

Necrolytic Acral Erythema – A Case Series

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Abstract

It is currently accepted that necrotic acral erythema (NAE) represents a separate clinical entity, unlike earlier when it was a part of necrolytic migratory erythema. It manifests clinically as symmetrically distributed, well-defined, hyperpigmented papules and plaques with thick adherent scales over the dorsum of the feet. According to some theories, the underlying pathogenic mechanism of NAE is hepatic dysfunction leading to metabolic abnormalities such as hypoalbuminemia, hypoaminoacidemia, hyperglucagonemia, and transitory zinc insufficiency. To differentiate NAE from other necrolytic erythemas, a deeper comprehension of the etiopathogenesis and histological characteristics is necessary. Here, we report a case series of patients with necrolytic acral erythema & zinc deficiency, as evaluated, who showed significant improvement with oral zinc supplementation.

Key words: Hepatitis C, Necrolytic acral erythema, Zinc

Introduction

Necrolytic acral erythema (NAE) is a dermatological condition characterised by pigmented to erythematous patches and plaques with hyperkeratosis usually over the dorsum of hands and feet. El Darouti and Abu el Ela reported the first case of NAE in Egypt in 1996. Earlier, it was considered characteristic of active Hepatitis C virus infection, but now cases of NAE have been reported in seronegative patients as well.¹ Hepatic cirrhosis, neoplasms, nutritional deficiencies, and hepatitis C virus (HCV) infections are among the causes of necrolytic erythemas. Necrolytic erythemas enable the early identification of severe underlying illnesses when properly diagnosed.² Patients may have uncommon clinical characteristics and rare acute presentations of NAE; in these situations, suspicion of an HCV infection may not be raised for weeks or months until more typical chronic lesions appear. NAE frequently manifests before an HCV infection diagnosis is made for the patient.³

Case Report

Case 1: A 29-year-old male patient came to our dermatology OPD with complaints of dark coloured skin lesions on both feet for the past 6 months. The patient was a daily wage laborer by occupation. The patient did not complain of any itching or irritation. There is no history of any topical application on the feet. On examination, symmetrical, well-defined, pigmented plaques with hyperkeratosis and scaling were observed on the dorsum of the bilateral feet (Figure 1A). Hepatitis C Virus (HCV) serology was negative, and liver enzymes were within normal limits. Serum Zinc levels were significantly low (24 µg/dL). Serum Glucagon levels were within normal limits. A punch biopsy of the skin from the lesion was done and sent for histopathological examination showed marked hyperkeratosis with foci of necrosis. Epidermis shows marked irregular hyperplasia and acanthosis. A few necrotic keratinocytes are present. Papillary dermis shows diffuse lymphocytic infiltrate (Figure 2).

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The patient was given 50mg elemental zinc for 2 months, and improvement in the lesions was noted (Figure 1B).



Figure 1A: Symmetrical hyperpigmented scaly plaques over the dorsum of both feet. Figure 1B: Significant reduction in the lesions after treatment with 50mg elemental zinc daily for 2 months.

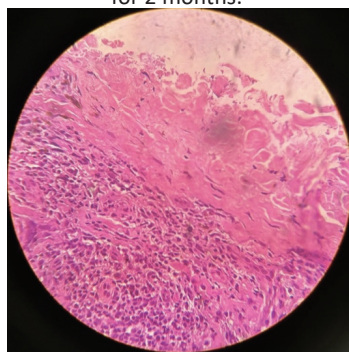


Figure 2: Marked hyperkeratosis with foci of necrosis.

Epidermis shows marked irregular hyperplasia and acanthosis. A few necrotic keratinocytes are present; the papillary dermis shows diffuse lymphocytic infiltrate. (H&E stain, 40x)

Case 2: A 46-year-old female came to the dermatology OPD complaining of dark coloured skin lesions on both feet for the past 8 months. The patient was a homemaker, and she did not have complaints of itching or burning sensations over the lesions. Patient denies any history of topical application. On examination, there were well-defined hyperpigmented scaly plaques on the dorsal surface of both feet (Figure 3A). Patient refused a punch biopsy of the skin to be taken. A diagnosis of NAE was made when the serum Zinc levels of the patient turned out to be 32 μ g/dL. The patient was started on 50mg elemental zinc per day, and improvement in the lesions was noted after 1 month of taking oral zinc (Figure 3B).



Figure 3A: Hyperpigmented scaly plaques on the dorsum of

both feet. Figure 3B: Improvement noted in the lesions after 1 month of treatment with oral zinc.

Case 3: A 53-year-old female came to the dermatology OPD complaining of asymptomatic dark skin lesions on both feet for the past 11 months. The patient was a homemaker & denies any history of topical application. On examination, there were well-defined hyperpigmented scaly plaques on the dorsal surface of both feet (Figure 4). The patient could not be convinced to undergo a biopsy of the skin to be taken. A presumptive diagnosis of NAE was made when the serum Zinc levels of the patient turned out to be 28 μ g/dL. The patient was started on 50mg elemental zinc per day and is yet to come back for follow-up.



