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Clinical vignette

A nuclear beacon of hope: an advanced, metastatic glucagonoma treated with [^{177}Lu]Lu-DOTA-TATE

Martyna Klosinska, Joanna Kolodziej, Adrianna Mroz, Weronika Madra, Grzegorz Kaminski
Department of Endocrinology and Radioisotope Therapy, Military Institute of Medicine — National Research Institute, Warsaw, Poland

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Abstract

Glucagonoma is a rare pancreatic neuroendocrine tumor (panNET) that can be characterized by increased secretion of glucagon and distinguishing symptoms — glucagonoma syndrome with a typical dermatosis, necrolytic migratory erythema, being its most common manifestation. While surgery and somatostatin analogs remain first-line therapeutic options in panNETs, radioligand therapy with [^{177}Lu]Lu-DOTA-TATE is a recommended second-line palliative treatment in advanced, metastatic cases. However, its prospects and efficacy are still not vastly researched in less frequent neuroendocrine neoplasms. Here, we present an extraordinary case of a metastatic glucagonoma treated with [^{177}Lu]Lu-DOTA-TATE used as a second-line treatment in progressive disease.

KEYwords: glucagonoma; pancreatic neuroendocrine tumor; radioligand therapy; [^{177}Lu]Lu-DOTA-TATE; lutetium, necrolytic migratory erythema

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Introduction

Glucagonoma is an extremely rare pancreatic neuroendocrine tumor (panNET) oversecreting glucagon with distinctive clinical manifestations known as glucagonoma syndrome, which consists of skin lesions, diabetes mellitus, deep vein thrombosis, and depression. A typical dermatosis, necrolytic migratory erythema (NME), is its most characteristic and frequent representation as it affects up to 70–90% of patients. While complete surgical resection is the cornerstone of treatment, in inoperable cases, somatostatin analogs (SSAs) are used as the first-line therapeutic option because of their remarkable efficiency in reducing hormonal imbalance. However, in advanced, metastatic, and progressive cases novel treatment approaches are needed. Radioligand therapy (RLT) is a method that combines long-acting SSAs with radiolabels such as ^{177}Lu which emit localized radiation in panNETs overexpressing somatostatin receptors (SSTRs). RLT with [^{177}Lu]Lu-DOTA-TATE is a safe and efficacious palliative treatment in advanced, metastatic panNETs. However, literature about its efficiency in rare neuroendocrine neoplasms such as glucagonoma is very limited. We report a case of a patient with metastatic glucagonoma treated with RLT. Despite the first promising effects with good symptom control, the observed progression-free survival (PFS) was relatively short. RLT treatment in glucagonomas requires further research to better investigate its efficacy in this special subgroup of panNETs.

Case report

A 69-year-old patient was admitted to the hospital due to diffuse erythematous lesions and ulcerations on the skin of lower limbs suggestive of NME (Fig. 1). An abdominal computed tomography (CT) scan revealed a tumor-like lesion of the tail of the pancreas and multiple heterogeneous hypodense lesions in the liver. A thick-needle biopsy of the focal lesion of the liver confirmed the presence of a well-differentiated NET G3 — Ki67 30%, chromogranin A (+), synaptophysin (+), glucagon (+). Laboratory determinations showed increased levels of chromogranin A — 165.1 ng/mL and fasting glucagon — 2928 ng/L. A [^{99m}Tc]Tc-HYNIC-TOC scintigraphy revealed an overexpression of SSTRs in all pathological lesions observed in CT — Kenning 4 (Fig. 2). Thus, the patient

Correspondence to: Joanna Kolodziej, Department of Endocrinology and Radioisotope Therapy, Military Institute of Medicine — National Research Institute, Szaserow 128, 04–349 Warsaw, Poland
e-mail: jkolodziej1@wim.mil.pl

