

Carcinoid crisis induced by radioligand therapy: a rare but life-threatening complication in patient with neuroendocrine tumor

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Abstract

Carcinoid crisis (CC) is a rare but potentially life-threatening complication that may occur in patients with neuroendocrine tumor (NET). The pathophysiology of CC involves the sudden, massive release of vasoactive substances. This article presents a unique case study of a patient with a disseminated NET of the pancreas, who developed CC after radioligand therapy (RLT). Despite its rarity, awareness of CC as a potential severe complication of RLT is essential for timely and effective management and better prognosis for affected patients.

KEYwords: carcinoid crisis; neuroendocrine tumor (NET); radioligand therapy (RLT); somatostatin analogs (SSA);

¹⁷⁷Lu-DOTA-TATE

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Introduction

Carcinoid crisis (CC) is a rare but potentially life-threatening complication that may occur in patients with neuroendocrine tumor (NET). The pathophysiology of carcinoid crisis (CC) involves the sudden, massive release of vasoactive substances, primarily serotonin, leading to systemic effects such as hypotension, cardiac arrhythmias and bronchospasm.

Case report

A 60-year-old male with a disseminated neuroendocrine tumor (NET) of the pancreas, metastasized to the liver, lymph nodes, peritoneum and bones, previously treated with a short-acting somatostatin analog (SSA), was referred to the Department of Endocrinology and Radioisotope Therapy of the Military Institute of Medicine — National Research Institute for Radioligand Therapy (RLT) with ¹⁷⁷Lutetium (¹⁷⁷Lu) and somatostatin analogs (SSA) —

[¹⁷⁷Lu]Lu-DOTA-TATE. The first course of RLT was well tolerated, and the patient experienced no significant adverse effects. Post-therapeutic [^{99m}Tc]Tc-HYNIC-TOC scintigraphy revealed numerous disseminated *foci* of increased radiotracer uptake, especially in the liver, pancreas, and abdominal lymph nodes (Fig. 1).

Three months later, the patient underwent a second course of RLT. He was administered 7.4 GBq of [¹⁷⁷Lu]Lu-DOTA-TATE along with amino acid infusion. Compared with previous imaging, post-therapeutic scintigraphy revealed significant regression of the lesion in the liver (Fig. 2). On the first day after RLT, the patient's condition deteriorated rapidly. He developed severe hypotension, atrial fibrillation, abdominal pain, diarrhea, oliguria, peripheral edema, and facial flushing. Laboratory results indicated myocardial injury and severe infection (Tab. 1).

The patient was initially managed with antibiotics, fluids, vaso-pressors, antiarrhythmics, and prophylactic anticoagulation. The persistence of severe hypotension, tachycardia, and flushing led to the suspicion of CC. He was administered a short-acting somatostatin analog — octreotide. This intervention led to significant clinical improvement: stabilization of blood pressure, return to sinus rhythm, resolution of diarrhea and abdominal pain, reduction in facial flushing, and improvement of diuresis. After only a few days, the patient, in good general condition and without complaints, was discharged from the hospital.

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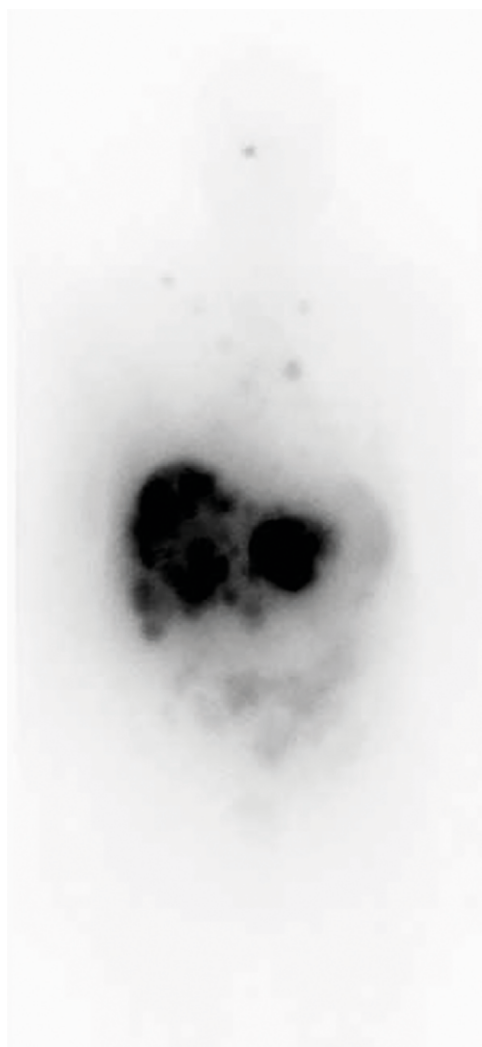


