

## Case Report

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# Drug induced bullous erythema multiforme in a 75-year-old male: A case report

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### Abstract

Erythema multiforme is an autoimmune mediated reaction pattern with diverse clinical manifestations characterized by the formation of multiple areas of erosion and ulcer in the oral cavity and haemorrhagic crusting of lips. such a case of Erythema multiforme in a 75 -year-old male is described here. The management of bullous form of erythema multiforme involves symptomatic treatment with topical anesthetics, topical or systemic steroids or antihistamines and treating the underlying etiology, if known. Recurrent erythema multiforme associated with the herpes simplex virus should be treated with prophylactic antiviral therapy. Severe mucosal erythema multiforme require hospitalization and must be treated in critical intensive care unit such as treating for burn in a Burn unit for intravenous fluids and depletion of electrolytes.

**Keywords:** Erythema multiforme; fluorescent antibody technique; lip; target lesion.

### Case presentation

A 72-year-old-male reported with a chief complaint of bleeding from the lips and soreness due to the presence of erosion and ulcers for the past 1 month (Figure 1). He also complaints of burning quality of intense pain in his mouth and difficulty to consume beverages or eat food. Patient visited a dentist in a private dental clinic and was prescribed Amoxicillin and aceclofenac for the pain, but the lesion hasn't subsided. He had no history of deleterious habits of chewing or smoking tobacco or consumption of alcoholic beverages. His family history was non-contributory. Extraoral examination revealed no cervical lymph-

adenopathy. Extensor aspect of the arm revealed target eye lesion- central area of scab surrounded by a paler ring like area bordered by pigmentation (Figure 2). Flexor aspect on the skin of left forearm revealed Bull-eye lesion consisting of a central paler area bordered by popular area of pigmentation (Figure 3).

Intraoral examination revealed multiple areas of erosion and ulcer on his right and left buccal mucosa and labial mucosa. Haemorrhagic crustations present on his vermilion border of lip.



**Figure 1:** Extraoral profile showing Haemorrhagic crusting on the vermilion border of lips



**Figure 2:** Extensor aspect of the arm revealed target eye lesion-central area of scab surrounded by a paler ring like area bordered by pigmentation.



**Figure 3:** Flexor aspect on the skin of left fore arm revealed Bull-eye lesion consisting of a central paler area bordered by popular area of pigmentation.

## Discussion

Erythema Multiforme is an autoimmune mediated reaction pattern with diverse clinical manifestations characterized by multiple areas of erosion and ulcer in the oral cavity and characteristic haemorrhagic crusting on the vermilion border of lip. Erythema multiforme is a cell mediated immune reactions that can be triggered by medications such as analgesics like acetaminophen, oxicam derivatives like piroxicam, antiepileptics such as Phenytoin, valproic acid. antibiotics such as Penicillin-aminopenicillin, Tetracycline, Erythromycin, sulphonamides, Fluoroquinolones, cephalosporins, Antihyperlipidemic drugs like statins, and infections like Herpes zoster and Mycoplasma Pneumoniae, cytomegalovirus, Epstein-Barr virus, Hepatitis-C, Influenza, Herpes simplex Type 1 and 2. Vaccines like small-pox, measles, mumps, rubella, hepatitis-B, varicella, Influenza, Pneumococcal, Haemophilus influenza can induce Erythema multiforme [1]. Herpes antigen present within the epidermis, activate the alternative complement pathway. Fungal infections like Histoplasmosis, coccidiomycosis can also elicit Erythema Multiforme. Patients with leukaemia, renal cell carcinoma, gastric adenocarcinoma, cholangiocarcinoma [2-5]. Patients with inflammatory bowel disease also associated with erythema multiforme. Consumption of food preservatives like Benzoic acid in excess are reported with the occurrence of Erythema multiforme reactions [6].

**Bastuji-Garin et al classification of erythema multiforme:** EM Minor (Bullous form) and EM Major (Steven-johnsons syndrome) [1].

**Recurrent erythema multiforme:** The occurrence of Erythema Multiforme over a period of years with a mean duration of about 6-10 years [7].

**Persistent erythema multiforme:** A rare form of Erythema multiforme characterized by the continuous occurrence of typical lesions without interruption [7].

Mild prodromal symptoms include malaise, sore throat often precede eruptions and drugs given for these symptoms are usually blamed for Erythema Multiforme. Individual areas of erosions were painful. In severe ill patients there is high fever, cough, sore throat, myalgia, malaise and severe pain in the areas of mucosal erosion with secondary photophobia and inability to ingest food or fluids [7].

