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Journal
Dermatology Online Journal, 22(9)

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Publication Date
2016

DOI
10.5070/D3229032507

Volume 22 Number 9
September 2016

Case presentation

Necrolytic migratory erythema associated with fatty liver disease and the psuedoglucagonoma syndrome

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Dermatology Online Journal 22 (9): 12

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Abstract

We report a 48-year-old woman with a past medical history of psoriasis, nonalcoholic steatohepatitis (NASH), and type II diabetes mellitus, who presented to the emergency department with a 1 week history of erosive annular plaques with associated atrophy and telangiectasias on her legs bilaterally, thighs and buttock, histopathologically consistent with necrolytic migratory erythema. Although classically associated with a pancreatic glucagonoma, this patient experienced this figurate erythema in the setting of fatty liver disease with no glucagonoma. The rarity of pseudoglucagonoma syndrome, or necrolytic migratory erythema occurring in the absence of a glucagonoma, warranted the discussion of this case.

Keywords: necrolytic migratory erythema, pseudoglucagonoma syndrome, figurate erythema

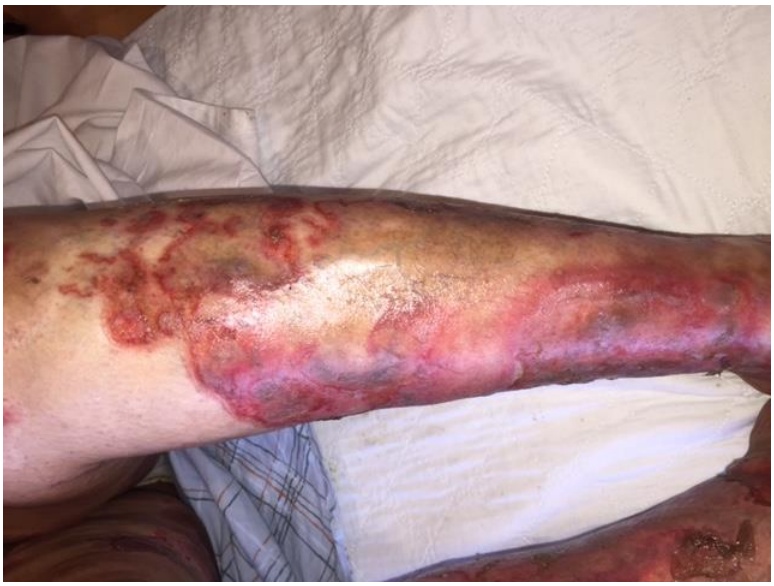

Figure 1. At presentation, the patient was noted to have tender erosive, annular plaques on the distal legs which were characterized by crusting of advancing borders, atrophy and telangiectasias.

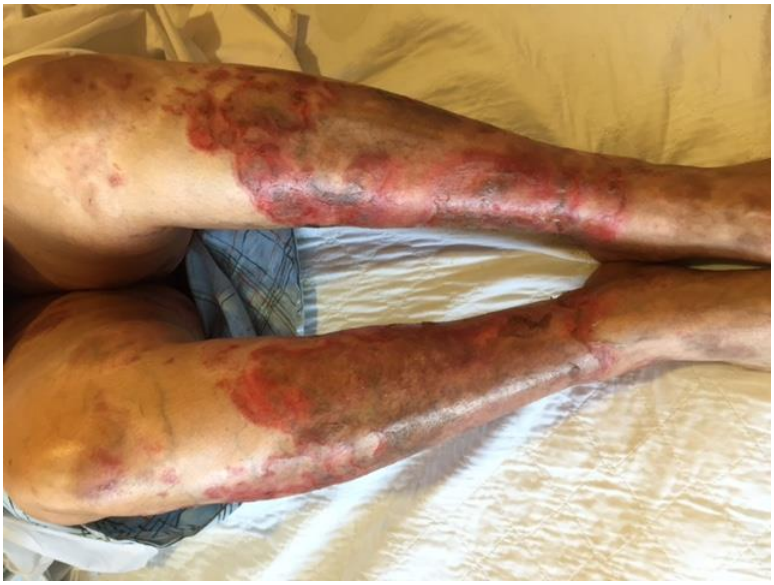

Figure 2.
The patient presented with tender erosive, annular plaques on the distal legs characterized by crusting of advancing borders, atrophy and telangiectasias.

