

Case Report / Olgu Sunusu**Oral lesions of drug induced erythema multiforme – report of three cases****İlacın İndüklediği Eritema Multiformenin Oral Lezyonları- Üç Olgunun Sunusu**Shruthi Hegde¹, Sumona Pal², Vidya Ajila¹, Harini K³, Babu S¹

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ÖZET

Eritema Multiforme (EM) belirli enfeksiyon ve ilaçlarla ilişkili bir hipersensitivite reaksiyonu olarak Kabul edilen, ani, kendini sınırlayan ve bazen tekrarlayan cilt bulgularına olması durumudur. Geniş bir ilaç grubu EM'yi tetikleyebilir. Ağrı kesici olarak en sık reçete edilen ilaçlardan olan non steroid antiinflamatuvar ilaçlar EM gibi yan etkilere de yol açabilir. EM'nin klinik olarak major ve minor formları vardır. EM'nin üçüncü bir varyantı olarak oral EM bir kaç raporda sunulmuştur. Bununla birlikte oral mukozayı tutan EM'nin ayrı bir antite mi yoksa minör EM formunun bir parçası mı olduğu hale açık değildir. Bu olgu sunusunda üç EM olgusu tartışılmıştır, ikisinde yalnız oral mukozal lezyonlar, diğerinde ise deri belirtileri ile oral mukoza lezyonları gözlenmiştir. Ayrıca bu sunuda NSAID'lerin nadir yan etilerine bu durumu yönetimi ile birlikte vurgulanmıştır.

Anahtar Kelimeler: eritema multiforme, ilaç, oral mukoza

Abstract

Erythema multiforme (EM) is an acute, self-limited, and sometimes recurring skin condition considered to be a hypersensitivity reaction associated with certain infections and medications. A range of medications can trigger the EM. Non-steroidal anti-inflammatory drugs (NSAIDS) which are most commonly prescribed for pain relief can also produce rare adverse reactions such as EM. EM is clinically characterized by a "minor" form and a "major" form. Only few reports have stated about oral EM as the third variant of EM. However it is unclear whether EM involving only oral mucosa is a separate entity or is a part of minor form of EM. In this report three cases of EM are discussed , in which two cases involved exclusively oral mucosal lesions and in one case skin manifestations along with oral mucosa was observed. Also the uncommon adverse effects of NSAIDS is highlighted in this report along with its management.

Key words: Erythema multiforme, drugs, oral mucosa

Introduction

Non-steroidal anti-inflammatory drugs are commonly prescribed by medical and dental practitioners for pain relief. Diclofenac sodium is a widely used non-steroidal anti-inflammatory drug (NSAID) for pain relief. Adverse reactions to NSAIDs are rare.(1) Systemic administration of medications can cause potential intraoral complications. Erythema multiforme is one such adverse drug reaction.(2) Erythema multiforme is an ulcerative and bullous disorder, characterized by cutaneous eruption which may or may not be followed by oral involvement and may occasionally involve the mouth in an isolated manner.(3) Three cases of Erythema multiforme with oral lesions are described in this report. The uncommon adverse effects of diclofenac sodium are highlighted along with the management. We hope that this report will add to the existing scanty literature and draw attention on the occurrence and manifestation of this condition and also on potential drawbacks of self-medication.

Case Report

Case 1

A 22 years-old-male presented with ulcers and blister formation on lips and mouth since 5 days. He gave history of pain in the right mandibular posterior teeth region 5 days back for which he had taken over the counter medication (tablet diclofenac sodium 50mg, twice). He noticed blisters in lips and mouth after taking the medications. The blisters ruptured spontaneously with discharge of blood tinged fluid. Patient had pain on touching, difficulty in swallowing and speech. He had no similar past history and his medical history is non-contributory. On examination encrusted lesions were present on both upper and lower lips. Irregular erythematous area measuring about 2x3 cm covered by yellowish slough was present on the palatal mucosa(Figure 1). Based on the history and clinical examination diagnosis of erythema multiforme was made. He was advised to apply fluticasone 0.05% cream on the lips twice daily, and Tablet prednisolone 20 mg once per day for 7 days. Patient was recalled after a week. On follow up visit he gave history of relief of symptoms. Encrusted lesions and erosions were healing. Dosage of prednisolone tablet was tapered and stopped over next 7days.

