy to accelerate the onset of the wound healing process, to relieve tissue inflammation, to improve local immunity and to normalize periodontal microcirculation in vivo studies during chemotherapy.<sup>3,4</sup> In addition to LLLT, antimicrobial photodynamic therapy (aPDT) has been

used for the treatment of infections, based on the concept of a photosensitizing agent that absorbs and is activated by a specific wavelength of light in the presence of oxygen, producing physicochemical reactions that culminate in the formation of oxygen-reactive species, mainly singlet oxygen, which are cytotoxic to microorganisms.<sup>5</sup> With a specific mechanism of action, aPDT has an immediate advantage in microbial reduction.<sup>6</sup>

There are few studies in the literature that treat simple tooth socket infections after extraction with aPDT.<sup>7,8</sup> A study carried out on humans showed beneficial results using a-PDT for the prevention of post-extraction alveolitis<sup>7</sup>. In another study, carried out on rats, it was concluded that aPDT was an effective antimicrobial treatment for tooth sockets in areas affected by induced periodontitis.<sup>8</sup>

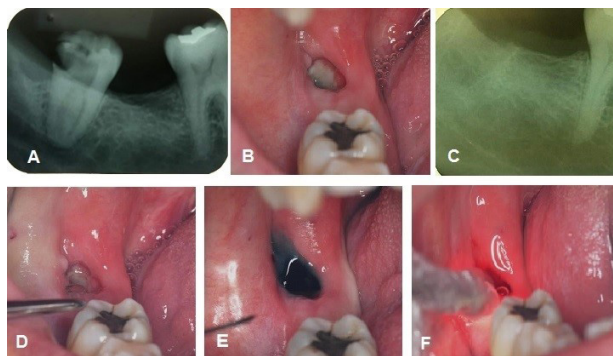
Thus, the aim of this article was to report the results of a rare case of alveolar osteitis treatment with aPDT in a patient with ALL.

## Case Report

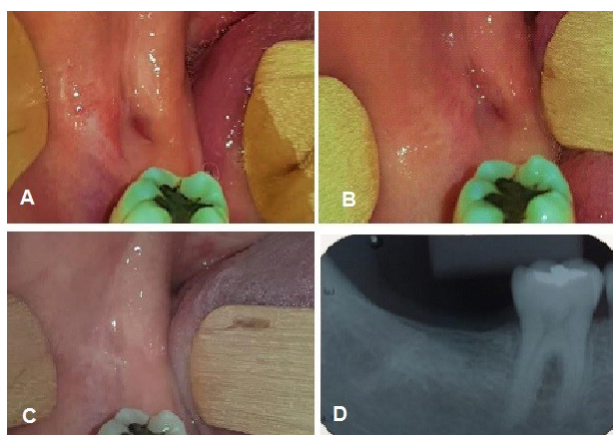
A 33-year-old white male patient, diagnosed with ALL in

2017, attended the clinic of the Faculty of Dentistry of the Federal University of Goiás, Goiânia, Brazil, complaining of pain in the region of tooth 48. He reported that he was a calm person and had no history of genetic diseases in his family and that he was in his 17th chemotherapy cycle (Medicines: Mercaptopurine 50 mg, vincristine 1.4 mg associated with prednisone 20 mg and omeprazole 20 mg). Clinical and radiographic findings showed an extensive open cavity at the subgingival level in tooth 48 (Figure 1A) and with no masticatory function. Due to the requirement to eliminate the infectious focus due to ALL, tooth extraction was performed with the agreement of the patient and his hematologist. His doctor sent us a report authorizing the surgical procedure, assuring us that he was undergoing chemotherapy, he adhered well to the treatment, and he presented 6.930 microliters of the blood of leukocytes at the moment, with other blood exams within normal limits. We were also assured that it would be important to perform the extraction since the patient was in pain and the tooth was without function and with an extensive caries lesion.

After tooth extraction, analgesics and antibiotics were prescribed (following the recommendation of the



**Figure 1.** (A) Extensive radiolucent image suggestive of caries lesion with the pulp involvement of tooth 48; (B) Initial appearance of alveolitis; (C) Radiography 14 days after extraction; (D) Curettage of the socket; (E) Application of the blue methylene photosensitizer at 0.005%; (F) Application of the low-level laser.



**Figure 2.** (A) Clinical aspect 7 days after a-PDT; (B) Clinical aspect 15 days after a-PDT; (C) Clinical follow-up after 7 months; (D) Radiographic appearance after 7 months.

hematologist). After 7 days, the patient returned for postoperative examination and suture removal, and he reported mild pain in the alveolus. There was a pink mucous stain without bleeding and edema. The suture was removed, and the tissues around the alveolus were irrigated with 0.12% chlorhexidine, as there was food accumulation at the site. The patient was instructed on hygiene. Seven days later, the patient returned, complaining of severe pain and a bad smell in the alveolar region. After lymph node palpation, a slight increase in the right submandibular ganglia was noted. On clinical examination, the presence of alveolar osteitis was observed; the alveolus had a whitish center and reddish edges (Figure 1B). On periapical radiography of the region (Figure 1C), no significant alteration was found. After local anesthesia, curettage of the alveolus (Figure 1D) associated with aPDT was performed in two sessions with an interval of 7 days between them. A 0.005% methylene blue photosensitizer was applied to the alveolus with a syringe (Figure 1E) and was reapplied every minute, remaining in the region for a total of 5 minutes, and then a LLL (Laser Device: Therapy EC, DMC, São Carlos-Brazil) was applied at a wavelength of 660 nm and a 321-J/cm<sup>2</sup> dose during 90 seconds (P=100 mW, E= 9 J; spot area= 0.028 cm<sup>2</sup>) – Table 1, with the spot in direct contact with the mucosa (Figure 1F). At the end of the session, an analgesic, in case of pain, was prescribed to the patient.

