Journal of Chemical Health Risks

www.jchr.org

JCHR (2026) 16(3), 34-37 | ISSN:2251-6727

Necrolytic Acral Erythema Associated with Chronic Hepatitis C: A Case Report

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(Received: 16 March 2026 Revised: 14 April 2026 Accepted: 01 May 2026)

KEYWORDS

Zinc deficiency, Acral plaques, Psoriasiform dermatitis

ABSTRACT:

Necrolytic acral erythema (NAE) is an uncommon clinicopathological dermatosis strongly associated with chronic hepatitis C virus (HCV) infection and frequently linked to abnormalities in zinc metabolism. It typically presents as a symmetrical acral eruption over the dorsa of the feet, evolving from erythematous papules to hyperkeratotic, hyperpigmented scaly plaques, with histopathology showing psoriasiform epidermal hyperplasia and focal necrolytic changes. We report a case of a 45-year-old man who presented with painful, pruritic lesions over both feet for six months. Cutaneous examination revealed bilaterally symmetrical, well-defined hyperpigmented plaques with thick adherent dark scales and peripheral erythema over the dorsae of the feet and toes, with sparing of the palms, soles, nails, and mucosa. Laboratory investigations showed low serum zinc levels of 45 mcg/dL, positive HCV serology, and HCV RNA viral load of 2.5 million IU/mL, along with mildly elevated liver transaminases. Histopathological examination of a lesional skin biopsy demonstrated psoriasiform epidermal hyperplasia, focal parakeratosis, pallor of the upper epidermis, scattered necrotic keratinocytes, and mild superficial perivascular lymphocytic infiltrate, confirming the diagnosis of NAE. The patient was treated with oral zinc sulfate 220 mg three times daily and showed significant clinical improvement within four weeks, with marked reduction in erythema, scaling, and plaque thickness. This case highlights the importance of recognizing NAE as a cutaneous marker of underlying HCV infection and zinc deficiency, enabling timely diagnosis and appropriate management.

Introduction

Necrolytic acral erythema (NAE) is an uncommon clinicopathological dermatosis characterized by a symmetrical acral eruption that predominantly involves the dorsa of the feet and toes and, less frequently, the hands, whereas the palms, soles, and nails are usually spared.(1) Although rare, NAE shows a strong association with chronic HCV infection; in a study of 300 patients with chronic HCV, Raphael et al. identified NAE in 5 patients, corresponding to a prevalence of 1.7% (95% confidence interval 0.5%–3.8%).(2) Clinically, the lesions evolve through stages from erythematous papules and plaques to well-developed hyperkeratotic, hyperpigmented plaques with adherent scale, and patients commonly report pain, pruritus, or a burning sensation. The pathogenesis of NAE remains incompletely understood and appears multifactorial, with proposed contributions from chronic liver dysfunction, hypoalbuminemia, amino acid imbalance, and disturbances in zinc metabolism; zinc is particularly relevant because it is essential for epidermal integrity and repair. Histopathological changes are stage-dependent but classically include psoriasiform epidermal hyperplasia, hyperkeratosis with parakeratosis, epidermal pallor or spongiosis, focal keratinocyte necrosis, and a superficial dermal inflammatory infiltrate. Oral zinc therapy has been reported as one of the most consistently effective treatments, with successful remission documented in case-based literature even when the precise mechanism is not fully understood.(3, 4) The present case was documented in the Department of Dermatology, Venereology and Leprosy, Sree Balaji Medical College and Hospital, Chennai.

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JCHR (2026) 16(3), 34-37 | ISSN:2251-6727

Case Report

A 45-year-old man presented with painful, pruritic lesions over both feet that had been progressively evolving for six months. The eruption began as erythematous papules and gradually developed into scaly plaques associated with increasing hyperpigmentation and discomfort. He denied any previous similar episodes, antecedent drug intake, or accompanying systemic symptoms. Cutaneous examination showed bilaterally symmetrical, well-defined hyperpigmented plaques with thick, adherent dark scales and peripheral erythema over the dorsae of the feet and toes (Figure 1). The lesions were limited to acral sites, with no involvement of the palms, soles, nails, or mucosa. Systemic examination was unremarkable. Laboratory evaluation revealed a low serum zinc level of 45 mcg/dL (reference range: 70–120 mcg/dL). Serological testing for hepatitis C virus was positive, and HCV RNA polymerase chain reaction showed a viral load of 2.5 million IU/mL, confirming active infection. Liver function tests demonstrated mildly elevated transaminases, with alanine aminotransferase of 120 U/L and aspartate aminotransferase of 95 U/L. Histopathological examination of a lesional skin biopsy revealed psoriasiform epidermal hyperplasia with focal parakeratosis, pallor of the upper epidermis, scattered necrotic keratinocytes, and a mild superficial perivascular lymphocytic infiltrate in the dermis, findings consistent with necrolytic acral erythema. The patient was started on oral zinc sulfate 220 mg three times daily, following which significant clinical improvement was noted within four weeks, with marked reduction in erythema, scaling, and plaque thickness.

