ACUTE ORAL ULCERATION IN A YOUNG LADY- ERYTHEMA MULTIFORME ASSOCIATED WITH DICLOFENAC: REPORT OF CASE WITH MANAGEMENT AND REVIEW.

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ABSTRACT

Erythema Multiforme is an acute; immune mediated mucocutaneous disorder, triggered by medications and viral infections. It includes a wide range of clinical presentations: mucocutaneous forms of varying severity with one or more mucosal localizations, forms affecting large body surface areas and a form with oral involvement only. Diclofenac is a non-steroidal anti-inflammatory drug, used as an effective analgesic. It is one of the well-tolerated NSAIDS and its over-the-counter use is approved in some countries. There are very few reports of developing a hypersensitivity reaction to Diclofenac. We report one such unique case of a 20–year-old lady, who developed acute and severe oral ulceration, which was treated effectively on an out patient basis itself.

KEYWORDS: Diclofenac, Erythema Multiforme, muco-cutaneous, hypersensitivity reaction.

INTRODUCTION

Erythema Multiforme (EM) is an acute mucocutaneous inflammatory and hypersensitivity reaction. It is characterized by acrally distributed, distinct target lesions with concentric colour variation, sometimes accompanied by oral, genital, or ocular mucosal erosions or a combination of these. “Erythema” means redness and as it can present with a wide range of
clinical presentations, it is termed as “multiform”. Most of the cases have no cause, while other causes include medications, infections, immunotherapy or illness.[1] EM most commonly occurs in young adults, having an acute onset with mild or no prodromal symptoms of fever, malaise, headache, cough, sore-throat, noticed 1 week before the onset of mucocutaneous lesions.[2] EM may be classified as minor, major, Stevens-Johnson syndrome or toxic epidermal necrolysis.[3] This is a report of a case of EM in a 20-year-old lady after the intake of diclofenac sodium.

CASE SYNOPSIS
A 20-year-old female patient, reported to us with a complaint of painful sores in the mouth with difficulty in opening the mouth for duration of 2 days. She gave a history of shoulder pain, for which she had taken medications (diclofenac sodium) for two days one-week back, after which she developed fever and sore throat. Four days later, she developed multiple ulcers, which involved the whole mouth within a day. She had excruciating pain with severe bleeding on slightest provocation with difficulty in eating and swallowing. Past history also revealed that she did not have such attacks previously.

Past medical and dental history was unremarkable. Extra-oral examination, revealed shallow irregular erosions involving the entire vermilion zone of both lips and extended intra-orally [Figure-1]. The surface was covered with blood crusts and dried serous exudates, which when removed revealed raw erythematous floor. On palpation there was severe tenderness with bleeding on slight provocation. Mouth opening was restricted to 20mm. On intra oral examination, the labial and buccal [Figure-2] mucosa showed extensive epithelial denudation covered with necrotic slough.

A clinical working diagnosis of Erythema Multiform was made. Local debridement with hydrogen peroxide and saline was done. Serologic tests revealed no infection with HSV. Instead of prescribing high dose systemic steroids, so as to minimize the adverse effects, she was given Betnesol (Betamethasone soluble tablets), which was to be used as a mouth-wash. 0.5mg of the tablet was to be dissolved in 10ml of water and swished and spit for three times a day for one week along with an optimal dose of systemic steroids, Prednisolone - 30mg/day in 3 divided doses for 7 days followed by tapering of the dose. Her weight, blood pressure and blood sugar levels were periodically checked and were within the normal limits during the review visits. She was also given antihistamines for one week. She was advised to have plenty of fluid intakes. She was reviewed everyday for the first one - week and every
alternate day for the next week. The lesions healed completely on the twenty first day of review [Figure-3 & 4] and had no recurrence after one year of follow up.

Figure 1: A 20-year-old lady, presenting with irregular erosions, surface covered with blood crusts and serous exudates on the lips.

Figure 2: Right buccal mucosa showing extensive epithelial desquamation.

