

## Case Report

# Necrolytic migratory erythema presenting with annular erosive patches over gastrostomy site

## 壞死鬆解性遊走性紅斑於胃造口手術部位呈環型糜爛性斑片疹

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A 75-year-old gentleman presented with annular erythematous patches with erosions and crusting at the periphery. The annular lesions coalesced to form a geographical pattern involving eighty percent of the body surface. Skin biopsy showed characteristic features of necrolytic migratory erythema.

75 歲男患者，出現環型紅色斑片疹，其四週有糜爛及結痂。此環型病損融合成地圖狀，累及體表八成面積。皮膚活組織檢查顯示壞死鬆解性遊走性紅斑的特徵。

**Keywords:** Glucagonoma, hyperglucagonaemia, necrolytic migratory erythema

**關鍵詞：**胰高血糖素瘤，高血糖素血症，壞死鬆解性遊走性紅斑

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## Introduction

Necrolytic migratory erythema (NME) is the cutaneous reaction pattern of hyperglucagonaemia. It is classically associated with pancreatic glucagonoma. The diagnosis is based on the

characteristic clinicopathological features. Zinc deficiency should be ruled out as it shares similar clinical features.

## Case report

A 75-year-old gentleman presented with itchy and weepy rash over whole body for 2 months. He was an ex-smoker and had a history of stroke, ischaemic heart disease and chronic obstructive pulmonary disease with regular follow-up at a medical clinic for over 20 years. He suffered from cancer of the larynx in 1996 which had been successfully treated with radiotherapy. However, he suffered from recurrent aspiration pneumonia due to poor coordination of swallowing after radiotherapy

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necessitating the insertion of a gastrostomy tube for feeding. He was chair-bound with limited mobility.

The skin lesions started initially as erythematous patches over the peri-gastrostomy area, and gradually progressed to blister formation over the next week. Erosions, weeping and crusting appeared after the blisters ruptured. The involvement extended to the whole trunk, limbs, perineum and face over two months. The individual patches extended centrifugally in an annular configuration with post-inflammatory hyperpigmentation in the centre and weeping erosions and crusting at the periphery. The annular lesions coalesced to form a geographical pattern involving as much as eighty percent of the body surface area (Figures 1 and 2).

Wound swab was negative for bacterial culture and skin scrapings were negative for fungal elements. Blood tests for complete blood count, fasting glucose, renal and liver function were unremarkable except for a low albumin level of 24 g/l. The anti-nuclear antibody and anti-skin antibody were both negative. The serum zinc level was on the low side: 8.5  $\mu\text{mol/L}$  (normal range: 9.4-18.4  $\mu\text{mol/L}$ ).

The clinical differential diagnoses included necrolytic migratory erythema, acquired zinc deficiency, drug eruption and pemphigus foliaceus.

A skin biopsy for histological examination was performed over one of the established lesions over the trunk. The histological features were shown in Figures 3 & 4. The epidermis was acanthotic and necrotic with cellular pyknosis. The Malpighian layer showed cellular pallor and ballooning. There were also clefts between the pale epidermis and necrotic cells. There was perivascular lymphocytic infiltrate in the dermis. Immunofluorescence study was negative.

Overall, the clinicopathological features were highly suggestive of necrolytic migratory erythema.

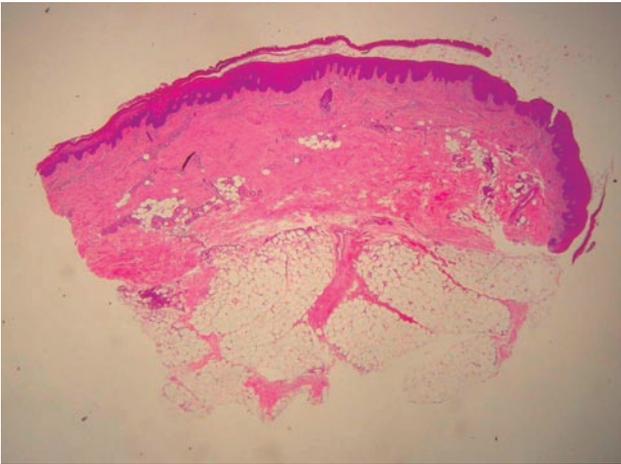
An abdominal ultrasound was unremarkable, while doppler ultrasonography of the lower limbs revealed no evidence of deep vein thrombosis. Serum glucagon level was not available at the local laboratory.



