

Necrolytic acral erythema without hepatitis and hypozincemia: a rare presentation

Tasleem Arif, Dinesh Raj, Syed Suhail Amin

Jawaharlal Nehru Medical College (JNMC), Aligarh Muslim University (AMU), Aligarh, India.

Abstract Necrolytic acral erythema (NAE) is a recently described entity from Egypt by El Darouti and Abu el Ela in seven patients with associated hepatitis C virus infection. It is characterized by its distinguishing psoriasiform skin lesions, an acral distribution, and histological features. The cause of the disease is not clear, though zinc deficiency, hypoaminoacidemia and hyperglucagonemia have been proposed. There are few reports in which it has occurred independently without associated HCV infection. However, NAE without associated HCV infection and normal serum zinc levels has been rarely reported till date. Herein, the authors report a rare case of NAE from India without associated HCV infection and with a normal serum zinc concentration.

Key words

Hepatitis C, hypoaminoacidemia, necrolytic acral erythema, zinc deficiency.

Introduction

Necrolytic acral erythema (NAE), first reported from Egypt, is considered a rare cutaneous marker of HCV infection.¹ It is characterized by pruritic, well-defined, symmetric dusky discoloration with peripheral blistering which may later progress to erythematous, hyperkeratotic to violaceous lichenified plaques with peripheral dusky red erythema distributed mainly on the dorsal aspects of the hands and feet.² However, some researchers have described the same cutaneous findings without associated HCV infection. In this article, the authors report a seronegative case of NAE with normal serum zinc levels which has rarely been reported.

Case Report

A 35-year-old female patient presented with a

history of erythematous skin lesions on hands, feet and knee since 3 months. These lesions started as erythematous papules which progressed to form erythematous plaques and first appeared over hands then involved dorsum of feet and subsequently knees. Cutaneous examination showed well-demarcated, erythematous to light brownish hyperpigmented, hyperkeratotic plaques involving the dorsal aspects of hands, feet, elbows and knees (**Figure 1 and 2**). The plaques from hands extended proximally to forearm in a linear distribution (**Figure 3**); while the plaques from feet extended proximally onto the legs with a clear cut demarcation from the adjoining normal skin (**Figure 4,5**). Auspitz sign was negative. Rest of the cutaneous and systemic examination was unremarkable. The patient tested seronegative for hepatitis C and B virus. Serum zinc was 89.19 µg/dl (Normal range for adult female: 65-256 µg/dl). Other laboratory investigations were unremarkable. Histopathological examination of a punch skin biopsy showed hyperkeratotic epidermis with focal parakeratosis, irregular acanthosis, and elongated rete ridges. In the dermis, periadnexal and perivascular

Address for correspondence

Dr. Tasleem Arif
Department of Dermatology,
Jawaharlal Nehru Medical College (JNMC),
Aligarh Muslim University (AMU),
Aligarh, India
Email: dr_tasleem_arif@yahoo.com



Figure 1 Erythematous scaly plaques in a bilaterally symmetrical distribution over dorsal aspects of hands and feet.



Figure 2 Erythematous scaly plaques over dorsal feet and knees.



Figure 3 Erythematous to light brownish scaly plaques in a linear distribution over forearms.



Figure 4 Erythematous plaques over feet with extension on to the legs.



Figure 5 Close view showing well demarcated erythematous plaques with extension on to the legs and clear cut demarcation from the adjoining normal skin.

lymphocytic infiltration was seen. Based on history, suggestive clinical examination and further supported by histopathological findings, the diagnosis of NAE was established.

Discussion

NAE is a rare condition which has been recently described. In most of the cases, it is associated with hepatitis C infection. It presents with a well-demarcated psoriasiform eruption mainly over the acral sites. Other sites which can be involved include knees, thighs, abdomen, and genitalia. In our case, knees, elbows, legs and forearm were also involved. However, palms, soles, nail bed, nail plates, and mucous membranes are usually not affected in this disease. Though, most of the earlier reported cases were suffering from hepatitis C infection, only a few cases of seronegative NAE have been reported. However, clinical features of these patients were similar to seropositive NAE. Males and females are equally affected by this disease.¹

The etiopathogenesis of NAE has not been elucidated till date. However, certain factors have been incriminated which include hypoaminoacidemia, hyperglucagonemia, hypoalbuminemia, and low serum zinc level. But none of the above lab abnormalities were seen in our patient. Hypoaminoacidemia and hyperglucagonemia may reflect hepatocellular dysfunction seen in these patients. Hypoaminoacidemia may induce epidermal protein depletion which can explain the keratinocyte necrosis seen in this condition. High serum glucagon level yields greater amount of arachidonic acid and its metabolites which can induce inflammatory changes seen in NAE.³ Albumin sequesters the fatty acids released from tissue membranes, making them inaccessible to further degradation to metabolic products such as prostaglandins.

