Case Report

Treatment of Ulcerative Lesions with Low-level Laser Therapy in a Patient with SARS-CoV-2

Abstract

Ulcerated lesions have been observed in SARS-CoV-2 patients and their treatment is a challenge. We aim to report the treatment of oral lesions with low-level laser therapy (LLLT) in a patient with SARS-CoV-2. The patient diagnosed with COVID-19 was admitted to the intensive care unit, on mechanical ventilation, and on a nasogastric tube diet that persisted due to oral lesions. Painful ulcerated lesions, clinically diagnosed as viral ulcer, were found on the tongue, palate, labial commissure, and oropharynx during the oral evaluation. An antimicrobial photodynamic therapy with methylene blue and red laser (high energy) was performed, followed by treatment with LLLT with red laser. Significant clinical improvement of the lesions was observed after seven sessions of LLLT, with the oral diet being reestablished. Oral mucosal lesions in patients with COVID-19 are usually symptomatic and with onset after systemic symptoms. LLLT has been used in the management of these lesions, with promising results.

Keywords: *Laser therapy, photodynamic therapy, SARS-CoV-2*

Evllen do Vale Castro[1], Joao Victor de Paula Freitas[1], Francisco Artur Forte Oliveira[1], Lucas Alexandre Maia[1], Thinali Sousa Dantas[2], Clarissa Pessoa Fernandes Forte[1]

[1]Christus University Center, Fortaleza, Brazil, [2]Department of Dentistry, Christus University Center, Fortaleza, Brazil

Introduction

COVID-19 was the name given to the pandemic disease that emerged in late 2019, caused by a single-stranded RNA virus called SARS-CoV-2.[1,2] This virus predates patients with established systemic diseases such as hypertension, diabetes, and obesity.[1] When this virus comes into contact with the host cell, it triggers an excessive immune reaction that causes extensive tissue damage, called a cytokine storm.[1] Patients who develop the disease symptomatically present mainly fever, headache, sore throat, dyspnea, dry cough, hyposmia, hypogeusia, and in more severe cases, pneumonia.[2,3]

Angiotensin-converting enzyme 2 (ACE-2) receptors are the main gateway for the virus to enter host cells. They can be found at multiple sites, which contributes to the multisystemic involvement of COVID-19.[4] The oral cavity is one of the sites where there is high expression of ACE-2 in epithelial cells, suggesting that it is a susceptible site for SARS-CoV-2 infection to occur. Furthermore, it has been observed that the interaction of SARS-CoV-2 with ACE-2 may disrupt the functions of oral keratinocytes, resulting in painful ulcers in patients diagnosed with COVID-19.[5]

The oral lesions in patients with COVID-19 present three main etiological hypotheses. The first etiological hypothesis suggests that the oral lesions are not originated from SARS-CoV-2, but are infections caused by other viral diseases, such as herpes simplex virus or cytomegalovirus, that appear when the patient is infected with SARS-CoV-2 due to immunosuppression.[4] The second hypothesis claims that the oral lesions appear in consequence of possible adverse effects caused by the treatments used by SARS-CoV-2-infected patients,[4] and the third hypothesis relates the onset of the lesions to the presence of ACE-2 receptors in the oral epithelium.[6]

Regarding these oral lesions, the literature reports the appearance mainly of petechiae, ulcers, blisters, vesicles, macules, papules, plaques, pigmentation, and hemorrhagic crust in patients diagnosed with COVID-19.[2,3]

This article presents a case of treatment of ulcerated oral lesions with low-level laser therapy (LLLT) in a patient admitted to the intensive care unit (ICU) due to complications caused by SARS-CoV-2 infection.

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Address for correspondence:
Prof. Thinali Sousa Dantas, Department of Dentistry, Christus University Center, 133 João Adolfo Gurgel Street, Fortaleza, Brazil.
E-mail: thinali@hotmail.com

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Case Report

An 80-year-old woman, F. C. L., was diagnosed with COVID-19 and was admitted to the ICU of a large reference hospital (Unimed Regional Hospital) on April 27, 2021, due to acute respiratory distress syndrome. She was tracheostomized, on mechanical ventilation, and on a nasoenteral tube diet that persisted even after the removal of the orotracheal tube due to the presence of painful ulcerations in the oral cavity.