Almost 25-60% of the affected patients clinically present with mucosal involvement. Mucosal lesions are characterized by areas of erosions and pseudomembranes, painful. The target lesions or Bulls-eye lesions are more commonly occur on the extensor acral location in Bullous Erythema multiforme. They consist of a central vesicle or livid erythema surrounded by a concentric pale and then red ring. The mucosal lesions are present in 25% to 90% of the cases and usually start at the same time as skin lesions. Pulmonary involvement can occur in the presence of a negative chest x-ray with involvement of the bronchial epithelium causing Dyspnea, Bronchial hypersecretion and Hypoxemia [8]. The differential diagnosis include fixed drug eruptions, Bullous pemphigoid, Paraneoplastic pemphigus. The ocular involvement of bullous pemphigoid is not seen in patients with erythema multiforme. Pemphigoid is character-

ized by the occurrence of thick walled, tense bullae that do not rupture easily. whereas in patients with erythema multiforme the bullae if occurred in the oral mucosa gets easily ruptured by the teeth during mastication or speaking resulting in the formation of large areas of erosions leaving a raw erythematous area and there is characteristic haemorrhagic crusting on the vermilion border of the Lip. Fixed drug eruptions usually occur at one particular area in the oral cavity. The lesion occurs in the same site when there is any medical history of drug intake of the offending drug. Erythema multiforme is usually associated with haemorrhagic crusting on the vermilion border of lip, which are spared in fixed drug eruptions. Erythema multiforme usually have a chronic course of months to years, whereas fixed drug eruptions usually resolve in a week after drug intake. Paraneoplastic pemphigus resemble erythema multiforme. A complete blood profile and clotting factors helps in ruling out leukemia occurring in Paraneoplastic pemphigus. Cutaneous T-cell lymphoma and Thymoma, Waldenström's macroglobulinemia were the neoplasias that were encountered in patients with Paraneoplastic pemphigus. Leukemia, hepatic cholangiocarcinoma [9,10].

The earliest histological findings of EM are endothelial cell swelling, dermal papillary edema and perivascular lymphohistiocytic infiltrate. Later epidermal necrosis, dermal-epidermal interface alteration, subepidermal or intraepidermal separation and bulla formation occur. Herpes simplex Deoxyribonucleic Acid (DNA) is found primarily in the skin lesions of recurrent EM, with the viral antigens being present for as long as 3 months with no evidence of clinical disease. The Herpes simplex DNA is found in peripheral white blood cells only during an acute episode of Erythema Multiforme [11]. Tzanck test -reveal acantholytic keratinocytes. Herpes simplex antigen has been detected by Polymerase chain reaction in biopsy specimens of active lesions. Direct immunofluorescence test of biopsy of skin region reveals granular deposition of C3 and immunoglobulin M (IgM) at the dermo-epidermal junction and the superficial blood vessels. In addition, homogeneous C3 and IgM staining of focal epidermal cells can be seen in regions of epidermal necrosis. serum assay for complements helps in diagnosing erythema multiforme. Increased levels of Tumour necrosis factor- $\alpha$  occur in Drug induced Erythema multiforme. Throat swab test followed by Polymerase chain reaction helps in assessing erythema multiforme induced by Herpes simplex virus. Erythrocyte sedimentation rate (ESR), White blood cells, Liver function tests, electrolytes can be assayed [12,13].

### Management

Patients affected by Erythema Multiforme must be treated in a burn's unit. The main aim of therapy is to provide replenishing of the body electrolytes that were lost by the erosions occurring after rupture of the flaccid bullae. Treatment aims at removing the cause. Systemic potent corticosteroids are beneficial. Open wet compresses. Burow's solution (Domeboro compresses, one packet in 1 pt of water) followed by silver sulfadiazine cream (Silvadene) twice daily for bullous or erosive lesions. 1.5 % Hydrogen peroxide mouthrinse two-five times a day. 1% Dyclone solution, viscous lidocaine or a mixture of Kaopectate in elixir of diphenhydramine applied directly to the lesions for pain. Analgesics like Aspirin 600 mg q4h. Acyclovir 200 mg five times a day or 400 mg PO b.i.d in case of Herpes associated Erythema Multiforme. Patients can be prescribed Prednisolone 100-250 mg per day but must be started before blistering occurs. Pulse therapy: Treatment with Methylprednisolone 4 mg/kg bolus in-

fusion everyday is given until the disease responds and is then tapered over 2-3 weeks [14,15].

### Clinical significance

A proper history of drug intake is helpful in identifying drug induced erythema multiforme cell mediated immune reactions characterized by the presence of target or Bulls eye lesions on the extensor aspect of forearms. The diagnosis of such drug induced erythema multiforme aids in prompt initiation of treatment and thereby helps in preventing life threatening skin scalding reactions like Steven Johnson syndrome.

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