

## CASE REPORT

# A Rare Case of Pseudoglucagonoma Syndrome Masquerading as Necrolytic Migratory Erythema

Nikita, Siba Prasad Dalai, Samir Sahu, Aswini Kumar Sahoo

## Abstract

Necrolytic migratory erythema (NME) is pathognomonic of glucagonoma syndrome associated with pancreatic neoplasm. Pseudoglucagonoma syndrome, which is extremely rare, refers to NME without a glucagon-secreting tumor. We describe a rare case of NME in a 45-year-old female who presented with a skin rash associated with scaling, cheilitis, glossitis, hair loss, and weight loss. Serum glucagon and serum zinc levels were normal. Skin biopsy was suggestive of necrolytic erythema migrans. Ultrasonography (USG) and computed tomography (CT) of the abdomen showed chronic pancreatitis. Resolution of lesions was observed with topical steroids, emollients, intravenous (IV) protein infusions, and other supplements.

## Keywords

Pseudoglucagonoma, Necrolytic migratory erythema, Glucagon secreting tumor

## Introduction

Necrolytic migratory erythema (NME) is a characteristic skin rash often associated with glucagonoma, an alpha-cell tumor of the pancreatic islets. It is usually seen as a part of the glucagonoma syndrome, a paraneoplastic syndrome. NME is also rarely seen as a part of other clinical entities, such as liver disease and intestinal malabsorption, called the pseudoglucagonoma syndrome. The condition is frequently misdiagnosed due to its rarity and often the presenting symptom of glucagonoma.<sup>[1]</sup>

## Case Presentation

A 48-year-old female patient presented with a complaint of low-grade fever for the last 1 year. She developed erythematous papulosquamous rash over both thighs, legs, and feet, followed by a flexor aspect of both arms and hands for the last 6 months, which remitted and relapsed (*Fig 1*). The rash was associated with itching and swelling of both the legs and left hand. There was a significant history of loss of appetite, loss of weight, and

cheilitis with diffuse, non-scarring alopecia. She also complained of repeated episodes of vomiting for the last three months, associated with steatorrhea. There was no history of abdominal pain or loose stools. She denied any history of diabetes, tuberculosis, or a family history of any chronic illness. She visited multiple local practitioners who have been diagnosing skin lesions to be fungal or bacterial, prescribing antifungals and antibacterials, which showed no improvement.

The patient had a BMI of 17.31 Kg/m<sup>2</sup>. On examination, there was pallor and bilateral pitting pedal edema with no lymphadenopathy. Per-abdomen examination was soft non-tender without organomegaly.

On laboratory investigation, Hemoglobin was 7.4 mg/dl, total leucocyte count was 11,260 cells/ $\mu$ l, and total platelet count was 1,96,000 cells/ $\mu$ l. Peripheral smear showed macrocytes with hyper-segmented neutrophils. Blood glucose levels, Fasting lipid profile, and Liver function

PG Department of Medicine, IMS & SUM Hospital, Bhubaneswar, Odisha, India

Correspondence to: Dr. Siba Prasad Dalai, Associate Professor, PG Department of Medicine, IMS & SUM Hospital, Bhubaneswar, Odisha

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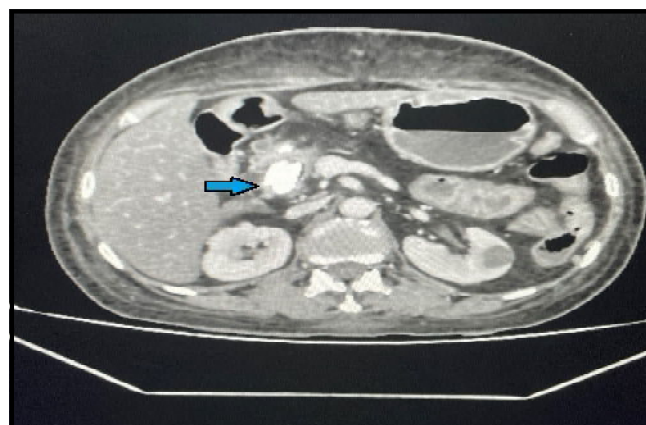
tests were normal. Serum amylase and lipase levels were 47 U/L and 64 U/L, respectively. Serum calcium was 7.17 mg/dl. Serum Vitamin B12 levels were >2000pg/ml (Normal range- 197-816pg/ml). Serum glucagon levels were 63pg/ml (50-200pg/ml), and serum zinc was 93µg/dl.

Upper gastrointestinal endoscopy showed antral erosions. Ultrasonography (abdomen and pelvis) showed fatty liver, atrophic pancreatic parenchyma with dilated main pancreatic duct (8.5mm) with multiple intraductal and pancreatic parenchymal calcific foci suggestive of chronic calcific pancreatitis (CCP). Contrast-enhanced computed tomography (CECT) abdomen showed atrophic pancreatic parenchyma with multiple intraparenchymal and ductal calcification; the largest calculus measuring 36×14 mm in the pancreatic head within the duct, dilated main pancreatic duct with side branches (maximum diameter 8.7 mm) with no obvious surrounding fat stranding, collection, postcontrast enhancement or focal lesions (Fig 2). Skin biopsy showed moderately dense, superficial, perivascular mixed infiltration of lymphocytes and neutrophils with mild ballooning of the upper epidermis. The keratinocytes in the upper dermis showed pink staining of cytoplasm and darkly stained small nuclei suggestive of pyknosis. These findings pointed towards NME. (Fig 3).

