Skin Lesions Still the “Sine Qua Non” for Diagnosing Erythema Multiforme? - A Case Report with Critical Literature Review

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Abstract

Erythema multiforme (EM) is an uncommon, acute inflammatory vesiculobullous disorder affecting the skin and/or mucous membranes. The oral variant of this condition is even more uncommon. Here we present a case of herpes-associated EM affecting the oral cavity where the skin lesions, which were considered the “sine qua non” for EM diagnosis, were absent. The case was promptly and precisely diagnosed and treated using a standardized regime of systemic corticosteroid therapy with supportive care to which he responded well and continues to be disease-free at 1 year follow-up.

Keywords: Erythema multiforme minor, Herpes associated erythema multiforme, Oral erythema multiforme

INTRODUCTION

Although first recognized in early 19th century, it was not until 1860 that Ferdinand von Hebra coined the term “erythema multiforme (EM)” to denote this disease.¹ It is basically a hypersensitivity reaction believed to be a sequelae of a cytotoxic immunologic attack on keratinocytes expressing non-self antigens, which are primarily caused by microbes (viruses), drugs or food additives. When herpes simplex virus (HSV) infection is implicated, the diagnosis is herpes-associated EM (HAEM). There may be a genetic predisposition to EM. Human leukocyte antigen DQ3 has been proven to be especially related to recurrent EM and maybe a helpful marker to distinguish HAEM from other diseases with EM-like lesions.²⁻⁶ EM typically affects teenagers, and young adults (20-40 years).³⁻⁶ It affects males more than females in a ratio of 3:2.² Here we share a case of oral EM without skin involvement presenting as acute onset stomatitis which can be a diagnostic dilemma to an oral physician.

CASE REPORT

A 32-year-old male reported to the dental clinic complaining of extensive oral ulcerations, pain, inability to eat and burning sensation since 3 days. There was a history of sudden onset of fluid-filled blisters in the mouth, rapidly increasing in number and size, spontaneously bursting thereafter.

Patient was afebrile with no lymphadenopathy present. Odynophagia and dysarthria were present. Cracking and encrustations were seen on the edematous lips. The oral variant of this condition is even more uncommon. Here we present a case of herpes-associated EM affecting the oral cavity where the skin lesions, which were considered the “sine qua non” for EM diagnosis, were absent. The case was promptly and precisely diagnosed and treated using a standardized regime of systemic corticosteroid therapy with supportive care to which he responded well and continues to be disease-free at 1 year follow-up.
There was history suggestive of herpes labialis 2 weeks before the episode. Based on this along with the history, a provisional diagnosis of HAEM oral variant was made. Incisional biopsy proved non-specific as expected showing focal ulcerations with dense sub-epithelial infiltration especially in the peri-vascular areas (Figure 4). Direct immunofluorescence showed non-specific deposits of IgG, IgM and C3 at basement membrane and peri-vascular areas. A herpes culture taken from the lip erosions was negative. However, serology for HSV came out to be positive for IgG confirming the diagnosis of HAEM.

The patient weighed 62 kg and was put on a course of systemic corticosteroids (tablet prednisone 20 mg BD for 7 days which was quickly tapered off and stopped in 2 weeks), capsule erythromycin estolate 500 mg TID for 3 days and topical anesthetic agent (lignocaine). Careful oral hygiene and soft diet were advised to the patient. The patient was able to eat and drink pain-free within 48 h. A follow-up oral examination at 7 days showed complete healing of the oral ulcerations (Figures 5-7). 1 year after the episode, the patient continues to be a disease free.

DISCUSSION

The presentation of EM ranges from the self-limited, mild form (EM minor) to progressive, and aggressive form like EM major Steven Johnson syndrome and toxic epidermal necrolysis\(^\text{10}\) (Table 1).
Diagnosis of EM, tends to be centered on dermatologic lesions of the extremities, with mouth ulcers regarded as a secondary finding. The concept of pure oral EM is controversial and not universally accepted since some dermatologists believe that the characteristic appearance and distribution of skin lesions are the “sine qua non” for its diagnosis. Kenett described EM affecting the oral cavity. Since then, many reports have been published describing EM sans skin lesions. It has been suggested that a third category, i.e., the oral variant of EM be incorporated into the current classification. The diagnosis of oral EM is one of exclusion.

The differential diagnosis for the case presented here included pemphigus vulgaris, cicatricial pemphigoid, bullous lichen planus, major oral aphthous ulcerations, HSV infection and EM. The biopsy helped rule out the first three. Also, our case was acute in onset in contrast to a chronic nature of these conditions. It would be clinically challenging to distinguish major aphthae from EM, if EM occurs sans the pathognomonic target lesions. Here, histopathological and direct immunofluorescence findings were found compatible with the diagnosis of EM. Furthermore, there was a history of preceding HSV infection. But the lip erosions were negative for HSV culture. Hence, the question of herpetic gingivostomatitis (primary/secondary) was nullified. The clues mentioned hereby would help an oral physician unerringly to arrive at the diagnosis of oral EM.

Spontaneous healing of EM can be slow, up to 2-3 weeks in minor and up to 6 weeks in major. Treatment is thus indicated but controversial. Precipitating factors should be dealt with immediately. The use of corticosteroids is controversial.

<table>
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<tr>
<th>Condition</th>
<th>Pattern of skin lesion</th>
<th>Body surface area with epidermal detachment (%)</th>
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<tbody>
<tr>
<td>EM minor</td>
<td>Typical target lesions, raised atypical target lesions, minimal mucous membrane involvement and when present at only 1 site (most commonly the mouth). Oral lesions; mild to severe erythema, erosions and ulcers.</td>
<td>&lt;10</td>
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<tr>
<td>EM major</td>
<td>Cutaneous lesions and at least 2 mucosal sites (typically oral mucosa) affected. Symmetrically distributed typical target lesions or atypical, raised target lesions or both. Oral lesions usually widespread and severe.</td>
<td>&lt;10</td>
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<tr>
<td>SJS</td>
<td>Main difference from EM major is based on the location of lesions and the presence of systemic symptoms primarily atypical flat target lesions and macules rather than classic target lesions. Generally widespread rather than involving only the acral areas. Multiple mucosal sites involved, with scarring of the mucosal lesions. Prodromal flu-like systemic symptoms also common.</td>
<td>&lt;10</td>
</tr>
<tr>
<td>Toxic epidermal necrolysis</td>
<td>No typical targets, flat atypical targets; begins with severe mucosal erosions and progresses to diffuse, generalized detachment of the epidermis</td>
<td>&gt;10</td>
</tr>
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EM: Erythema multiforme, SJS: Stevens-Johnson syndrome

In our case, since the patient was culture negative at the time of presentation and had reported relatively early on, a systemic corticosteroid regime was adopted with dosing as per literature (0.5-1.0 mg/kg/day). Also supportive care was provided alongside. We thereby conclude that with careful diagnosis and case selection, the management...
CONCLUSION

The idea of classic textbook “target lesions” of EM may hamper the oral physician in considering the diagnosis of oral EM in acute onset stomatitis. This condition of varied etiologies, mimics several other conditions of the oral cavity and can be misleading, therefore, prompt and precise diagnosis is required in order to initiate early management to reduce the associated comorbidity. As more cases of oral EM get reported, this condition will definitely carve its niche into the current spectrum of such diseases. Moreover, by educating the patient about this condition, future recurrences may be prevented.

Differential features of EM minor, EM major, Stevens-Johnson syndrome and toxic epidermal necrolysis.

REFERENCES


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