Hypoalbuminemia will lead to higher levels of prostaglandins which can induce inflammatory process in NAE. Since albumin is the carrier for zinc, its deficiency can lead to deficiency of zinc. How zinc deficiency is related to NAE is still not clear, but there are reports of improvement of skin lesions of NAE with zinc supplementation even in patients with normal serum concentration of zinc.⁴

Clinically NAE has been characterized by three evolutionary stages: the initial acute stage is characterized by scaly, erythematous papules that may have a dusky hue and deep-red center. Appearance of flaccid blisters and erosions may be seen in this stage. During the fully developed lesional stage there is confluence of erythematous to violaceous lichenified plaques with sharply defined margins surrounded by adherent scales. In late stage, progressive thinning with increased hyperpigmentation is seen. In some cases, erosions and crusting can occur during this stage. It is during this stage that spontaneous remission or exacerbation may occur.⁵

Histopathologically the findings may differ depending upon the stage. Acute NAE shows acanthosis, individual keratinocytes necrosis, confluent upper epidermal necrosis with necrosis tracking perpendicular to the surface of the epidermis. Dermis shows a superficial and deep perivascular infiltrate of lymphocytes. Chronic lesions demonstrate parakeratosis, irregular acanthosis, papillomatosis, epidermal pallor, and a superficial and deep perivascular inflammatory infiltrate.^{6,7}

The differential diagnosis includes psoriasis, hypertrophic lichen planus, atopic dermatitis, necrolytic migratory erythema, and other necrolytic erythemas. Psoriasis can be easily excluded clinically by the absence of silvery white scales and Auspitz sign, and

histopathologically by the absence of spongiosis and necrotic keratinocytes.⁶ Other necrolytic erythemas such as acrodermatitis enteropathica, pellagra and biotin deficiency can be differentiated from NAE clinically by specific predilection of sites, periorificial and mucosal involvement; more erythematous, blistering and erosive lesions while less common hyperkeratotic and verrucous lesions; and associated systemic symptoms. Although majority of cases which have been reported tested positive for hepatitis C infection; there are few reports of NAE without hepatitis C coinfection. While there are some reported cases which were seronegative to hepatitis C infection but with low serum zinc levels; the present case is very rare as the patient was seronegative for hepatitis C infection and was also having normal serum zinc level. This suggests that NAE could be an isolated entity which can occur independently in a setting with normal hepatic function and with a normal serum zinc level.

Conclusion

NAE is a distinct entity which can occur independently without confection with hepatitis C virus or low serum zinc level.

References

1. El Darouti M, Abu el Ela M. Necrolytic acral erythema: A cutaneous marker of viral hepatitis C. *Int J Dermatol*. 1996;**35**:252-6.
2. Patel U, Loyd A, Patel R, Meehan S, Kundu R. Necrolytic acral erythema. *Dermatol Online J*. 2010;**16**:15.
3. Nofal AA, Nofal E, Attwa E, El-Assar O, Assaf M. Necrolytic acral erythema: A variant of necrolytic migratory erythema or a distinct entity? *Int J Dermatol*. 2005;**44**:916-21.
4. Abdallah MA, Hull C, Horn TD. Necrolytic acral erythema: A patient from the United States successfully treated with oral zinc. *Arch Dermatol*. 2005;**141**:85-7.
5. Abdallah MA, Ghozzi MY, Monib HA, Hafez AM, Hiatt KM, Smoller BR *et al*. Necrolytic acral erythema: A cutaneous sign of hepatitis C virus infection. *J Am Acad Dermatol*. 2005;**53**:247-51.
6. Wu YH, Tu ME, Lee CS, Lin YC. Necrolytic acral erythema without hepatitis C infection. *J Cutan Pathol*. 2009;**36**:355-8.
7. Bentley D, Andea A, Holzer A, Elewski B. Lack of classic histology should not prevent diagnosis of necrolytic acral erythema. *J Am Acad Dermatol*. 2009;**60**:504-7.