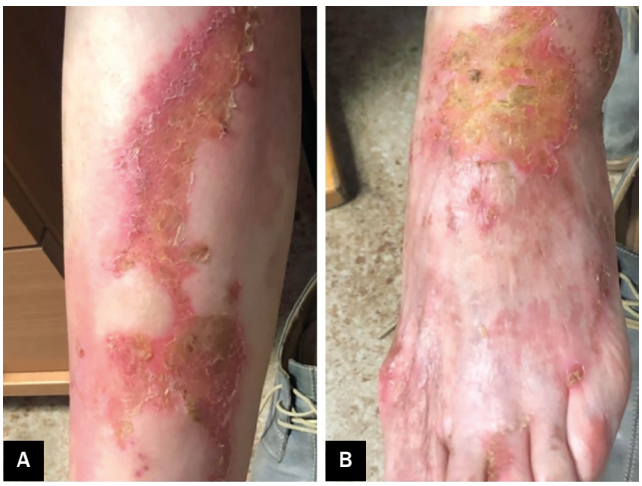

Figure 1. Changes in skin lesions on the left lower leg shank and foot following treatment. Skin lesion upon admission (**A**, **B**)

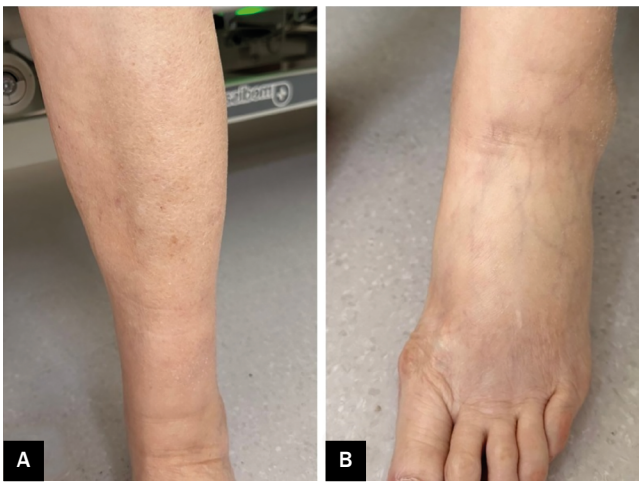

Figure 3. Changes in skin lesions on the left lower leg shank and foot following treatment. Relief of skin lesions after completion of all treatment courses (**A**, **B**)

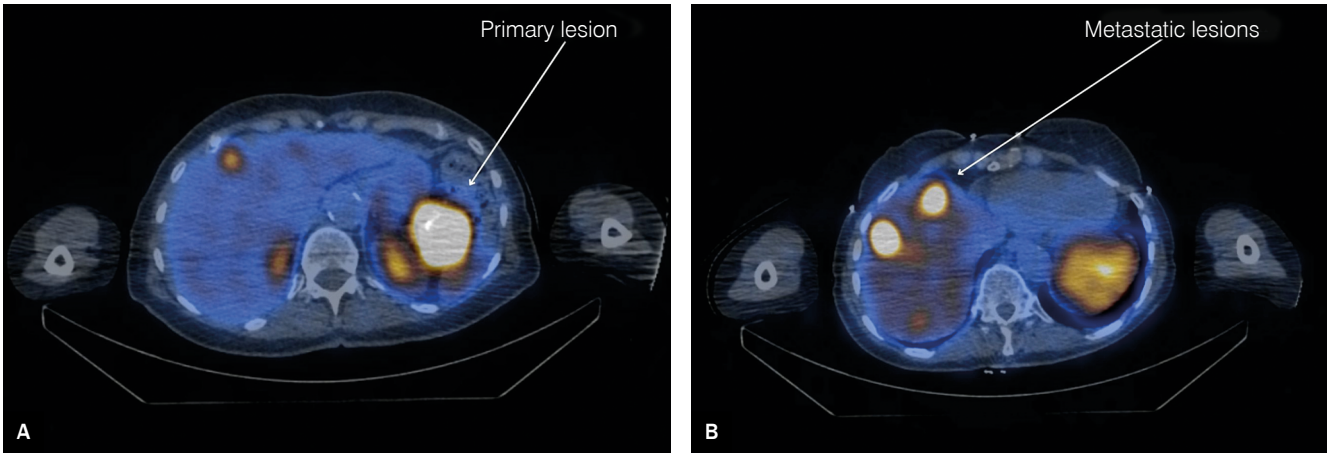

Figure 2. Axial fused [^{99m}Tc]Tc-HYNIC-TOC single-photon emission computed tomography (SPECT)/CT image of the abdomen revealed a focus of intense tracer uptake in the tumor of the tail of the pancreas (**A**) and several foci of tracer uptake in the liver metastases (**B**)