Figure 4: Well-defined hyperpigmented scaly plaque with peripheral erythema on the dorsal surface of both feet

Discussion:

NAE is frequently observed in HCV-infected patients. Males and females are both equally affected by the condition. Patients with NAE typically fall within the 19–58 years.¹ Although the exact origin of NAE is unknown, hypoaminoacidemia, hypoalbuminemia, hyperglucagonemia, and zinc insufficiency are thought to be likely contributors. Hyperglucagonemia and hypoaminoacidemia can be caused by hepatocellular dysfunction. Necrolysis can result from the loss of epidermal proteins caused by hypoaminoacidemia. Increased production of arachidonic acid and its metabolites due to elevated serum glucagon levels causes inflammatory alterations in NAE.⁴

Given the inconsistent reactions to supplementation shown in the literature, zinc might be a contributing factor. The divalent cation is a cofactor in protein synthesis, hepatic mobilization of vitamin A, DNA and RNA replication, and apoptosis inhibition. A zinc shortage lowers serum transport proteins, which might hinder the delivery of nutrients to tissues. For example, vitamin A, which is necessary for normal epidermal proliferation and differentiation, is delivered by a retinol-binding protein and prealbumin complex.²

It primarily affects the acral sites and manifests as a psoriasiform eruption. The abdomen, genitalia, thighs, and knees are additional areas of involvement. In this situation, the mucous membrane, nail bed, nail plates, palms, and soles are typically unaffected.⁵

Dermatological conditions presenting with psoriasiform plaques and acral erythemas are among the differential diagnoses. Psoriasis, eczema, dermatophytosis, erythrokeratoderma, and paraneoplastic acrokeratosis or Bazex syndrome make up the former group. The latter group includes pellagra, zinc-responsive acral hyperkeratosis, biotin deficiency, acrodermatitis enteropathica, and fatty acid deficiency.¹ Necrolytic migratory erythema (NME), a necrolytic erythema traditionally linked to glucagonoma syndrome due to pancreatic islet cell neoplasia, is the condition most frequently confused with NAE. However, it has been proposed that NAE might actually be an acral form of NME.³ Three stages of progression define NAE in therapeutic settings: In the initial acute stage, scaly, erythematous papules with a deep-red center and possibly a dusky color are characteristic. In this stage, flaccid blisters and erosions may be observed; in the fully developed stage, erythematous to violaceous lichenified plaques with well-defined boundaries and adherent scales encircling them appear. There is gradual

thinning and enhanced hyperpigmentation in the late stage. Crusting and erosion may occasionally follow at this point. An aggravation (flare) or spontaneous remission could happen in the latter stages.⁵

Oral zinc supplements are part of the treatment for NAE. Within a few weeks of oral medication, there is a very noticeable response to oral zinc (identical findings were observed in the index case). Interferon-alpha, with or without ribavirin, is the definitive treatment for NAE in patients who test positive for hepatitis C. In most cases, this medication has improved skin disease. Oral amino acid, systemic, and topical corticosteroid supplements play a negligible part in treating NAE. According to Manzur et al., topical tacrolimus was successfully used in NAE, with lesions completely resolved four weeks after administration.⁵

It is important to recognise the condition early so that its underlying cause can be detected and treated. HCV serology is to be done in every patient with suspected NAE as HCV infection is seen in 75% of the cases.

