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Case Report

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Low-Level Laser Therapy Approach of Bilateral Necrotizing Sialometaplasia of the Hard and Soft Palates

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Abstract

Introduction: Necrotizing sialometaplasia (NS) is a rare locally destructive inflammatory benign disease that commonly affects the minor salivary glands. It is frequently associated with the glands located in the posterior portion of the hard and soft palates. Low-level laser therapy (LLLT), also called photobiomodulation therapy (PBMT), has been deemed a substantial method for the regenerative wound process.

Case Presentation: A 32-year-old male patient was referred with a chief complaint of two asymptomatic crater-like ulcers measuring approximately 1.5 cm wide on the right side of the hard and soft palates, and another measuring 0.3 cm wide on the left side of the hard palate. The lesion had two weeks of evolution followed by a previous infectious "sore throat" event that kept the patient hospitalized for 4 days. A clinical diagnosis of NS was made. LLLT was applied during 2 sessions per week, favoring the total wound healing within 2 weeks. At 3 months of clinical follow-up, the patient did not present any complication or relapse and was thus released.

Conclusion: This is, to our knowledge, the first clinical report of LLLT applied for the management of NS. Large palatal ulcers caused by NS usually have long healing periods. The shortened healing period observed in this case encourages the inclusion of LLLT in any treatment protocol for similar lesions.

Keywords: Necrotizing sialometaplasia; Low-level laser therapy; Photobiomodulation therapy; Palate; Pharyngitis.

Introduction

Necrotizing sialometaplasia (NS) was first described by Abrams et al in 1973 as the necrotizing inflammatory affliction of minor salivary glands misdiagnosed as a malignancy.[1] It is a rare benign lesion mimicking a malignant tumor, characterized by a self-healing inflammatory necrotizing disease of the minor salivary glands, and manifested as an ulcerative lesion commonly on the hard palate. There is a close histopathological and clinical similarity with squamous cell carcinoma and mucoepidermoid carcinoma, which can lead to a misdiagnosis.[2]

Although it is believed to be the result of local prolonged ischemia of the salivary glands, some potential predisposing factors can be considered, such as traumatic injury, ill-adapted prosthesis, post-surgical complications, and/or respiratory infection.[3] Even if NS simulates a malignant condition, no treatment is required due to second-intention wound healing. Healing periods ranging from 4 to 10 weeks have been reported.[2,4] The healing period depends mostly on the size of the lesion, proper wound care from the patient, and systemic factors such as comorbidities, age, gender, and secondary infection. An incisional biopsy is indicated to rule out the suspicions of malignancy if there is no regression after 3 months of follow-up.[2]

Low-level laser therapy (LLLT), also called photobiomodulation therapy (PBMT), has been widely associated with favoring tissue regeneration and wound healing.[5] LLLT/PBMT provides an anti-inflammatory effect on the oral mucosa cells, which the mechanism of action develops at the mitochondrial cellular level,

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related to cytochrome c oxidase absorbing light for cell metabolism.[6] LLLT/PBMT accelerates wound healing and reduces pain by stimulating the process of oxidative phosphorylation in the mitochondria. This increases the synthesis of adenosine triphosphate (ATP), produces inflammatory responses, and exhibits beneficial effects on inflammation and healing.[5] Cell proliferation via LLLT/PBMT action has been described in cell types such as fibroblasts, endothelial cells, neoplastic cells, stem cells, smooth muscle cells, lymphocytes, and osteoblasts.[7-10]

The aim of this case report is to suggest a novel approach to NS, with LLLT being a noninvasive and rapid wound healing promoter. This is, to our knowledge, the first report of the appliance of such technology for this purpose.

Case Presentation

A 32-year-old man was referred to the oral medicine clinics of the author's institution with a chief complaint of a lesion on the palate. He explained that he had acquired measles 1 month prior to the appointment and underwent symptomatological treatment of the disease. After 2 weeks of evolution, he sought medical assistance due to a purulent discharge in the affected area. He complained of a sore throat and noticed the development of a large palatal ulcer. He was hospitalized for 4 days, and during this time, it was not possible to reach a final diagnosis of the infection. Finally, the patient was referred to dental care.