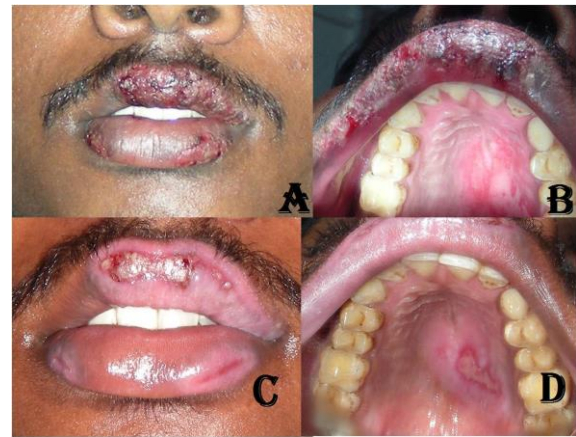


Figure 1
A) Ulceration of the labial mucosa, with hemorrhagic crusting of the vermilion zone of the lips. B) Diffuse ulcerations and erosions involving the hard palate. C) Healing lesions in the vermilion zone of lips D) Healing lesions in the hard palate)

Case 2

A 18- years-old male presented to the department with the complaint of ulcers on the lip and inside the mouth since 4 days . Patient had headache 1 week back for which he took over the counter medication (details not known). Following self-medication he developed blisters and painful ulcers in the mouth and lips. He also developed blisters on hand , back of neck which burst open. Medical history was noncontributory. On examination lips were swollen with severe bloody encrustations ,vesicles and bullae were present on neck , flexor aspect of right forearm(Figure 2). Based on the history and clinical examination diagnosis of erythema multiforme was made. Patient was advised Tab. Betamethasone 0.5mg, twice daily for 1 week , triamcinolone acetonide 0.1% ointment , twice daily for one week. Following the medication the ulcers healed without scarring.



Figure 2
A) Ulceration of the labial mucosa, with hemorrhagic crusting of the vermilion zone of the lips. B) Diffuse ulcerations and erosions involving the hard palate. C) Blisters below the lower lip D) Erosions and vesicles in the neck region.)

Case 3

A 35 years- old- male patient reported to the department of Oral Medicine and Maxillofacial Radiology with a complaint of bleeding and crusting of the lips since the past 2 days. There was history of intake of medication 4-5 days earlier for throat pain. Two days later, he developed vesicles on the labial and buccal mucosa which ruptured leading to severe burning sensation over the mucosa, bleeding from the lesions and difficulty in eating. He reported a similar episode after intake of diclofenac tablets few years ago. On examination, crusting of the lips was seen with bilateral submandibular lymphadenopathy. Crusting was prominent along the vermilion border of the upper and lower lips with bleeding on provocation. Erosions and ulcerations were seen in the labial and buccal mucosa concentrated mainly in the anterior part of the oral cavity(Figure 3). There were no lesions elsewhere in the body. Based on the history and clinical findings a diagnosis of erythema multiforme was made. He was then treated with prednisolone 10mg thrice daily for 1 week, twice daily for 2nd week and once a day for third week. Topical medication was also prescribed as follows-Clobetasol dipropionate 0.05%, Chlorhexidine gel 1% and Benzocaine gel 20% thrice daily. The lesions resolved within 2 weeks.

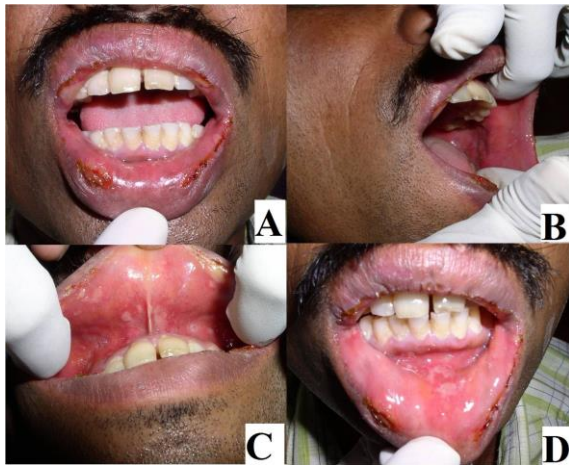


Figure 3

A) Crusting of the lips, B) Erosions along the occlusal line of left buccal mucosa C) Upper labial mucosa with multiple erosions, D) Irregular eroded areas in the lower labial mucosa

