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## Case report

### NECROLYTIC ACRAL ERYTHEMA: HIGH DEGREE OF SUSPICION FOR DIAGNOSIS

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## ABSTRACT

Necrolytic Acral Erythema (NAE) is a recently described, poorly understood, rare dermatological entity, which is frequently associated with Hepatitis C Virus (HCV) infection. This report describes a 53 year old male with a 6 month history of well demarcated, reddish brown to hyperpigmented, scaly skin over dorsum of both hands and feet. Investigations revealed hypothyroidism and low serum zinc levels. Patient also tested seropositive for HCV. Histopathological examination revealed hyperkeratosis and subcorneal clefting along with areas of necrosis. Patient was started on oral zinc along with treatment for hypothyroidism, and improved symptomatically in 2 weeks. Early recognition of NAE is of prime importance to dermatologists as it allows diagnosis of HCV in previously unaware patients and gives way for efficacious treatment.

**Keywords:** Necrolytic erythema, Hepatitis C, HCV

## INTRODUCTION

Necrolytic acral erythema (NAE) belongs to the group of necrolytic erythemas which include acrodermatitis enteropathica, pellagra, biotin deficiency, essential fatty acid deficiency and necrolytic migratory erythema. These conditions are both histologically and clinically similar but differ in their etiology. [1] NAE is a recently described, poorly understood, rare dermatological entity. NAE is characterised by erythematous to violaceous, scaly plaques on the acral sites. It is frequently associated with Hepatitis C Virus (HCV) infection and is now considered a diagnostic cutaneous marker for the disease. Recognition of NAE requires clinico-pathological correlation and a high degree of suspicion. NAE responds well to oral zinc therapy and treatment of the underlying HCV infection with interferon alpha. We report a case of NAE from Southern India.

## CASE REPORT

A 53 yr old man, farmer by profession, presented to the dermatology department with dry, rough, thickened skin over the hands and legs for the past 6 months. The lesions initially started on the legs and then progressed to involve the hands in about 2 weeks. It was associated with itching and burning sensation on sun exposure. Patient also gave history of loose stools since 3 weeks. Stools were watery in consistency, about 4-5 episodes per day, not associated with blood or mucus. It was associated with pain abdomen. Patient was not an alcoholic or on any medications. Family and personal history were non-contributory in our case.

Cutaneous examination showed well demarcated, reddish brown to hyperpigmented, rough, thick, scaly skin with cracks over both lower limbs extending up to the knee and both upper limbs extending just above the elbow joints (Figures 1a and b).

Diffuse, erythematous patches were present over the face (Figure 2) and 'V' region of neck with hyperpigmentation and a few papules, suggestive of Casal's necklace. Rest of the examination including that of oral cavity and genitalia did not show any abnormality. Deep tendon reflexes were sluggish.

A skin biopsy specimen taken from the lesions over the forearm demonstrated hyperkeratosis and clefting present subcorneally, extending up to subepidermal levels (Figure 3). Areas of epidermis showed necrosis. Dermis showed sparse inflammatory infiltrate along with congested blood vessels.

Liver function tests were altered - Alkaline phosphatase was elevated (332 IU/L) but Aspartate transaminase and Alanine transaminase were normal. Electrocardiogram showed low voltage complexes. ECHO revealed mild pericardial effusion with no ischaemic changes. Thyroid hormone levels were suggestive of hypothyroidism (free T3 - 0.15 pg/ml, free T4 - 0.07 ng/dl, serum TSH - 57  $\mu$ IU/ml). Serum zinc levels were low (47.3 $\mu$ g/dl). Patient tested seropositive for Hepatitis C virus. Other routine investigations were normal.

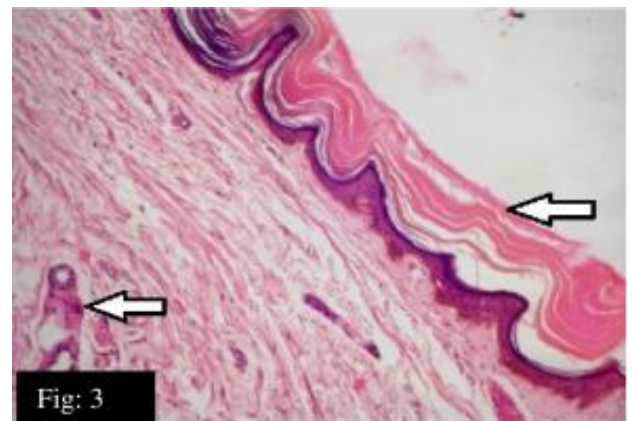
Patient was started on oral Zinc sulphate 440 mg/day in two divided doses, as the mainstay treatment. He was also put on Thyroxine 100  $\mu$ g once a day. Patient improved symptomatically in about 2 weeks (Figures 5a and 5b). Patient was continued on low doses of zinc sulphate for a period of one year and followed up at regular intervals. There was no recurrence of lesions.