A 48-year-old woman with a past medical history of psoriasis, nonalcoholic steatohepatitis (NASH), and type II diabetes mellitus, presented to the emergency department with a 1 week history of erosive annular plaques with associated atrophy and telangiectasias on her legs bilaterally, thighs, and buttock. The patient was afebrile with normal vital signs; review of systems was negative aside from pain associated with her cutaneous findings. Of note, she had also presented to the same emergency department one year earlier with a similar eruption that was thought to be an atypical psoriasis presentation and was treated with topical steroids and excimer laser therapy.

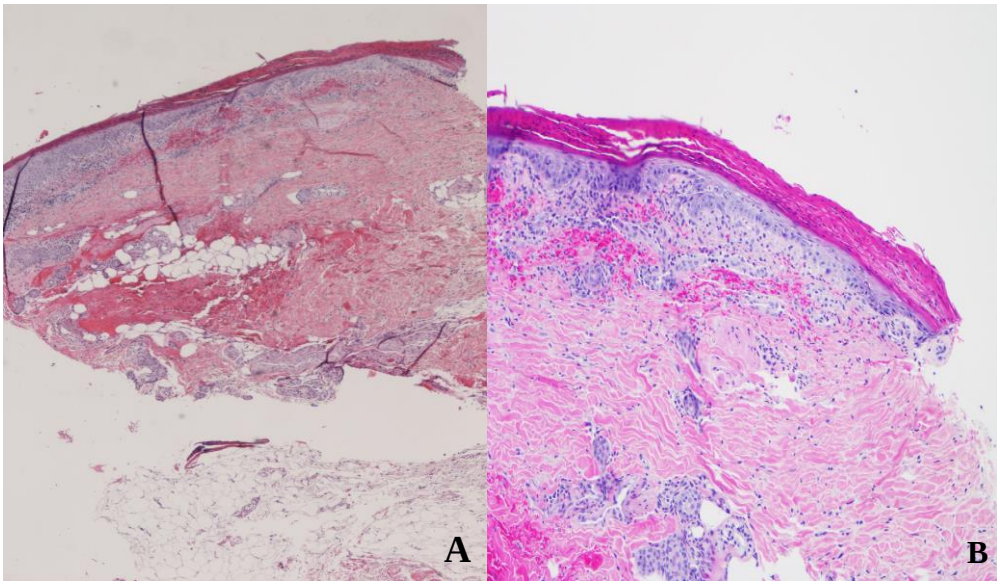

Figure 3A, B. Histopathology from our patient at 10x and 20x

3A. On histopathology, confluent parakeratosis, scattered necrotic keratinocytes and collections of neutrophils were noted in the epidermis.

3B. Marked papillary dermal edema and hyperplasia was noted in addition to collections of neutrophils, parakeratosis and necrotic keratinocytes in the epidermis. Direct immunofluorescence was negative.

The suspected diagnosis of necrolytic migratory erythema (NME) was confirmed via punch biopsy, which revealed confluent parakeratosis with collections of neutrophils and scattered keratinocyte necrosis in superficial epidermis consistent with NME. Direct immunofluorescence was negative. Our patient's laboratory results showed normal glucagon levels, zinc levels, and amino acid levels with only a mild reduction in histidine. An abdominal CT scan showed no evidence of a glucagonoma.

