Portuguese Journal of Dermatology and Venereology

PERMANYER

Check for updates

Port J Dermatol and Venereol.

CASE REPORT

Zinc supplementation possibly resolving pancreatic metastatic tumor-associated necrolytic migratory erythema. A new therapeutic approach?

Resolução de eritema necrolítico migratório associado a tumor pancreático após suplementação com zinco. Uma nova arma terapêutica?

Ana L. Matos[a], Duarte Flor, Rebeca Calado, and José C. Cardoso*

Department of Dermatology, Coimbra University Hospital Center, Coimbra, Portugal
ORCID: [a]0000-0003-1441-0601

Abstract

Necrolytic migratory erythema (NME) is a rare skin disease typically associated with glucagonoma syndrome, although it can be associated with other non-tumoral diseases. We present the case of a 71-year-old man with a pancreatic neuroendocrine tumor diagnosed with ENM. Although zinc levels were normal, after zinc oral supplementation, there was complete resolution of NME lesions that persisted even after chemotherapy with concomitant somatostatin analog therapy. This has already, although rarely, been reported. NME pathogenesis is not yet fully understood. Hyperglucagonemia contributes to the dysfunction of the epidermis but its pathogenesis most likely results from numerous aspects including hypoaminoacidemia or zinc and essential fatty acids deficiency.

Keywords: Paraneoplastic syndromes. Necrolytic migratory erythema. Zinc. Therapeutics. Pancreatic diseases.

Resumo

O eritema necrolítico migratório (ENM) é uma doença cutânea rara, tipicamente associada à síndrome do glucagonoma, embora possa associar-se a outras doenças não tumorais. Apresenta-se o caso de um homem de 71 anos com um tumor neuroendócrino pancreático que foi diagnosticado com ENM. Verificou-se resolução completa das lesões de ENM após suplementação oral com zinco, que haviam persistido mesmo após quimioterapia e terapêutica com análogo da somatostatina. Tal foi já ocasionalmente reportado. A fisiopatologia do ENM não é inteiramente compreendida. A hiperglucagonémia contribui para a disfunção da epiderme mas a sua patogénese é, provalvemente, multifatorial, incluindo determinantes como a hipoaminoacidémia ou a deficiência de zinco e ácidos gordos essenciais.

Palavras-chave: Síndromes paraneoplásicas. Eritema necrolítico migratório. Zinco. Terapêuticas. Doenças pancreáticas.

***Correspondence:**
Ana L. Matos
E-mail: ana.luisa.rodrigues.matos@gmail.com

Received: 15-08-2023
Accepted: 02-11-2023
DOI: 10.24875/PJDV.23000068

Available online: 20-12-2023
Port J Dermatol and Venereol. 2024;82(1):54-56
www.portuguesejournalofdermatology.com

2795-501X / © 2023 Portuguese Society of Dermatology and Venereology. Published by Permanyer. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Introduction

Necrolytic migratory erythema (NME) is a rare skin disease typically associated with the glucagonoma syndrome, although it can be associated with other non-tumoral diseases such as nutritional deficiencies, chronic pancreatitis, or inflammatory bowel disease[1]. Glucagonomas are exceptionally rare tumors of the pancreatic alpha-cells, and their syndromic presentation includes NME, glossitis, cheilitis, venous thrombosis, diabetes mellitus, anemia, anorexia, and neuropsychiatric disorders[2]. NME treatment is closely related to oncologic treatment, with most cases showing improvement after successful tumor surgery, somatostatin analog therapy, or chemotherapy, in parallel with decreasing levels of glucagon or neuroendocrine markers[1,3,4].

