

Oral Erythema Multiforme: Report of Two Cases

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Case Report

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Abstract: Erythema multiforme (EM) is an acute, self-limited, widespread cutaneomucous disorder. Basically, we distinguish two variety of EM that depend on the severity of the lesions: minor EM and major EM. However, some clinicians consider that oral EM is a separate entity which involve only the oral and labial mucosa without typical skin target lesions. The absence of skin lesions may lead to misdiagnose EM with other inflammatory conditions that involve oral cavity. Thus, it is important to recognize this entity for early diagnosis and proper management. The aim of our paper is to present two cases of oral EM and to emphasize on the importance of distinguishing this particular entity.

Keywords: erythema multiforme, mouth diseases, lip diseases, oral pathology, steroids

INTRODUCTION

Osseointegration was defined as the direct structural and functional connection between living bone and implant surface under load [1]. The importance of creating roughness on the implant surface to enhance osseointegration was suggested by Andrew Schroeder [2]. Various surface modification techniques have since been tested, either by addition methods, such as plasma titanium spray [2], plasma spraying hydroxyapatite [3] and anodizing [4] or subtraction methods, such as sandblasting [5], etching [6], sandblasting followed by etching [7] and laser [8]. The creation of hydrophilic surfaces is among the most recent advances under investigation in this subject [9].

INTRODUCTION

Erythema multiforme, first described by Ferdinand von Hebra and termed as erythema multiform exudativum, is an acute, self-limited, widespread cutaneomucous disorder characterized by the onset of several skin and mucosal lesions [1]. These lesions are the expression of a hypersensitivity reaction which involves cytotoxic T lymphocytes in the epithelium that induce focal cell necrosis [2-4]. Clinical classification of the EM is typically based on the severity of the condition including minor erythema multiform in which lesions involve one mucous membrane with typical skin target lesions and major erythema multiform in which lesions involve two or more mucous membrane (oral, genital, conjunctival, nasal) with more severe skin lesions [5-7]. On 1968, Kennett proposed the term "oral erythema multiforme" to describe a variety of EM that involve only the labial and the oral mucosa without skin lesions [8]. This variety is rare and still underrecognized by clinicians.

The aim of our paper is to present two cases of oral erythema multiforme and to emphasize on the importance of distinguishing this particular variant of EM.

CASE REPORT

Case one

50 years old female was referred from oncology department for evaluation of upper and lower cheilitis appeared 2 weeks ago. The onset of these lesions was on the seventh day after administration of the first cycle FEC (5 fluorouracil, epirubicin, and cyclophosphamide) of neoadjuvant chemotherapy for an invasive ductal carcinoma of the breast. The first diagnosis made was a chemotherapy-induced oral mucositis but these lesions didn't respond to local treatment of sodium bicarbonate and antifungal therapy. Medical history revealed also epilepsy treated with valproate de sodium and allergy to penicillin and acetylsalicylic acid.

Clinical exam on the referral day has shown crusty cheilitis with shallow erosion of the labial mucosa (Figure 1,2). According to the clinical aspect and medical history of the patient, erythema multiform and paraneoplastic pemphigus were the main differential diagnosis.



Fig-1: Crusty cheilitis of the labial mucosa



Fig-2: Swelling and redness of the labial mucosa

Management include removal the labial crust under local anesthesia with oxygenated water to facilitate healing of the lesions and prescription of strong dermocorticoid cream (Dermocort 0.05%) three times daily, along with local anesthetic gel (xylogel

2%) to decrease pain and allow alimentation (Figure3). Furthermore, the patient was advised soft, bland diet. The patient responded dramatically to the treatment and the labial lesions almost resolved within 10 days on the follow-up (Figure 4).



Fig-3: Clinical aspect after crust removal



Fig-4: Healing of the lesions within ten days

The incisional biopsy on the perilesional mucosa was done, and the histopathological features has shown an acanthotic squamous epithelium with few necrotic keratinocytes and many lymphocytes exocytosis associated with focal spongiosis. The

underlying chorion is congestive seat of a diffuse inflammatory cell infiltration without the presence of polynuclear eosinophils or vasculitis (Figure 5,6). The direct immunofluorescence was negative. There features were suggestive of erythema multiform.

