Case study

NATUROPATHIC DRUG ERYTHEMA MULTIFORME MAJOR - A RARE CASE REPORT

ABSTRACT

Erythema multiforme (EM) is an acute self-limiting hypersensitive mucocutaneous lesion with varied etiologies. It is classified as spectrum of disorders with Erythema multiforme minor, Erythema multiforme major. Herpes virus infection is considered to be involved more than 90% of cases. Drug associated EM is rare and reported to be less than 10%. EM affects most commonly teenagers and young adults with more predilection to males. Oral lesions are seen on the lips and buccal mucosa which appear as erythematous macules, and bloody encrustations involving lips with classic target like lesions. Here is a case report of erythema multiforme major which was induced by naturopathic medications in a middle-aged woman who presented with classic target lesions and was effectively treated with systemic corticosteroids which showed complete remission and no recurrence had been noted till date.

KEYWORDS: Erythema multiforme, mucocutaneous lesions, target lesion, drug induced, case report

INTRODUCTION

Erythema multiforme is a well-recognized acute mucocutaneous disease that involves the skin and sometimes the mucosa[1]. The etiology of which may be related to herpes simplex virus, use of certain medications, autoimmune disease, radiation, immunization, pregnancy, period, and food additives or chemicals. It is a condition that occurs predominantly in young adults, with a slight female preponderance[2]. EM clinically represents 2 variations such as major and minor form, Erythema minor affects only the skin and erythema major includes mucocutaneous involvement[3,4] Although it was previously thought that erythema multiforme was on the same pathologic spectrum as Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis, it is now accepted that erythema multiforme is a distinct disease[5].Here we report a

rare case of drug induced erythema multiforme of skin and oral cavity affecting a middle aged woman. Along with its etiology, pathogenesis and diagnostic criteria and management have been emphasized.

CASE REPORT

A 45-year-old female patient [figure1] reported to the department of oral medicine and radiology with the chief complaint of presence of ulcerations and bleeding from lips for the past 15 days which is associated with severe continuous throbbing type of pain which aggravates during mastication with no relieving factors and intermittent profuse bleeding from ulcerations during brushing and mastication. Pt gives history of taking siddha medicine for joint pain before 1 month after which she had developed skin ulcer in the back in the beginning ,later ulcers started spreading in skin involving upper and lower extremities and later around after a period of 1-week ulcers started developing in lips. Her past medical history revealed pt. has joint arthritis for 6 months. Her extraoral examination revealed [figure2] on inspection, presence of healed diffuse multiple target like lesions of varying sizes with superficial dry flecks seen on lumbar region, thighs, flexor surface of hands and neck region. The surface of the ulcers appears grayish black with mild erythematous areas with sloping edges. On palpation, it is non-tender, non-indurated with no evidence of bleeding or pus discharge. On examination of lips [figure 3], presence of edematous lips with multiple diffuse ulcerated areas seen on upper and lower lips of size approximately 5 x 5 cm with superficial encrustations and bleeding points were evident. The surface of the ulcer appears dry with blood discharge and the periphery of ulcer is erythematous while the center is violaceous and dark, the margins of the ulcer irregular and appears raised to the surrounding mucosa. On palpation it was tender, non-indurated with evidence of bleeding. Her intraoral examination[figure 3] reveals on inspection Presence of multiple erythematous diffuse ulcerated areas of varying sizes seen on hard palate of size approximately 1 x 0.5 cm, 1x 0.6 cm and 1.5 x 0.5 cm. the surface of the ulcer appears erythematous and is continuous with the surrounding mucosa. On palpation, it is tender with no evidence of bleeding. Based on history and clinical examination, provisional diagnosis of Erythema multiforme of skin and oral cavity. The patient was subjected to routine blood investigation which revealed all the parameters were within normal

range, and she was subjected for skin biopsy and given for histopathological analysis. The H&E stained specimen showed presence of loose epidermis with apoptotic keratinocytes and lymphocytic Infiltration giving a histopath diagnosis of erythema multifome. Based on history, clinical and investigations , a final diagnosis of erythema multiforme major was given and the lesions were treated pharmacologically with combination of topical and systemic corticosteroids. The systemic corticosteroids were given 10 mg BID for 14 Days and tapered to once daily for next 10 days and intermittent dosage was given for the next 1 week and intermittent dosage was reduced to half in the next week and dosage were stopped. Complete healing[figure 4] of ulcerations in skin and oral cavity were observed in a period of 1 month and patient is kept under regular follow up till date.