**Fig 1a and b: Well demarcated, reddish brown, rough, hyperpigmented, thick, scaly skin with cracks over both upper limbs extending just above the elbow joints.**



**Fig 2: Diffuse, erythematous patches were present over the face**



**Fig 3: Hyperkeratosis with sparse inflammatory infiltrate seen around blood vessel and adnexae.**



**Fig 4a and b: Resolution of lesions with oral zinc in about 2 weeks**

## DISCUSSION

NAE is an infrequently described dermatologic entity.<sup>[2]</sup> It was first described by El Darouti et al in a case series of 7 Egyptian patients in 1996.<sup>[3]</sup> It belongs to the group of necrolytic erythemas. This group of dermatoses also includes acrodermatitis enteropathica, pellagra, biotin deficiency, essential fatty acid deficiency, and necrolytic migratory erythema. These conditions share many histological and clinical similarities but have diverse etiologies. NAE is often associated with HCV infection.

The initial lesion is often erythema with vesicles and flaccid bullae, especially around the periphery of plaques.<sup>[3,4,5]</sup> Chronic lesions appear as erythematous to violaceous plaques with thick scale, erosions and crusting, and often have a dark red rim.<sup>[1,3,4,5,6]</sup> Lesions are predominantly found on acral sites.<sup>[1,4,7,8]</sup> The most common site of NAE plaques is the dorsal aspect of feet.<sup>[1,3,4,7,8,9]</sup> However, absence of lesions over feet is not critical for diagnosis.

Scaly, erythematous lesions on acral locations can be observed in both psoriasis and NAE. NAE has dark, verrucous scales as opposed to the silvery white scales of psoriasis. Furthermore, NAE can present with flaccid blisters and it typically spares the palms and soles. Histologically, the lesions of psoriasis do not possess the necrotic keratinocytes seen with NAE.<sup>[5, 9]</sup>

Histologically, NAE resembles findings of other necrolytic erythemas. Abdallah et al found that in the early stages, NAE shows acanthosis, epidermal spongiosis and superficial perivascular dermatitis. In the late stages, it shows psoriasiform hyperplasia and prominent papillomatosis with parakeratosis, subcorneal pustules, epidermal pallor and necrotic keratinocytes.<sup>[4,10]</sup> Confluent necrosis of the keratinocytes in the upper parts of the epidermis may lead to cleft formation.<sup>[4,5]</sup> Since there are no specific histopathological features, correct diagnosis requires clinico-pathologic correlations and a high degree of suspicion.<sup>[4,11]</sup>

The exact pathogenesis of NAE is not known, but the etiology of NAE seems to be multifactorial. Several mechanisms have been put forward, including zinc deficiency, hypoaminoacidemia, hypoalbuminemia, hepatocellular dysfunction, hyperglucagonemia and diabetes.<sup>[4, 5]</sup> Zinc deficiency has been suggested as an etiologic factor in the skin lesions. The presence of

zinc deficiency in a subset of patients with the disease and the clinical response to zinc supplementation substantiates this theory. According to Najarian et al, even patients with normal serum zinc levels may harbour occult cutaneous zinc deficiency.<sup>[12]</sup>

Treatment of NAE is initiated with oral zinc sulphate supplementation, and response is often noted within several weeks of beginning therapy. The recommended dose is 440 mg/day in 2 divided doses.<sup>[1,4,9]</sup> In many patients, including ours, complete or near-complete resolution of skin lesions is attained with zinc treatment alone.<sup>4,5,9,12</sup> Other modalities of treatment like oral amino acid supplementation, topical corticosteroids and intralesional triamcinolone have been tried, but efficacy in skin disease has been minimal.<sup>[1,3,4,5,7,9]</sup>

Treatment of underlying hepatitis C (with interferon-alpha with or without ribavirin) is the definitive treatment and has led to improvement of skin disease in a majority of patients.<sup>[1, 3, 4, 6, 8]</sup>

## CONCLUSION

The incidence of Hepatitis C infection worldwide is rising and NAE is a diagnostic cutaneous marker. Early recognition of NAE is of prime importance to dermatologists as it allows diagnosis of HCV in previously unaware patients and gives way for efficacious treatment.

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**Conflict of Interest:** None

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