DOI: 10.1111/pde.13719

CASE REPORT

WILEY Pediatric Dermatology

Treatment of oral manifestations of toxic epidermal necrolysis with low-level laser therapy in a pediatric patient

Amanda Leal Rocha DDS[1] | Alessandra Figueiredo De Souza DDS, MSc[2] | Laiz Fernandes Mendes Nunes DDS[3] | Nayara Dias de Souza Cunha MD[4] | Célia Regina Moreira Lanza DDS, MSc, PhD[1] | Denise Vieira Travassos DDS, MSc, PhD[2] | Tarcília Aparecida da Silva DDS, MSc, PhD[1]

[1]Department of Oral Surgery and Pathology, Faculty of Dentistry, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil

[2]Department of Community and Preventive Dentistry, Faculty of Dentistry, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil

[3]Dental Surgeon Resident, Hospital das Clinicas, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil

[4]Department of Medicine, Hospital das Clinicas, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil

Correspondence
Tarcília Aparecida da Silva, DDS, MSc, PhD, Department of Oral Surgery and Pathology, Faculty of Dentistry, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil.
Email: silva.tarcilia@gmail.com

Abstract

Drug-induced reactions are complications associated with high mortality and significant morbidity. Stevens–Johnson Syndrome (SJS) and toxic epidermal necrolysis (TEN) are examples of these conditions, which are characterized by skin and mucous lesions. Here, we report a case of a 9-year-old girl who presented with blisters associated with an extensive vesicular rash and multiple ulcerations on the lips and oral cavity. A drug-induced hypersensitivity reaction to antibiotics was suspected, and a diagnosis of TEN was made. The patient was managed with withdrawal of the suspected causative agent, and the oral lesions were treated with low-level laser therapy (LLLT) and oral hygiene. This case highlights that TEN requires interdisciplinary intervention with dental assistance and follow-up to improve symptoms, nutrition, systemic condition, and quality of life.

KEYWORDS
low-level light therapy, oral manifestations, toxic epidermal necrolysis

1 | INTRODUCTION

Drug-induced hypersensitivity reactions are the most frequent cause[1] of toxic epidermal necrolysis (TEN). Mucosal erosions are always present and are responsible for major functional impairments,[2] including poor oral intake.[3] Loss of the integrity of the mucosa and skin also increases the risk of local[4] and systemic secondary infections.[4,5]

Low-level laser therapy (LLLT) has been used for clinical management of oral lesions in pediatric and adult patients given its analgesic, antiinflammatory, and reparative actions.[6–8]

Given the rarity of TEN, evidence-based treatment protocols for mucosal lesions are lacking. Although no previous cases of TEN mucosal lesions were treated with LLLT, it was employed here on the basis of international guidelines, demonstrating its efficacy for the management of oral mucositis.[8] Therefore, the purpose of this report is to present a severe oral manifestation of TEN in a pediatric patient and treatment with LLLT.

2 | CASE REPORT

A 9-year-old girl with cystic fibrosis was admitted for management of a pulmonary exacerbation. Oxygen therapy and antibiotics, including ceftazidime, oxacillin, and amikacin, were initiated.

On the 12th day of hospitalization, she developed ocular conjunctival hyperemia, edema, and itching. On the following day, blister formation was initially observed on the lower lip with subsequent involvement of all labial mucosa (Figure 1). Subsequently, a rapid and abrupt progression of the lesions was noted with the development of vesicles and blisters over the trunk and limbs (Figure 2). She developed multiple painful and deep ulcerations on the buccal

mucosa. Hemorrhagic lesions on the lips resulted in areas of labial collapse (Figure 3). The skin and mucosal findings progressed, and the patient could not speak or open her mouth, preventing intake of solid foods and necessitating initiation of parenteral nutrition.

Management included discontinuation of suspected causative agents (ceftazidime, oxacillin, amikacin) and initiation of meropenem due to extensive skin and oral involvement and concerns for the development of secondary infection. She was febrile without hemodynamic instability or blood count abnormalities. Analgesia was optimized with tramadol (1.5 mg/kg) every 6 hours.

The hospital dentistry team was consulted on the fourth day after skin findings. The treatment of oral lesions was performed by daily application of an InGaAlP low-level laser (*laser duo/MMOpstics*, *São Carlos*, *SP*, *Brazil*) (Figure 4). The laser is portable and lightweight, and treatment was performed by a trained dentist. Intraoral and labial mucosa was irradiated with a 2-4 J^9 per point energy with a red light 660-nm, power of 100 mw. The laser settings were 66.66-133.33 J/cm^2 with a laser-beam spot size of 0.03 cm^2 for 20-40 s/cm^2. The treatment was delivered daily with the laser tip in direct contact with and perpendicular to the affected area of the oral mucosa. The total irradiation time by session was 8-10 minutes depending on the affected area.

