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Case Report

# Acute necrotizing acral erythema associated with hepatitis C: Histopathological dermoscopic correlation

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ABSTRACT

Necrotizing acral erythema (NAE) is a rare disease associated with hepatitis C and is considered as diagnostic marker. Clinical findings are well-circumscribed hyperpigmented papules and thick adherent scaly plaques symmetrically distributed on the dorsum of the foot. From a clinical perspective, NAE shares similarities with other conditions such as necrotizing erythema migrans (NME), enteropathic acrodermatitis (AE), and pellagra. To clearly distinguish NAE from similar conditions, a better understanding of its causes and histopathological features is important. NAE often follows a pattern of worsening and improving symptoms. Dermoscopy is noninvasive and can be an important tool in differentiating NAE from other necrotizing erythema and aids in diagnosis. Oral zinc therapy is the most effective treatment method regardless of HCV infection. Here, we present rare case report of a 46-year-old male patient who presented with clear fluid bullae and surrounding erythema in the lower extremity due to HCV infection with improvement after oral zinc treatment.



## 1. Introduction

Necrotizing acral erythema (NAE) is a rare disease associated with hepatitis C.[1] It has two stages: the acute stage is characterized by erosions, bullae, and erythematous or purple papules. In chronic stage, well defined plaques with erythema, lichenification, secondary pigmentation and thin surface scales form in the marginal layer. Treatment with oral zinc therapy has achieved incredible results.

## 2. Case Report

A 46-year-old chronic alcoholic male patient came to our dermatology department with complaints of edema, numerous blisters with few raw areas on the both leg including feet, for 15 days. Additionally, he had been complaining of yellowing in his eyes and abdominal pain for 15 days. There is no history of similar complaints like before. Skin examination revealed an erythematous ring with abundant clear fluid filled bullae approximately 2x2 to 3x4 $cm^2$ and abundant clear fluid on the lower extremities (Figure 1 a-b). There is also pitting edema in the legs and feet. Yellowing of the sclera is appreciated. Routine blood investigation revealed increased total count, neutrophils, low haemoglobin, elevated serum alkaline phosphatase (ALP), total, direct and indirect bilirubin, C- reactive protein, erythrocyte sedimentation rate (ESR), decreased total protein and albumin. Raised prothrombin and activated partial thromboplastin time. Serological test shows Hepatitis C virus - Positive and HIV – Non reactive. Urine routine microscopy revealed bilirubin 3+++ and protein trace. Histopathological examination revealed acantholytic epidermis with subcorneal blistering, hypergranulosis, acanthosis and neutrophilic exocytosis. Dermoepidermal junction shows small foci of haemorrhage. Dermis

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shows perivascular and periadnexal mixed inflammatory infiltrate (Figure 2b). Dermoscopy revealed white globules, brown globules, reddish brown, red dots, and yellow globules associated with acanthosis, epidermal melanin, red cell extravasation, telangiectasia, and serous dryness, respectively (Figure 2a). Based on clinical, laboratory, dermoscopic and histopathological examination, we reached a diagnosis of necrotizing acral erythema. The patient was treated with 167.86 mg of zinc orally twice a day and topical 2% fusidic acid cream for 2 weeks, and a significant improvement in the lesions was observed (Figure 1c-d).


**Figure 1: a** and **b:** Pre-treatment; **c:** and **d:** Post-treatment

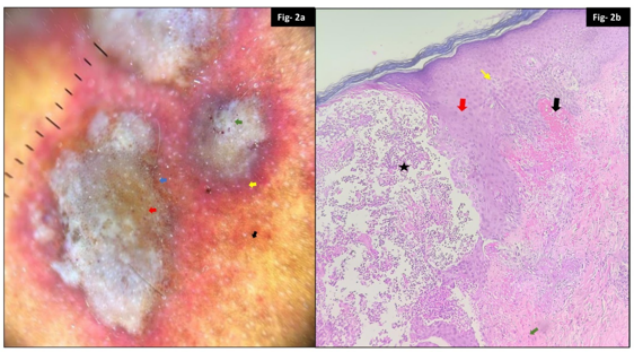


**Figure 2: a:** Dermoscopy showed white globules (green arrow), brown globules (black arrow), reddish-brown areas (yellow arrow), red dots (blue arrow) and yellow globules (red arrow); **b:** Histopathological examination revealed acantholytic epidermis with subcorneal blistering (black star), hypergranulosis (red arrow), spongiosis (yellow arrow), and neutrophilic exocytosis. The dermo-epidermal junction shows small foci of hemorrhage (black arrow). Dermis shows perivascular and peri adnexal mixed inflammatory infiltrate (green arrow).

## 3. Discussion

El Darouti and El Ela first published the definition of necrotizing acral erythema (NAE) in 1996, which is accepted as the diagnosis marker of hepatitis C infection.[2] There is no preference for either gender and age of onset range from 35 to 55 years.[3] Although the pathophysiology is not clear, hypoalbuminemia, hyperammonaemia, hyperglucagonemia, liver dysfunction and low zinc levels are thought to be responsible in this condition. Necrolysis and loss of epidermal proteins result from hyperammonaemia. Prostaglandin production increases with hypoalbuminemia which may contribute to the inflammatory response in NAE.[4] Since albumin is the protein that carries zinc, low albumin will reduce zinc. The degree of liver damage and skin severity are directly related to hepatitis C infection. Hepatitis C genotype and viral load are also important in the pathogenesis of NAE.[5,6] NAE lesions are usually located on the dorsum of the feet and toes; However, the disease can affect the Achilles tendon, legs and knees joint and malleolus with itching, pain, burning sensation and dysesthesia. Dermoscopic findings of NAE often include white and yellow globules as well as scattered red macules at the lesion site. The scales are white with brown spots often appearing around them.[7] The histopathological signs of NAE are acanthosis, epidermal spongiosis, and perivascular dermatitis in the acute stage. Therefore, in addition to the clinical lesions found in our case, dermoscopy and histopathological examination are additionally useful in the diagnosis of NAE. Differential diagnoses include psoriasis, pellagra, eczema, enteropathic acrodermatitis, and necrotizing erythema migrans.[8] Despite a persistent high viral load, treatment with ribavirin and interferon alpha has demonstrated efficacy in improving the condition in patients with hepatitis C infection. The positive clinical outcome, even without zinc deficiency, is associated with zinc's ability to modulate the immune system, combat viruses, reduce inflammation, and act as an antioxidant. Administering oral zinc at a dosage of 220mg twice daily for a duration of up to 8 weeks has proven highly effective in eliminating the lesions.[9] Additional therapeutic alternatives comprise systemic, intralesional, and topical corticosteroids, topical tacrolimus, and phototherapy.

## 4. Conclusion

Necrolytic acral erythema presents as a distinct condition characterized by specific clinical and histopathological features. It is consistently linked to hepatitis C infection and hepatic dysfunction. Oral zinc therapy, combined with antiviral treatment for hepatitis C, serves as the main approach for management. We highlight this case to raise awareness, as there's a risk of overlooking this condition, especially in areas where hepatitis C prevalence is low.

## 5. Source of Funding

None.

## 6. Conflict of Interest

None.

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