Journal of Pakistan Association of Dermatologists 2012;**22**:66-69.

Case Report

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

Wasfa Hayat, Kanwal Zahra, Lamees Mahmood Malik, Nadia Ali Azfar, Mohammed Jahangir

Department of Dermatology, Unit I, Allama Iqbal Medical College/Jinnah Hospital, Lahore, Pakistan

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.[1] 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.[2] NAE has its clinical and microscopic resemblance with necrolytic migratory erythema.

Reports are available regarding the association of HCV with NAE.[3] 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.

Address for correspondence
Dr. Wasfa Hayat
321 A-II BOR Society,
Johar Town, Lahore
Email: wasfa_hayat@yahoo.com
Ph# 0331-4404970

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

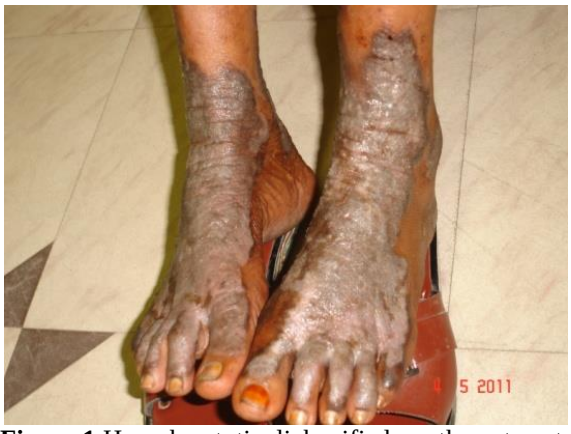

Figure 1 Hyperkeratotic, lichenified, erythematous to violaceous plaques on dorsum of both feet.

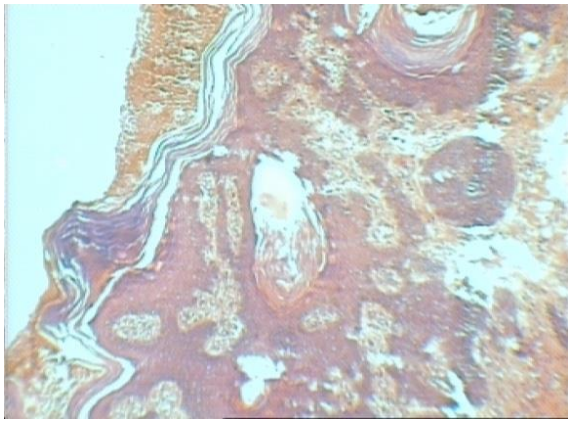

Figure 2 Hyperkeratosis, parakeratosis, acanthosis and superficial, perivascular inflammatory infiltrate.

on the dorsal aspects of feet, malleoli and ankles (**Figures 1**). Lesions with similar clinical morphology were present on hands, with erosions and excoriation marks. Face and scalp were spared. Nails, hair and mucosae were normal.

On laboratory analysis, hemoglobin 12.2g/dl, white cell count 6000/µl, ESR 36mm first hour, total bilirubin 0.5mg/dl, SGPT 188U/dl, ALP 396 U/l, BSR 246mg/dl, serum albumin and renal function tests were normal. Anti-HCV antibodies were reactive by ELISA.

Histopathology of the lesion revealed hyperkeratosis, parakeratosis, acanthosis and superficial, perivascular inflammatory infiltrate. 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, hypoaminoacidemia, 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.[5]

Three stages of lesions have been described on gross and histological examination (**Table 1**).[6]

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.

Initial stage	*Fully developed stage*	*Late stage*
Clinical features		
Erythematous papules or plaque with scale are present and have a dusky or eroded center	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	Thinning of lesions occurs, with continued hyperpigmentation. Demarcation continues, followed by spontaneous relapse and remission
Histological features		
Nummular dermatitis–like moderate and regular acanthosis • Variable spongiosis • Inflammatory infiltrate • Pigment incontinence	Psoriasiform epidermal hyperplasia • Marked papillomatosis • Parakeratosis • Focal hypergranulosis • Pigment incontinence • Occasional subcorneal pustules • Epidermal pallor • Vascular ectasia • Infiltrate of inflammatory cells in the papillary dermis • Necrotic keratinocytes - Sometimes become confluent in the upper epidermis, sometimes tracking along the acrosyringium	Minimal-to-moderate acanthosis • Minimal-to-moderate inflammatory cell infiltrate • Pigment incontinence

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.[5] 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

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. Najarian DJ, Lefkowitz I, Balfour E *et al*. Zinc deficiency associated with necrolytic acral erythema. *J Am Acad Dermatol* 2006;**55(**5 Suppl):S108-10.
3. Tabibian JH, Gerstenblith MR, Tedford RJ *et al*. Necrolytic acral erythema as a cutaneous marker of hepatitis C: report of two cases and review. *Dig Dis Sci* 2010; **55**:2735-43.
4. El-Darouti MA, Mashaly HM, El-Nabarawy E *et al*. Leukocytoclastic vasculitis and necrolytic acral erythema in patients with hepatitis C infection: do viral load and viral genotype play a role? *J Am Acad Dermatol* 2010;**63**:259-65.
5. El-Ghandour TM, Sakr MA, El-Sebai H *et al*. Necrolytic acral erythema in Egyptian patients with hepatitis C virus infection. *J Gastroenterol Hepatol* 2006;**21**:1200-6.
6. Abdallah MA, Ghozzi MY, Monib HA *et al*. Histological study of necrolytic acral erythema. *J Ark Med Soc* 2004;**100**:354-5.
7. Khanna VJ, Shieh S, Benjamin J *et al*. Necrolytic acral erythema associated with hepatitis C: effective treatment with interferon alfa and zinc. *Arch Dermatol* 2000;**136**:755-7.
8. Liu A, Erickson CP, Cockerell CJ, Hsu S. Necrolytic acral erythema: a case not associated with hepatitis C infection. *Dermatol Online J* 2008;**14**:10.
9. 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.
10. Khokhar N, Gill ML, Malik GJ. General seroprevalence of hepatitis C and hepatitis B virus infections in population. *J Coll Physicians Surg Pak* 2004, 149:534-6.
11. Syed AA, Rafe MJ, Qureshi H, Vermund SH. Hepatitis B and hepatitis C in Pakistan. *Int J Infect Dis* 2009;**13**:9-19.