Discussion

Erythema multiforme is an acute, self-limited, and sometimes recurring skin condition considered to be a hypersensitivity reaction associated with certain infections and medications.(4)EM and related diseases give rise to mucosal erythema and ulceration with or without a variety of cutaneous

rashes and pleomorphic eruptions.(5) EM is classified into several variants, mainly minor and major forms. EM minor occasionally may involve the oral cavity alone or may present with a skin eruption, with or without lesions of oral or other mucous membranes(6). EM minor is often also characterised by rashes, which are usually symmetrically distributed on the extensor surfaces of the arms and legs. Skin lesions are typically “iris” or “target” lesions or bullae on extremities, which may itch. Intraoral lesions predominantly occur on the non-keratinized mucosae and are most pronounced in the anterior part of the mouth, including the lips and tongue. Intraoral lesions present as widespread macules to blisters that coalesce to form large ulcerations.(7)

Few reports have stated about oral EM as the third variant of EM.(8) However it is unclear whether EM involving only oral mucosa is a separate entity or is a part of minor form of EM. Two of our reported cases showed exclusively oral mucosal lesions and in one case skin manifestations along with oral mucosal lesions.

EM is associated with an acute onset and usually with mild or no prodromal symptoms.(9)EM is a disorder that reacts primarily to antigens that are induced by exposure to microbes or drugs.(6) Both EM minor and major are considered to be delayed-type hypersensitivity reactions that result from a T-cell mediated immune reaction to the causative agent. This reaction leads to a cytotoxic immunological attack on keratinocytes.(10)

A range of drugs may precipitate EM. Drugs which may precipitate EM are sulphonamides, antibiotic drugs (cephalosporins, quinolones, aminopenicillins, tetracyclines, macrolides), imidazole antifungals, anticonvulsants (phenobarbital, phenytoin, valproic acid, carbamazepine, and lamotrigine), and then non-steroidal anti-inflammatory drugs (especially oxicam), allopurinol, and others.(1,6) Previous use of medication has been identified in 59% of cases.(6) In an international case control study on severe cutaneous adverse reactions of non-steroidal anti-inflammatory drugs, oxicams were associated with highest risk which was followed by ibuprofen and diclofenac sodium.(11) Roujeau JC et al (12) suggested that the use of oxicam were associated with significantly higher risk than for diclofenac and propionic acid derivatives among NSAIDs. They also stated that for none of the drugs does the excess risk exceed five cases per million users per

week.(12) The known adverse effects of diclofenac is gastrointestinal effects, CNS effects, rashes, allergic reactions, fluid retention, and rarely impairment of renal function.(13) Analgesic diclofenac sodium was the causative agent in two of our cases since there was no evidence of intake of any other drug. Diclofenac sodium (50-mg tablets) was taken twice in case 1. In case 2 details of drug is unknown.

Besides EM, several allergic mucosal reactions to systemic drug administration have been reported which include anaphylactic stomatitis, intraoral fixed drug eruptions, lichenoid drug reactions, lupus erythematosus like eruptions, pemphigus like drug reactions, nonspecific vesiculoerosive lesions.(2) The differentiation between these lesions are based on the patterns of mucosal alterations.

There are no specific diagnostic tests for EM.(14) Features more suggestive of EM are the acute onset (or recurrent nature), oral erosions typically located on the lip and anteriorly in the mouth, and pleomorphic skin and other lesions. Biopsies are advised in early vesicular lesions. In ulcerative lesions histopathologic appearance can be nonspecific and nondiagnostic.(8) In our cases advanced ulcerative lesions were present, hence biopsy was not advised. Diagnosis was arrived on the basis of history of drug intake, clinical appearance of the lesions and exclusion of other ulcerative lesions.

For the management of EM, precipitants should be removed or treated. Causal drugs should be stopped and relevant infections treated. Antiviral agents may be indicated in Herpes associated erythema multiforme. No specific treatment is available for EM, palliative treatment is done with analgesics, lidocaine rinses, soothing mouth rinses and soft bland diet may be necessary. Systemic and topical antibiotics are prescribed in order to avoid secondary infections. Corticosteroids are the most commonly used drugs in the management of EM. EM minor usually respond to topical corticosteroids. In severe cases systemic corticosteroids are indicated.(8,14) In all our cases, the lesions regressed after corticosteroid therapy.

In this report rare adverse reaction of NSAIDS is highlighted. Also the varied clinical features of EM such as exclusive oral mucosal lesions were described.

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