A dental report was requested for the patient on May 17, 2021, when painful ulcerated lesions were observed. The ulcers were well demarcated, shallow, ovoid, with yellow-gray pseudomembrane, red halo, and with areas of hemorrhage. They were located on the tongue (left side and apex), soft palate (left side), and lip commissure (left side) [Figure 1]. Considering the clinical aspect of the lesions, they were diagnosed by the dental team as viral ulcers. The ulcers located on the tongue and lip commissure were larger and had an aspect of infection. The treatment started on the same day since the patient was in pain and the ICU team was eager to remove the nasoenteral tube diet to discharge the patient. Due to the urgency of the treatment, the pandemic of COVID-19, and the typical clinical aspect of the lesions, no further serological examinations were carried out.

Photobiomodulation (PBM) sessions were indicated to treat all ulcers. In addition, antimicrobial photodynamic therapy (aPDT) was performed in the larger ulcers with the aspect of infection, located on the tongue and lip commissure [Figure 2]. The LLLT used had a power of 100mW and a tip area of 0.028cm2 (DMC Equipaments®). The aPDT was performed on the 1st day of treatment using the photosensitizer methylene blue at 0.010%, with 5 min of preirradiation time and high energy of red laser (9 J), with a wavelength of 660 nm. After the aPDT treatment, the PBM protocol was performed on the other ulcerated lesions using low energy of red laser (1 J) and side-by-side points. Table 1 shows the used protocols.

After the 1st day of low-level laser therapy treatment, the dental team was able to conclude that the prognosis was good and the treatment was working since the patient reported pain improvement and the oral lesions started to heal. The patient adherence and tolerability of the treatment were very satisfactory, given that the LLLT did not have side effects, the application was painless and fast (approximately 10 min), and the lesions were improving.

The PBM protocol was performed daily, with the exception of weekends, during subsequent LLLT treatment sessions, in all ulcerated lesions, with a standardized protocol of 1 J of energy of red laser applied using side-by-side points. By the time of the third session, the patient reported overall improvement of the painful symptoms. A clinical improvement of the ulcerated lesions was observed in the fourth session, with the exception of the lesions located on the tongue and lip commissure [Figure 3].

During the treatment and consequent improvement of the oral lesions, the speech therapy team started the tests to remove the nasoenteral tube. After the seventh PBM session, it was possible to observe total regression of the patient's oral lesions [Figure 4], and from then on, the solid diet was reestablished.

Discussion

The present study reports a case of ulcerated oral lesions associated with COVID-19 successfully treated with LLLT and aPDT. The LLLT helped to heal, in only a few days, painful oral lesions that were preventing the patient to start solid diet and be discharged from the ICU.

The coronavirus, the virus that causes COVID-19, is known to have the oral cavity as one of the sites of

Table 1: Protocols used during patient treatment

Protocol	Energy/ point	Fluence	Irradiation time/point
aPDT	9J	321.4J/cm^2	90 sec
Photobiomodulation	1J	35J/cm^2	10 sec

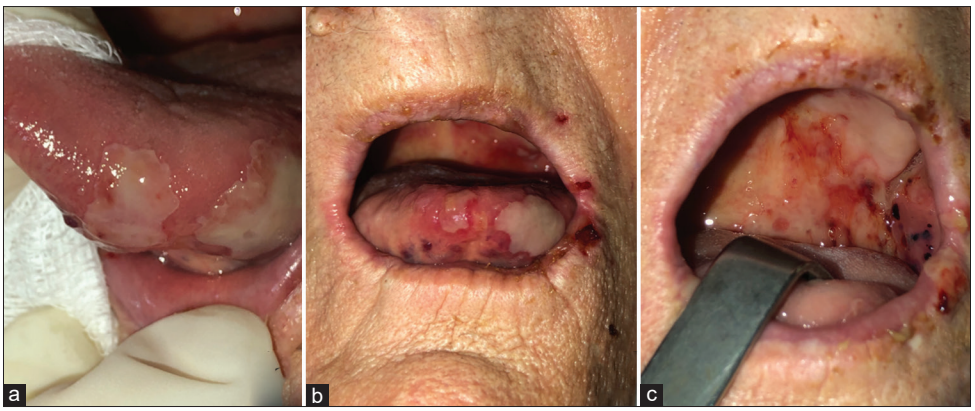

Figure 1: Initial examination. Ulcerated lesions with the presence of a fibrinopurulent membrane and hemorrhagic points on the left side of the tong (a), apex of the tong and left side of labial commissure (b), and soft palate (c)

