

Drug induced erythema multiforme of the oral cavity

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ABSTRACT

Drug induced erythema multiforme (EM) is a rare clinical entity which majorly involves the oral cavity. It commonly occurs due to intake of drugs such as NSAID'S, certain antibiotics, and anticonvulsants. It is characterized by rapidly rupturing vesicles leading to ill-defined erosions in the oral cavity and encrusted lip lesions. These lesions are usually difficult to differentiate from other vesiculo bullous and ulcerative lesions which would have a similar presentation and the absence of skin lesions can sometimes lead to misdiagnosis. Drug induced EM has an acute onset and is a self-limiting inflammatory hypersensitivity reaction that causes blistering and ulcerations of the skin and mucous membrane. The lesions heal following the discontinuation of the causative medications. This case report describes a case of drug induced erythema multiforme of the oral cavity that occurred consequent to the intake of Tab. Diclofenac Sodium and Tab.Cephelexin. The patient developed painful, bleeding, burning ulcerations with severe crustations on the upper, and lower lip, lateral and ventral surface of tongue, hard palate and retro molar regions. The case was managed with corticosteroids.

KEYWORDS: Erythema Multiforme; drug-induced; oral ulcerations; acute self-limiting inflammation

INTRODUCTION

The term "Erythema Multiforme" was first coined by Ferdinand Von Hebra in the year 1866. Erythema Multiforme (EM) is a self-limiting, acute, mucocutaneous, inflammatory condition which is caused by an immunologic reaction. Regardless of various etiological factors that have been listed as a cause for this condition, the exact mechanism of EM remains unclear [1]. Antigens induced by the exposure to certain medications or viral infections, induces apoptosis of Keratinocytes due to a hypersensitivity reaction caused by Cytotoxic T lymphocytes [2]. In more than 80% of the cases, infections caused by Herpes simplex virus (HSV) 1 and 2 are the main triggers followed by Epstein-Barr virus (EBV) and Mycoplasma pneumoniae [3]. Other triggering factors include various drugs such as non-steroidal anti-inflammatory drugs, antibiotics, anticonvulsants and others [4]. Less than 10% of cases of EM occur due to drugs.

Drug induced EM typically involves lips, oral mucosa, and sometimes the bulbar conjunctiva. The bullae that are formed initially rupture to form erosions on lips and oral cavity. Though each type of EM is well defined, it may be difficult to differentiate in clinical practice due to their overlapping features. The aim of our case report is to present a case of

drug induced oral erythema multiforme and to highlight the distinct features of this particular variant of EM.

CASE REPORT

A 49-year-old male patient was referred to the oral medicine clinic by a dental practitioner with chief complaints of burning sensation in the mouth, difficulty in eating, swallowing since three days. Patient gave a history of developing multiple painful ulcerations in the mouth and lips subsequent to the intake of medications following a tooth extraction 4 days ago. History also revealed that the patient developed burning sensation, a day after intake of medications and subsequently developed painful blisters which ruptured to form ulcers. Patient was on anti-hypertensive medications for the past 15 years.

On clinical examination, bilateral submandibular lymph nodes were tender and palpable. Extra-orally, there was severe crusting of upper and lower lips with multiple eroded areas. White to greyish necrotic slough were present all over the upper and lower lips and also the commissures of lips bilaterally which readily bled on touch. On intra-oral examination multiple superficial ulcers were seen with irregular margins on the lateral surface of the tongue bilaterally and on anterior two-third of ventral surface of tongue. Diffuse erosions were also seen on the left side of hard palate and left retromolar region. Multiple pinpoint ulcers were seen on the labial mucosa of lower lip (Figure 1). There was no involvement of other mucosal

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Fig. 1. Pre-treatment aspect. A) Patient profile B) Extra-oral picture showing crusting of upper and lower lips and erosions with white slough C) Intra-oral picture showing erosions and ulceration of hard palate and retromolar region D) ulceration on the ventral surface of anterior 2/3rd of the tongue E) Multiple pinpoint ulcerations present on the lower labial mucosa.

and dermal surfaces. Routine hematological investigations were within the normal range (Table 1). Based on the positive drug history, acute onset and clinical presentation a clinical diagnosis of Drug induced Erythema Multiforme was made. Histopathological examination was nonspecific and showed the presence of lymphocytic infiltrates.