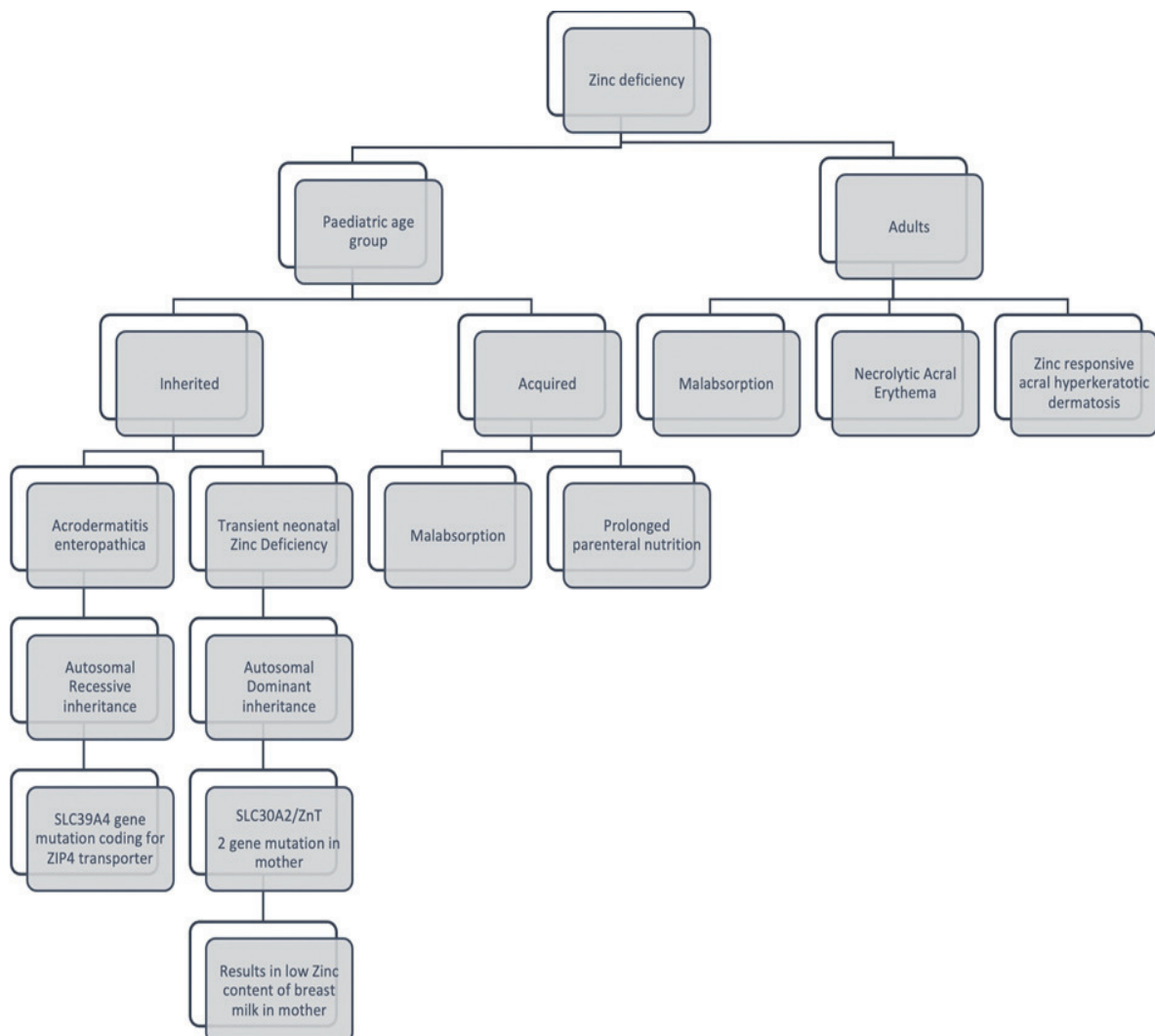


Figure 5 shows flow-chart showing zinc deficiency in adult and paediatric age groups with their aetiology

Table 1: Summary of Seronegative Necrolytic Acral Erythema Cases

Reference	Age/ Sex	Duration	Site	Initial presentation	Symptoms	HPE findings	Serum zinc / labs	Underlying disorder	Treatment given	Course / Outcome
Present case 1	29 / M	6 months	Dorsa of both feet	Well-defined pigmented plaques with hyperkeratosis and scaling	Asymptomatic (no itching/ irritation)	Hyperkeratosis, irregular hyperplasia, acanthosis; necrotic keratinocytes; dermal lymphocytic infiltrate	24 µg/dL (low)	-	Oral zinc 50 mg/day for 2 months	Marked improvement after 2 months
Present case 2	46 / F	8 months	Dorsa of both feet	Well-defined hyperpigmented scaly plaques	Asymptomatic	Not done (biopsy refused)	32 µg/dL (low)	-	Oral zinc 50 mg/day	Improvement after 1 month
Present case 3	53 / F	11 months	Dorsa of both feet	Well-defined hyperpigmented scaly plaques	Asymptomatic	Not done (biopsy refused)	28 µg/dL (low)	-	Oral zinc 50 mg/day	Follow-up pending
Pandit et al., 2016 (Case 1)	24 / M	3 weeks	Dorsa of feet, index fingers	Erythematous-to-hyperpigmented plaques with vesicles & bullae	Burning sensation	Hyperkeratosis, irregular elongated rete ridges	~54.6 µg/dL (low)	-	Oral zinc	Near complete resolution after 2 weeks
Pandit et al., 2016 (Case 2)	40 / M	5 months	Dorsa of feet	Well-defined hyperpigmented plaques	Asymptomatic	Not done (biopsy refused)	Low	-	Oral zinc	Complete clearance in 4 weeks
Wei et al., 2022	17 / F	4 years	Bilateral dorsal feet & ankles	Well-demarcated erythematous scaly plaques with inflamed erosive rim	Pruritic, painful	Parakeratosis, psoriasiform hyperplasia, epidermal pallor, focal necrosis	51 µg/dL (slightly low); iron deficiency anemia	Iron deficiency anemia	Oral zinc 150 mg/day	Dramatic improvement, residual hyperpigmentation
Baroudi et al., 2023	—	—	Feet (acral)	NAE-like plaques	—	—	Not significantly low; seronegative for HCV	Hypothyroidism	Zinc + thyroid management	Improvement reported

Conclusion

Necrolytic acral erythema (NAE) is a distinctive skin manifestation associated with active HCV infection, presenting as dusky-red plaques that may show vesiculation or thickened scaling in a dorsal acral

distribution. It is considered the only pathognomonic cutaneous sign of HCV, making it important for dermatologists and primary care physicians to recognize this condition. It is important to recognize the condition early so that its underlying cause can be detected and treated.

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