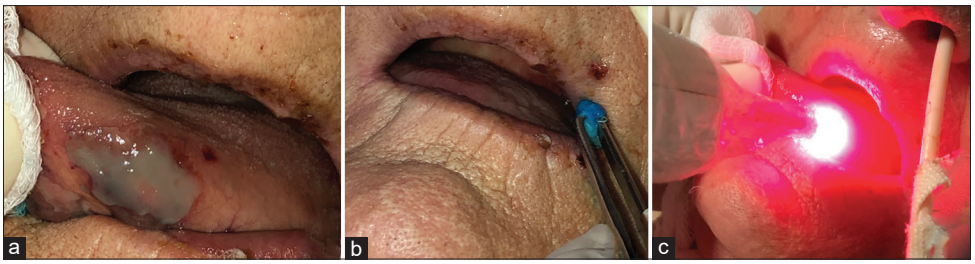

Figure 2: Antimicrobial photodynamic therapy. Left side of the tong lesion after the application of methylene blue at 0.010% (a), application of the photosensitizer on the labial commissure (b), and red laser irradiation (c)

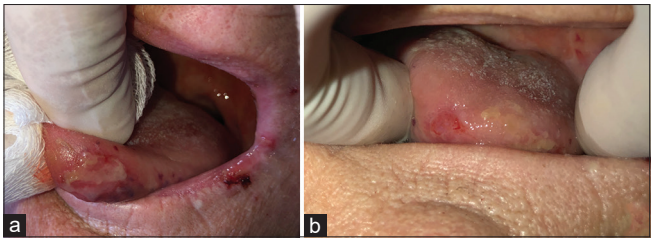

Figure 3: Clinical aspect of oral ulcerated lesions of the left side of the tong (a) and apex of the tong (b) after four sessions of photobiomodulation

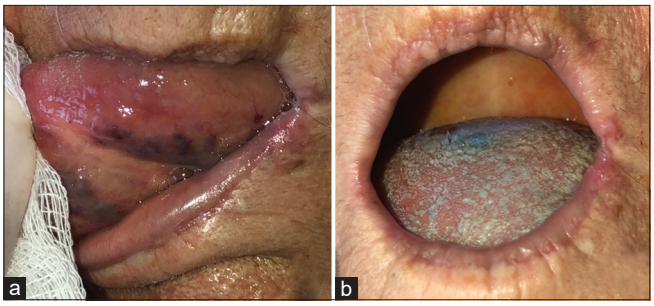

Figure 4: Clinical aspect of tong (a), labial commissure (a and b), and palate (b) after photobiomodulation treatment without oral ulcerated lesions

colonization, being detected in the saliva of patients with COVID-19.[7] In this context, oral lesions associated with COVID-19 have been increasingly reported in the literature. Martín Carreras-Presas *et al*. (2021),[3] Chaux-Bodard *et al*. (2020),[8] and Galván Casas *et al*. (2020)[9] were the first researchers to characterize this condition.

Oral lesions caused by SARS-CoV-2 have a higher prevalence on the tongue, labial mucosa, palate, gingiva, oral mucosa, oropharynx, and a small percentage on tonsils.[7] The clinical features of these lesions are varied, with no specific pattern present. Studies report aphthous, hemorrhagic, and necrotic ulcers, petechiae, herpetic lesions, geographic tongue, vesiculobullous lesions, and even pigmentation as possible clinical manifestations.[7,8] Corroborating previous findings in the literature, our patient presented ulcerated aphthous lesions and necrotic areas on the tongue, palate, lip commissure, and oropharynx.

These lesions usually manifest with the presence of painful symptoms, burning sensation, or itching.[7] Its epidemiology does not present a defined prevalence of gender[7] but presents a mean age in affected patients of 42.5 years.[10] The latency between the onset of systemic symptoms and oral lesions is between 4 days and 12 weeks after the first systemic symptoms.[7]

According to the research conducted by Riad *et al*. (2022),[11] which evaluated 26 patients diagnosed with COVID-19, the presence of a higher incidence of ulcers located mainly on the dorsum of the tongue was observed, followed by the lateral of the tongue, body of the tongue, hard palate, and mucosa lips. The number of ulcers among patients varied between 1 and 7 ulcers, with sizes between 1 and 5 mm.[11] In contrast, the research of Iranmanesh *et al*.[11] observed that the oral lesions would heal in 5–15 days, and the regression of these lesions was directly associated with the systemic improvement of the patient.[7] Our patient presented six oral lesions, with ulcerated characteristics, and the complete regression of the lesions occurred after 7 sessions of treatment with PBM.