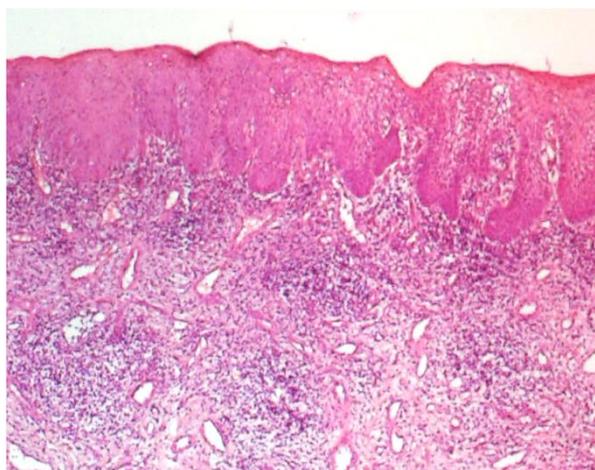


Fig-5: Histological section 40× magnification: Acanthotic squamous epithelium with diffuse inflammatory cell infiltration without the presence of polynuclear eosinophils or vasculitis in the underlying chorion

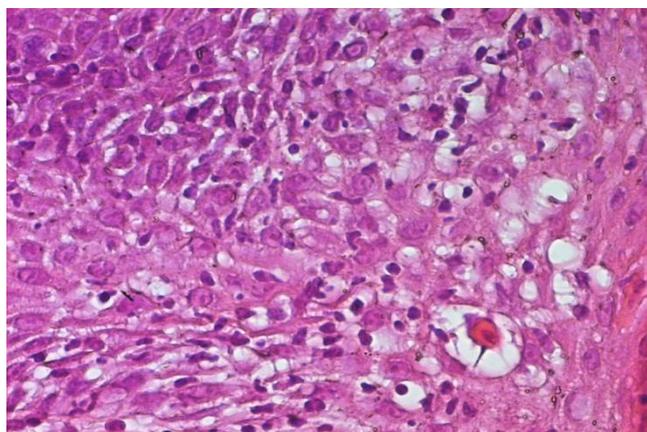


Fig-6: Histological section 400× magnification: Necrotic keratinocytes and many lymphocytes exocytosis associated with focal spongiosis

Serological investigation of HSV-1, HSV-2, HBV, HVC, VIH, *chlamydia pneumonia*, *Chlamydia trachomatis* and *mycoplasma pneumonia* were not found to be significantly elevated thereby eliminating the possible role of this infection in the aetiopathogenesis of the erythema multiform.

After the administration of the second cycle of chemotherapy, there was no recurrence of the erythema multifome, thus the drug-related hypothesis was also excluded.

Case two

A 30 years old female was referred by her general dentist after the onset of deep erosion and crusty lesions of the lips appeared three days ago (Figure 7). Her medical history was unremarkable and the patient didn't report any drug intake during the last two weeks or recent infection. The patient reported a similar anterior attacks three months ago that resolved spontaneously. The diagnosis of erythema multiforme was made based on the clinical aspect, the acute onset and the recurrent aspect of the disease. To confirm the diagnosis, an incisional biopsy was done and has shown the histopathological feature of erythema and negative direct immunofluorescence.



Fig-7: Crusty cheilitis associated with deep erosion and blistering of the lip mucosa

Treatment includes removal of the labial crust under local anesthesia with oxygenated water thus facilitating healing of the lesions. Since the attack was severe, we prescribed systemic corticosteroid 60mg of

prednisone at a posology of 1mg/Kg/day for 7 days. Serological investigation for HSV-1 and HSV-2 was negative. The lesions were almost healed on the seventh day follow-up (Figure 8).



Fig-8: Lesions almost healed on the seventh day follow-up

DISCUSSION

Erythema multiforme is thought to belong to the same spectrum as well as Stevens Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN)

as it share common symptoms (skin lesions and oral ulcer) and common histopathological features (keratinocyte necrosis). Although, an international study for severe cutaneous adverse reaction (SCAR) has

shown that, in one hand EM is a distinct entity with distinctive demographic characteristics and risks factors (affect younger patients with male predilection), a high rate of recurrence (herpes simplex as principal trigger factor), in the other hand SJS and TEN are two stages severity of the same pathological condition [9].

