Clinical and Histopathologic Findings

A 37-year-old male presented with a history of gradually progressive darkening of dorsa of hands and feet with overlying hyperpigmented plaques since 5 months. It was associated with mild pruritus, and there were no systemic symptoms. On examination, there were well-defined hyperpigmented plaques distributed symmetrically over dorsa of hands and feet with overlying thick adherent scales. A diffuse hyperpigmentation of the surrounding skin was noted extending till lower third of both legs and the metacarpophalangeal joint (MCP) joints of upper limbs [Figure 1a]. No changes were observed in hair, nail, and oral mucosa. Complete Hemogram, urine routine, liver function test, and renal function test were within normal limits. Serology for Hepatitis B, HIV, and ELISA were negative, but Hepatitis C serology was reactive with hepatitis C virus (HCV) Genotype 3 and viral load of 3,050,000 IU/mL. Skin biopsy obtained from one of the plaques revealed hyperkeratotic epidermis with acanthosis, psoriasiform hyperplasia, and hypergranulosis. Dermis had peri-vascular and peri-appendageal inflammatory infiltrate comprising of lymphocytes, macrophages, and melanin incontinence [Figure 2a and b]. The patient was started treatment. A near complete resolution of lesions was seen at the end of 1.5 months of the treatment [Figure 1b].

Question

What is your diagnosis?
**Answer**

Necrolytic acral erythema (NAE).

**Discussion**

Necrolytic acral erythema (NAE) was first described in Egyptian patients as a specific cutaneous manifestation of infection by hepatitis C virus. However, very few cases of seronegative NAE have been reported in literature. Its etiopathogenesis is not known; however, hypo-aminoacidemia, hypoalbuminemia, hyperglucagonemia, and zinc deficiency are considered as probable causes.

Clinically, it is characterized by three stages of evolution: Initial acute stage characterized by scaly, erythematous papules or sometimes by appearance of flaccid blisters and erosions. Fully developed stage shows confluence of erythematous to violaceous lichenified plaques with sharply defined margins surrounded by adherent scales resembling erythrokeratoderma. In late stage, progressive thinning with increased hyperpigmentation is seen. Spontaneous remission or exacerbation may occur during late phase.

Histologically, early stage of NAE resembles nummular dermatitis, manifested as spongiosis and perivascular dermatitis, and lesions in late stages show psoriasiform hyperplasia, hyperkeratosis, parakeratosis, papillomatosis, focal hypergranulosis, pigment incontinence, and inflammatory cells in papillary dermis and necrotic keratinocytes.

NAE shows dramatic response to oral zinc therapy within few weeks of treatment, but the definitive management in patients seropositive for hepatitis C is the treatment of underlying infection. Our patient was started on oral zinc sulphate 200 mg thrice daily along with treatment of hepatitis C. However, the antiviral drugs were started 2 weeks after the zinc therapy. The lesions started showing slight clinical improvement immediately after zinc therapy indicating potential role of zinc in causation of the disease. A near complete resolution of lesions was within 1.5 months of the treatment.

The closest differential diagnosis in our patient is zinc responsive acral dermatitis that is a rare clinical entity distinctive in its clinical, histopathological features and remarkable in showing a significant response to zinc therapy. Clinically, it is characterized by persistent well-defined hyperpigmented, psoriasiform plaques, with occasional rim of erythema, distributed symmetrically over the acral regions of the body mostly over dorsum of feet and hands. These cases were distinctive in their complete lack of response to all modalities of treatment such as topical steroids, tacrolimus, and oral methotrexate. Histologically, it shows hyperkeratosis, focal parakeratosis, hypergranulosis, acanthosis with paler keratinocytes, and intact basal cell layer. The rete ridges shows hyperplasia with sparse infiltrate of lymphocytes and histiocytes in upper dermis and around the blood vessels. Treatment consists of zinc supplementation 0.5-1 mg/kg in divided doses. There are no recommended guidelines for the duration of therapy, and treatment should be tailored for individual patients.

NAE is a rare cutaneous marker for hepatitis C infection. Early diagnosis and treatment of this condition reduces the morbidity and clinical outcomes such as chronic hepatitis, hepatic cirrhosis, and hepatocellular carcinoma.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

**Conflicts of interest**

There are no conflicts of interest.

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