Figure 3: Post treatment photograph of the right buccal mucosa.
DISCUSSION

EM is an immune mediated, hypersensitivity reaction with a wide range of etiology, most often an infectious agent or drugs. Infections such as Herpes Simplex, Mycoplasma, drugs such as β-lactams (penicillin, cephalosporins) and non-β-lactam antibiotics (clindamycin, trimethoprim–sulfamethoxazole, ethambutol, tetracycline-like drugs, clindamycin, rifampicin), anticonvulsants (carbamazepine, phenytoin, phenylbutazone, phenothiazine-like drugs, barbiturates), allopurinol, NSAIDs, oralanti-diabetics (sulfonamides, chlorpropamide, tolbutamide), codeine, furosemide, gold, and protease inhibitors may cause EM. There is a genetic component of EM. It is linked to specific HLA types such as HLA-DQ3, HLA-B15 (B62), HLA-B35, HLA-A33, HLA-DR53 and HLADQB1*0301. Extensive mucosal involvement may be exceptionally associated with HLA allele DQB1*402 patients. From immunopathologic aspect, mild forms of EM begin as type III hypersensitivity reaction, involving immune complex reaction of antigen and antibody. There is deposition of immune complexes inside and outside blood vessels, causing vasculitis and increases its permeability. These immune complexes deposit in tissues and cause fever, urticaria, arthralgia, and lymphoid gland expansion. An autoimmune process causes severe EM. Drug administration is considered as foreign antigen, which will be absorbed by cell surface and trigger chemical reaction with hapten, which could change the immunogenicity. The involvement of microbial infection causes microbial endotoxin release, and later produces autoantibody detectable in serum.

EM typically affects young adults, and 20% in children. It has an acute onset with or without prodromal symptoms. The skin lesions start as macules, papules or vesicles, which collapse and enlarge to form large plaques. Blisters may appear in the center of the skin.
lesion, resulting in concentric rings resembling a bull’s eye (target lesion). Oral lesions appear as epithelial necrosis with encrustation on lips. The different types of EM include, minor form (mostly affecting one site, commonly oral mucosa with <10% of body surface area are affected), major (cutaneous lesions and at least 2 mucosal sites, oral lesions are wide spread and severe &<10% of body surface area is involved), Stevens-Johnson syndrome (Main difference from major form is based on the typology and location of lesions and the presence of systemic symptoms &< 10% of the body surface area is involved), Overlapping Stevens-Johnson syndrome and toxic epidermalnecrolysis (No typical targets, up to 10%–30% of the body surface area is affected) and Toxic epidermal necrolysis (characterized by epidermal detachment of > 30% of the body surface and widespread purpuric macules or flat atypical targets). Both HSV 1 & 2, have been shown to precipitate EM, typically lesions begin 10-14 days following the clinical manifestation of HSV and the lip being the most common site.

Diagnosis is made by exclusion of other similar diseases with a detailed clinical examination. When lesions are confined to the oral cavity the differential diagnosis would include Herpes and Pemphigus. In acute herpetic infections, the gingiva is most commonly involved and is smaller with regular borders but in the present case, ulcers were irregular with no gingival involvement and serologic tests for HSV were negative. In our case there was a positive drug history and acute onset, which helped us to differentiate from Pemphigus. EM is self limiting and mild cases usually heal within 2-4 weeks with local debridement, plenty of fluid intake and topical analgesics. Oral antihistamines and topical steroids provide symptomatic relief. Severe cases require intensive management with systemic steroids and intravenous fluid replacement. EM associated with herpes is treated with acyclovir 200mg five times a day for five days, if started within the first few days. Recurrence is seen approximately in 20-25% of case with two to four episodes a year. If there is recurrence low dose acyclovir is necessary for prevention – 200 to 800mg per day for 26 weeks.

CONCLUSION
In our case EM had occurred as a result of drug intake and such cases with severe oral lesions can be management effectively on outpatient basis itself by reducing the dosage of systemic steroids, so that there are minimal side effects. Betnesol when used as an oral rinse, there can be consideration reduction in local symptoms.

Conflicts of Interest: The authors declare that they have no conflict of interest.
REFERENCES