Figure 1. Post-therapeutic ^{99m}Tc -HYNIC-TOC planar scintigraphy scan after the first course of 7.4 GBq ^{177}Lu -DOTA-TATE reveals numerous disseminated foci of increased radiotracer uptake in liver, pancreas, peritoneum, abdominal, hilar, supra- and subclavicular lymph nodes, bones and right orbit

Table 1. Laboratory test results of the patient

Test	Result	Reference range
WBC	18.30	4–10 [$\times 10^9/\text{L}$]
RBC	5.26	4.5–6.0 [$\times 10^{12}/\text{L}$]
HGB	13.9	13.8–17.2 [g/dL]
MCV	80	80–100 [fL]
PLT	254	150–450 [$\times 10^9/\text{L}$]
CRP	37	0–5 [mg/dL]
Procalcitonin	20.15	0.05–0.5 [ng/mL]
Creatinine	1.7	0.6–1.2 [mg/dL]
Albumin	2.6	3.5–5.0 [g/dL]
AST	23	10–40 [U/L]
ALT	16	7–56 [U/L]
CK	827	20–200 [U/L]
CKMB	1262	0–25 [U/L]
hs-Troponin T	107.1	< 22 [ng/L]

ALT — alanine aminotransferase; AST — aspartate aminotransferase; CK — creatine kinase; CKMB — creatine kinase muscle-brain; CRP — C-reactive protein; HGB — hemoglobin; MCV — mean corpuscular volume; PLT — platelets; RBC — red blood cells; WBC — white blood cells

Discussion

Carcinoid crisis is a rare but serious complication of NETs with an incidence ranging between 1 and 10% among NET patients [1]. The main triggers of CC are invasive procedures, such as surgery, liver embolization, biopsy and general anesthesia [1, 2]. As illustrated in the presented case, RLT can also induce CC. The precise mechanism of CC during treatment is not fully understood due to limited case reports in the literature [3–5]. Proposed pathomechanisms include tumor lysis from beta radiation by ^{177}Lu , SSA discontinuation, amino acid co-administration, and emotional stress [5]. The massive release of vasoactive substances may lead to a sudden onset of hemodynamic instability. It is important in that case to recognize that other medical conditions, such as severe infections or cardiac event, which