Clinical case

A 71-year-old man, with no other relevant medical history, was diagnosed with a stage II pancreatic neuroendocrine tumor. A few months after surgery, a positron emission tomography-computed tomography (CT) scan showed hepatic metastasis and suggested a local relapse of the primary tumor, later confirmed by hepatic magnetic resonance and thoraco-abdominopelvic CT

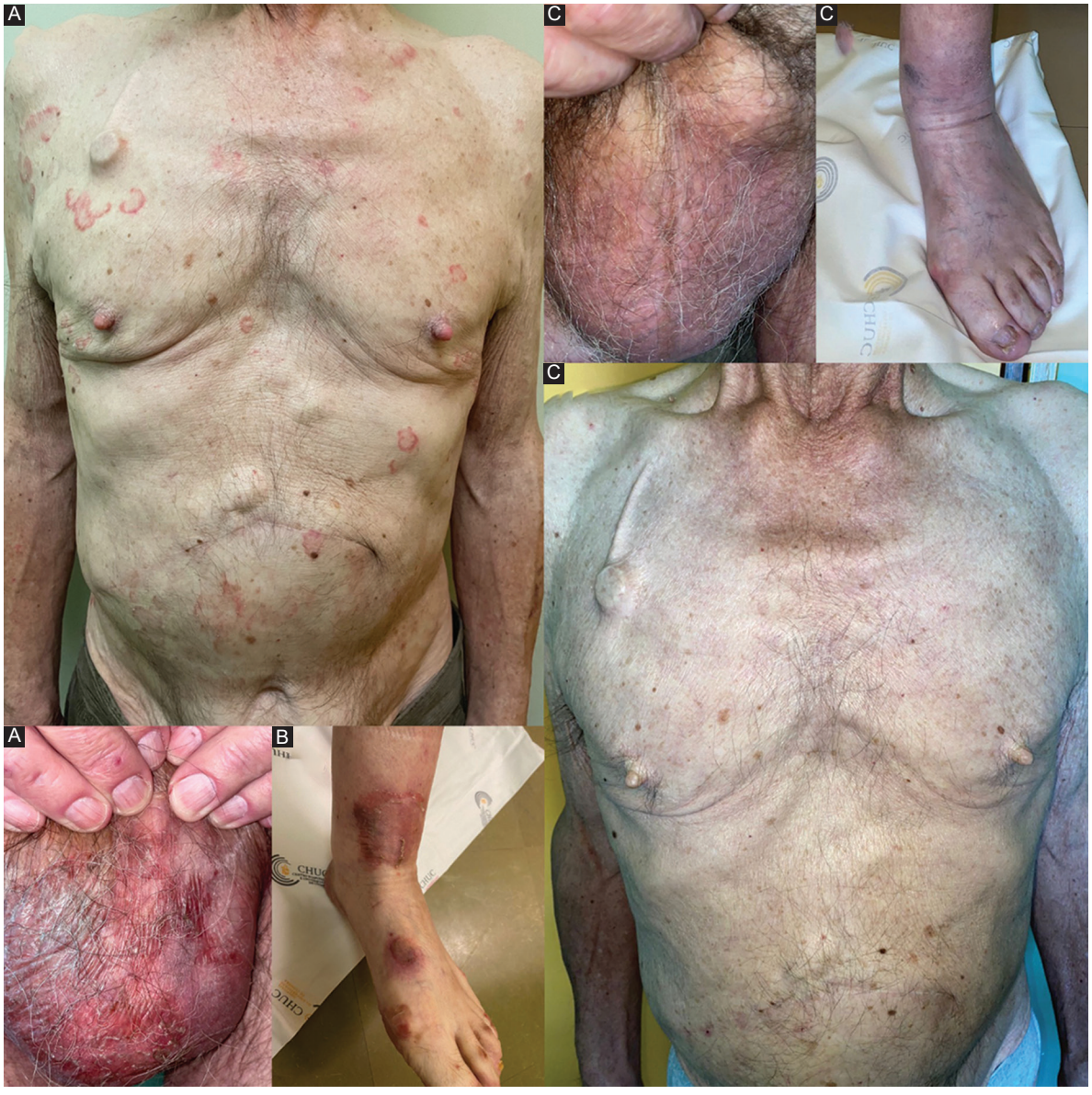

Figure 1. A: polycyclic erythematous scaly lesions, predominantly on the torso and upper limbs, also involving the genitals. **B**: large erosive, crusted, and painful plaques, also involving the feet. **C**: complete clinical resolution.

