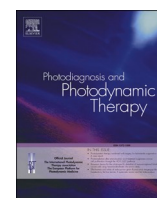




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Case report

A combination of phototherapy modalities for extensive lip lesions in a patient with SARS-CoV-2 infection

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ABSTRACT

Many oral signs and symptoms related to the novel coronavirus disease (COVID-19) have been reported; however, both prevalence and etiology are still undetermined. Since the clinical features of the oral lesions seen in COVID-19 are highly heterogeneous and the treatments differ considerably in the literature, the present study aimed to report a clinical case in which a combination of antimicrobial photodynamic therapy (aPDT) and photobiomodulation therapy (PBMT) was used for extensive lip lesions in a patient suffering from COVID-19. Within 4 days and without any systemic drug administration, after two sessions of aPDT and one session of PBMT, the lip lesions were completely healed, and the patient recovered her orofacial functions satisfactorily. According to the current case report and taking into consideration the evident lack of information about many aspects of COVID-19 infection, this combination of phototherapy modalities seems to be a promising tool for managing COVID-19-related lip lesions; however, more studies are necessary.

1. Introduction

The novel coronavirus disease (COVID-19) is caused by a single-chain RNA virus popularly known as Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) [1,2]. According to the World Health Organization on 29 December 2020, over 79 million cases and 1.7 million deaths have been reported globally since the start of the pandemic [3].

Although most cases are asymptomatic or produce mild symptoms, severe respiratory symptoms may be seen, resulting in acute severe respiratory distress and even multiple organ failure [1]. The most common clinical manifestations of COVID-19 are fever and dry cough; however, shortness of breath, dysosmia, and dysgeusia may also be encountered [4]. Other atypical presentations have been increasingly reported worldwide, including gastrointestinal and dermatological manifestations and chemosensory dysfunctions [1].

Several oral signs and symptoms related to COVID-19 have already been described, e.g. taste disorders, unspecific oral ulcerations, desquamative gingivitis, petechiae, and coinfections, but the exact

prevalence is still undetermined [4]. It is yet not possible to know the etiology of these oral manifestations but two hypotheses have already been raised: 1) direct mechanisms related to local viral replication due to cellular invasion via the receptor angiotensin-converting enzyme-2 (ACE2) present in the epithelial cells that leads to an inflammation response; 2) indirect results from the viral infection, as a consequence of the patients' systemic and psychological status or secondary to drugs administered [1,4].

Since the clinical features of the oral lesions seen in COVID-19 are highly heterogeneous, the treatments differ considerably in the literature, varying from mouthwashes to topical or systemic drugs (antifungals, antibiotics, antivirals, corticosteroids) and even photobiomodulation therapy (PBMT) [2]. In light of these facts, the present study reports a clinical case in which a combination of antimicrobial photodynamic therapy (aPDT) and PBMT was used for lip lesions in a patient with SARS-CoV-2 infection.

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Fig. 1. Clinical evaluation. (A) Initial presentation – extensive lip lesions; (B) Methylene blue solution applied over the lesions; (C) Four days after the first aPDT session, showing complete wound healing.

2. Case report

A Brazilian 50-year-old female, with obesity, hypertension, and type-2 diabetes mellitus, sought medical help owing to a flu-like syndrome suggestive of COVID-19 that appeared 7 days earlier. The real-time reverse transcription-polymerase chain reaction (RT-PCR) test confirmed the clinical suspicion.

She rapidly developed severe and progressive dyspnea ($SpO_2 = 88\%$) and did not have a favorable response to non-invasive ventilation and self-prone position, resulting in acute respiratory failure. Then, the patient was sent to the Intensive Care Unit for endotracheal intubation and mechanical ventilation, lasting approximately 20 days, besides supportive measures and medications. Four days after the extubation, it was noted the emergence of painful lip lesions. From the oral team's evaluation, it was noted extensive crusted ulcers on lip vermillion (both upper and lower lips) that sometimes bleeding spontaneously and impacted negatively on the patient's basic orofacial functions (Fig. 1A).