During an extra-oral examination, the patient presented good facial symmetry as well as the absence of swelling or lymphadenopathy in the face and cervical region. An intra-oral examination revealed two asymptomatic, non-bleeding, crater-like ulcers with whitish edges differing from adjacent mucosa, measuring approximately 1.5 cm wide on the right side of the hard and soft palates, and another measuring 0.3 cm wide on the left side of the hard palate (Figure 1). When asked about previous trauma in the region, the patient mentioned only food trauma as a possible source. Also, the use of a dental prosthesis, previous anesthesia in the region, smoking, drug usage or systemic disease were ruled out. Diagnostic hypotheses included bacterial or viral pharyngitis, tonsillitis, diphtheria, infectious mononucleosis, and noma.

The clinical findings were compatible with NS. Classic clinical characteristics sustained the diagnosis such as:

- Anatomic position: an asymptomatic crater-like ulcer on the posterior hard palate and the junction of the hard and soft palate areas, closely related to the palatal foramen;
- Particularities of the lesion: well-delineated borders, the absence of purulent secretion or granulation tissue;
- Regional and systemic factors: the absence of lymphadenopathy or the clinical course that could sustain any malignancy hypothesis.

With such strong clinical evidence of NS, the affected area was not biopsied, preventing further damage to the affected area. We opted for weekly LLLT (Bio Wave LLLT Dual, Kondortech, São Carlos - SP, Brazil) with a spectrum of red light 660 nm, 30 mW of power, a fluence of 1.1 J/cm^2 and irradiation time of 1 minute and 40 seconds per point. Only 2 weeks of this protocol showed the excellent recovery of the affected region, with complete wound healing.

The clinical diagnosis revealed to be precise since the lesion showed good clinical evolution after photobiomodulation treatment started, without the need for any other medications such as antibiotics, antifungal or steroids or NSAIDs. The patient was kept for a clinical control follow-up and was released after a 3-month visit without a relapse or further complications (Figure 2).

Discussion and Conclusion

Brannon et al studied 69 cases of NS and found that most of the lesions were unilateral and located on the posterior hard palate with a broad range of possible predisposing factors.[11] Often the lesion manifests as a crater-like ulcer and can or cannot be accompanied by pain.[12]

The etiology of NS is widely believed to be ischemia of the vascular supply of the salivary gland lobules. This process leads to necrosis and/or squamous metaplasia of the salivary gland tissue, which is usually eliminated through

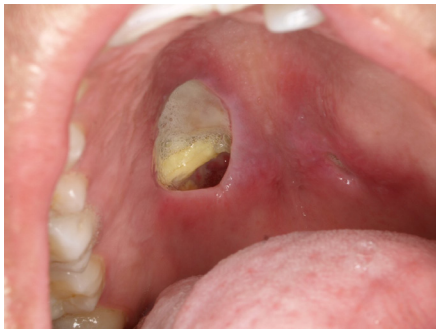

Figure 1. Extensive Palatal Ulcer Measuring Approximately 1.5 cm Wide on the Right Side of the Hard and Soft Palates, and Another Measuring 0.3 cm Wide on the Left Side of the Hard Palate, Asymptomatic, Compatible With a Diagnosis of NS.

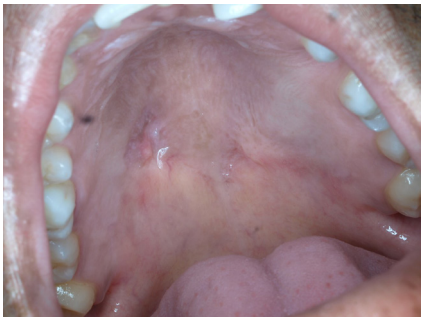

Figure 2. Clinical Aspect After 2 Sessions of LLLT Showing Excellent Wound Healing.

a long-lasting ulcer. Predisposing factors to ischemia can be related to a traumatic injury, local anesthesia, an ill-adapted prosthesis, alcohol use, smoking, a surgical procedure, and an upper respiratory infection.[3,4] The hard and soft palate junction is the most affected region of NS due to the limited blood supply from the palatal artery.

