

# Hyperkeratotic Lesions in a Patient With Hepatitis C Virus

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A 59-year-old man with a history of untreated hepatitis C virus presented with a pruritic rash on the extensor aspect of the extremities of 1.5 years' duration. He had been prescribed hydrocortisone ointment 2.5% and topical betamethasone-clotrimazole in the past but neither was successful. The patient denied a history of eczema, allergies, or asthma. Physical examination revealed multiple dark brown, slightly lichenified papules on the dorsal aspect of the hands, as well as thick, hyperkeratotic, fissured plaques on the bilateral elbows, knees, and dorsal aspect of the feet extending onto the malleoli and lower anterior shins. Laboratory test results revealed a low serum zinc level of 44  $\mu\text{g}/\text{dL}$  (reference range, 60–120  $\mu\text{g}/\text{dL}$ ).

## What's the diagnosis?

- acrodermatitis enteropathica
- necrolytic acral erythema
- necrolytic migratory erythema
- pellagra
- psoriasis vulgaris

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The authors report no conflict of interest.

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## The Diagnosis: Necrolytic Acral Erythema

**H**istopathologic analysis of a biopsy specimen from the right leg revealed an erosion with parakeratosis containing neutrophils and marked spongiosis favoring the upper layer of the epidermis with focal individual necrotic keratinocytes. In addition, there was a lymphocytic and neutrophilic exocytosis with edema of the papillary dermal papillae, mild papillary dermal fibrosis, and a mild perivascular lymphocytic infiltrate with neutrophils and occasional eosinophils. Clinicopathologic correlation led to a diagnosis of necrolytic acral erythema (NAE).

The patient was prescribed clobetasol propionate ointment 0.05% and oral zinc sulfate 220 mg twice daily but was initially noncompliant with the topical corticosteroid regimen. He did, however, initiate zinc supplementation, which was later increased to 220 mg 3 times daily. At 3-month follow-up, the lesions had nearly completely cleared (Figure) and the serum zinc level was within reference range at 81 µg/dL.

Necrolytic acral erythema is a rare dermatosis that was first described in 1996 by el Darouti and Abu el Ela<sup>1</sup> in a series of 7 Egyptian patients. Since then, most of the cases have reported concomitant hepatitis C virus (HCV) infection.<sup>2</sup> Necrolytic acral erythema classically presents with symmetric, well-defined, hyperkeratotic plaques in an acral distribution, typically on the dorsal aspect of the feet.<sup>2,3</sup> Lesions may involve the dorsal aspect of the toes

and the lower legs, with less common involvement of the elbows, hands, and buttocks. Patients often report pruritus and/or burning.<sup>3</sup>

Abdallah et al<sup>4</sup> proposed several stages of NAE development with erythematous papules with dusky eroded centers progressing to marginated, erythematous to violaceous, lichenified plaques. Over time, these lesions tend to thin with progressive hyperpigmentation.

Histologically, early findings of NAE include acanthosis with epidermal spongiosis and upper dermal perivascular dermatitis. Over time, lesions may exhibit psoriasiform hyperplasia with papillomatosis and parakeratosis, epidermal pallor, subcorneal pustules, vascular ectasia, papillary dermal inflammation, and necrotic keratinocytes. Minimal to moderate acanthosis with an inflammatory infiltrate may be observed later in disease progression.<sup>5</sup>

The differential diagnosis of NAE includes many benign inflammatory skin diseases. Given the acral/extensor distribution of hyperkeratotic lesions and psoriasiform pattern on histopathology, NAE initially may be misdiagnosed as psoriasis. Unlike psoriasis, however, NAE rarely involves palmoplantar skin or nails<sup>4</sup> and may respond dramatically to treatment with zinc supplementation.<sup>6,7</sup> Necrolytic acral erythema also may be confused with other necrolytic erythemas, including necrolytic migratory erythema, acrodermatitis enteropathica, and pellagra. A deficiency of biotin or essential fatty acids also may mimic NAE. Necrolytic acral erythema can be distinguished from these entities based on its characteristic appearance and distribution, along with comorbid HCV infection.<sup>2,4</sup>

Several reports of NAE have revealed an associated zinc deficiency.<sup>2,8</sup> The underlying pathophysiology of zinc deficiency in NAE has not been elucidated but is thought to be related to HCV infection.<sup>2</sup> Clinical improvement has been reported with zinc supplementation in patients with NAE at dosages of 220 mg twice daily, even in those with initial serum zinc levels within reference range.<sup>6,7</sup> Our patient was observed to have a low serum zinc level that dramatically improved with oral supplementation.

The recognition of this uncommon entity is critical for dermatologists and dermatopathologists, as NAE has been proposed as an early cutaneous marker of HCV and may prompt the initial diagnosis of HCV.<sup>1-10</sup> The severity of NAE has even been linked to HCV severity.<sup>1,8</sup> Treatment of HCV has cleared NAE in several cases,<sup>4,10</sup> implicating



Necrolytic acral erythema lesions had nearly completely cleared at 3-month follow-up after zinc supplementation.

the virus in its pathogenesis. A proper workup for liver dysfunction and follow-up with an appropriate health care provider for HCV treatment is crucial. Our patient was encouraged to follow up with the hepatology department, as he had not been evaluated in several years.

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