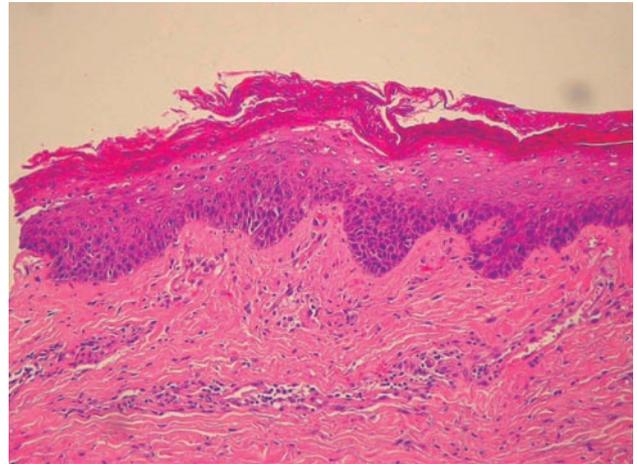
**Figure 1.** Annular erythematous erosive patches over trunk and limbs.



**Figure 2.** Annular erythematous erosive patches over the pubic, groin and perineal area.



**Figure 3.** This biopsy shows intraepidermal vesiculation and underlying psoriasiform epidermal changes. (H&E, Original magnification x 20)



**Figure 4.** High power shows epidermal pallor with cytoplasmic ballooning and vacuolation as well as confluent parakeratotic necrosis of upper epidermis. (H&E, Original magnification x 100)

The condition of the patient gradually deteriorated. He developed generalised oedema with severe hypoalbuminaemia. The patient died of pneumonia six months after the initial onset of the skin lesions.

## Discussion

Necrolytic migratory erythema is the cutaneous reaction pattern of hyperglucagonaemia. It was first described by Becker et al.<sup>1</sup> It is classically associated with pancreatic glucagonoma.<sup>2</sup> It is also associated with pancreatic insufficiency, internal causes of malabsorption, cirrhosis and ectopic glucagon secreting tumours such as bronchogenic carcinoma and nasopharyngeal carcinoma.<sup>3</sup>

Most of the symptoms and signs can be attributed to the metabolic effects of excess glucagon. Amino acid levels are depressed as a result of glucagon stimulating consumption of amino acid substrates for gluconeogenesis and increasing amino acid oxidation.<sup>4</sup>

Epidermal protein deficiency and consequent necrolysis ensue as a result of insufficient amino acids. Excess glucagon also increases the cutaneous levels of arachidonic acid, which increases downstream inflammatory mediators such as prostaglandin and leukotrienes, which perpetuate the cutaneous inflammation.

The skin lesions of necrolytic migratory erythema are polymorphous, but erosions and crusts are usually apparent. Primary lesions include erythematous macules or patches which progress to plaques that may develop central blister formation. The blisters may erode rapidly and form crusts. The erythematous and eroded annular patches and plaques coalesce into large geographic areas. The eruption disappears and reappears spontaneously over a course of weeks. The distribution of necrolytic migratory erythema is characteristic and includes the intertriginous areas (groin, perineum, buttocks, lower abdomen), the central face (especially periorally) and the distal extremities. Mucosal involvement manifests as angular cheilitis, atrophic glossitis and stomatitis.<sup>5</sup>

Pruritus and pain are common cutaneous symptoms. Weight loss is the most common presenting systemic feature. Other systemic features include sore mouth, diarrhoea, weakness, mental status changes and diabetes mellitus.

The serum glucagon level, if available, is usually grossly elevated with a value over 1000 pg/mL (normal range 50 to 150 pg/mL). Most patients have hyperglycaemia and a normochromic normocytic anaemia. The serum zinc level may be on the low side, but not to the degree of zinc deficiency, which is usually lower than 7  $\mu\text{mol/L}$  (normal range: 9.4-18.4  $\mu\text{mol/L}$ ). Acquired zinc deficiency should be ruled out as it shares similar cutaneous features.<sup>6</sup>

The characteristic histological feature of NME is the well demarcated necrosis of the outer layers in the Malpighian stratum. Early lesions may demonstrate dyskeratotic dermatitis with superficial perivascular inflammation in the dermis and minor spongiosis and dyskeratotic epidermal cells.<sup>7</sup> Chronic lesions also show a psoriasiform dermatitis with parakeratosis and loss of the granular layer.

Treatment of the underlying disease is the mainstay of management. For patients with glucagonoma, resection of the tumour is the treatment of choice. Unfortunately, by the time of diagnosis, such tumours are frequently large and have already metastasised in most cases. The results of chemotherapy have been disappointing. Measures to correct nutritional deficiencies and glucagon levels may provide

symptomatic relief. The intravenous somatostatin analogue, being a glucagon antagonist, has been shown to improve the cutaneous symptoms of the syndrome.<sup>8</sup> Supplementation to correct zinc, amino acid, or fatty acid deficiencies has been reported to be beneficial in a case series.<sup>9</sup>

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