Differential diagnosis should be properly considered for NS that has developed on the palate after or in association with an upper respiratory infection, as the swelling of the mucous membrane might compromise the vascular supply.[6] The diagnosis of oral ulcerative lesions might be a challenge, and this implies that it is important to deeply investigate the patient's history, causative factors, and presenting features. In our case, the patient complained of a sore throat after noticing a palatal ulcer, and this perhaps demonstrates a previous infection, which may have been bacterial or viral pharyngitis, tonsillitis, diphtheria, infectious mononucleosis, or noma.

Oral ulcerative lesions that have developed from infectious diseases might be difficult to diagnose due to a wide potential range of non-specific symptoms. For bacterial infections, oral ulcerations are typically present in syphilis and tuberculosis, but the palate is a less common site of involvement and the patient may manifest cervical lymphadenopathy.[13,14] Viral infections related to oral ulcers comprise herpes simplex virus 1, herpes simplex virus 2, Epstein-Barr virus and cytomegalovirus, human herpesvirus 8 (Kaposi's sarcoma herpes virus), and the human immunodeficiency virus.[13-15] It has also been suggested that the infections of some herpes viruses, such as cytomegalovirus, may lead to decreased local immunity and cause noma development.[16-18] Such an infectious disease as measles is a predisposing factor to noma, a fulminant infection of oral facial tissue.[18]

The most common findings for bacterial pharyngitis and tonsillitis are a sore throat, palatine petechiae, cervical lymphadenopathy, and tonsillopharyngeal erythema, with or without exudates. Ulcerative lesions are typically associated with a viral rather than a bacterial etiology.[19] Diphtheria infection usually localizes in the upper respiratory tract, ulcerates the mucosa, and induces the development of an inflammatory pseudomembrane, although skin lesions may be present. It can involve the posterior structures of the mouth and the proximal pharynx, but hard and soft palates are unusual sites for diphtheria with oral mucosal lesions.[20] Diphtheria is also a potential infectious cause of palatal perforation.[21]

Another differential diagnosis of ulcers that can lead to palatal perforation should be considered, comprising traumatic, infectious, granulomatous, neoplastic, collagen vascular, idiopathic, and chemical irritants, as the clinical features of chemical lesions are similar and can lead to bone necrosis or even fistulas.[22] Even simple traumatic ulcers, when addressed with the improper application of chemicals and/or medications, could develop extensive palatal necrosis, leading to palatal perforation.[23]

Although different pathogens may cause infectious ulcers on the oral cavity, it is important to observe specific clinical characteristics that could support the diagnostic hypothesis. Table 1 provides the most relevant oral features of bacterial, viral and fungal ulcers for differential diagnosis, as well as the need for biopsy procedures and the usual therapeutic approach.

The previous diagnosis of measles made on the public health institution prior to the referral to our service was clinical. Since we could not obtain a conclusive serological exam that could confirm the measles infection, we cannot discard the possibility of other infections.

It is important to highlight that political and economic crisis scenarios can impact the public health care system.[38] Outbreaks of vaccine-preventable diseases, such as measles, diphtheria, and malaria, have been reported across Brazil after the Venezuelan migration from 2016-2018.[38]

NS ulcers can mimic a malignant form. Misdiagnosis of NS should always be considered. This possibility was discarded due to a cause-effect relation with the measles event, as well as the clinical aspects found in the lesion. Yagihara et al[39] discussed clinical characteristics that mimic those of a malignant tumor, such as severe pain during swallowing, an ulceration with no apparent cause, and a deep, irregular ulcer with irregular edges. In situations like these, a histopathological examination is a golden standard for the diagnosis of NS. None of these characteristics was presented in our case when the patient sought our institution. The treatment of NS comprises surgical excision as seen in the cases described by Abrams et al[1] and Brannon et al.[11] Current case reports point to the fact that unnecessary radical intervention can be avoided due to the self-healing nature of the lesion.[2,12]

Because it appeared to us that this was an unusual approach to NS, we established a systematic review searching for similar cases in the literature. The following databases were accessed: PubMed, Lilacs, BVS, and Scielo. The following descriptors were used during this search: *biostimulation, laser therapy, photobiomodulation therapy, low-level laser therapy,* with "necrotizing sialometaplasia" and "salivary glands." The following PRISMA flow chart represents the task (Figure 3).[40] Eligible papers included were English-language studies published regarding the therapeutic low-level laser only in human clinical studies with complete clinical follow-up compatible with the evolution of NS. Studies with other types of therapeutic modalities, subjects not related to NS, animal studies, and/or papers in languages other than English were excluded.