An aPDT session was then performed for 2 days. For that, methylene blue at 0.01 % was applied over all lesions and (Fig. 1B), after 5 min (time pre-irradiation), the laser device Therapy EC® (DMC, São Carlos, SP, Brazil) was used at 660 nm, on contact mode, point by point, with 100 mW, 32.14 J/cm^2 , 9 J, and 9 s per point. A total of 30 points were distributed throughout the effected areas: 20 points on the upper and 10 on the lower lip. Moreover, on the second day, a PBMT session was conducted. The same areas previously described were irradiated with the same equipment, but using 100 mW, 17.8 J/cm^2 , 1 J, and 10 s of irradiation per point in 660 and 808 nm, employing a programming tool of the laser device that exchanges the wavelength periodically (every 5 s).

After 4 days from the first laser application, the lip lesions were completely healed and the patient recovered satisfactorily her basic orofacial functions (Fig. 1C). Eventually, the patient recovered completely from the effects of COVID-19, no longer requiring intensive care after a few days.

3. Discussion

In the current case report, a combination of aPDT and PBMT resulted in an important clinical improvement of the patient's orofacial condition related to the ulcerative lip lesions within around four days. To the best of the authors' knowledge, this is the first case on the benefits of this

phototherapeutic approach to a patient hospitalized for COVID-19 in an Intensive Care Unit. Even with the clear limitations of a case report, this article can add valuable information to the understanding of the disease, since the first outbreak of COVID-19 has been reported very recently and standard prospective randomized studies are virtually impossible.

Considering that aPDT has proved effective in inhibiting bacterial, fungal, and viral infections (including those caused by viruses with an envelope such as the coronaviruses) [5] and the lack of reliable information on the etiology of oral lesions related to COVID-19 (maybe a direct local replication of SARS-CoV-2 or opportunistic coinfections) [4], the protocol used herein was based on a previous report of the same research group in which lesions of oral cytomegalovirus reactivation on lips were successfully treated in a systemic compromised patient [6].

PBMT, in its turn, reduces the concentration of signaling molecules such as nuclear factor-kappa beta and tumor necrosis factor-alpha and inhibits prostaglandin E2, cyclooxygenase-2, and interleukin 1 beta, resulting in analgesia and mitigation of the inflammatory process [6].

As shown in the current case report and taking into consideration the evident lack of information about many aspects of SARS-CoV-2 infection, this combination of phototherapy modalities seems to be a promising tool for managing COVID-19-related labial lesions; however, much more studies are necessary.

References

- [1] E. Halboub, S.A. Al-Maweri, R.H. Alanazi, N.M. Qaid, S. Abdulrab, Orofacial manifestations of COVID-19: a brief review of the published literature, *Braz. Oral Res.* 34 (2020) e124, <https://doi.org/10.1590/1807-3107bor-2020.vol34.0124>.
- [2] B. Iranmanesh, R. Amiri, H. Zartab, M. Aflatoonian, Oral manifestations of COVID-19 disease: a review article, *Dermatol Ther.* (2020), <https://doi.org/10.1111/dth.14578>.
- [3] World Health Organization, Weekly Epidemiological Update - 29 December 2020, 2020. <https://www.who.int/publications/m/item/weekly-epidemiological-update-29-december-2020>.
- [4] J. Amorim dos Santos, A.G.C. Normando, R.L. Carvalho da Silva, A.C. Acevedo, G. De Luca Canto, N. Sugaya, A.R. Santos-Silva, E.N.S. Guerra, Oral manifestations in patients with COVID-19: a living systematic review, *J. Dent. Res.* (2020), <https://doi.org/10.1177/0022034520957289>.
- [5] A. Almeida, M.A.F. Faustino, M.G.P.M.S. Neves, Antimicrobial photodynamic therapy in the control of COVID-19, *Antibiotics* 9 (2020) 320, <https://doi.org/10.3390/antibiotics9060320>.
- [6] S.B. Rezende, L. Campos, L.F. Palma, R.Y. Tateno, A. Simões, M.C. Macedo, R.L. da Silva, Photobiomodulation and antimicrobial photodynamic therapy for oral cytomegalovirus reactivation following acute graft-versus-host disease, *Photodiagnosis Photodyn. Ther.* 32 (2020) 101849, <https://doi.org/10.1016/j.pdpdt.2020.101849>.