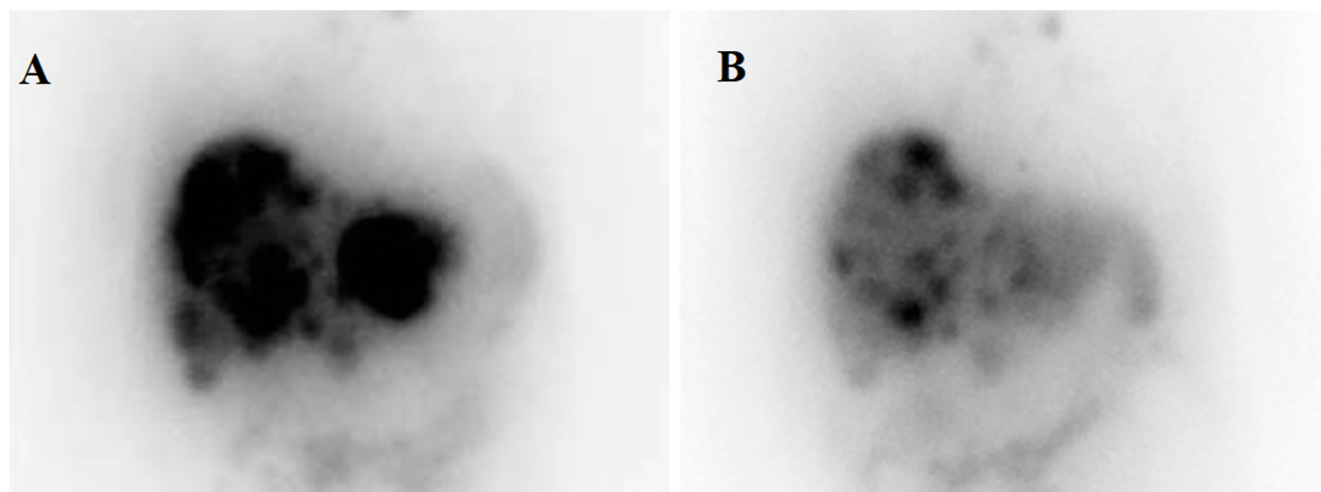


Figure 2. Post-therapeutic ^{99m}Tc -HYNIC-TOC planar scintigraphy scans after first (A) and second (B) course of 7.4 GBq ^{177}Lu -DOTA-TATE show significant regression of the lesions in the liver

may mimic and overlap the symptoms of CC, as it was seen in our patient. This can complicate the clinical picture and potentially delay the diagnosis. Due to the life-threatening nature of CC, it is essential to consider this diagnosis in a patient with rapid deterioration after RLT or other triggering procedures. As demonstrated in our case, prompt recognition and treatment with octreotide can significantly improve outcomes [5]. Despite its rarity, awareness of CC as a potential severe complication of RLT is essential for timely and effective management and better prognosis for affected patients.

Article information and declarations

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Author contributions

The authors' contributions to the work were as follows: conception of the article — DB-K, MS; design of the article — DB-K, MS, NO; acquisition of data, analysis and interpretation of data — DB-K, NO, MK; writing of the manuscript — DB-K, NO; revising the article critically for important intellectual content, final approval of the version to be published — MS, GK.

Conflicts of interest

The authors report no competing interest.

Ethics statement

The research was conducted ethically in accordance with World Medical Association Declaration of Helsinki. Data were collected retrospectively.

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Supplementary material

None.

References

1. Bardasi C, Benatti S, Luppi G, et al. Carcinoid crisis: a misunderstood and unrecognized oncological emergency. *Cancers (Basel)*. 2022; 14(3), doi: [10.3390/cancers14030662](https://doi.org/10.3390/cancers14030662), indexed in Pubmed: [35158931](https://pubmed.ncbi.nlm.nih.gov/35158931/).
2. Gade AK, Olariu E, Douthit NT. Carcinoid syndrome: a review. *Cureus*. 2020; 12(3): e7186, doi: [10.7759/cureus.7186](https://doi.org/10.7759/cureus.7186), indexed in Pubmed: [32257725](https://pubmed.ncbi.nlm.nih.gov/32257725/).
3. Yadav SK, Jha CK, Patil S, et al. Lutetium therapy-induced carcinoid crisis: a case report and review of literature. *J Cancer Res Ther*. 2020; 16(Supplement): S206–S208, doi: [10.4103/jcrt.JCRT_22_18](https://doi.org/10.4103/jcrt.JCRT_22_18), indexed in Pubmed: [33380679](https://pubmed.ncbi.nlm.nih.gov/33380679/).
4. Tapia Rico G, Li M, Pavlakis N, et al. Prevention and management of carcinoid crises in patients with high-risk neuroendocrine tumours undergoing peptide receptor radionuclide therapy (PRRT): literature review and case series from two Australian tertiary medical institutions. *Cancer Treat Rev*. 2018; 66: 1–6, doi: [10.1016/j.ctrv.2018.03.002](https://doi.org/10.1016/j.ctrv.2018.03.002), indexed in Pubmed: [29602040](https://pubmed.ncbi.nlm.nih.gov/29602040/).
5. Del Olmo-García MI, Muros MA, López-de-la-Torre M, et al. Prevention and management of hormonal crisis during theragnosis with LU-DOTA-TATE in neuroendocrine tumors. A systematic review and approach proposal. *J Clin Med*. 2020; 9(7): 2203, doi: [10.3390/jcm9072203](https://doi.org/10.3390/jcm9072203), indexed in Pubmed: [32664679](https://pubmed.ncbi.nlm.nih.gov/32664679/).