DISCUSSION

Drugs are double edged sword, which gives beneficial results and can also cause adverse reaction in certain conditions. Adverse drug reaction can manifest as many forms like Erythema multiforme, fixed drug eruption and anaphylactic reactions[6]. Erythema multiforme was first reported in literature by Bateman and Bulkey in 1846 followed by Hebra[7] in 1866 who described as erythema exudative multiforme. In 1922 Stevens and Johnsons reported severe form of erythema multiforme with involvement of oral and conjunctival mucous membrane along with skin lesions.[8] EM due to drugs is rare, most common drugs which induce reactions are non-steroidal anti-inflammatory drugs and antibiotics very few cases of EM have been reported with the ingestion of paracetamol and diclofenac sodium[6]. Apart from drugs, Erythema multiforme is a cell-mediated immune response, and infections are associated with 90% of cases, although herpes simplex virus (HSV) type 1 is the most commonly identified etiology, HSV-2 also has been shown to cause erythema multiforme[9] . Mycoplasma pneumoniae is the second most common etiology, especially in children[10]. Recently certain naturopathic medicines are also said to initiate a cell mediated immune response leading to erythema multiforme. The Genetic susceptibility can be a predisposing factor in some patients with EM. Specifically, in a study of 35 EM patients and 80 control subjects, 66% of EM patients were found to carry the HLA-DQB1*0301 allele compared with 31% of control subjects.[11] This association was stronger in patients with HSV-associated EM. Among patients with recurrent EM, reports exist of increased disease susceptibility in

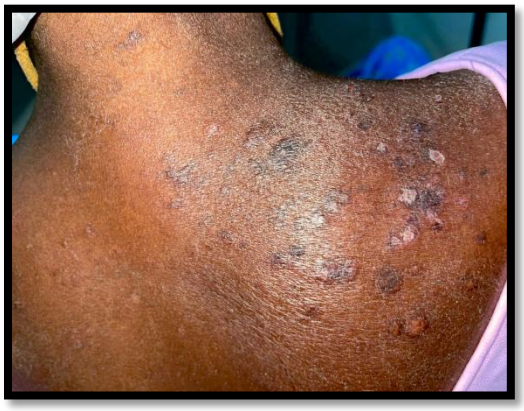
association with the HLA-B35, HLA-B62,15 and HLA-DR5320 alleles[3]. In drug induced cases, activation of tumour necrosis factor-a (TNF-a), perforin, and granzyme B, causing the epidermal destruction seen in the disease[12,13]. The clinical presentation of earliest lesions of EM are usually round, erythematous, oedematous papules surrounded by areas of blanching that may resemble insect bites or Papular urticaria. These papules may enlarge and develop concentric alterations in morphologic features and colour, resulting in the well-known targetoid lesions of EM.[14] The morphologic features of a targetoid lesion include a central portion of epidermal necrosis that can appear as a dusky area or blister. Immediately outside the central portion is a dark red, inflammatory zone surrounded by a lighter oedematous ring with an erythematous zone on the extreme periphery[3]. Lesion distribution in classic EM, the lesions are most commonly distributed symmetrically on the acral extremities and show a predilection for the extensor surfaces. Although lesions ultimately may spread in a centripetal fashion, the trunk is usually far less affected than the extremities[15].oral involvement is estimated to occur 1ith 25% -60% patients with erythema multiforme[16]. Diagnosis usually entails excluding other similar diseases by careful review of the clinical history and detailed clinical examination. Features more suggestive of EM are the acute onset (or recurrent nature), oral lesions typically located on the lip and anteriorly in the mouth, and pleomorphic skin lesions (typical and atypical target lesions). The diagnosis is usually supported by peri-lesional tissue biopsy and exclusion of other causes[17]. No available diagnostic laboratory tests assist in making a diagnosis of EM[9,18] Histological examination and immunostaining often shows moderate to dense perivascular inflammatory infiltrate (CD4 lymphocytes and histocytes) within the papillary dermis, hydropic degeneration of basal keratinocytes and non-specific immune deposits of IgM, C3 and fibrin along basement membrane[19] The management of EM can be difficult. There are no available systematic reviews, and randomized controlled trials are scarce. Any precipitants should be removed or treated. Causative drugs should be stopped and relevant infections treated[17]. Corticosteroids are the most commonly used drugs in the management of EM, despite the lack of evidence. Erythema multiforme may respond to topical corticosteroids. Patients with EM should be treated with systemic corticosteroids or azathioprine, or both or other immunomodulatory drugs such as cyclophosphamide, dapsone, cyclosporine, levamisole, thalidomide or interferon-a[20]. Cyclosporine given intermittently may control recurrent EM[17]

CONCLUSION

The myriad of cutaneous and mucosal hypersensitivity reactions with characteristic clinical presentation of lesions are triggered by certain antigenic stimulus, thus represents a various acute condition which involves both skin and mucous membrane. Due to the varied nature of these diseases with overlapping clinical signs and symptoms , it still remains a diagnostic dilemma in many clinical scenarios. Drug induced Oral erythema multiforme is a rare variant and needs to differentiate from another oral ulcerative lesion for prompt management and follow-up. As an oral physician ,we play a vital role in diagnosing and management of those diseases by careful evaluation of combined history, clinical and histological data .A multidisciplinary approach to treat this condition along with proper follow up would aid in managing the acute nature of these diseases and improves the well-being of patients.