scan. The patient was then subjected to thermal ablation of liver metastases and proposed for systemic therapy with the somatostatin analog drug lanreotide. One month later, the patient was referred to the dermatology department for a 2-year worsening dermatosis. He presented with polycyclic erythematous and scaly lesions, predominantly on the torso and upper limbs, also involving the genitals, with erythematous and vaguely erosive scrotal plaques (Fig. 1A). There was no mucosal involvement, and the patient showed an adequate nutritional status. After a non-diagnostic skin biopsy, there was worsening of the dermatosis and a subsequent histological evaluation showed confluent parakeratosis, keratinocyte vacuolization with neutrophil exocytosis, and a dermal lymphomononuclear perivascular infiltrate with scattered neutrophils, confirming the diagnosis of NME. Zinc levels were normal (0.7 mg/L, normal levels between 0.66 and 1.5 mg/L) and serum neuroendocrine markers were high (neuron-specific enolase 26 ng/mL, normal levels < 15 ng/mL; chromogranin A 350.7 ng/mL, normal levels < 85 ng/mL). Glucagon levels were also significantly elevated (1295 pg/mL, normal levels < 210 pg/mL). At the time of dermatology referral, the patient also showed progression of the disease on a CT scan. For that reason, by the time, NME diagnosis was confirmed, he began chemotherapy with capecitabine and temozolomide, maintaining lanreotide therapy. A month later, he maintained significant skin lesions, mainly affecting the lower limbs, with large erosive, crusted, and painful plaques, also involving the feet (Fig. 1B). Hepatitis C serology was negative. Zinc supplementation was initiated at a 220 mg twice daily dose for 2 months. At 3-month follow-up, there was a complete resolution of the dermatosis (Fig. 1C).

Discussion

NME pathogenesis is not yet fully understood. Hyperglucagonemia contributes to the dysfunction of the epidermis but most likely numerous aspects including hypoaminoacidemia or zinc and essential fatty acids deficiency are involved in the pathogenesis of NME. In our patient, after zinc oral supplementation, in the context of normal serum zinc levels, there was complete resolution of NME lesions that had persisted even after chemotherapy with concomitant somatostatin analog therapy. This has already been reported[5], although rarely, and supports the role of zinc deficiency in the pathogenesis of NME.

Conclusion

In our patient, after zinc oral supplementation, in the context of normal serum zinc levels, there was complete resolution of NME lesions that had persisted even after chemotherapy with concomitant somatostatin analog therapy. This has already been reported, although rarely, and supports the role of zinc deficiency in the pathogenesis of NME.

Funding

None.

Conflicts of interest

None.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

Use of artificial intelligence for generating text. The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript, nor for the creation of images, graphics, tables, or their corresponding captions.

References

1. Liu JW, Qian YT, Ma DL. Necrolytic migratory erythema. JAMA Dermatol. 2019;155:1180.
2. Feldmann R, Wahl S, Steiner A. Normoglycemic glucagonoma syndrome associated with necrolytic migratory erythema. J Eur Acad Dermatol Venereol. 2018;32:e306-7.
3. Banerjee A, Shah SR. Necrolytic migratory erythema associated with a glucagonoma. New Engl J Med. 2020;383:e39.
4. Aragón-Miguel R, Prieto-Barrios M, Calleja-Algarra A, Pinilla-Martin B, Rodriguez-Peralto J, Ortiz-Romero P, et al. Image gallery: necrolytic migratory erythema associated with glucagonoma. Br J Dermatol. 2019;180:e1.
5. Sinclair SA, Reynolds NJ. Necrolytic migratory erythema and zinc deficiency. Br J Dermatol. 1997;136:783-5.