Patient was advised to discontinue all medications. Patient was prescribed with Systemic steroids (Oral prednisolone) 5 mg thrice a day initially for 3 days and the dose was increased to four times a day for next 3 days after which tapering of the medication was done for the next one week. In addition to this patient was also prescribed chlorhexidine gluconate mouthwash. The patient was recalled after a week. Partial healing of the ulcers on upper, lower lips and labial mucosa and complete healing of erosions was seen on hard palate. After 2 weeks complete healing of lesions was seen both intra-orally and extra-orally with post inflammatory pigmentation on the upper lip (Figure 2).

DISCUSSION

Erythema multiforme (EM) is an acute, immunological, vesiculobullous disorder that primarily affects the skin and mucous membranes. EM is broadly divided into two types which includes EM major and EM minor. Other types include Stevens-Johnson syndrome (SJS), Toxic Epidermal Necrolysis Syndrome (TENS). EM major is characterized by symmetrically distributed typical target lesion which presents as cutaneous lesions and a minimum of two

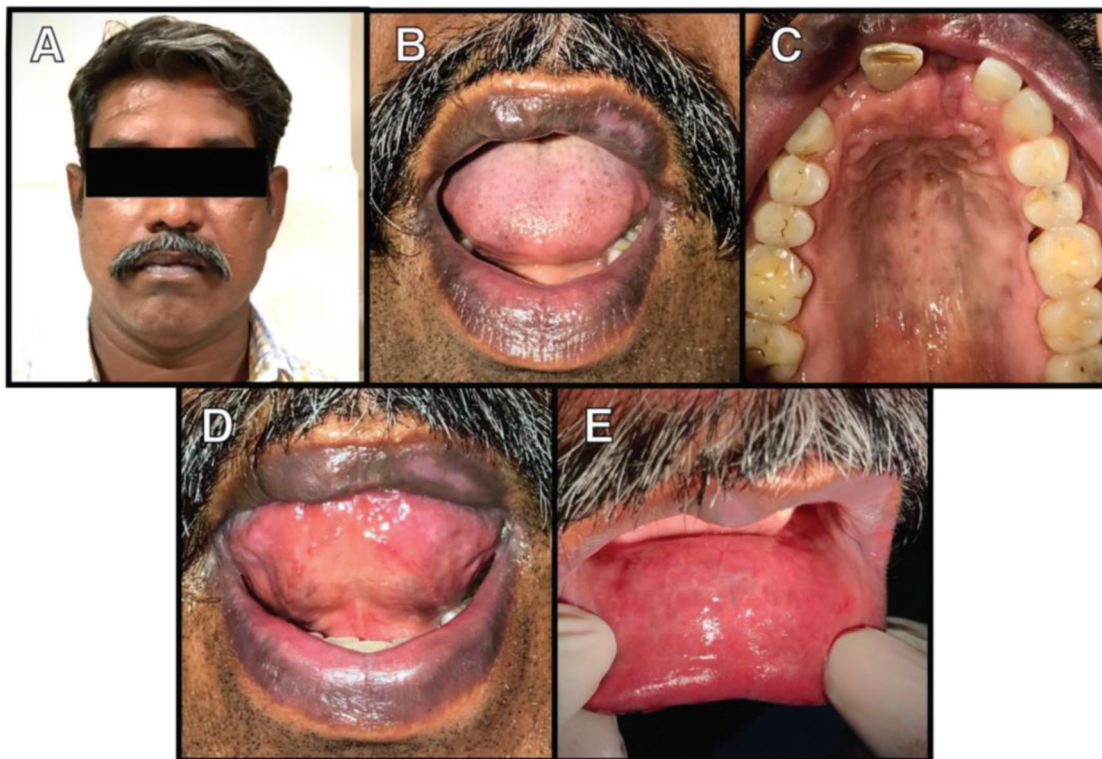
mucosal sites will be affected while body surface affected is less than 10%. EM minor is characterized by typical or raised atypical lesions with involvement of any one mucosal site (mostly the oral cavity) with body surface affected is usually less than 10%. SJS is primarily characterized by widespread atypical flat target lesions rather than classic target lesions. Detachment of less than 10% of body surface area seen. TENS has detachment of more than 30% of the body surface area and widespread purpuric macule or flat atypical target lesions [5]. SJS and TENS are considered to be the two stages severity of the same pathological condition [6]. The incidence of EM is reported to be far lesser than 1%. While the cause for more than half of the cases of EM are unknown others are considered to be caused by medications, infections, immunotherapy, or illnesses [7,8].