No pain and no adverse events occurred, and seven days after the second session of aPDT (the same application mentioned above), there was a significant improvement in the healing of gingival tissue and almost complete closure of the socket (Figure 2A). Fifteen days later, the total

**Table 1.** Laser Parameters

Type of laser	Low-Level As-Ga-Al Laser
Emission mode	Continuous
Time on/Time off	10 seconds
Delivery system	Optical fiber
Energy distribution	by point
Peak power	not applicable
Average power	0.1 W
Spot diameter at focus	0.3 cm
Focus spot area	0.028 cm <sup>2</sup>
Spot diameter at tissue	0.3 cm
Focus-to-tissue	Against the tissue
Spot area at tissue	0.028 cm <sup>2</sup>
Peak power density at spot area	3.57 W/cm <sup>2</sup>
Peak power density at tissue	321 J/cm <sup>2</sup> (E= 9 J/tooth)
Average power density at spot area	Not applicable
Average power density at tissue	Not applicable
Beam divergence	Not applicable
Water irrigation	Not applicable
Air and aspirating airflow	Not applicable

closure of the alveolar mucosa was clinically noticeable without any sign of inflammation or infection in the gingival tissue (Figure 2B). In a maintenance consultation 7 months after the procedure, a complete recovery of the alveolus and radiopacity in the alveolus region compatible with the natural bone repair was observed (Figure 2C and 2D).

## Discussion

Alveolar osteitis is one of the most common complications after the extraction of permanent teeth and may be more frequent in immunosuppressed patients.<sup>9</sup> Treatment consists mainly of reassuring the patient and relieving pain. Several drugs have been used as local drug therapies, such as zinc oxide and eugenol, salicetin adhesive (Salicapt), and lyophilized acemannan hydrogel, the most common being Alveogyl. In a systematic review with a meta-analysis carried out by Shafae et al<sup>2</sup> it was observed that patients treated with photobiomodulation therapy reported a reduction in the level of pain around 3.41-fold greater than those treated with Alveogyl.<sup>2</sup> This was consistent with the findings of Rani et al,<sup>10</sup> who demonstrated more rapid improvement in pain and healing of osteitis in the group treated with a diode laser than in groups treated with Er: Cr: YSGG and Alveogyl.

The positive results regarding tissue healing observed in the present case are consistent with those described by Lins et al,<sup>11</sup> who evaluated the clinical findings of tissue repair after teeth extractions (36 and 47) by comparing a region treated with photobiomodulation with a region that did not receive this intervention. Twenty-four days after the surgical procedure, the region around the extraction sites treated with photobiomodulation therapy (tooth 47) showed the presence of pink color in the border area, the absence of an inflammatory reaction and edema resulting from the surgical procedure, and the absence of extravasation of blood from the alveolus walls, as observed in the present case report. In the region around extracted tooth 36, which was not treated with LLLT, pink color was observed in the border area, along with the presence of an inflammatory reaction and edema, exuberant blood leakage from the alveolus walls, and the presence of pain.<sup>11</sup>

Studies related to the use of aPDT in immunosuppressed patients with malignant lesions/diseases are scarce. It is known that photobiomodulation can accelerate the healing process, increasing the mobility of keratinocytes, the proliferation of fibroblasts, and consequently more rapid epithelialization and extracellular matrix synthesis and angiogenesis. This minimizes the effects of chemotherapy, inhibiting the proliferation of cells with mitotic activity.<sup>3</sup> aPDT is a promising treatment for the eradication of microorganisms and has been shown to be effective against bacteria, viruses, fungi and parasites, as well as in the degradation of its external virulence factors.<sup>6,12</sup> Macêdo et al<sup>12</sup> published two case reports using

aPDT in oral lesions in patients with leukemia, and they observed that aPDT had positive results and was well accepted by the patient, presenting an important adjuvant therapy to reduce the course of infectious lesions in cancer patients, as in the current clinical case.

In another study carried out in rats treated with chemotherapy, it was demonstrated that multiple sessions of LLLT as adjuvant therapy favored the healing process at sites with periodontitis, minimizing the magnitude of the local inflammatory response and accelerating the process of tissue restructuring in these animals.<sup>3</sup> These results are quite encouraging when it comes to tissue repair in patients undergoing chemotherapy.

In another recent survey, Theodoro et al<sup>5</sup> evaluated the effect of aPDT associated with photobiomodulation therapy on rats undergoing chemotherapy. The authors observed lower immunostaining for TNF- $\alpha$  and IL-6, thus demonstrating that both adjuvant therapies were effective at reducing these pro-inflammatory biomarkers. The reduction in the levels of these pro-inflammatory cytokines may have interfered in the reduction of the bone damage process aggravated by chemotherapy.<sup>5</sup> In the present case report, although no histological analysis or evaluation of pro-inflammatory markers was performed, the application of aPDT led to complete repairs of the alveolar soft tissues and the absence of signs of inflammation 15 days later.

Within the limitations of the present study, the authors suggest that aPDT could be a safe and efficient alternative of treatment in the resolution of alveolar osteitis in a patient with ALL, with a 7-month follow-up. Longitudinal studies evaluating the effectiveness of aPDT in the treatment of this type of infection, as well as in the resolution of other bone disorders, are warranted.

## Ethical Considerations

Informed consent for the execution of the procedures was obtained from the patient.

## Conflict of Interests

The authors declare that they have no conflict of interest.

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