Necrolytic acral erythema: an unusual cutaneous presentation of hepatitis C virus infection

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Abstract

Necrolytic acral erythema (NAE) is a newly recognized dermatosis which has been regarded as early cutaneous marker of hepatitis C virus (HCV) infection. It presents as a well demarcated, dusky, symmetrically distributed erythematous to violaceous eruption with marked hyperkeratosis and lichenification associated with pruritus or burning on the dorsal aspects of feet extending to the toes. It shows clinical and histopathological resemblance to other necrolytic erythemas. We report a case of a 55-year-old woman with itchy hyperpigmented papules and plaques on the feet for the last 6 months. Histopathology showed the features of necrolytic acral erythema.

Key words
Necrolytic acral erythema, hepatitis C virus infection

Introduction

Necrolytic acral erythema (NAE) is closely related to a group of necrolytic erythemas and metabolic syndromes. NAE was first described in 1996 by Egyptian physicians M. El Darouti and M. Abu El Ela. It presents as well circumscribed, dusky, erythematous to violaceous plaques with adherent scales with marked hyperkeratosis and lichenification. It is associated with itching or burning sensation and has an acral distribution. NAE has its clinical and microscopic resemblance with necrolytic migratory erythema.

Reports are available regarding the association of HCV with NAE. Its association with HCV infection makes it a distinct clinical entity. It is speculated that viral load and genotype might play some role in NAE. We report a case of a middle aged HCV positive female who presented with typical clinical and histopathological features of NAE.

Case report

A 55-year-old woman presented in our outpatient department with the complaint of erythematous papules on the dorsum of feet which were associated with intense itching for the last 6 months. These papules gradually increased in size to form plaques over the next few weeks. She took treatment in the form of local applications but no treatment proved beneficial in relieving her symptoms. There was occasional purulent discharge from the lesions. Similar lesions developed on the upper limb and trunk which were also intensely itchy. The patient had recently been diagnosed as a case of diabetes mellitus.

Dermatological examination revealed well demarcated, symmetrical, hyperkeratotic, erythematous to violaceous, lichenified plaques...
There was absence of band like infiltrate (Figure 2).

Patient was treated with oral cetirizine, oral zinc, topical tacrolimus and salicylic acid.

Discussion

Necrolytic acral erythema (NAE) has been described as an early cutaneous marker for hepatitis C virus (HCV) infection. The ages of the patients with NAE have ranged from 11-60 years, but the onset typically occurs between 35-55 years. No sex predisposition is reported. It presents as a well-defined, dusky, erythematous eruption with marked hyperkeratosis and a dark red rim associated with pruritus or burning. Proposed theories for the cause of NAE describe alterations in some metabolic factor, many of which are seen in other necrolytic erythemas, including necrolytic migratory erythema, pellagra, essential fatty acid and biotin deficiency, and acrodermatitis enteropathica. The hypothesized causes for the metabolic alteration include hypoalbuminemia, hyperaminoacidemia, low zinc level, increased glucagon, liver dysfunction, or diabetes. Only hepatitis C is universally present in all persons with NAE.

The most common sites of involvement are the dorsal aspects of the feet, over the Achilles tendons, malleoli, legs, and knees. Less frequent sites of involvement include the elbows, hands, buttocks, and genitalia. There is sparing of the palms, soles, face, and mucous membranes.

Three stages of lesions have been described on gross and histological examination (Table 1).

NAE can be difficult to distinguish from certain groups of necrolytic erythemas, which include necrolytic migratory erythema, acrodermatitis
Table 1 Clinical and histological features in three stages.

<table>
<thead>
<tr>
<th>Clinical features</th>
<th>Fully developed stage</th>
<th>Late stage</th>
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<tbody>
<tr>
<td>Initial stage</td>
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<td>Erythematous papules or plaque with scale are present and have a dusky or eroded center</td>
<td>A confluence of papules and plaques with sharply defined margins and adherent scale develops. Increased hyperpigmentation and decreased redness may be present. Lesions may be lichenified. Pustules also may occur at this stage</td>
<td>Thinning of lesions occurs, with continued hyperpigmentation. Demarcation continues, followed by spontaneous relapse and remission</td>
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<table>
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<tr>
<th>Histological features</th>
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<tr>
<td>Nummular dermatitis–like moderate and regular acanthosis</td>
<td>Psoriasiform epidermal hyperplasia</td>
</tr>
<tr>
<td>• Variable spongiosis</td>
<td>• Marked papillomatosis</td>
</tr>
<tr>
<td>• Inflammatory infiltrate</td>
<td>• Parakeratosis</td>
</tr>
<tr>
<td>• Pigment incontinence</td>
<td>• Focal hypergranulosis</td>
</tr>
<tr>
<td></td>
<td>• Pigment incontinence</td>
</tr>
<tr>
<td></td>
<td>• Occasional subcorneal pustules</td>
</tr>
<tr>
<td></td>
<td>• Epidermal pallor</td>
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<tr>
<td></td>
<td>• Vascular ectasia</td>
</tr>
<tr>
<td></td>
<td>• Infiltrate of inflammatory cells in the papillary dermis</td>
</tr>
<tr>
<td></td>
<td>• Necrotic keratinocytes - Sometimes become confluent in the upper epidermis, sometimes tracking along the acrosyringium</td>
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enteropathica, biotin deficiency, pellagra, and essential fatty acid deficiency. However, these entities can be distinguished on the basis of clinical and laboratory evaluation.7 The next most consistent finding associated with NAE is zinc deficiency, which may result from HCV infection. Even in patients with normal serum zinc levels, zinc supplementation has lead to clinical improvement of NAE. It is thought that zinc deficiency may occur in the skin prior to the development of clinical zinc deficiency as assessed by serum zinc levels.8

The optimal treatment for NAE is the optimal treatment of hepatitis C combination therapy with interferon and ribavirin. In one patient, ribavirin in addition to the interferon alfa therapy improved NAE despite the presence of a continued high viral load.

Oral zinc replacement has been successful in some cases.8,9 Interferon alfa monotherapy has been reported to be effective treatment.8 Amino acid replacement therapy, both orally and parenterally, has yielded some improvement.

Forty-two cases of NAE have been described internationally, mostly in Egypt.7 The reason for this disproportionate distribution is perhaps due to the prevalence of HCV infection in Egypt which is estimated to be 15 to 20 percent while worldwide it is 3 percent and in Pakistan it is 5.31 to 7.5 percent.10,11 Despite the high prevalence of HCV in Pakistan very few cases of NAE have been reported from Pakistan. The reason for this may be that physicians may not be aware of this relatively new entity and it may be misdiagnosed as it has clinical resemblance to other dermatoses including lichen planus and other necrolytic erythemas. As it has a very
strong association with HCV infection, physicians and dermatologists should be aware of this as a cutaneous marker of HCV infection.

References