Topical chlorhexidine digluconate (0.12%) was prescribed for oral hygiene to prevent secondary infections. After six sessions of LLLT, the patient could ingest liquids, and solid oral intake recovered after eight sessions. The patient was discharged from the hospital after 12 sessions of LLLT and remained in outpatient follow-up for two further sessions until the lesions were completely healed. Three weeks after discharge from the hospital, the patient exhibited good healing of the skin lesions and complete resolution of the oral lesions (Figure 5).

FIGURE 1 Clinical appearance of the oral lesion on the 2nd day of TEN manifestations and the start of the dental follow-up with LLLT. The patient presented a single blister involving both the upper and lower lips

FIGURE 2 Clinical photograph of the patient with widespread blisters on the arm

3 | DISCUSSION

Oral care must be considered an essential component of the management of TEN. In our case, the oral manifestations were the primary cause of functional impairment. The administration of an

FIGURE 3 Hemorrhagic erosions and crusts on the lips, resulting in areas of labial collapse on the fifth day of TEN manifestation

FIGURE 4 The laser duo/*MMOpstics* (InGaAlP) is portable, lightweight, and practical. It contains two wavelengths on the same devise, Red Laser (660 nm) and Infrared Laser (808 nm). *SP*, *Brazil: São Carlos*

FIGURE 5 Total remission of oral lesions after 3 weeks of dental follow-up. Areas of depigmentation in the perioral region and pigmentation of the lips were observed

antiinflammatory oral rinse or the use of topical anesthetics are employed for pain control.[10] Topical corticosteroids are widely prescribed in oral Stevens-Johnson syndrome (SJS)/TEN, but there is limited evidence of efficacy.[10] The use of an oral rinse with an antiseptic reduces bacterial colonization of the mucosa.[11] The patient in this report was instructed to perform oral hygiene with topical use of chlorhexidine digluconate (0.12%) to prevent secondary infections.

Herein, we report the use of LLLT to treat oral lesions with favorable results. One previous report described LLLT in the treatment of oral ulcers of an SJS patient exhibiting pain relief and improvement in oral functions.[4] The Multinational Association of Supportive Care in Cancer and the International Society of Oral Oncology have reported the efficacy of LLLT for prevention of chemotherapy-induced oral mucositis.[8] Therapeutic LLLT used to treat oral mucositis induced by chemotherapy also demonstrated positive results.[12] Importantly, the American Academy of Pediatric Dentistry recognizes the use of laser as beneficial for the treatment of infants and children, providing pain relief and reducing inflammation associated with ulcers and herpetic lesions.[6] Furthermore, a systematic review and meta-analysis of the effect of LLLT in pediatric and young patients revealed reductions in the severity of oral mucositis and pain.[12] Moreover, a double-blind randomized clinical trial demonstrated the efficacy of LLLT in reducing oral mucositis-associated pain in children, whereas no significant benefit in reduction of the oral mucositis score was verified.[13] This apparent discrepancy can be explained by the wavelengths used (830 nm). Accordingly, Schubert et al demonstrated that wavelengths of 632-660 nm are more effective in preventing mucositis possibly due to the release of energy in the superficial layers.[14]

LLLT induces nonthermal photochemical reactions called photobiomodulation.[15,16] Radiation in the visible spectrum is absorbed by chromophores in the mitochondrial respiratory chain, and its effects involve enhancement of adenosine triphosphate production[17] and cell metabolism, thereby accelerating healing.[9,18] LLLT also results in modulation of the inflammatory process[19] by reducing the levels of prostaglandin E2, cyclo-oxygenase, and cytokines.[16] Moreover, effects on nerve impulse transmission, including alterations in the pain threshold of nociceptors, the release of endorphins, and a reduction in acute pain,[16,18,20] were described.

Lasers offer several benefits for oral care in children.[7] LLLT has proven to be useful in hospitalized patients and outpatients due to its easy application, noninvasiveness, good response, and no adverse effects.[4,6,7] When using dental lasers, adherence to the infection control protocol is also necessary.[7] Additional care with antiseptic mouth rinses should be implemented. Importantly, precisely predicting the number of sessions necessary for the treatment of lesions is not possible given that it depends on the nature of the lesions and different factors, for example, host response and secondary infection.

4 | CONCLUSION

We demonstrate that LLLT may be an effective treatment of TEN-related oral lesions. The therapy was well tolerated and might be considered as a routine protocol in the treatment of mucosal drug-induced reactions. Definitive conclusions about the real contribution of LLLT for noncancer patient improvement depend on further studies.

