

Treatment Following Erythema Multiforme in the Oral Mucosa After qHPV Vaccine with Low-Level Laser Therapy: Case Report

Tratamiento del Eritema Multiforme en la Mucosa Oral Después de la Vacuna Contra el qHPV con Terapia con Láser de Baja Potencia: Reporte de un Caso

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MAGALHÃES, A. P.; BALBINO, J. A.; ARAÚJO, S. C. S.; BOMBARDA-NUNES, F. F. & PIGATTI, F. M. Treatment following erythema multiforme in the oral mucosa after qHPV vaccine with low-level laser therapy: Case report. *Int. J. Odontostomat.*, 15(1):222-225, 2021.

ABSTRACT: Erythema multiforme (EM) is a mucocutaneous condition of uncertain etiology, although the hypersensitivity reaction to a wide variety of agents may be related to the onset of the lesions. In about half of the affected patients it is possible to identify a previous infection. This article aims to report a case of EM in the oral mucosa after qHPV vaccine (Gardasil®), to highlight the diagnostic process and the proposed treatment. Female patient, 16 years old, after 10 days of receiving the first dose of the qHPV vaccine. On physical examination, she presented multiple ulcers and hemorrhagic crusts to the touch, based on the clinical picture and the history of the disease, a diagnostic hypothesis was EM. Low-level laser therapy (LLLT) was chosen as an alternative treatment, since the exercises applied were not successful. The patient was followed up, reported decreased pain and burn and, after one year of treatment, there was no recurrence of the lesions. Laser treatment showed an effective treatment alternative, in addition to the low cost and ease of application.

KEY WORDS: erythema multiforme, human papillomavirus recombinant vaccine quadrivalent, lasers.

INTRODUCTION

Erythema multiforme (EM) is an acute self-limiting disease that is typically associated with hypersensitivity reactions to viruses as well as drugs (Samim *et al.*, 2013; Lerch *et al.*, 2018). Infrequently vaccination is linked as a triggering factor for EM (Katoulis *et al.*, 2010; Chahal *et al.*, 2018). Oral involvement is symptomatic and often shows characteristic crusting ulceration of the lips and ulcerations often involving buccal mucosa or other mucosal surfaces (Fitzpatrick *et al.*, 2019).

Quadrivalent human papillomavirus (qHPV) vaccine is a non-infectious vaccine developed for the

prevention of cervical cancer and condyloma acuminatum. It was approved in September 2006 in the European Union for use in females 9–26 years of age, following its approval in the USA in June 2006 (Katoulis *et al.*). In 2008, the mass media reported suspected links between the qHPV vaccine and serious adverse events; however, several studies have found that the vaccine is safe, and the main adverse events are mild local reactions (Pérez-Carmona *et al.*, 2010). Herein, we discuss a case of oral EM in a 16-year-old woman who received the qHPV vaccine. We also discuss the management of this patient with low-level laser therapy.

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CASE REPORT

A 16-year-old female presented with several oral lesions associated with dysphagia and dysphonia of a few days' duration. The patient did not report any relevant



Fig. 1. Initial clinical aspect of the lesions, with multiple ulcers and bleeding crusts in the lip.



Fig. 2. Appearance of the ulcers and bleeding crusts in lower lip mucosal.



Fig. 3. Appearance of the ulcers and bleeding crusts in upper lip mucosal.

systemic alterations. However, the mother said that approximately ten days before the onset of oral lesions the patient had received an intramuscular injection of a second dose of the qHPV vaccine (Gardasil®).

Extra-oral examination revealed multiple ulcers and bleeding crusts on touch. The lesions were located on the lip, mainly in the lower lip vermillion (Figs. 1, 2 and 3). The intraoral examination revealed lesions in the labial mucosa and bilateral buccal mucosa characterized by membrane-covered ulcerations.

A low-energy AsGaInP laser (Therapy XT, DMC São Carlos/SP, Brazil) 660 nm, 0.028 cm beam diameter, exposure $35\text{J}/\text{cm}^2$ (100mW), with 1 J per point of application and 10 seconds irradiation time per point were respectively used. Laser irradiation was initiated immediately on the first appointment. This treatment was repeated four times at 48-hour intervals while signs and symptoms persisted. The method of application of the laser was point contact directly on the lesions over their entire extension. With the following applications, there was a gradual improvement in the clinical picture (Figs. 4, 5 and 6). The patient was followed up, and after one year of treatment, there was no recurrence of lesions.



Fig. 4. Clinical aspect 48 hours after laser therapy.



Fig. 5. Clinical aspect of lower lip mucosal 48 hours after laser therapy.



Fig. 6. Clinical aspect of upper lip mucosal 48 hours after laser therapy.