LLLT has been applied to accelerate the regenerative processes of tissues, which is possible due to its low-energy densities and wavelengths that easily infiltrate, leading to biomodulation effects on cells and tissues.[41,42] Several cells can be affected and proliferate from the action of LLLT, such as fibroblasts, endothelial cells, neoplastic cells, stem cells, smooth muscle cells, lymphocytes, and

Table 1. Oral Features for Differential Diagnosis of Infectious Ulcers of the Oral Cavity Regarding the Type of Pathogen, Clinical Presentation, Need for Biopsy and Usual Treatment

Lesion	Diagnosis	Clinical Manifestation	Biopsy	Treatment
Noma	Clinical presentation; Cultures	Acute necrotizing gingivitis, often accompanied by a swelling that can progress to symptomatic necrosis, increasing to a blackish furrow where intraoral tissue is being lost, with a well-demarcated perimeter surrounding a blackened necrotic center.[18,24]	Indicated	Antibiotic with rehydration, dietary rehabilitation and treatment of associated diseases[18]
Syphilis	Clinical presentation; Dark-field microscopy, PCR, and direct fluorescent antibody testing for *T. pallidum*; Serological test[26,28]	Primary stage - oral chancre or ulcer typically indurated and is usually without exudate. There may be regional lymphadenopathy.[25,26] Secondary stage - diffuse maculopapular skin rash involving the trunk, extremities, palms, and soles.[26,27] Tertiary stage - formation of destructive granulomas (gummas). In the tongue, involvement is painless, with thickening and induration of the organ. Gummatous lesions may invade and perforate the palate and destroy the osseous base of the nasal septum[28]	Indicated	Antibiotic therapy[26]
Tuberculosis	History; clinical presentation; chest X-ray; cultures[36]	Deep, irregular single painless ulcer with inverted margins and granulations on the floor with sloughing tissue associated with enlarged regional lymph node, tuberculomas, and nodules, commonly affecting the tongue[29,36]	Indicated	Anti-TB therapy[36]
Aspergillosis	PAS-stained sections; Cultures; serological test of circulating antigen galactomannan *Tachypleus* or limulus assay (1→3)-β-d-glucans; PCR[36]	Yellow-black, necrotic ulcerations[30] or black central crusting and edematous-erythematous changes of the surrounding tissues of painful palatal lump[31]	Indicated	Antifungal therapy[36]
Histoplasmosis	Clinical presentation; Cultures; Serology (complement fixation test, immunodiffusion, and histoplasmin skin test)[36]	Granular ulcerations, deeper painful ulcers surrounded by erythematous or white irregular areas, and verrucous nodule[32,33]	Indicated	Antifungal therapy[36]
Paracoccidioidomycosis	Clinical presentation; Cultures; Periodic acid–Schiff staining (PAS) and Grocott's silver staining[34]	Granulomatous, erythematous ulceration with hemorrhagic dots, known as moriform stomatitis and can affect lips, gingiva, buccal mucosa, palate, tongue, and floor of the mouth[34]	Indicated	Antifungal therapy[34]
Infectious mononucleosis	Clinical presentation; Heterophile antibody test/ monospot test; Enzyme immunoassays[36]	May manifests sore throat and development of palatal petechiae exudative pharyngitis, tonsillitis, and posterior cervical lymphadenopathy are common[35,36]	Not indicated	Supportive treatment, rest, and analgesics; Antiviral or corticosteroids treatment[36]
Cytomegalovirus infection	Serological test of CMV-specific antibodies or IgG; CMV-specific IgM antibodies[36]	Persistent, solitary or numerous, painful or painless, shallow ulcerations, with a base covered by a yellow slough or pseudomembrane, and the margins can be rolled, elevated, with or without induration[36,37]	Not indicated	Antiviral drugs[36]
Herpes simplex virus	Clinical presentation; Virologic tests; Cytology smears stained with Giemsa or Papanicolaou stain; PCR; Serological tests[36]	Blisters or vesicles with eruptions extremely painful and break in tiny, shallow-grey ulcers on a red base[29,36]	Indicated	Analgesics and antipyretics, topical anesthetics, and antiviral therapy[36]

osteoblasts.[7-10]