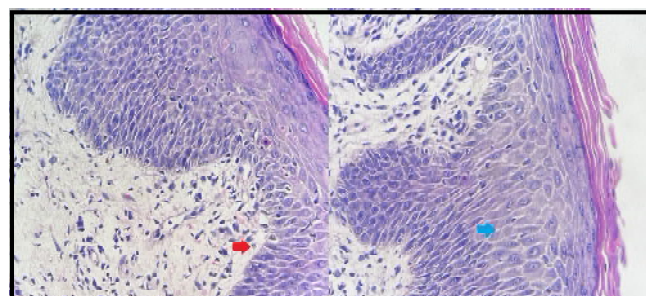
Based on clinical, laboratory, radiological, and histopathological findings, the diagnosis of pseudoglucagonoma syndrome secondary to chronic calcific pancreatitis was considered. The patient was treated with topical steroids, emollients, zinc for skin lesions, pancreatic enzyme supplements, vitamins, and intravenous protein supplements for chronic calcific pancreatitis. Skin lesions resolved over the next 14 days, and she was subsequently discharged (Fig 4). The patient was followed up for 3 months and had no recurrence of skin lesions.



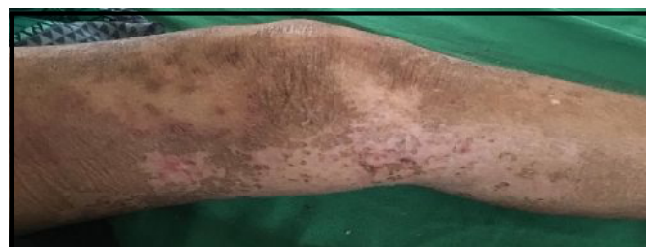
**Fig 1. Papulo-squamous and erythematous rash and swelling over affected areas**



**Fig 2. CECT abdomen showing pancreatic calculi (blue arrow)**



**Fig 3. Skin biopsy showing superficial, moderately dense, perivascular mixed infiltrate of lymphocytes and neutrophils with mild ballooning of upper epidermis (red arrow) and keratinocytes in the upper dermis with darkly stained small nuclei suggestive of pyknosis (blue arrow)**



**Fig 4. Resolution of the skin lesions after treatment**

### Discussion

Pseudoglucagonoma syndrome refers to NME in the absence of glucagon-secreting tumor that characterizes glucagonoma syndrome. This may occur in pancreatitis, gastrointestinal disorders like inflammatory bowel disease, iatrogenic causes, and odontogenic abscesses.<sup>[2]</sup> NME typically presents as waves of irregular erythema followed by erosions and crusting. Initially, a pinkish maculopapular rash with irregular edges and arcuate or polycyclic patternis observed. Sometimes, there is the formation of flaccid bullae that rupture easily, forming crusts, while

new vesicles continue to develop along the edges.<sup>[3]</sup> The progression would be confluent, annular, pruritic, and painful plaques, waxing and waning course, developing in friction areas involving the perineum, groin, buttocks, lower abdomen, and lower limbs.<sup>[4]</sup> Glossitis, cheilitis, and stomatitis are common mucosal findings.

NME usually occurs in pancreatic neoplasm glucagonoma with very high serum glucagon levels. However, cases of NME with normal glucagon levels have been reported in celiac sprue and pancreatitis. One of the underlying mediators proposed is enteroglucagon, a substance produced by the crypt cells of the small intestine. In the malabsorptive states, unabsorbed nutrients are present in the lumen, which release enteroglucagon, which can cause NME by an undetermined mechanism.<sup>[5]</sup>

Some patients are misdiagnosed as having chronic candidiasis and usually report with prior treatment with antibiotics and antifungal agents without improvement before a conclusive diagnosis is reached. Only a few cases of NME without glucagonoma have been reported in the literature. A case of NME was reported in a heroin-dependent patient.<sup>[6]</sup> Iatrogenic etiology leading to NME has been documented<sup>[7]</sup>, and another case due to zinc deficiency has been reported earlier.<sup>[8]</sup> Rare associations between NME and non-glucagon-secreting tumors have been reported, leading to pseudoglucagonoma syndromes, such as small-cell lung cancer, liver cancer, insulin-secreting tumors, and duodenal neoplasms. Only two cases of NME were recently reported with acute pancreatitis and alcoholic etiology.<sup>[9]</sup>

Our case, with a chronic history of skin lesions misdiagnosed as fungal lesions by multiple local practitioners, was treated with antifungals and over-the-counter topical applications without resolution. Dermatitis could be resolved only after proper pathology identification and treatment of the underlying etiology. Skin biopsy showed mixed infiltrates in the upper epidermis with parakeratosis and pyknotic changes. CECT revealed multiple pancreatic calculi, pathognomonic of chronic calcific pancreatitis leading to the diagnosis of NME secondary to chronic pancreatitis, hence diagnosed as pseudoglucagonoma syndrome.

NME associated with glucagonomas has a rapid rash resolution following surgical resection of the tumor. Pseudoglucagonoma syndrome has a protracted course as the underlying factors, such as pancreatitis, are almost irreversible, and treatment should be directed toward the underlying condition. As malnutrition seems common in pseudoglucagonoma syndrome, nutritional repletion with zinc, amino acids, and essential fatty acids can be considered. Supplementation with essential amino

acids (EAA), zinc, and essential fatty acids (EFA) improved NME in some patients.<sup>[10]</sup>

### Conclusion

NME is a rare dermatosis that raises suspicion of glucagonomas; however, in the absence of a tumor, the diagnosis of pseudoglucagonoma syndrome should be considered. Hence, our case raises the necessity of a thorough understanding of the course of illness with evaluation of different systems involved for the identification of pathology and for delineating the underlying etiology- pancreatitis and liver and GI disorders apart from glucagonoma in cases of NME.

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### Conflicts of Interest

There are no conflicts of interest.

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