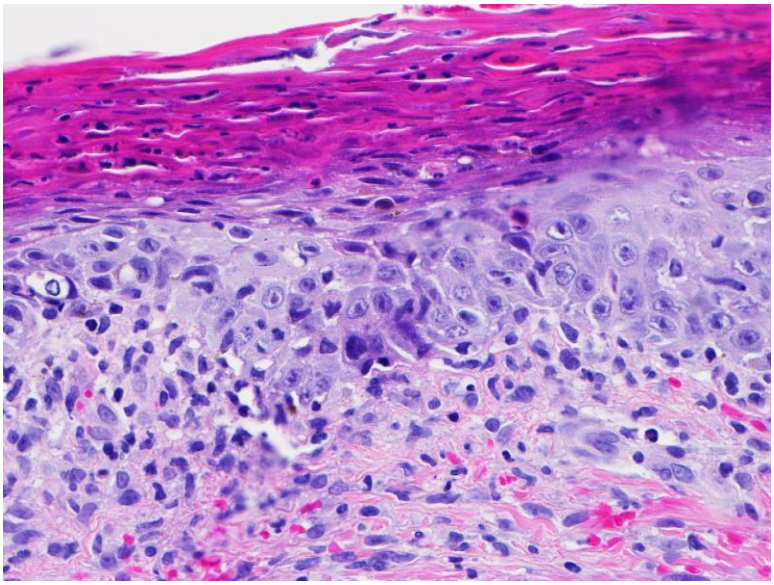

Figure 4. Histopathology from our patient at 40x

We believe the diagnosis was most consistent with pseudoglucagonoma syndrome secondary to liver disease (reflected by the elevated liver function tests and a history of NASH). Additional case reports have described various liver diseases including hemochromatosis as well as alcoholic cirrhosis associated with pseudoglucagonoma. After 4-week follow up, the patient had complete resolution of the eruption.

NME is a cutaneous finding most often considered a paraneoplastic manifestation of a pancreatic glucagonoma (a glucagon-secreting tumor of pancreatic alpha cells). The term necrolytic migratory erythema, was first coined by Dr. DS Wilkinson [1] in 1973 to describe a transient, painful, and psoriasiform eruption found in approximately 70% of patients with a glucagonoma [2]. Glucagonoma syndrome is overall a rare disease process that is not frequently encountered. In 38-75% of cases of glucagonoma, patients present with concomitant diabetes mellitus [3]. Other common manifestations of the glucagonoma syndrome include glossitis, weight loss, diarrhea and venous thrombosis.

A distinct entity, NME occuring in the absence of a pancreatic glucagonoma is known as the pseudoglucagonoma syndrome. Whereas the pathogenesis of NME in pseudoglucagonoma syndrome remains unknown, it has been reported in the literature to be associated with liver disease, such as cirrhosis and hepatitis, inflammatory bowel disease, pancreatitis, nutritional deficiencies, and celiac disease. Less commonly, conditions like heroin abuse and odontogenic abscess have also been associated with pseudoglucagonoma syndrome [4].

Clinically, NME can present as a figurate erythema with flaccid bullae that later rupture leaving erosions and scale. The mucous membranes may also be involved, presenting as angular cheilitis, glossitis, and stomatitis. To prevent recurrence, management is typically aimed at treatment of the underlying cause. In NME associated with a glucaganoma, identification of the mass through imaging and ultimately surgical removal is performed [5]. Treatments for pseudoglucagonoma have been aimed at nutritional replacement with zinc, amino acids and fatty acids [6].

The pathogenesis of NME is multifactorial and may be related to nutritional deficiencies in zinc, amino acids or fatty acids, elevated glucagon levels, and liver disease. It is speculated that hyperglucagonemia may produce NME by either changing the levels of amino acids or by increasing epidermal levels of arachidonic acid [7]. When NME occurs in the absence of a glucagonoma, the pathogenesis is less clear. It has been hypothesized that liver disease can increase glucagon levels in the blood due to a decrease in liver degradation of the peptide mimicking the heightened glucagon concentrations seen with a glucagonoma [8].

Diagnosis of NME is made by clinicalpathologic correlation. Histopathological findings of NME typically demonstrate psoriasiform hyperplasia with parakeratosis, pallor of the superficial epidermis with or with necrosis of keratinocytes. Neutrophils may also be seen in the upper dermis. When NME is suspected, laboratory tests should include serum levels of glucagon, amino acids, zinc, and essential fatty acids. To assess for underlying diabetes mellitus, a glucose tolerance test and hemoglobin A1c should be ordered. The differential diagnosis of NME includes other nutritional deficiencies including acrodermatitis enteropathica, subacute cutaneous lupus erythematous, and immunobullous diseases like pemphigus vulgaris.

In conclusion, we report a woman with necrolytic migratory erythema secondary to underlying hepatic disease. The pathogenesis of this is condition is most likely multi-factorial and requires more research. Although classically associated with glucagonoma syndrome, NME has also been associated with a host of other conditions, such as hepatic disease and nutritional deficiencies.

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