CASE REPORT

Necrolytic Acral Erythema in a hepatitis C negative patient: A Case report

Sadiq Mahdi, MD, AlMutairi A.

Department of Internal Medicine, Salmaniya Medical complex, Manama, Bahrain

ABSTRACT

Necrolytic acral erythema (NAE) is a rare distinctive skin disorder. Most studies report an association of NAE with hepatitis C virus (HCV) infection. It is characterized by its distinguishing acral distribution, psoriasiform skin eruption and histological features. It's etiopathogenesis is not fully understood though hypo amino acidemia, hyperglucagonemia and Zinc deficiency are considered as probable causes. Several small studies and cases have been reported around the world. Nevertheless, it may occur independently without HCV association, as have been reported recently in few cases. We report here a case of Necrolytic Acral Erythema in a 53 years old female with negative hepatitis C marker and abnormal presentation as well.

INTRODUCTION

Necrolytic Acral Erythema (NAE) was first described in Egyptian patients in 1996 by El Darouti and Abu El Ela.[1] NAE has been referred to as a cutaneous marker of hepatitis C infection owing to its strong association with the infection. Necrolytic acral erythema manifests as well-circumscribed, dusky erythematous plaques with adherent scale. Lesions classically have an acral distribution. While the plaques are psoriasiform, they do not manifest an Auspitz sign as be seen in psoriasis. Burning or pruritus may occur with active disease.[2] The etiopathogenesis of NAE is not known yet; hypoaminoacidemia, hypoalbuminemia, hyperglucagonemia, and zinc deficiency are considered probable causes. Hepatocellular dysfunction may result in hypoaminoacidemia and hyperglucangonemia. Hypoaminoacidemia may induce epidermal protein depletion which leads to necrolysis. High serum glucagon level yields greater amount of arachidonic acid and its metabolites, which induce inflammatory changes of NAE.[3] The histological findings are similar to those of necrolytic erythema characterized initially by acanthosis, epidermal spongiosis, and superficial perivascular dermatitis.[4] The differential diagnosis of NAE includes chronic eczema, psoriasis, necrolytic migratory erythema, acrodermatitis enteropathica, and pellagra. This can be differentiated by clinical presentation or histological and laboratory examination. The treatment of NAE is difficult, as it is frequently resistant to most topical and systemic agents. The optimal treatment for necrolytic acral erythema (NAE) involves the treatment of hepatitis with combination therapy of interferon and ribavirin. Patients have been responsive to oral zinc supplementation in several cases.[5]

Correspondence: *Dr. Sadiq Mahdi1, Department of Internal Medicine, Salmaniya Medical complex, Manama, Bahrain*

CASE REPORT

A 53 year old female presented to our clinic with a 10-12 years history of lesions all over her body. The lesions were slightly itchy and sometimes painful. They are slowly growing in size and extended all over different areas. She was diagnosed and treated before as Lichen planus, eczema and psoriasis. She had received topical medication in the form of emollients and topical steroids with minimal improvement. There was no history of significant weight loss or trauma on the affected area. She was otherwise healthy. Her physical examinations were unremarkable. On skin examination we found bilaterally symmetrical well-defined brownish hyperkeratotic plaques with an erythematous rim located on both legs extending to involve the soles as well. Both wrists were affected with the involvement of the palms also. The lesions extended to cover the knees and sporadic affection of the trunk. The scalp, mucous membranes and nails were normal (Fig. 1,2,3,4). We put differential diagnosis of necrolytic migratory erythema, erythrokeratoderma, eczematous dermatitis, lichen planus and psoriasis. Laboratory finding including anti-hepatitis C virus (HCV) antibodies as well as hepatitis B surface antigen and antibody were negative. Her fasting blood sugar was 109 mg/dL and her plasma zinc level was 81 µg/dL (normal 70-120 µg/dL). A bunch biopsy was taken from the leg lesion and revealed parakeratosis and epidermal hyperplasia, focal epidermal necrosis and dyskeratotic cells which was matching with the diagnosis of Necrolytic acral erythema. We started her on oral zinc supplementation, topical steroid combined with salicylic acid and tacrolimus with good response.