Oral EM is a distinct variety but underrecognized variant of the EM spectrum. Although this form is not universally accepted, it is widely accepted as separate entity by many authors [2, 8, 10-12].

The diagnosis is often difficult to establish in the absence of typical skin target lesions, since the clinical aspect of crust, erosion, erythema and bullae may mimic other oral inflammatory diseases such as auto-immune blistering disorders [8]. The rapid onset of the attack, the spontaneous resolution, the recurrent aspect of the attacks and the involvement of lip mucosa and the vermillion are the most suggestive criteria of oral EM [11].

According to sanchis and al.'s study, oral mucosa is the most frequent site affected with EM. Within the affected oral mucosa sites, lip and lip mucosa was seen in 95.5%, cheek in 90% and tongue in 86.4%. Less frequent site is soft palate, hard palate and gums. In our cases, we notice only the involvement of the lip and the lip mucosa and no other site of the oral cavity was affected [13].

The histopathological features of EM are those of nonspecific inflammatory process. Although a wide spectrum of tissue change could be observed, Amos and al. when studying twenty-five specimens of oral EM found that the main epithelium change consists of inter and/or intracellular edema and acanthosis of the spinous layer, sometimes irregular elongation of rete ridges. In the connective tissue a combination of vascular dilatation and congestion, perivascular infiltrate of mononuclear cells, and edema of the upper portion of the lamina propria⁷. Direct immunofluorescence are also important to rule out others inflammatory condition of the oral cavity such as pemphigus vulgaris, mucous membrane pemphigoid and lichen planus. The result may be negative or nonspecific [10].

Oral EM occur most frequently in adolescent and young adult but it can also occur at any age with slight predominance to female [12]. Herpes simplex infection was found to be the most trigger factor in the onset of acute oral EM¹⁵. Many other viral and bacterial infection are also implicate on the etiology of EM. Less frequently, oral EM can be induced by drug as opposed to SJS and NET where drug had higher etiologic fractions [6].

Mucosal involvement of EM especially oral mucosa is very painful and can interfere with

mastication, swallowing and speech. Therefore, the main recommendations of the SJS's pain may be proposed [14]. The first line of treatment is the topical lidocaid gel application to avoid discomfort and allow alimentation. In our cases, the topical anesthetic agent was sufficient and there were no needs to morphemic administration to relief pain.

Although there is no clinical trials that deal with treatment of EM, there is a widely acceptance of corticosteroid in the management of EM [15]. Despite that EM is a self-limited condition that resolve spontaneously within at most one month, corticosteroid provides fast healing of the lesions and good recovery duration of the outbreak. Different route administration of steroids is proposed depending on severity of lesions. Topic form of strong corticosteroid is restricted to the mild form although systemic administration is reserved for more severe lesions. As we have shown for case 1 and case 2, both topic and systemic corticosteroid are efficient in healing of the lesions.

For patients with positive history of HSV infection or recurrent episode of EM, antiviral therapy may be recommended to avoid relapses [16]. Tatnall and al. has proven the efficiency of 400mg twice daily of continuous acyclovir therapy for 6 month to prevent new attacks and to obtain complete remission for cases of recurrent EM [14]. He also noticed that one patient with no herpes simplex-precipitated disease has also been disease free after the antiviral therapy. In cases where acyclovir had fail, valaciclovir 500mg or famciclovir 500 mg twice daily or for 6 months may be also prescript [17, 18].

Even though almost cases of oral EM resolve spontaneously without any sequelae, the most redoubtable complication ever is synechia [19, 20]. Depending on the location of ulcer, synechia may occur between the lip mucosa and gingiva, cheek mucosa and gingiva, tongue and the mouth floor and between the lower and the upper lip. To avoid such sequelae, patient should be advised to make lip movements and maximum mouth opening several times a day as soon as possible. Indeed, as burns, some days are sufficient for the formation of adhesions if two mucosal lesions are in contact [20]. These complications are more seen with SJS and NET.

CONCLUSION

Clinicians must recognize this particular variety of EM since the typical skin target lesions are absent and the diagnosis may be delayed. Oral EM should be considered on the differential diagnosis in the event of an acute onset of stomatitis especially when lip is involved. Incisional biopsy is indicated to rule out other inflammatory conditions that can affect the oral mucosa.

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