Based on Wilden and Karthein's research,[43] a relevant subject arises from the wavelength (energy range) between 600-700 nm; it is effective in triggering cell proliferation and differentiation. Hence, in a systematic review from 2015 to evaluate the scientific literature in the last 12 years related to the use of LLLT, it is clarified that the spectrum of visible red light varying from 600 to 700 nm contributes to more biostimulation.[7]

The two following points regarding LLLT doses are most important in a study by Evans and Abrahamse: (1) a decrease in cell viability and proliferation with a significant amount of damage to the cell membrane and deoxyribonucleic acid by higher doses (10 and 16 J/cm^2), and (2) an inhibitory effect by multiple exposure at higher doses.[42]

PBMT approach also successfully controls secondary infection. Different illumination wavelengths induce different bacteria. Clinically, PBMT at 830 nm controls infection of different etiologies at different stages, and

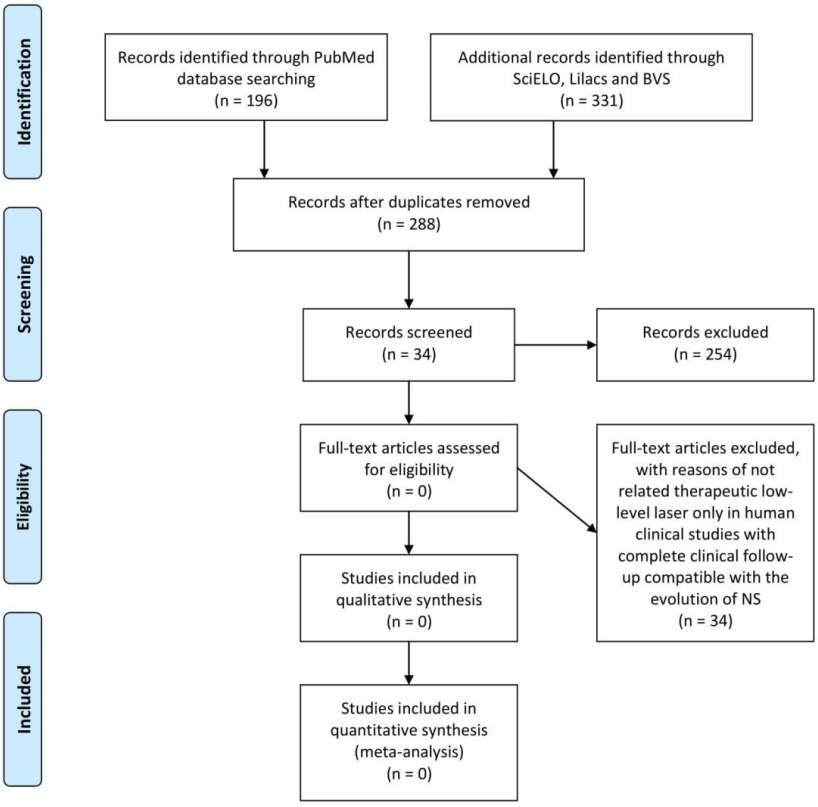

Figure 3. PRISMA Flow Diagram, Systematic Review Searching for Studies Published Regarding the Therapeutic Low-Level Laser Only in Human Clinical Studies With Complete Clinical Follow-up Compatible With the Evolution of NS.

visible light at a high intensity can decrease bacteria in infected wounds. However, it is necessary to identify the type of bacterial infection before initiating local irradiation.[44]

Extensive NS lesions that reach the size described in our case usually achieve complete recovery within 4 to 10 weeks.[2,4] The LLLT/PBMT was effective reducing this healing period. Therefore, such a noninvasive procedure as LLLT/PBMT for NS treatment is an excellent option of interest for shortening the healing period. This is, to our knowledge, the first case described in the literature of this treatment.

Ethical Considerations

All procedures performed in this study were in accordance with the ethical standards of the institutional research committee of Amazonas State University (document number #17299119.5.0000.5016) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The patient provided his written consent, and no identifier information is included in the case report.

Conflict of Interests

The authors declare no conflict of interest.

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