Discussion

Necrolytic acral erythema (NAE) is a distinctive acral dermatosis first described by el Darouti et al. in 1996 in seven patients with active hepatitis C virus (HCV) infection, in whom lesions characteristically involved the dorsa of the feet and evolved from dusky erythematous areas with early blistering to chronic hyperkeratotic plaques.(1) Davis & Creditt (2020) and Inamadar et al. (2020) have established NAE as a rare but recognizable extrahepatic cutaneous manifestation of chronic HCV infection, although the estimated prevalence among patients with chronic HCV appears to be low, at about 1.7%.(5, 6) The present patient therefore fits a classic epidemiologic and clinicovirologic context for NAE: a middle-aged man with active HCV viremia, acral dorsal foot involvement, and compatible histopathology. The morphology and distribution in this case are particularly characteristic. NAE typically presents as a symmetrical acral eruption affecting the tops of the toes and feet, with lesions progressing from erythematous papules or plaques to well-demarcated, hyperpigmented, thickened plaques with adherent scale; pain, pruritus, and burning are common symptoms, while the palms, soles, and nails are usually spared. Yost et al. described later-stage lesions as hyperkeratotic targetoid plaques with a peripheral erythematous rim, secondary lichenification, hyperpigmentation, and overlying micaceous or necrotic-appearing scale.(7) The patient's six-month evolution from erythematous papules to painful, pruritic, bilaterally symmetrical hyperpigmented plaques with thick dark scale and peripheral erythema over the dorsae of the feet and toes, together with sparing of palms, soles, nails, and mucosa, closely mirrors this well-developed chronic phase of NAE. His age of 45 years is also concordant with the reported mean onset of approximately 40–45 years.

Histopathology in NAE is stage-dependent, and clinicopathologic correlation is central to diagnosis. In the detailed histologic study by Abdallah et al., early lesions showed acanthosis, spongiosis, and inflammation resembling eczema, whereas fully evolved lesions demonstrated psoriasiform epidermal hyperplasia with marked papillomatosis, parakeratosis, focal hypergranulosis, epidermal pallor, necrotic keratinocytes, vascular ectasia, and papillary dermal inflammation; pigment incontinence could be seen throughout the disease course.(8) Srisuwanwattana & Vachiramon (2017) have emphasized that fully developed NAE may show subcorneal pustules and upper-epidermal necrosis in addition to psoriasiform change.(9) The biopsy in the present case showed psoriasiform epidermal hyperplasia, focal parakeratosis, pallor of the upper epidermis, scattered necrotic keratinocytes, and a mild superficial perivascular lymphocytic infiltrate, a constellation that aligns closely with the described fully evolved histologic pattern and strongly supports the diagnosis.

The main clinical differentials in this setting include psoriasis, chronic eczema, acrodermatitis enteropathica, pellagra, and necrolytic migratory erythema. Psoriasis may simulate NAE because both can produce sharply

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JCHR (2026) 16(3), 34-37 | ISSN:2251-6727

demarcated hyperkeratotic plaques with psoriasiform histology, but NAE is favoured when lesions are restricted to acral dorsal sites in a symmetric pattern and are accompanied by HCV infection and/or zinc deficiency.(10) Chronic eczema is more likely to show prominent spongiosis clinically and histologically and lacks the characteristic necrolytic changes. Acrodermatitis enteropathica classically presents with periorificial and acral dermatitis associated with alopecia and diarrhea, which were absent here. Necrolytic migratory erythema of glucagonoma syndrome typically occurs with systemic manifestations such as weight loss, stomatitis, diabetes, anemia, or thromboembolic disease, rather than a purely localized dorsal foot eruption. Thus, the combination of lesion topography, sparing of palms and soles, low serum zinc, active HCV infection, and compatible biopsy makes NAE substantially more likely than its mimics in this patient.

