Erythema Multiforme Minor - Report of a Case with Review of Literature

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Abstract

Erythema Multiforme (EM) is an acute, immune–mediated condition characterized by the appearance of distinctive target like lesions on the skin. It is triggered by a variety of conditions including infections, drug use, vaccines etc. It has a spectrum of manifestations from mild to fulminating variants creating a diagnostic dilemma. The incidence of EM has been estimated to be between 0.01 and 1%. Prevalence of oral EM varies from 35% to 65% among patients with skin lesions. However, in patients where EM was diagnosed by oral lesions, prevalence of skin lesions ranged only from 25% to 33%. We report a case of erythema multiforme minor in a 30 year old male patient managed with topical corticosteroids with complete remission.

Keywords: erythema multiforme, oral ulcers, acute onset, topical corticosteroids.

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Introduction

Erythema multiforme is an acute mucocutaneous hypersensitivity reaction with a variety of etiologies. Ferdinand Von Hebra described erythema multiforme (EM) in the year 1866 as a self-limited and acute skin disease that is symmetrically scattered on the extremities with a typical recurring concentric pattern in the form of “target lesion.” It is characterized by a skin eruption, with or without oral or other mucous membrane lesions. It can be induced by drug intake or several infections, in particular herpes simplex virus (HSV) infection, which has been identified in up to 70% of erythema multiforme cases. It comprises of variants in a range from a mild, exanthematous, self-limited and cutaneous variant with least oral involvement known as EM minor; to a more severe, fulminating and progressive variant with an extensive mucocutaneous epithelial necrosis known as Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN); hence the name multiforme. The clinical classification of these disorders is variable, thus making definitive diagnosis difficult.

Early recognition and prompt management will benefit the patients. We present a classic case of extensive erythema multiforme minor with a follow up of complete remission.

Case Report

A 30 year old male patient visited the department with a chief complaint of multiple ulcers on oral mucosa with pain in the mouth since one week. The pain was sudden in onset, continuous in nature and pricking type which aggravated on eating or drinking. The lesions first appeared on the palate and after a few days similar lesions came everywhere in the mouth. Patient also noticed blood in his sputum. As said by the patient the lesions were present only on the oral mucosa; no other mucosa or skin was...
involved. He also gives a history of mild fever for 3 days before the appearance of the lesions. No history of previous episodes of such lesions was present. No relevant medical, dental, stress or drug history was known. Patient gives a history of alcohol consumption three to four times a week. No other tissue abuse habit was reported.

Extraoral examination showed presence of multiple erosions with bloody crustings involving the entire lower lip. Introral examination revealed multiple large confluent erythematous ulcerations with irregular margins and covered with yellowish pseudomembrane on the entire surface of right and left buccal mucosa, upper and lower labial mucosa, vestibular mucosa, floor of the mouth, palate, lateral surface, tip and ventral surface of the tongue (fig. 1).

![Figure 1. Bloody crustings involving the entire lower lip and multiple large confluent erythematous ulcerations with irregular margins and covered with yellowish pseudomembrane on the entire oral mucosa.](image)

On palpation the ulcers were shallow, tender, soft in consistency and bled on provocation. There was no presence of intraoral bullae on the mucosa. The history of acute onset of the lesions with mild fever and presence of bloody crustings on the lip led to a classic provisional diagnosis of erythema multiforme minor. The differential diagnosis considered was of pemphigus vulgaris, erosive lichen planus and allergic stomatitis.

Incisional biopsy was performed from the right buccal mucosa of the lesional and the perilesional site. The tissue was stained with hematoxylin and eosin and direct immunofluorescence was done. The H & E stained section showed that the epithelium was ulcerated with presence of subepithelial vesicle and necrotic basal keratinocytes. The connective tissue showed mature connective tissue stroma with chronic inflammatory infiltrate. Perivascular inflammatory cell infiltrate was also evident (fig. 2).

![Figure 2. H & E section (40x) shows subepithelial vesicle and necrotic basal keratinocytes.](image)

Correlating history, clinical findings and histopathology a final diagnosis of erythema multiforme was made. The patient was prescribed with triamcinolone acetonide 0.1% to be applied on the entire oral mucosa three times a day after meals for 15days. The patient was
recalled after 7 days (fig. 3) and then after 15 days (fig. 4). The patient responded well to the therapy given with 90% of the lesions healed after 7 days and complete healing was seen after 15 days.

**Figure 4.** Recall visit after 15 days shows complete remission of the lesions.

**Discussion**

The term erythema multiforme (EM) is a clinical condition which reflects the broad morphological spectrum of the lesions. The peak age at presentation is between 20 and 40 years although 20% of cases occur in children. The oral lesions are accompanied by rapidly rupturing vesicles and bullae leading to diffuse sloughing and ulceration of the whole surface of the skin and mucous membrane.

Erythema multiforme has been reported to be triggered by numerous agents, particularly viruses, especially herpes simplex virus (HSV) but other herpesviruses (varicella-zoster virus, cytomegalovirus, Epstein-Barrvirus), adenoviruses, enteroviruses (Coxsackie virus B5, echoviruses), hepatitis viruses (A, B and C), influenza, paravaccinia, parovirus B19, poliomyelitis, vaccinia and variola have all been implicated. Drugs such as sulphonamides (e.g. co-trimoxazole), cephalosporins, aminopenicillins, quinolones, chloromezanol, barbiturates, oxicam non-steroidal anti-inflammatory drugs, anticonvulsants, protease inhibitors, allopurinol or even corticosteroids may be implicated. Food additives or chemicals such as benzoates, nitrobenzene, perfumes have also been reported as aetiological agents. Over 50% of patients have unknown aetiology with stress or emotional factor as the second largest category. In the present case the patient gave a history of mild fever before the onset of the intraoral lesions which could suggest a viral etiology.

The exact pathogenesis is unknown. It has been suggested that EM results from T-cell-mediated immune reaction to the precipitating agent, which lead to a cytotoxic immunological attack on keratinocytes that express non self-antigens, which subsequently leads to subepithelial and intra-epithelial vesiculation; that causes widespread blistering and erosions. A better understanding of the molecular and immunologic events underlying HSV-associated EM (HAEM) and their main differences with respect to drug induced EM has been provided by recent studies. It is suggested that disease development begins with HSV infection of epithelial skin cells, and subsequently circulating mononuclear CD34 cells (Langerhans cell precursors). This transporst the HSV-DNA fragments to distant skin sites, where an immune mediated epidermal damage occurs due to production of interferon-γ (IFN-γ). Conversely, in drug-induced EM, tumour necrosis factor alpha (TNF-α) induces keratinocyte apoptosis which is released from keratinocytes, macrophages, and monocytes causing the tissue damage. A subset of EM patients has been reported to have autoantibodies against desmoplakins I and II and antiepidermal autoantibodies. In addition to a cellular immune response, humoral immune mechanisms may be involved in the pathogenesis of EM-like disease.

**Conclusions**

The management of EM can be difficult. An important element in EM treatment is the discontinuation of all inciting factors. In addition, disease management depends on other factors, such as the presence of mucosal disease, the development of recurrent disease and overall disease severity. Mild forms usually heal in 2–6 weeks; local wound care, topical analgesics or anesthetics for pain control and a liquid diet are often indicated in these situations. For more severe cases, intensive management with intravenous fluid therapy may be necessary. Oral antihistamines and topical steroids may also be necessary to provide symptom relief. Systemic corticosteroids have been used successfully in some patients.
Declaration of Interest

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References