FIGURE 1 : PROFILE

FIGURE 2 : skin lesions



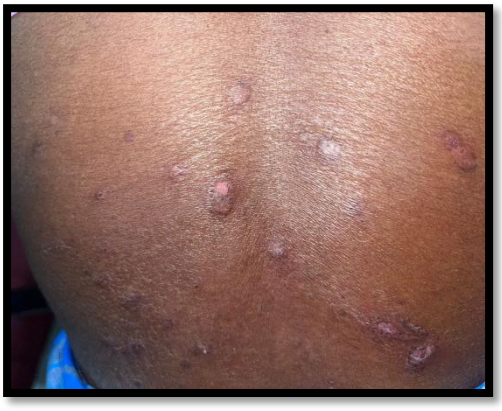
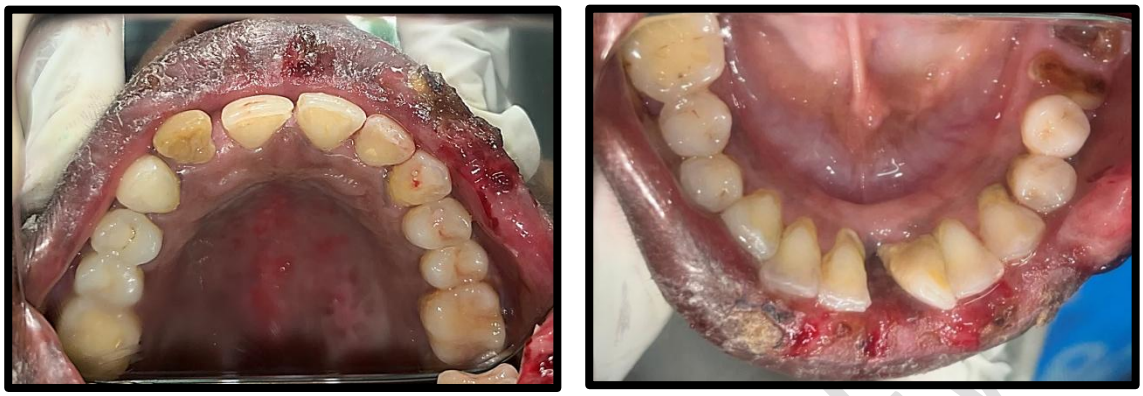


FIGURE 3 : lip and intraoral lesions



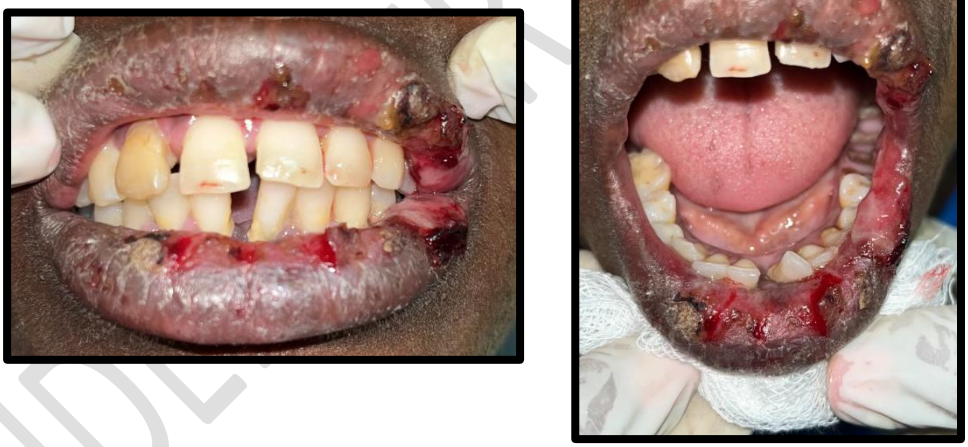
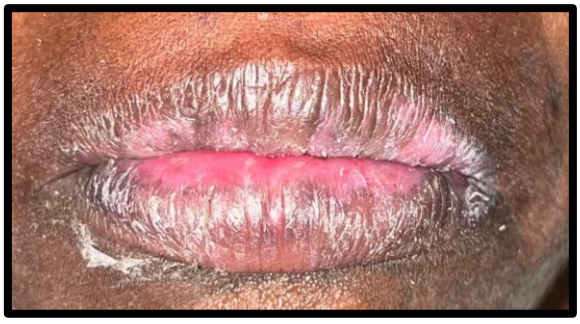
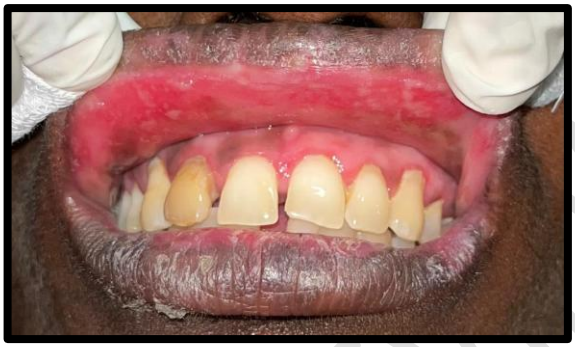


FIGURE 4 : Post-treatment





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