Journal of Endocrinology, Metabolism and Diabetes of South Africa 2020; 25(3):80–81
https://doi.org/10.1080/16089677.2020.1793487

JEMDSA
ISSN 1608-9677 EISSN 2220-1009

CASE REPORT

Necrotising migratory erythema leading to the diagnosis of a metastatic glucagonoma without diabetes

Rahm Makan* **and Cloete Van Vuuren**

Department of Health Sciences, University of the Free State, Bloemfontein, South Africa
**Correspondence: rahm@live.co.za*

A case of necrotising migratory erythema (NME), which is one of the distinctive paraneoplastic skin manifestations associated with the glucagonoma syndrome, is described and discussed. In 80% of all patients with glucagonoma, NME is the first clinical sign. The glucagonoma syndrome is a constellation of clinical features: NME, weight loss, anaemia, diabetes, diarrhoea, thromboembolism and neuropsychiatric symptoms. The global incidence of glucagonoma is one in 20 million people per year. The male to female ratio is 0.8:1 with the mean age of diagnosis being 52.2 years. The median time in relation to the initial onset of symptoms and the correct diagnosis is 3.5 years. The 10-year survival rate in patients with metastatic disease is 51.6% and without metastatic disease 64.3%. SPECT scan has a sensitivity range of 67–100% for detecting neuroendocrine tumours. Differential diagnoses of other skin conditions that mimic NME are: bullous pemphigoid, vasculitis, acrodermatitis enteropathica, chronic mucocutaneous candidiasis, seborrhoeic dermatitis, contact dermatitis, pellagra, inflammatory bowel disease, liver cirrhosis, coeliac disease, chemical burns, eczema, herpes etc. A satisfactory response to somatostatin as medical therapy in a case-study patient with metastatic disease is reported.

Keywords: dermatitis, diarrhoea, glucagon, groin, neuroendocrine, octreotide, pancreas, pulmonary embolus, rash, skin, somatostatin, SPECT, venous thromboembolism, zinc

A 54-year-old woman presented with a four-month history of a diffuse skin rash, which did not respond to oral corticosteroids prescribed by a dermatologist. She also complained of diarrhoea, loss of appetite and weight loss of 39 kg over a year. She had a 27 pack/year smoking history, and was on thyroid hormone replacement therapy. There was no significant family history of any medical conditions.

She had an erythematous, scaly skin rash with areas of crusting, distributed on her sub-mammary folds, anterior surfaces of her upper and lower limbs, abdomen and groin with areas of healing skin lesions characterised by brownish-bronze hyperpigmentation (Figure 1). Her mucosal surfaces were dry and she had conjunctival pallor. She had normal blood glucose but was anaemic with a haemoglobin of 10.7 g/dl.

On abdominal computerised tomography (CT) scan there was a large heterogeneous mass in the liver and multiple sclerotic lesions in vertebrae, pelvis and proximal femurs in keeping with metastatic foci. Single photon emission computerised tomography (SPECT) with Octreoscan™ (octreotide uptake scan) had focal increased areas of uptake in the head of the pancreas consistent with a glucagonoma and increased uptake in the liver, as well as skeletal metastases. The immunohistochemical stains on liver biopsy showed metastatic neuroendocrine tumour cells. Confirmation using a monoclonal antibody stain specifically for glucagon confirmed a glucagonoma. Serum glucagon levels were unavailable at the laboratory.

Our diagnosis was a metastatic glucagonoma presenting with necrotising migratory erythema (NME).

NME is a cutaneous, paraneoplastic manifestation due to long-standing high glucagon levels[1] causing diarrhoea as well as malabsorption with deficiency of zinc and other essential fatty acids and minerals.[2,3] Excess glucagon leads to increased arachidonic acid formation in the skin.[1] Friction in the intertriginous areas causes activation of the inflammatory cascade.[1] A differential diagnosis includes: bullous pemphigoid, vasculitis, acrodermatitis enteropathica, chronic mucocutaneous candidiasis, seborrhoeic dermatitis, contact dermatitis, pellagra, inflammatory bowel disease, liver cirrhosis, coeliac disease, chemical burns, eczema, herpes, etc.[4]

The global incidence of glucagonoma is one in 20 million people per year.[5] A functional glucagonoma presents with a glucagonoma syndrome: NME, weight loss, anaemia and diabetes;[6] however, all features may not be present concomitantly. Additional clinical features may include diarrhoea, thromboembolism and neuropsychiatric symptoms.