Drugs that can cause EM include NSAIDs, b-lactam antibiotics like (penicillins, cephalosporins) non-b-lactams like (clindamycin, trimethoprim) etc., anticonvulsants like (carbamazepine, phenytoin) barbiturates, oral anti-diabetics like (sulfonamides, chlorpropamide, tolbutamide) codeine, furosemide, gold, and protease inhibitors [7]. One of the studies have reported that 2.06% of cases of EM were due to diclofenac sodium, 6.17% of cases due to paracetamol, 5.65% due to anti-tubercular drugs, 5.39% due to penicillins, 3.34% due to anti-retro virals and 3.08% due to uptake of cephalosporins [8].

In our case, the clinical manifestation of the lesions might have appeared after the intake of NSAIDs and b-lactams. Patient did not reveal history of any other infections. The sudden appearance of oral lesions the next

Table 1. Routine Haematological Test Results.

| Test Name | Result | Normal Range |
|-------------------------|------------------------------|---|
| Hemoglobin | 16.7 g% | Male - 13.4–18 g% Female - 11.2–16 g% |
| Total WBC count | 7900 cells/mm ³ | 4000 - 11000 cells/mm ³ |
| Neutrophils count | 77% | 40–60% |
| Lymphocytes | 20% | 20–40% |
| Eosinophils | 2% | 00–05% |
| Monocytes | 1% | 01–04% |
| Basophils | 0% | 00–01% |
| ESR (30 mins) | 06 mm | 00–08 mm |
| ESR (60 mins) | 15 mm | 05–15 mm |
| Total RBC count | 6.0 millions/mm ³ | Male - 4.5–6.0 millions/mm ³ Female - 3.5–5.0 |
| Platelet count | 140,000/mm ³ | 150,000–400,000/mm ³ |
| PCV | 59% | Male - 40–55% Female - 35–48% |
| MCV | 97 fL | 76–96 fL |
| MCH | 27 pg | 27–35 pg |
| MCHC | 28 g/dl | 32–38 g/dl |
| Glucose (fasting) | 67 mg/dl | 70–110 mg/dl |
| Glucose (post prandial) | 88 mg/dl | 80–160 mg/dl |
| Urea | 25 mg/dl | 14–40 mg/dl |

**Fig. 2.** Post-treatment photos shows complete healing of the lesions.

consecutive day after ingestion of drug reveals that it was probably a case of Drug induced Erythema Multiforme. Oral EM is a less common variant of EM and is confined only to oral mucosa on primary attack. Subsequent attacks may also have cutaneous involvement. Among the oral mucosa, the most common sites involved are labial mucosa, buccal mucosa, lips followed by palatal mucosa. Management includes stopping the usage of the suspected drug followed by administration of topical and systemic

steroids for a period of one week with consecutive tapering of the dose.

■ CONCLUSION

Drug induced erythema multiforme of oral cavity are considered as an uncommon variant and proper history taking and knowledge is required to differentiate from other

oral ulcerative lesions so as to provide prompt and necessary treatment.

Informed consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Declaration of interest

The authors have no competing interests to declare.

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