Erythema multiforme following non steroidal anti-inflammatory drug ingestion in a case of rheumatoid arthritis

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Abstract:
Erythema multiforme is an acute reactive mucocutaneous inflammatory and hypersensitivity reaction characterized by skin eruptions, with erythematous edematous or bullous lesion of the skin or mucous membrane. Only 4% of EM reactions are caused by drugs. Here we report a case of 40 year old Indian female receiving medication of rheumatoid arthritis for past 10 years experienced extensive ulceration of vermilion surface of lip and intra oral ulceration with involvement of buccal mucosa but without any skin target lesions after taking over the counter NSAIDs.

Key words: Erythema multiforme, NSAID, rheumatoid arthritis

Case Report
A 40 year old female with a history of rheumatoid arthritis on medication was admitted with the complaint of fever, malaise, swelling of lip, ulceration of oral cavity and pain and inability to eat for past 5 days. She gave a history of fever and malaise for which she took an over the counter NSAIDS to which she developed multiple small ulcerations that later transformed into extensive, irregular ulceration of the oral cavity.

Fig 1: Irregular hemorrhagic ulcers with encrustation

Since she was a patient of rheumatoid arthritis with deformed joint and decreased range of mobility her treatment regimen included methotrexate 7.5mg, sulphasalzine 500mg, hydroxychloroquine 400mg,other concomitant medication included pantaprazole 20mg, domperidone 10mg, folic acid

5mg, vitamin D 60000 IU weekly. No past history of allergic diathesis was noted. The patient was well oriented and on examination was hypotensive and lethargic with mild fever. Extra oral examination revealed irregular ulceration of vermilion surfaces of lip. The ulcers' were hemorrhagic and tender on palpation with crusted erosion. Bilateral submandibular lymph node was enlarged and tender. Intra oral examination revealed irregular erythematous buccal mucosa with tongue ulceration. The hard palate and gingival surface were spared.

The vital sign were reported as follows, temperature (axillary) 100.5F, respiratory rate 25/min, pulse 96/min, blood pressure 100/70mmhg. The laboratory test revealed elevated markers of inflammation, white blood cell count 15x10^3/ul, RBC count 4.37x10^6/ul, platelets count 324 x10^3/ul, serum creatinine 0.9mg/dl, blood urea 18mg/dl ,liver function test were normal. Anti HBSAg and Anti HCV were negative. Reports of blood and urine culture were awaited. Skin biopsy was not done. Chest x ray and USG

Fig 2: Four days post treatment.

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abdomen were normal. The sudden onset, positive drug history, extensive irregular ulceration of the oral cavity, cracking and fissuring of lips with bloody crusting lead to the diagnosis of oral erythema multiforme after ruling out the other differentials. After initial assessment patient was started on steroid to facilitate oral fluid intake. The patient was advised to stop the current medication. Healing was noted after removing the offending drug and on steroid therapy.

Discussion

Erythema multiforme (EM) is an acute, self-limited, and sometimes recurring skin condition that is considered to be a type IV hypersensitivity reaction associated with certain infections, medications, and other various triggers. Globally, the frequency of erythema multiforme is estimated at approximately 1.2-6 cases per million individuals per year. According to von Hebra, who first described the disease in 1866, the patients with erythema multiforme should have acrally distributed typical target lesions or raised edematous skin papules with or without mucosal involvement.¹

In 1968, Kenneth described an inflammatory oral disorder with oral lesions typical of EM but without any skin involvement. He reported nine cases seen at the East Man Dental Hospital. The common sites involved were lips, checks, and tongue. These patients had irregular large ulcers with necrotic tags attached to the borders. When lips are involved the typical blood encrusted lesions were seen. In this series of cases, the typical target skin lesions were seen during the recurrences not in their initial attacks.² Many investigators have suggested this as a third category of EM known as oral EM that is characterized by typical oral lesions of EM but no target skin lesions. Oral EM is a distinct but less well-recognized variant of EM. The diagnosis has to be established by excluding other oral inflammatory and vesiculobullous lesions.

The pathophysiology of erythema multiforme (EM) is still not completely understood, but it is probably immunologically mediated and appears to involve a hypersensitivity reaction that can be triggered by a variety of stimuli, particularly bacterial, viral, or chemical products. The following medical conditions seem to predispose individuals to a higher risk of developing the disorder: HIV infection, corticosteroid exposure, bone marrow transplant, systemic lupus erythematosus (SLE), graft versus host disease (GVHD), and inflammatory bowel disease (IBD). Individuals undergoing radiation, chemotherapy, or neurosurgery for brain tumors are also at higher risk.³ No specific laboratory tests are indicated to make the diagnosis of erythema multiforme (EM), which should be arrived at clinically. The clinical picture can guide laboratory testing in severe cases. Biopsies are advised only in early vesicular lesions of erythema multiforme not in ulcerated ones since histopathology appearances are nonspecific and no diagnostic.⁴ Cultures are indicated in severe cases and should be obtained from blood, sputum, and mucosal lesions.

No specific imaging studies are necessary in most cases, although chest radiography may be useful in cases with respiratory symptoms or signs. The most common drugs that trigger EM lesions are barbiturates, hydantoin, penicillin, phenothiazines, sulphonamides, co-trimoxazole, phenytoin, carbamazepine and non-steroidal anti-inflammatory drugs such as diclofenac, ibuprofen, and salicylates. The diagnosis of mucosal EM has always been a challenge because it mimics other mucosal diseases like aphthous ulcers, bechets disease, pemphigus vulgaris, mucous membrane pemphigoid, mucosal lichen planus, and paraneoplastic pemphigus. After HSV, if the drug is suspected as culprit as in our case it was some NSAID, it is immediately stopped followed by appropriate supportive care which includes viscous lidocaine rinses, bland soft diet, soothing eye drops, antibiotics to prevent secondary infection with steroids. Lesions of EM usually respond to topical steroids, for more severe cases systemic corticosteroids are recommended.⁵

Conclusion

Oral EM is a rare and less described variant of EM. The rapid onset and progression with no cutaneous involvement, pattern of mucosal involvement and immediate relief by short course corticosteroid and withholding culprit drug along with no recurrence, and mucosal biopsy with classical features clinch the diagnosis of mucosal erythema multiforme. Though rare, cases of drug induced mucosal EM is on rise. Early recognition, therapy and regular follow-up of this acute mucocutaneous disease spectrum are critically important to prevent cicatrical morbidities.

Declaration of consent

The author certifies that written informed consent was obtained before publication. The patient understands that no identifying information will be published and identity of the patient will be completely concealed.

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Conflict of interest

None declared.

References