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Drug induced Erythema Multiforme and its Oral Manifestations: A case report

Rajesh Bhatia*, Vishal Mehrotra, Kriti Garg, Rahul Srivastava, Sachin Kushwah,

Rama Dental College, Rama University, Mandhana Kanpur, U.P, India

ABSTRACT:

Erythema multiforme is an acute muco-cutaneous lesion affecting the skin, oral mucosa, genitals, eyes etc. If untreated then it may be fatal. Reporting a case report on erythema multiforme with various oral and skin manifestations

INTRODUCTION:

A well-known acute mucocutaneous illness that affects the skin and occasionally the mucosa is erythema multiforme. Although the precise etiopathogenesis of EM is unknown, immune-mediated disorders are thought to be its cause [1]. While a considerable percentage of EM cases are still idiopathic, other possible causes of the condition include infections (such herpes simplex virus and Mycoplasma pneumonia), drug exposure (like antibiotics), immunization, and autoimmune disorders [2–3]. When cytotoxic T cells are activated in the epithelium during clinical manipulations of EM, keratinocytes undergo apoptosis, which results in necrosis of satellite cells. Traditionally, EM starts with symmetric involvement of the extremities and the development of lesions known as "targets," which typically dispersed across the trunk centripetally [3]. An important characteristic that helps distinguish EM from cutaneous symptoms of other immune-mediated illnesses, like urticarial and allergic rashes, is that EM skin lesions typically stay fixed for at least seven days. clinical manifestations that can be mild (EMminor, EM major), fulminant, or severe (Steven-Johnsonsyndrome); it can even result in toxic epidermal necrolysis(TEN) [4-5]. EM manifests as skin eruptions with or withoutoral or other mucous membrane lesions [6, 7] and candevelop at any age, but it develops most frequently in youngadults [8].The aim of this study is to report a case of oral erythema multiforme (EM) manifesting as oral, lip, and skin lesions.

CASE REPORT:

A forty-year-old man came into the dental office complaining of painful oral ulcers and deposits. He reported a past of intense pain that started with redness in his mouth and lips. When he consulted a local doctor in Rajasthan two years ago, the doctor recommended oral prophylaxis and medication for symptom relief. After that, during the Covid 19 era, he continued to wear the mask for a long period of time, which triggered his allergy and caused itching, redness, and swelling in the affected area. He took the doctor's prescribed medications once more, but they didn't help; instead, that made the symptoms worse, causing

a severe type of allergy, fever, and a general sense of unease, occasionally accompanied by arthralgia or even joint swelling. After receiving blood tests, he was diagnosed with typhoid and malaria. He was then treated with intravenous antibiotics and other medications, which made his systemic diseases worse and made his oral lesion worse, making it difficult for him to even swallow. He then complained of debris and widespread tartar on his teeth when he came to our clinic. Oral prophylaxis was performed and oral antibiotics(Ornidazole 500mg Bid for 5 days), and topical ointments were then administered.On clinical examination, multiple ulcers involving all areas of the oral cavity including keratinized and lining mucosa bilaterally. (Fig 2). The ulcers involving the tongue dorsum, oral floor and ventral surface of the tongue showed a tendency to bleed. Intra-oral ulcerations were accompanied by haemorrhagic crusting of the lips (Fig 1) The ulcers were extremely painful and interfered with eating and drinking. There were also a few macules and hyperemic papules.Upon closer inspection, many ulcers were seen on both the upper and lower lips' vermilion borders. The encrusted ulcers varied in size from 1 to 2 mm. Examination of the larynx and pharynx was normal. There were no palpable neck nodes. The existence of target lesions on the abdomen, the eye's sclera(Fig 3 & 4). Upon follow-up, it was determined that the second round of oral prophylaxis could not be continued due to an abrupt flare-up of the mucosal and lip lesions. As a result, he was recommended to undergo testing for food and drug allergies.Drug-induced erythema multiforme was the preliminary diagnosis made in considering the patient's positive drug history and lesions.