was qualified for a treatment with a long-acting SSA — lanreotide 120 mg every 28 days and surgical removal of the pancreatic tumor was performed. Subsequently, a complete regression of NME and a normalization of fasting glucagon level were achieved (Fig. 3).

Three years after the surgery progressive disease (PD) was diagnosed in a scheduled CT scan with no concomitant symptoms present and a normal level of fasting glucagon. Follow-up scintigraphy revealed an overexpression of SSTRs in all tumor *foci*. Therefore, the patient was qualified for RLT — four courses of [^{177}Lu]Lu-DOTA-TATE (7.4 GBq each) were administered every 10 weeks with good treatment tolerance and no adverse events (Fig. 4). The PFS lasted 7 months until a further progression resulted in patient's transfer to an oncology department to undergo chemotherapy.

In the presented case NME was the only clinical manifestation of metastatic G3 glucagonoma, and its complete regression along with fasting glucagon level normalization were achieved after surgery and during SSAs treatment, which is extremely rare [1]. Previous reports describe cases of progressive disseminated G1 and G2 glucagonomas treated with RLT with good response and achieved median PFS of approximately 23–30 months [2, 3]. The PFS in G3 gastroenteropancreatic NETs treated with RLT is estimated in a wide range of 9–23 months [4]. Noteworthy, there is a lack of research regarding PFS in G3 panNETs, especially in a small subgroup such as glucagonomas. We believe this case is the first to describe G3 glucagonoma treated with RLT due to good tracer uptake in scintigraphy, which allowed us to postpone the chemotherapy.