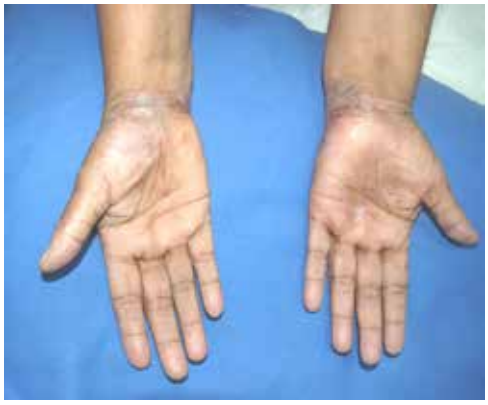

Fig. 1 Scaly brownish lesions located on wrists and palms.

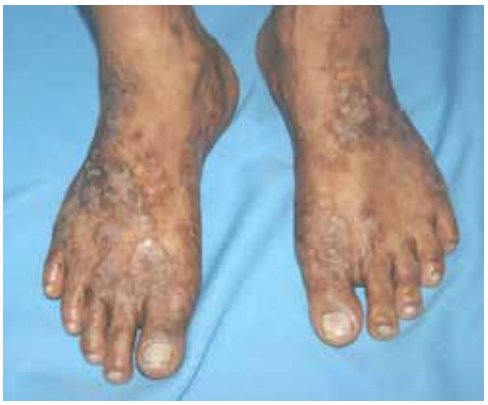

Fig. 2 Dusky red plaques on legs and feet.

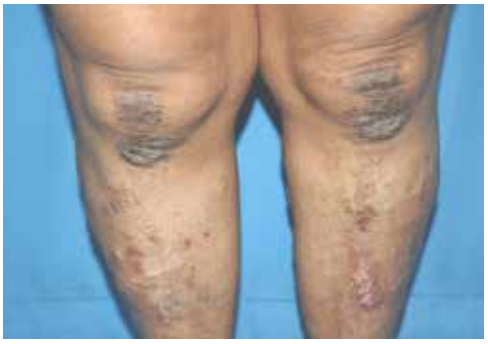

Fig. 3 Multiple reddish brownish macules, papules and plaques on legs and knee.

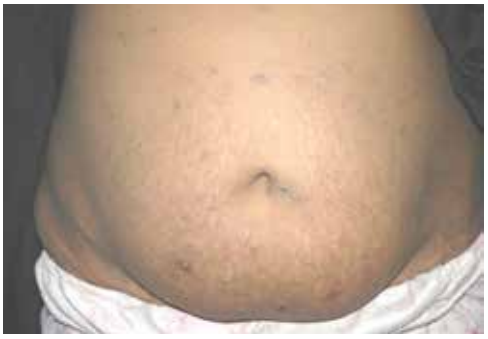

Fig. 4 Scattered lesions over the trunk.

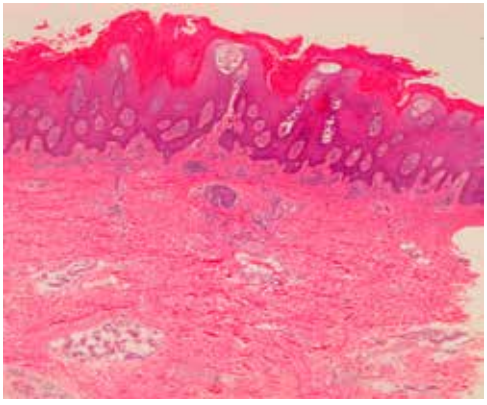

Fig. 5 Parakeratosis and epidermal hyperplasia.

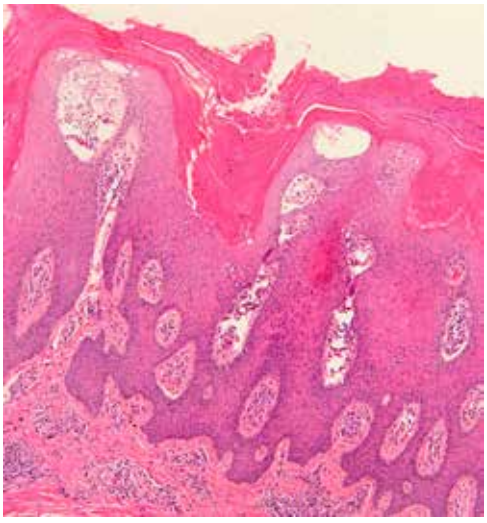

Fig. 6 Parakeratosis, focal epidermal necrosis and dyskeratotic cells.