ORCID

Tarcília Aparecida da Silva http://orcid.org/0000-0001-9623-7835

REFERENCES

1. Maverakis E, Wang EA, Shinkai K, et al. Stevens-Johnson syndrome and toxic epidermal necrolysis standard reporting and evaluation guidelines results of a national institutes of health working group. *JAMA Dermatol*. 2017;153(6):587-592.
2. Schwartz RA, McDonough PH, Lee BW. Toxic epidermal necrolysis. Part I. Introduction, history, classification, clinical features, systemic manifestations, etiology, and immunopathogenesis. *J Am Acad Dermatol*. 2013;69(2):185-186.
3. Oba U, Yamada H, Suenobu SI, et al. Toxic epidermal necrolysis in a child 6 months post-hematopoietic stem cell transplantation. *Pediatr Transplant*. 2017;21(5):1-4.
4. Simões A, Freitas PM, Bello-Silva MS, Tuner J, Eduardo CP. Laser phototherapy for Stevens-Johnson syndrome: a case report. *Photomed Laser Surg*. 2011;29(1):67-69.
5. Wong A, Malvestiti AA, Hafner MFS. Steven-Johnson syndrome and toxic epidermal necrolysis: a review. *Rev Assoc Med Bras*. 2016;62(5):468-473.
6. American Academy of Pediatric Dentistry. AAPD. Reference Manual 2013;37(6):15-16.
7. Caprioglio C, Olivi G, Genovese MD. Paediatric laser dentistry. Part 1: General introduction. *EJPD*. 2017;18(1):80-82.
8. Lalla RV, Bowen J, Barasch A, et al. MASCC=ISOO clinical practice guidelines for the management of mucositis secondary to cancer therapy. *Cancer*. 2014;120:1453-1461.

9. Simunovic Z, Ivankovich A, Depolo A. Wound healing of animal and human body sport and traffic accident injuries using low-level laser therapy treatment: a randomized clinical study of seventy-four patients with a control group. *J Clin Laser Med Surg*. 2000;18:67-73.
10. Creamer D, Walsh SA, Dziewulski P, et al. U.K. Guidelines for the management of Stevens-Johnson syndrome/toxic epidermal necrolysis in adults. *Br J Dermatol*. 2016;174:1194-1227.
11. Mockenhaupt M. The current understanding of Stevens-Johnson syndrome and toxic epidermal necrolysis. *Expert Rev Clin Immunol*. 2011;7(6):803-815.
12. He M, Zhang B, Shen N, Wu N, Sun J. A systematic review and meta-analysis of the effect of low-level laser therapy (LLLT) on chemotherapy-induced oral mucositis in pediatric and young patients. *Eur J Pediatr*. 2018;177(1):7-17.
13. Amadori F, Bardellini E, Conti G, Pedrini N, Schumacher RF, Majorana A. Low-level laser therapy for treatment of chemotherapy-induced oralmucositis in childhood: a randomized double-blind controlled study. *Lasers Med Sci*. 2016;31:1231-1236.
14. Schubert MM, Eduardo FP, Guthrie KA, et al. A Phase III randomized double-blind placebo-controlled clinical trial to determine the efficacy of low level laser therapy for the prevention of oral mucositis in patients undergoing hematopoietic cell transplantation. *Support Care Cancer*. 2007;15(10):1145-1154.
15. Mester E, Spiry T, Szende B, Tota JG. Effect of laser rays on wound healing. *Am J Surg*. 1971;122(4):532-535.
16. Fulop AM, Dhimmer S, Deluca JR, et al. A meta-analysis of the efficacy of laser phototherapy on pain relief. *Clin J Pain*. 2010;26 (8):729-736.
17. Hashmi JT, Huang YY, Sharma SK, et al. Effect of pulsing in low-level light therapy. *Lasers Surg Med*. 2010;42(6):450-466.
18. Navarro R, Marquezan M, Cerqueira DF, et al. Low-level-laser therapy as an alternative treatment for primary herpes simplex infection: a case report. *J Clin Pediatr Dent*. 2007;31(4):225-228.
19. Silva GB, Sacono NT, Othon-Leite AF, et al. Effect of low-level laser therapy on inflammatory mediator release during chemotherapy-induced oral mucositis: a randomized preliminary study. *Lasers Med Sci*. 2015;30(1):117-126.
20. Ahmed KM, Hussein SA, Noori AJ, Abdulateef SN, Abdulla BK. Evaluation of low level laser therapy in the management of chemotherapy-induced oral mucositis in pediatric and young cancer patients: a randomized clinical trial. *ESJ*. 2015;11(27):209-222.

How to cite this article: Rocha AL, Souza AF, Nunes LFM, et al. Treatment of oral manifestations of toxic epidermal necrolysis with low-level laser therapy in a pediatric patient. *Pediatr Dermatol*. 2018;00:1–4.
https://doi.org/10.1111/pde.13719