

## Case Report

# Drug induced mucosal erythema multiforme

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### ABSTRACT

Erythema multiforme (EM) is a hypersensitivity reaction to different antigenic stimuli, commoner being infection followed by drugs. It occurs predominantly in younger age group. EM has benign course but frequent recurrences are common especially secondary to HSV infection. Erythema multiforme present as classical cutaneous target/ targetoid lesions and mucosal bullae/erosions. Though almost 70% of patients suffer from mucosal involvement, isolated mucosal affection is very rare. Fuchs syndrome/ectodermosis pluriorificialis is a rare variant characterized by severe involvement of two or three mucosal sites in the absence of skin lesions commonly triggered by *Mycoplasma pneumoniae*. Here we are reporting a rare case of mucosal erythema multiforme secondary to drug and highlighting the importance of distinguishing it from other similarly presenting mucosal disorders.

**Keywords:** Erythema multiforme, Fuchs syndrome, Mucosal EM

### INTRODUCTION

Erythema multiforme (EM) is a reactive mucocutaneous disorder that presents with either milder variant known as EM minor or a toxic and extensive mucocutaneous necrosis named as EM major.<sup>1</sup> These variants share two common features: typical or less typical cutaneous target lesions and satellite cell or more widespread necrosis accompanied by erosions or bullae in various mucosae.<sup>2</sup> Certain unusual variants are also erroneously included under this spectrum like annular urticaria or serum sickness like reaction. EM occurs as a result of an allergic host response to an antigenic challenge. Many patients react to infectious diseases, representing approximately 90% of cases, the most common agent being HSV (Herpes Simplex Virus).<sup>3,4</sup> Other triggering factors are drugs, malignancy, vaccination, autoimmune diseases, and radiotherapy.<sup>5</sup> The most common drugs that trigger EM lesions are long acting sulfa drugs especially sulphonamides, co-trimoxazole, phenytoin, carbama-

zepine and non-steroidal anti-inflammatory drugs (NSAID's) such as diclofenac, ibuprofen, and salicylates. Mucosal lesions are present in around 70% of cases, most commonly involving oral mucosa especially in recurrent EM. Other mucosae involved are ocular, nasal, pharyngeal, laryngeal, tracheal, oesophageal, urethral and ano-genital. It is important to differentiate such isolated mucosal lesions of EM from other similarly presenting mucosal disorders.

### CASE REPORT

A 24-year-old male patient came to skin OPD with the complaint of painful raw areas in the mouth with pain and watery discharge from eyes since 5 days.

On further enquiry, he gave history of fever with throat congestion for which he consulted and took painkillers given by private practitioner for 5 days, 2 days after which he developed swelling of lips and multiple painful

raw areas in the mouth leading to oral intolerance to food. On examination, patient was tachycardiac with rest of the general and systemic examination within normal limit.



**Figure 1: Haemorrhagic crusting and erosions over lips.**



**Figure 2: Healing lip erosions after 7 days of treatment.**

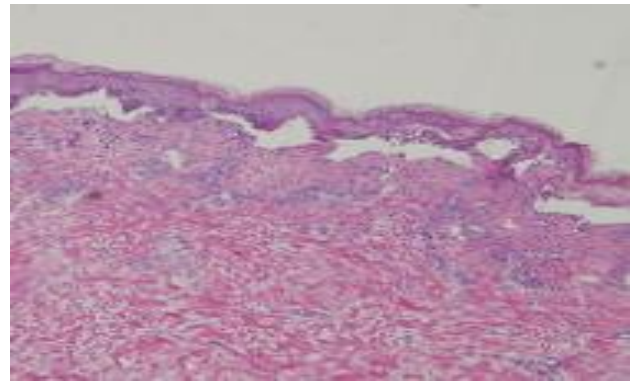


**Figure 3: Conjunctival congestion.**

On oral examination, the swollen lower lip, bilateral buccal mucosae showed extensive irregular ulcers, haemorrhagic crusts with superimposed yellowish slough, sparing the gingivae (Figure 1). Bilateral ocular congestion was also seen (Figure 3). Rest of the mucosae were normal. No skin lesions were observed.