Figure 1, 2: multiple bleeding erosive areas involving buccal/labial mucosa, tongue, palate

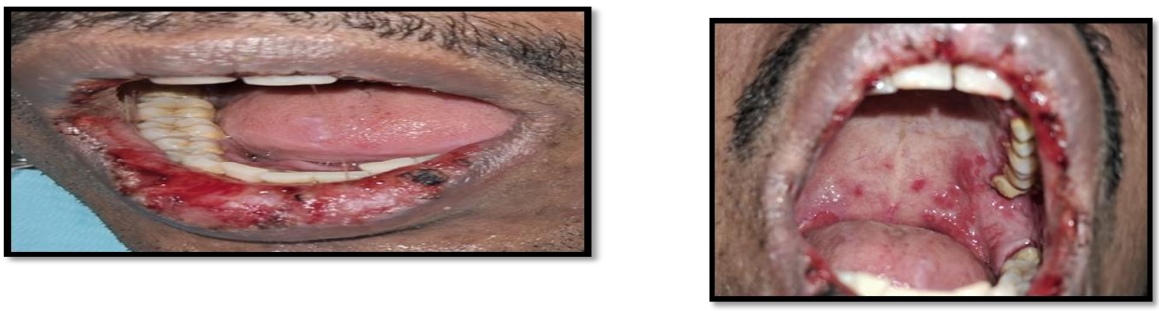
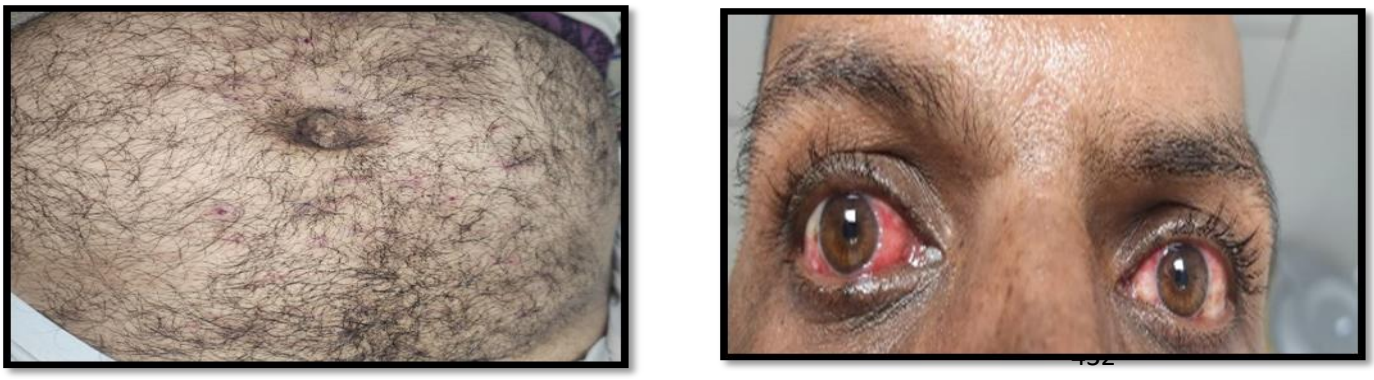


Figure 3,4: Target lesions over the abdomen and sclera of the eyes appears erythematous



DISCUSSION: Ninety percent of EM cases are linked to infectious organisms such Mycoplasma pneumonia in children and HSV in adults. Other etiologies connected with EM include medications, malignant tumors, and sarcoidosis. Seventy percent of individuals with either minor or major forms of EM have mouth lesions [11]. Mucosal lesions are rare but mostly affect the oral mucosa in cases of EM mild. Major lesions related to EM have been observed to manifest in more than two regions of the oral, genital, and ocular mucosa. Moreover, it has been noted that it only manifests itself in the oral cavity and not in skin lesions [10]. The oral cavity may be involved alone or in conjunction with additional lesions in the other stratified squamous epithelia [6]. The lips, buccal mucosa, and tongue are the primary sites for oral mucosa lesions, which usually manifest as hemorrhagic crusts on the lips [9]. Severe discomfort in the mouth and surrounding areas may cause problems with speech, nutrition, and hydration. Mouth and lip lesions heal without leaving scars. Recurrence occurs in roughly 25% of cases. Attacks can occur once or twice a year, with varying periods. They typically end after roughly six episodes over the course of ten years on average [12].