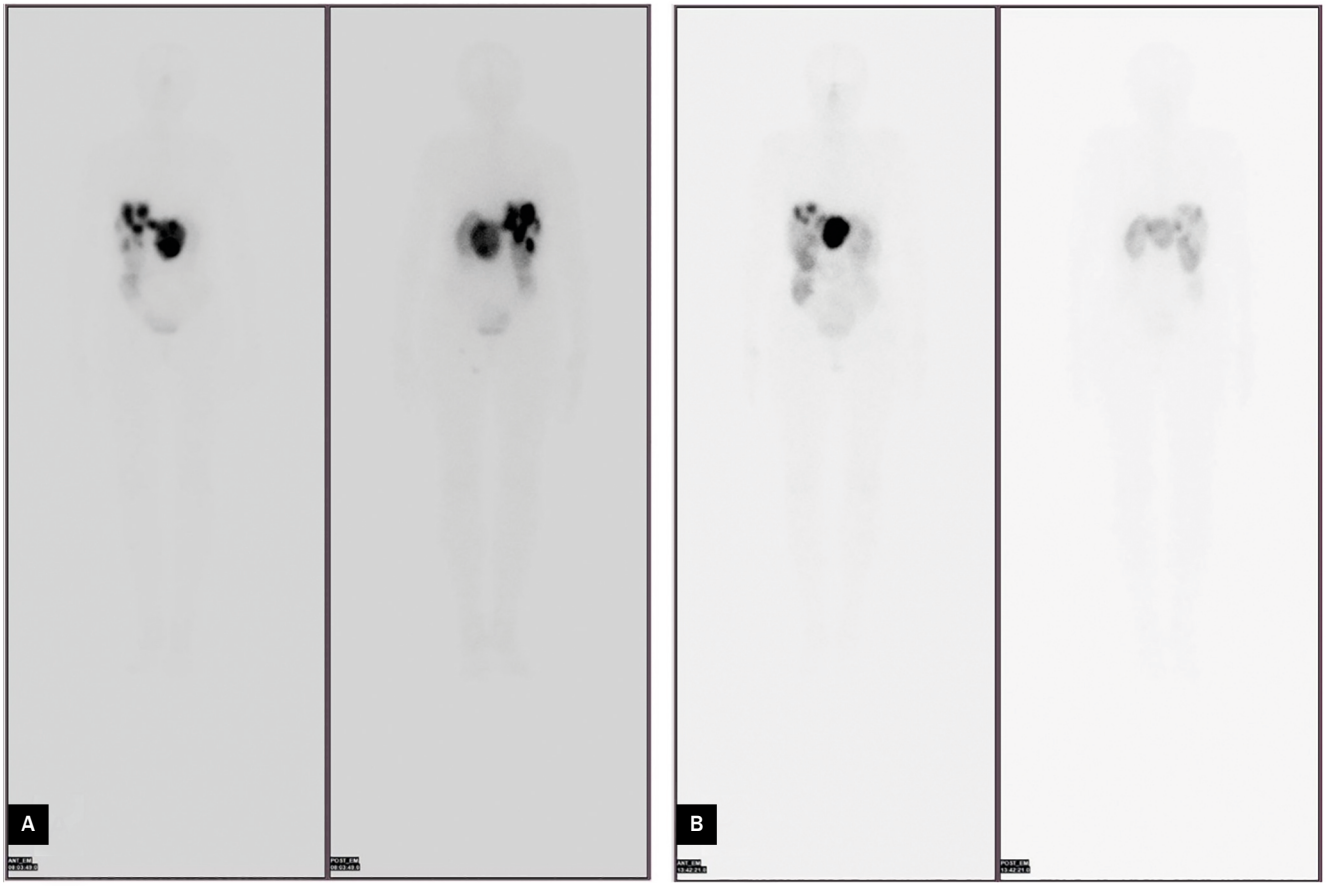

Figure 4. Post-therapeutic planar whole-body scintigraphy images after the first (**A**) and after the fourth (**B**) [177Lu]Lu-DOTA-TATE course

Article information and declarations

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None.

Author contributions

Collected the data and contributed to the conception and design of the article — MK, JK, AM, WM, GK; wrote the first draft of the manuscript — MK and JK; provided endocrinological care — AM; critically revised and supervised the project — GK. All authors provided critical feedback and helped shape the research, analysis, and manuscript. All authors have read and agreed to the published version of the manuscript.

Conflicts of interest

The authors declare no conflict of interest.

Ethics statement

An informed consent for publication was obtained from the patient.

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Supplementary material

None.

References

1. Qu Y, Li H, Wang X, et al. Clinical characteristics and management of functional pancreatic neuroendocrine neoplasms: a single institution 20-year experience with 286 patients. Int J Endocrinol. 2020: 1030518, doi: 10.1155/2020/1030518, indexed in Pubmed: 33204258.
2. Zandee WT, Brabander T, Blažević A, et al. Symptomatic and radiological response to 177lu-dotatate for the treatment of functioning pancreatic neuroendocrine tumors. J Clin Endocrinol Metab. 2019; 104(4): 1336–1344, doi: 10.1210/jc.2018-01991, indexed in Pubmed: 30566620.
3. Mavi ME, Tuncel M. Treatment of glucagonoma-related necrolytic migratory erythema with peptide receptor radionuclide therapy. Clin Nucl Med. 2021; 46(12): 1002–1003, doi: 10.1097/RLU.0000000000003731, indexed in Pubmed: 34034327.
4. Pavel M, Öberg K, Falconi M, et al. ESMO Guidelines Committee. Electronic address: clinicalguidelines@esmo.org. Gastroenteropancreatic neuroendocrine neoplasms: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2020; 31(7): 844–860, doi: 10.1016/j.annonc.2020.03.304, indexed in Pubmed: 32272208.