DISCUSSION

EM is considered a cell-mediated immune reaction, in which cytotoxic CD8+ T lymphocytes in the epidermis induce apoptosis of keratinocytes presenting viral antigens. Most authors agree that antigens in the vaccine act like keratinocyte-expressed antigens, thus similarly triggering EM (Katoulis *et al.*; Chahal *et al.*).

The prevalence of EM is less than 1 % and usually occurs in young people between 20 and 40 years old, being more common in women (Lerch *et al.*).

Clinically, erythema multiforme can be categorized into two variations. Acute EM refers to a single episode. Chronic EM can be a long-lasting evolution or recurrent which refers to repeated flares of EM over the years (Paulino *et al.*, 2018; de Risi-Pugliese *et al.*, 2019).

The EM is commonly found in the oral cavity, with prevalence ranging from 35 % to 65 %. Lesions in the oral mucosa ranging from diffuse erythema to multifocal ulcers. Initially it may be present in the form of vesicles or blisters, there may be oral pain that compromises food, food intake and speech (Samim *et al.*). Consequently, the patient evolves with dysphagia and dysphonia, as shown in the case reported.

Some vaccines have already been associated with EM (Katoulis *et al.*; Su *et al.*, 2020). According to reports by the Vaccine Adverse Event Reporting System (VAERS), between 1999 and 2017, 984 cases of EM emerged after vaccination, with smallpox being responsible for most cases (Samim *et al.*).

HPV vaccine probably was the causal agent in our patient in the absence of other known causes of EM and by the temporal relationship between the development of EM and the vaccination. However, as the age of immunization is also the age when EM is more frequent, the possibility of a coincidence cannot be ruled out (Kang *et al.*, 2008).

The literature reports a time interval between administration of the vaccine and the development of EM between 1 to 3 weeks, which corroborates the time of manifestation of the reported case (Samim *et al.*). In a recent study, 26 % of the reported cases of EM, occurred 7 to 14 days after vaccination (Su *et al.*).

The treatment of EM is not systematized, and several drugs with very different mechanisms of action are used, including antiherpetic drugs, corticosteroids, antibiotics, and immunosuppressive treatments (de Risi-Pugliese *et al.*).

Herein, we report the use of low-level laser therapy to treat oral lesions with favorable results. The LLLT is a phototherapy that stimulate tissue regeneration, reduce inflammation, and control pain (Anschau *et al.*, 2019). Previous reports described LLLT in the treatment of oral ulcers of a Stevens–Johnson syndrome patient exhibiting pain relief and improvement in oral functions (Simões *et al.*, 2011; Rocha *et al.*, 2019).

Treatment of EM is not codified, and the patient was exclusively managed with LLLT and oral care with a favorable outcome. Lasers offer several benefits due to its easy application, non-invasiveness, good response, and no adverse effects as an adjuvant to traditional treatment measures.

CONCLUSION

We report the first case of erythema multiforme following HPV vaccination treated by low-level laser therapy. The outcome in this case suggests that LLLT may be a new adjuvant modality for EM complications.

MAGALHÃES, A. P.; BALBINO, J. A.; ARAÚJO, S. C. S.; BOMBARDA-NUNES, F. F. & PIGATTI, F. M. Tratamiento del eritema multiforme en la mucosa oral después de la vacuna contra el qHPV con terapia con láser de bajapotencia: reporte de un caso. *Int. J. Odontostomat.*, 15(1):222-225, 2021.

RESUMEN: El eritema multiforme (EM) es una afección mucocutánea de etiología incierta, aunque la reacción de hipersensibilidad a una amplia variedad de agentes puede estar relacionada con la aparición de las lesiones. En aproximadamente la mitad de los pacientes afectados es posible identificar una infección previa. Este artículo tiene como objetivo informar un caso de EM en la mucosa oral después de la vacuna qHPV (Gardasil®), para resaltar el proceso de diagnóstico y el tratamiento propuesto. Paciente de 16 años, después de 10 días de recibir la primera dosis de la vacuna qHPV. En el examen físico, presentó múltiples úlceras y costras hemorrágicas al tacto, según el cuadro clínico y la historia de la enfermedad, una hipótesis diagnóstica fue EM. La terapia con láser de baja potencia (TLBP) se eligió como un tratamiento alternativo, ya que los ejercicios aplicados no tuvieron éxito. La paciente fue seguida, informó disminución del dolor y las quemaduras y, después de un año de tratamiento, no hubo recurrencia de las lesiones. El tratamiento con láser mostró una alternativa de tratamiento efectivo, además del bajo costo y la facilidad de aplicación.

PALABRAS CLAVE: eritema multiforme, vacuna tetravalente recombinante contra el virus del papiloma humano, rayos láser.

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