By sudden onset of mucosal affection, drug ingestion history, we kept the diagnosis of Drug induced mucosal Erythema Multiforme. Slit lamp examination was uneventful. Blood investigations were within normal limit and serostatus was negative. For confirmation of

causative agent, Tzanck smear was taken from scraping the base of fresh tiny erosion which did not show any multinucleated giant cells, also blood culture did not show any pathogenic organism. Throat swab was taken which showed only commensals. Anti HSV antibody levels were negative. Naranjo's algorithm showed probable drug cause as score came out to be 2+. Oral mucosal biopsy showed spongiosis, subepithelial tissue with mild infiltration by lymphocytes more in perivascular area and dermal edema (Figure 4). The patient was advised to stop all over the counter medications and was treated with tapering doses of systemic corticosteroids (40 mg prednisolone tapered down by 10 mg every 3 days) and mild analgesics, antihistaminics with local application of lignocaine gel to facilitate oral fluid intake. Frequent wet gauzes to reduce hemorrhagic crust and topical fusidic acid cream over lip erosions were given. Ocular congestion was treated by regular administration of lubricant eye drops. Symptoms were significantly relieved within 1 week of treatment.



**Figure 4: Oral mucosal biopsy showing interface dermatitis.**

## DISCUSSION

Erythema multiforme was first described by Hebra in 1866.<sup>6</sup> It usually occurs in young healthy individuals. The disease tends to have an episodic course with duration of 1 to 4 weeks.

Skin involvement in EM consists of typical target lesions which are individual lesions less than 3 cm in diameter with a regular round shape; well-defined border; and three different zones (central dusky erythema or purpura or vesicle/bulla surrounded immediately by paler peripheral edema, which is further encircled by well defined erythema) or raised atypical targets characterized by round, edematous, palpable lesions with only two zones or a poorly defined border located on the extremities or the face.

Amongst all the variants, mucosal EM variant is an under recognized and thus underreported form of EM. It has been reported that even if the primary attacks of EM are confined to the mucosa the subsequent attacks can produce more severe forms of EM involving the skin.<sup>7</sup>

It is characterized by episodic, recurrent bullae and erosions over lips, on both cutaneous and mucosal sides, non-attached gingivae, and the ventral side of the tongue. The hard palate is usually spared, as are the attached gingivae.<sup>8</sup> On the cutaneous part of the lips, identifiable target lesions may be discernible. The lesions rarely extend to the throat, larynx, and even the trachea and bronchi interfering with speech, mastication, and swallowing producing considerable morbidity. Eye involvement begins with pain and bilateral conjunctivitis in which vesicles and erosions can occur with lacrimation and photophobia.<sup>9</sup> Other mucosal surfaces like nasal, anogenital and urethral mucosae may be inflamed and eroded. Genital lesions are painful and may result in urinary retention. Scarring sequelae from ocular and pharyngeal involvement can cause morbidity.<sup>10</sup> In our case, prednisolone short course gave relief within 4 days (Figure 3) and on follow up of 3 months there was no recurrence.

The diagnosis of mucosal EM has always been a challenge because it mimics other mucosal diseases like aphthous ulcers, bechets disease, pemphigus vulgaris, mucous membrane pemphigoid, mucosal lichen planus, paraneoplastic pemphigus. To differentiate and confirm, mucosal biopsy with DIF is necessary. Management of mucosal EM involves identification of causative factor. After HSV (treated with acyclovir), if the drug is suspected as culprit as in our case it was some NSAID, it is immediately stopped followed by appropriate supportive care which includes viscous lidocaine rinses, bland soft diet, soothing eye drops, antibiotics to prevent secondary infection with topical and systemic steroids. To summarise, the rapid onset and progression with no cutaneous involvement, pattern of mucosal involvement and immediate relief by short course corticosteroid and withholding culprit drug along with no recurrence, and mucosal biopsy with classical features and negative DIF clinch the diagnosis of mucosal erythema multiforme. Though rare, cases of drug induced mucosal EM is on rise. Early recognition, therapy and regular follow-up of this acute oculocutaneous disease spectrum is critically important to prevent cicatricial morbidities.

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