Herpes Associated Erythema Multiforme: A Diagnostic Dilemma

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Abstract: Erythema multiforme (EM) is an acute mucocutaneous hypersensitivity reaction which usually affects young adults. Twenty percent of cases occur in children [1]. Erythema multiforme is a self-limiting illness. Herpes Simplex virus is the most common cause of EM, but a few medications like penicillin, barbiturates, NSAIDs, phenothiazines, hydantoins and sulfonamides also have etiological association. Here we report a case of EM with possible etiology of either HSV or drugs to discuss the clinical features, treatment and differentiating features between the two etiologies.

Keywords: Erythema Multiforme, Herpes Simplex Virus, Amoxycillin, Target Lesions

1. Case Report

A 9 year old male child was brought with ulcers noticed over both lips and oral cavity for 3 days. He had foul smelling breath and sore throat for one day. He did not have fever or rashes elsewhere in the body. He was vaccinated for varicella appropriately. On examination of oral cavity, erythematous macular rashes with few ulcers were noticed over both lips and inside the oral cavity (Fig 1). He had halitosis and his oral mucosa was congested. Hence a provisional diagnosis of herpetic gingivostomatitis was made and he was started on IV Acyclovir (10 mg/kg /dose) along with IV Amoxycillin to cover secondary bacterial infection. IV fluids were started because of poor oral intake. His oral lesions began healing but he developed fever on day 2 of admission and developed multiple vesicles with erythematous base over trunk, neck and limbs (Fig 2&3). Tzanck smear to look for multinucleated giant cells turned out negative. The diagnosis was revised as Erythema multiforme major and amoxycillin was stopped immediately as suggested by dermatologist. He had redness in both his eyes with thick discharge on day 3 which was treated with artificial tears as suggested by Ophthalmologist. He was started on saline compresses for lip lesions and mupirocin ointment for lesions on trunk, neck and limbs.

With the above management, he became afebrile and the oral ulcers as well as the rash got better. He was able to take oral feeds well.

2. Discussion

Erythema Multiforme, a self limiting illness, affects skin and mucosal surfaces. Depending on the number of sites and extent of involvement, it is usually differentiated into EM minor when cutaneous involvement is less than 10% of body surface area plus either no or one mucosal site (usually oral mucosa) involvement, and EM Major when cutaneous involvement is less than 10 % of body surface area plus 2 or more mucosal sites is involved [2].

Typically, the lesions of EM will develop after 10 to 14 days of HSV infection and lip is the most common site of HSV infection that precedes EM lesions [3]. In our case, the cutaneous lesions started within 4 days of onset of oral lesions. The oral lesions were beginning to heal whereas there were fresh flaccid bullae with erythematous bases seen.
in acral extremities and trunk. This was the strong reason for the clinical suspicion of EM major following probably the antibiotic given and was stopped immediately. The following table will help differentiate (Table 1) drug-induced EM with Herpes-associated EM [4].

The lesions of EM vary from erythematous macules, papules, vesicles, bullae to patches of confluent erythema and it is seen mostly on the extensor aspect of upper extremities. A few times these lesions might be confused with urticaria, with the difference being the EM lesions persisting beyond 24 hours. Steven-Johnson Syndrome and EM are two different entities [3].

Management of EM is primarily supportive care. Topical emollients along with systemic antihistamines would give symptomatic relief. In cases of EM caused by HSV, the lesions usually subside in 2 to 6 weeks of time, but recurrence is common. Hence oral Acyclovir 400 mg twice daily for a period of 6 months is advised as suppressive therapy to control recurrence of herpes-associated EM[5]. Those cases which does not respond to long term suppressive therapy of oral acyclovir can be managed with either dapsone, cyclosporine or thalidomide after consulting with a dermatologist[6]. Topical acyclovir is not advisable for Herpes associated EM lesions [7].

Table 1: Difference between herpes associated em and drug induced EM

<table>
<thead>
<tr>
<th></th>
<th>Herpes Associated EM</th>
<th>Drug Induced EM</th>
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<tbody>
<tr>
<td>Causes</td>
<td>HSV 1 and 2</td>
<td>Drugs</td>
</tr>
<tr>
<td>Disease Course</td>
<td>Acute, self-limiting, recurrent</td>
<td>Acute, self-limiting, not recurrent, does not follow HSV lesions</td>
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<tr>
<td>Distribution Of Lesions</td>
<td>Extremities, target lesions common</td>
<td>Face, extremities, target lesions rare, blisters seen</td>
</tr>
<tr>
<td>Mucosal Involvement</td>
<td>Absent/moderate</td>
<td>Present/severe</td>
</tr>
<tr>
<td>Mortality</td>
<td>none</td>
<td>5 – 15%</td>
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</tbody>
</table>

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References


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