The scientific studies of HSV associated EM (HAEM) are the basis of the pathogenic route of EM. It has been proposed that viral antigen-positive cells carrying the HSV-DNA polymerase gene trigger autoreactive T-cell responses [13]. The production of HSV-DNA fragments triggers EM. These fragments are most likely produced and transported by peripheral blood mononuclear cells, primarily macrophages and CD34+ Langerhans cell precursors, potentially via the vascular pathway. HSV-specific CD4+ Th1 cell recruitment and viral gene expression in the skin trigger the inflammatory reactions.As a result of enhanced sequestration of circulating leukocytes, monocytes, and NK cells as well as the migration of autoreactive T-cells to the epidermis, the reaction produces interferon-γ (IFN-γ), which upregulates cytokines and chemokines to exacerbate skin inflammatory processes [13]. It is yet unknown how autoreactive T-cells are produced. As a result, keratinocyte development inhibition, apoptosis, release of several cytotoxic agents, and lysis of peripheral keratinocytes cause damage to the epidermis. Unlike HAEM, drug-induced EM (DIEM) does not appear to be the outcome of a delayed-type hypersensitivity reaction. Instead, the disease is assumed to be generated by the reactive metabolites of the initial medication [14].TNF-α, which is produced by macrophages and monocytes and is present in keratinocytes, is the hallmark of drug-induced lesions, as demonstrated by immunocytochemical staining and in situ hybridization. T cells do not produce IFN-γ in these lesions. On the other hand, TNF-α was not found in HAEM, and it was proposed that this may be utilized as a lab test to differentiate HAEM from drug-induced lesions [13]. Given that it has been demonstrated to induce keratinocyte death [15], locally generated TNF-α may be significant in moderate cases of DIEM.

Substances and other antigens, such as the herpes virus, create circulating immune complexes that seep into the skin's and mucosa's basement membrane.These substances bind complement and cause a vasculitis that results in ischemia necrosis and thrombosis of the surrounding epithelium. This causes widespread erosions and blistering (16). Oral lesions

develop into blisters and ulcers after broad, extensive macular lesions. Approximately 70% of people with erythema multiforme had oral involvement (11).

Herpes, autoimmune vesiculobullous diseases like pemphius vulgaris or bullous pemphigoid, and other types of drug reactions should be taken into consideration as differential diagnosis when the oral mucosa is the only site affected. On keratinized mucosa, herpetic lesions are more prevalent. The potential of autoimmune vesiculobullous disease was ruled out in our case by the patient's positive drug history, clinical presentation, and lesion distribution.

Based on clinical pattern, other adverse drug reaction clinical patterns, such as lichenoid and pemphigoid drug reactions, can be distinguished. Anaphylactic stomatitis frequently manifests as urticarial skin responses, which are indicators of anaphylaxis. A fixed drug eruption limits the lesion to a specific region of the oral mucosa.The diagnosis of EM can be made without reference to any particular objective signs or criteria. The clinical history and clinical results are crucial indicators for diagnosis. Important aspects of the medical history consist of: (i) a sudden, self-limiting, or acute course; (ii) indications and symptoms of related infections, like HSV or M. pneumonia infection; and (iii) a medical history involving the use of new or recent drugs.The appearance of target lesions, elevated atypical papules, mucosal involvement, or a combination of these might all serve as clinical indicators of a diagnosis.

Although there isn't a specific treatment for EM, management of EM can be challenging, analgesics and a liquid diet may be necessary to manage symptoms. Hospitalization and supportive care are frequently necessary for severe cases of EM. This includes intravenous fluids, as well as early dermatological and ophthalmological consultations. (17)

CONCLUSION: Effective care of drug-induced oral EM requires differentiation from other oral ulcerative lesions, which is not common. For an early diagnosis, a thorough history taking and clinical examination are crucial.Since the majority of these cases go unreported because of patient ignorance and self-medication that results in serious adverse drug reactions, it is crucial that healthcare providers disclose these events in order to raise public awareness and sensitize people to the need of using pharmaceuticals responsibly. Prescriber and patient knowledge, coupled with a strong ADR monitoring system that includes a feedback mechanism, can greatly improve the identification, prevention, and treatment of these diseases.

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