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Small-Cell Lung Cancer and Necrolytic Migratory Erythema

TO THE EDITOR: Necrolytic migratory erythema is a rare inflammatory dermatosis, first described by Becker et al.,¹ which occurs in 70% of patients with the glucagonoma syndrome.² Its clinical features are polymorphic mucocutaneous manifestations, encompassing multiple annular erythematous scaling and crusting patches with hyperpigmentation. These lesions can affect the entire body with a predilection for the perineum, buttocks, groin, abdomen, and limbs — in other words, areas that are subject to increased pressure and friction.^{2,3} The only two reported oral findings are angular cheilitis and atrophic glossitis.²⁻⁵

A 73-year-old man was referred to our oral medicine unit for persistent and progressive mucocutaneous lesions. The oral mucosa showed bullous, erosive mucositis with several areas having lichenoid clinical features (Fig. 1A and 1B, next page). His body, including the genital area, was covered in purplish confluent erythematopapulous scaling and crusting lesions with a keratotic surface (Fig. 1C). Histologic analysis of lesions from skin and oral mucosa revealed mild hyperparakeratosis, spongiosis, necrotic keratinocytes, and a prominent neutrophilic, eosinophilic, and plasmacellular infiltrate (Fig. 1D).

The patient's nutritional status was normal. Routine hematologic tests revealed mild hyperglycemia, hypoalbuminemia, a glucagon level of 73 pg per milliliter (normal range, 25 to 250), and a zinc level of 134 μ g per deciliter (normal range, 60 to 250). Tumor markers showed a CA-125 level of 232 U per milliliter (normal range, 0 to 35) and a β_2 -microglobulin level of 2924 ng per milliliter (normal range, 600 to 2600). Total-body computed

tomography revealed the presence of an ovoid mass measuring 40 mm in diameter in the upper lobe of the right lung, with prominent striae hooking the apical and costal homolateral pleura. No evidence of a pancreatic tumor was detected. Needle biopsy of the lung with ultrasonographic guidance revealed a small-cell lung cancer. A diagnosis of nonglucagonoma-associated necrolytic migratory erythema was made. The patient died 2 months later.

The pathogenesis of this disorder remains unclear. Nonetheless, it appears that hypoaminoacidemia, a nutritional lack of zinc and fatty acids, or hepatocellular dysfunctions might be involved in triggering these mucocutaneous lesions.^{2,3} Less frequently, necrolytic migratory erythema has been seen with no glucagon-producing tumor, a condition that is termed the pseudoglucagonoma syndrome⁴ and is associated with various systemic diseases, such as celiac disease, ulcerative colitis, Crohn's disease, hepatic cirrhosis, and various extrapancreatic malignant neoplasms, such as hepatocellular cancer, bronchial cancer, tumors that secrete insulin or insulin-like growth factor II, and duodenal cancer.⁵ As in the case of our patient, necrolytic migratory erythema with oral bullous, erosive mucositis and lichenoid features can also be associated with small-cell lung cancer.

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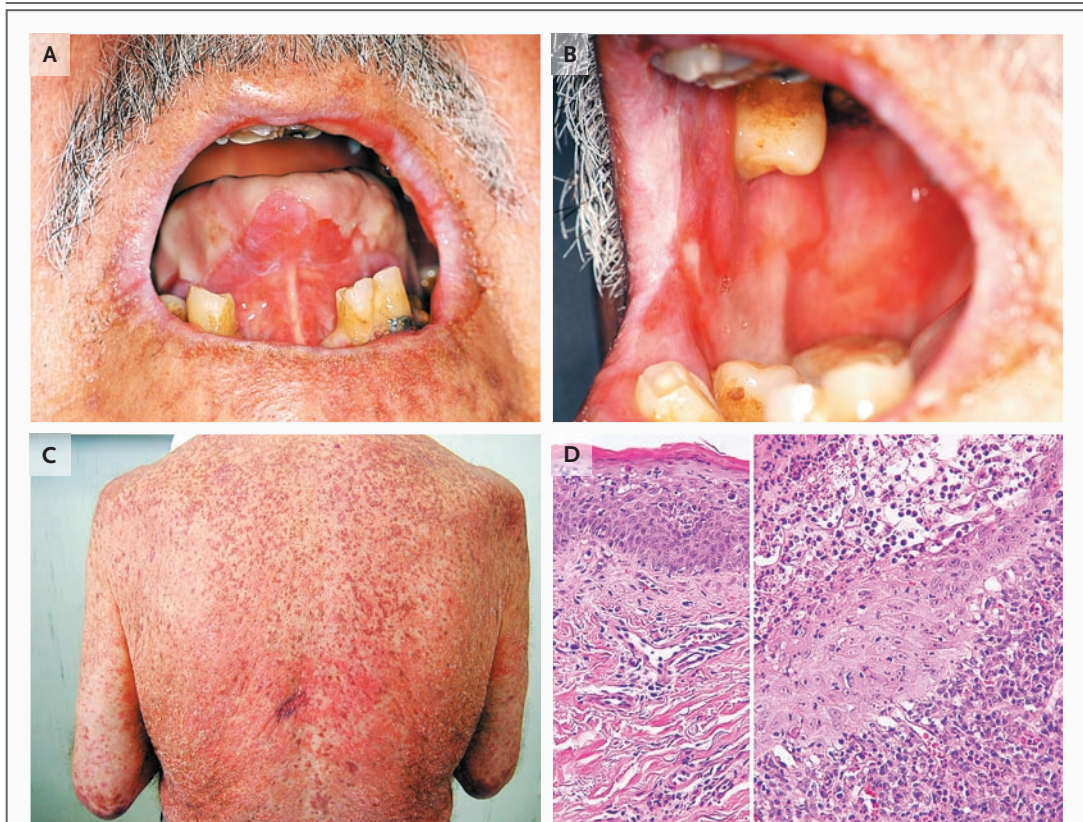


Figure 1. Mucocutaneous Manifestations of Necrolytic Migratory Erythema.

Bullous, erosive oral mucositis with areas having lichenoid features are visible on the tongue and the upper and lower lips (Panel A) and inside the right cheek (Panel B). The patient's entire body, including the back, is covered with purplish, confluent erythematopapulous scaling and crusting lesions with a keratotic surface (Panel C). Histologic analysis of the skin (Panel D, left) shows hyperparakeratosis and spongiosis, accompanied by the presence of necrotic keratinocytes, and vascular proliferation. Histologic analysis of the oral mucosa (Panel D, right) shows a prominent neutrophilic, eosinophilic, and plasmacellular infiltrate (hematoxylin and eosin).

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Prothrombin Time for Detection of Contaminated Heparins

TO THE EDITOR: The recent "heparin scandal" resulted from the use of contaminated heparin that caused serious adverse events including death.¹ The contaminant was identified as synthetically oversulfated chondroitin sulfate (OSCS).² Despite the missing final proof of a cause-and-effect re-

lationship, OSCS was shown to have pharmacologic effects that may contribute to the observed allergic-type reactions.³ Furthermore, OSCS is suspected to be responsible for an observed increased incidence of heparin-induced thrombocytopenia type 2.⁴ Revised monographs about heparin in