DISCUSSION

Necrolytic acral erythema (NAE) was first described in 1996 in Egypt as an association with Hepatitis C virus.[1] Some cases of NAE have been reported in the absence of HCV infection.[6,7] In our case, we report a case disseminated NAE and not associated with HCV. The most common NAE locations are the feet, follow by the lower legs, knees, thighs, genitalia, buttocks, and abdomen. Involvement of the upper extremities is generally mild and limited. The head and neck, palms, soles, nails, and mucous membrane are usually spared.

NAE manifests with several stages of involvement. In the initial stage, patients present with scaly erythematous papules or plaques which are deep red to violaceous at the center. Sharply demarcated scaly erythematous to violaceous lichenified plaques can be found in fully developed lesions. Superficial epidermal necrosis is occasionally observed over the dusky portions of the lesion. The pruritic plaque may remain unchanged for months. In the late stage, the lesions become progressively thinner, with some crusting and erosion.

NAE is a chronic relapsing and remitting disease, and spontaneous exacerbation can be expected.[8] As we can saw in our case all these areas were affected in addition to slight affection of the palms and soles.

Pathologically, fully developed NAE exhibits psoriasiform hyperplasia and prominent papillomatosis with parakeratosis, subcorneal pustules, epidermal pallor, and necrotic keratinocytes. Confluent necrosis of the keratinocytes in the upper parts of the epidermis may lead to cleft formation. Vascular ectasia, papillary dermal inflammation, and pigment incontinence are also seen.[4] Presence of foci of epidermal dyskeratosis and pale keratinocytes helps to differentiate NAE from psoriasis. Our patient's histological findings were compatible with necrolytic erythema. She had negative serology for HCV infection and a normal plasma zinc level.

The cause of necrolytic acral erythema (NAE) is uncertain, but a metabolic alteration due to hepatocellular degeneration from hepatitis C infection has been proposed. Many hypotheses describe deficiencies similar to those of the other necrolytic erythemas. Histological features are similar among necrolytic acral erythema and other nutrient deficiencies.

Zinc deficiency has been proposed to play a role in the pathogenesis of necrolytic acral erythema. Moneib et al studied zinc levels in the serum, lesional skin, and perilesional skin of 15 necrolytic acral erythema patients and found that all three were significantly decreased compared with levels in healthy subjects.[9] Low albumin levels have also been postulated as one of the causative factors. Albumin sequesters fatty acids and helps regulate prostaglandin levels. High levels of prostaglandins as a result of low levels of albumin may induce inflammation. Because, albumin is the main carrier of zinc in plasma, these two may be interrelated.[10]

Always keep in mind the differential diagnosis of lichen planus, acrokeratosis paraneoplastica, psoriasis and porphyria cutanea tarda. Hepatitis A, B, and C serologies are the most important tests, because necrolytic acral erythema (NAE) has a high association with hepatitis C. Serum zinc, serum glucagon, and serum amino acid values have been reduced in some reported cases.[11] With therapy, prognosis is fair. Some patients have a relapsing course.

Necrolytic acral erythema (NAE) has no known directly associated morbidly or mortality. Rather, the morbidity and mortality are related to the primary illness, hepatitis C. Treatment is mainly of HCV if present. On review of the literature we noted a case report describing treatment of hepatitis C with sofosbuvir and ledipasvir that resulted in clearance of necrolytic acral erythema from the skin.[12]

The goal of treatment is to decrease the burning and pruritus and improve the appearance of the lesions. Zinc sulfate,[13] amino acid supplementation, and interferon alfa have been successful in treating necrolytic acral erythema (NAE). Topical tacrolimus has been reported as an effective treatment for necrolytic acral erythema.[14] That's what we gave to our patient without interferon with a good response.

In conclusion NAE is a disease due to definite pathogenesis, not usually sticks to HCV. It may be related to abnormal metabolism of albumin and zinc, which needs further investigations.

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