It is worth noting that these lesions may or may not be directly related to COVID-19. The respiratory impairment of patients with the severe stage of the disease takes them to intensive care in ICUs, favoring the occurrence of traumatic injuries, caused by the use of orotracheal tubes, and the appearance of several opportunistic infections.[2] Furthermore, the oral cavity is a site of colonization of several microorganisms, which, with other factors such as immunosuppression, may lead to ventilator-associated pneumonia, periodontal infections, mucositis, hyposalivation, and viral and fungal infections, especially *Candida albicans*.[2]

Ulcers in the oral cavity may have many etiological factors, such as chemical or physical traumatic injuries, bacterial infections, systemic diseases, allergic reactions, and viruses.[1,2] It is important to consider, however, that the patient in our case was being treated for COVID-19 and presented clinical characteristics of virus ulcers that appear in immunosuppressed and hospitalized patients, as the ulcers were multiple, painful, well demarcated, shallow, ovoid, with yellow-gray pseudomembrane, red halo,[12,13] and with areas of hemorrhage.

Different treatments have been used for oral lesions in patients diagnosed with COVID-19. Chlorhexidine-based mouth rinses, topical or systemic corticosteroids, systemic

antibiotics, and low-intensity laser therapy were the most common.[7,11,14]

The PBM with low-intensity laser uses wavelengths within the red range (600 and 700 nm) to near infrared (700 and 950 nm).[4] The mechanisms of action of PBM are based on the interaction of the light length emitted by the device and its cellular targets, where the response is dose dependent and may have local and/or systemic action, with photostimulation or photoinhibition effects. The intracellular responses include an increase in cellular metabolism, cell proliferation, enzyme activation, DNA/RNA synthesis, alteration of the action potential of nerve fibers, and stimulation of local microcirculation.[4,15,16]

In this case, PBM was initiated after observing the existence of numerous painful ulcerated lesions that were making it impossible to re-establish the patient's oral feeding. The protocol used was based on the observational study by Eduardo *et al.* (2021),[6] who evaluated patients with COVID-19 who had oral lesions and were treated with PBM. In the study by Eduardo *et al.* (2021)[6] and the reported case, DMC's diode laser device, which has 100 mW of power and tip diameter of 0.028 cm^2, was used. The chosen wavelength was 660 nm, for 10 s, 1 J, and 35.7 J/cm^2 of energy density, continuously, in both cases. The number of points varied according to the size of the lesions, covering the entire lesion.

The low-power laser can also be used in aPDT, a treatment method that uses a light source, in this case, a red laser, in association with a photosensitizing agent in various concentrations, being methylene blue the most used.[4,15,16] This photosensitive compound accumulates in the pathological tissues, being able to absorb light in the wavelength between 600 and 1000 nm, called the phototherapeutic window. With this, the process of destruction of inappropriate cells present at the site of application of the photosensitizing agent is initiated.[17]

The mechanism of action of aPDT is based on the absorption of light photons capable of exciting electrons. Then, in the presence of oxygen, the photosensitizing agent transfers energy to the site, forming free radicals (singlet oxygen), which can cause damage to microbial cells and thus cause the death of microorganisms.[4,15,16,17]

The healing of lesions caused by the use of aPDT is associated with the absorption of the photosensitizer by the vascular network of the wound edges, being able to absorb more light and have a greater biological effect on local microorganisms.[17] Given the clinical and laboratory findings of the patient in our case, we chose to perform aPDT at the first moment to prevent the proliferation of possible viral infectious agents present in the lesions. This therapy is used in several cases in the dental clinic, such as in the treatment of labial herpes, candidiasis, and periodontitis, because it has antimicrobial action as a great advantage.[17]

The association of PBM with aPDT has been used in some cases of oral lesions in patients with COVID-19 published in the literature. The antimicrobial effect and the possible ability to inactivate viruses through aPDT in conjunction with PBM's modulating, repairing, and analgesic effects explain this association, which is defended by the positive results found in these cases published in the literature. In addition, the aPDT can cause viral inactivation, which stimulates lesion healing in conjunction with the action of PBM.[18]

In the cases published by Teixeira *et al.* (2021),[19] the PBM protocol used a wavelength of 660 nm in continuous mode, 0.5 J of energy, and 33 J/cm^2 of energy density. The authors also used aPDT, which was applied in one or two sessions before PBM for possible local decontamination, following a protocol of using 0.01% methylene blue with the preirradiation time of 3 min, a wavelength of 660 nm, and 4 J of energy per spot. Thus, it was possible to observe an improvement in the clinical picture of patients who underwent treatment with combined therapies (PBM + aPDT), corroborating the findings of our clinical case.

Oral lesions in patients with COVID-19 are a great challenge for dental surgeons, mainly due to the unclear etiopathogenesis. In addition, the lesions usually take a long time to heal, despite the various treatments applied. Therefore, we believe that photodynamic therapy, associated with PBM therapy, may accelerate the healing process, improve patients' quality of life, and contribute to dehospitalization.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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