The pathogenesis of NAE remains incompletely resolved and is probably multifactorial. Current understanding suggests an interplay among chronic liver dysfunction, nutritional disturbance, and HCV-related metabolic or immune effects, with zinc dysregulation playing a particularly important role. Inamadar et al. highlighted the probable contribution of abnormalities in albumin, amino acids, and zinc metabolism, while other sources note that HCV may contribute through direct viral, immune-mediated, or liver disease–related mechanisms.(5) Importantly, Moneib et al. demonstrated that patients with NAE had reduced serum and skin zinc levels, and that oral zinc supplementation corrected these biochemical deficits earlier than complete clinical improvement became evident.(11) The present patient's serum zinc of 45 mcg/dL therefore provides biologic support for the diagnosis and offers a plausible mechanistic explanation for both the epidermal injury and the subsequent therapeutic response.(12)

At the same time, this case also illustrates that zinc deficiency should be interpreted as contributory rather than exclusive. NAE has been reported in patients with normal plasma zinc levels, and remission with empiric zinc therapy has been documented even when baseline zinc was normal. Likewise, although HCV is the dominant association, a small number of seronegative or HCV-negative cases have been described in association with other disorders such as celiac disease, Crohn disease, sarcoidosis, and isolated nutritional deficiency.(4, 13) Accordingly, the diagnosis should not rest on a single laboratory marker alone, but on concordance among clinical morphology, distribution, histopathology, and systemic context. In the present patient, however, the coexistence of active HCV infection documented by HCV RNA, low serum zinc, mild transaminitis, and classic biopsy findings makes the diagnosis especially compelling. The absolute viral load of 2.5 million IU/mL confirms active infection, but available literature suggests that viral load itself does not consistently predict the occurrence of NAE.

The therapeutic response in this patient is also highly characteristic. Oral zinc is the most consistently effective treatment reported for NAE, regardless of whether serum zinc is frankly low, and commonly used regimens include zinc sulfate 220 mg twice daily; individual reports have documented improvement within 1–2 weeks in some patients and near-complete resolution over 5–8 weeks in others. Najarian et al. reported symptomatic improvement within 1 week and near-resolution by 5 weeks with zinc sulfate 220 mg twice daily,(3) while Abdallah et al. described gradual plaque resolution over 8 weeks with the same dose despite a normal plasma zinc level.(4) Khader et al. similarly documented regression within 2 weeks after zinc supplementation in seronegative disease.(13) Against that background, the marked improvement in erythema, scaling, and plaque thickness after 4 weeks of oral zinc sulfate 220 mg three times daily in the present case is entirely in keeping with a zinc-responsive NAE phenotype. Geria et al. (2009) and Hivnor et al. (2004) also shows that treatment of the underlying HCV infection with interferon and ribavirin could induce lesion resolution, and current HCV guidance recommends antiviral therapy for nearly all patients with active infection because virologic cure improves liver inflammation and reduces extrahepatic morbidity.(14, 15) For that reason, although zinc appropriately addressed the cutaneous eruption, recognition of NAE in this patient should also prompt definitive hepatology evaluation and HCV-directed antiviral therapy as part of comprehensive management.

Conclusion

In conclusion, this case highlights necrolytic acral erythema as an important cutaneous marker of underlying hepatitis C virus infection and associated zinc deficiency. The characteristic acral distribution,

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JCHR (2026) 16(3), 34-37 | ISSN:2251-6727

compatible histopathological findings, low serum zinc level, and prompt clinical response to oral zinc sulfate supported the diagnosis. Early recognition of this uncommon dermatosis is essential because it not only enables effective dermatologic treatment but also facilitates timely evaluation of the underlying systemic disease.

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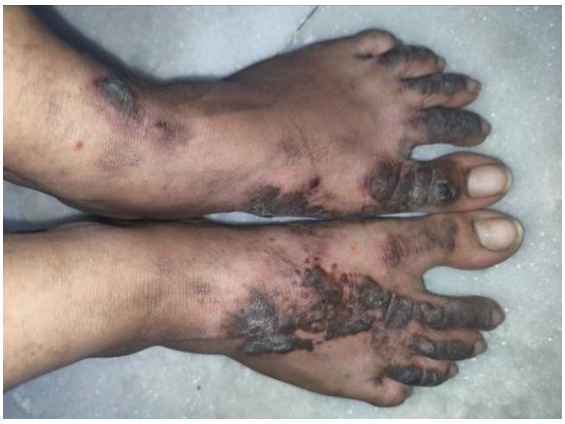

Figure 1: Bilateral dorsum of the feet showing multiple well-defined hyperpigmented plaques with surrounding erythema, predominantly over the toes and ankle region