Our patient was treated with zinc (50 mg eight hourly per os) and dietary protein supplementation (Fresubin®) on which the skin improved. She was then started on intramuscular octreotide injections (Sandostatin® LAR 20 mg IMI monthly).

At the initial follow-up, random glucose was still normal; the skin rash and diarrhoea had resolved. Follow-up SPECT was done at 12 months (no progression), 18 months (no progression) and two years (evidence of progression). Eighteen months after diagnosis the patient presented with a pulmonary embolus, confirmed by CT pulmonary angiogram.

With this case presentation, we wish to highlight NME as a paraneoplastic phenomenon of a functional glucagonoma that presented without diabetes. Prophylactic anticoagulation should be considered once the diagnosis of glucagonoma has been confirmed, due to the increased risk and the high mortality

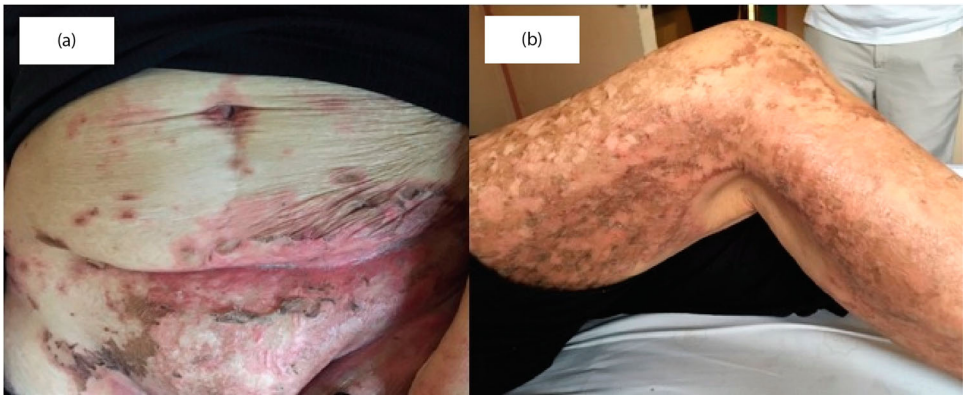

Figure 1. Image on the left shows clinical appearance of necrotising migratory erythema (NME) involving abdomen and groin, image on the right shows NME involving the lower limb.

associated with pulmonary embolism. Although patients diagnosed before the onset of metastatic disease may be cured surgically, medical therapy can still offer a good quality of life in the event of metastatic disease, as demonstrated in this case.

Disclosure statement – No potential conflict of interest was reported by the author(s).

ORCID

Cloete Van Vuuren http://orcid.org/0000-0002-9095-0039

References

1. Mullans EA, Cohen PR. Iatrogenic necrolytic migratory erythema: a case report and review of nonglucagonoma-associated necrolytic migratory erythema. *J Am Acad Dermatol*. 1998;38(5 II):866–73.
2. Tremblay C, Marcil I. Necrolytic migratory erythema: a forgotten paraneoplastic condition. *J Cutan Med Surg*. 2017;21(6):559–61.
3. Teixeira RC, Nico MMS, Ghideti AC. Necrolytic migratory erythema associated with glucagonoma: a report of 2 cases. *Clinics*. 2008;63(2):267–70.
4. Stacpoole PW. The glucagonoma syndrome: clinical features, diagnosis, and treatment. *Endocr Rev*. 1981;2(3):347–61.
5. Al-Faouri A, Ajarma K, Alghazawi S, et al. Glucagonoma and glucagonoma syndrome: a case report with review of recent advances in management. *Case Rep Surg*. 2016;2016(Figure 4):1484089.
6. Remes-Troche JM, García-de-Acevedo B, Zuñiga-Varga J, et al. Necrolytic migratory erythema: a cutaneous clue to glucagonoma syndrome. *J Eur Acad Dermatol Venereol*. 2004;18(5):591–5.

Received: 22-04-2020 Accepted: 6-07-2020