Submitted: 05.06.2024
Accepted: 08.08.2024
Early publication date: 25.11.2024

Endokrynologia Polska
DOI: 10.5603/ep.101015
ISSN 0423–104X, e-ISSN 2299–8306

Clinical outcomes and long-term follow-up after radioligand therapy in aggressive non-functioning pituitary neuroendocrine tumour

Dorota Brodowska-Kania, Marek Saracyn, Natalia Osial, Adam Daniel Durma, Maciej Kołodziej, Grzegorz Kamiński

Department of Endocrinology and Radioisotope Therapy, Military Institute of Medicine – National Research Institute, Warsaw, Poland

Key words: *pituitary neuroendocrine tumour (PitNET); aggressive pituitary tumour; non-functioning pituitary tumour (NF-PitNET); radionuclide ligand therapy (RLT); somatostatin receptors (SSTR); 177Lu-DOTATATE*

Pituitary neuroendocrine tumours (PitNETs) constitute approximately 15% of all intracranial neoplasms. While PitNETs are typically benign, they can exhibit aggressive nature in some cases, infiltrating surrounding tissues, growing rapidly, or recurring multiple times [1]. Therapeutic options for aggressive PitNETs are limited, primarily involving surgical intervention, followed by radiotherapy and conventional therapies, like temozolomide [2]. There is limited exploration of alternative modalities, such as radioligand therapy (RLT). We report a patient with aggressive PitNET, who underwent RLT over 12 years ago.

In 2007, a 33-year-old patient with newly diagnosed common variable immunodeficiency and chronic sinusitis underwent a computed tomography scan of the paranasal sinuses, which incidentally revealed a pituitary tumour. Magnetic resonance imaging (MRI) revealed a polycyclic nodular 45 mm lesion filling the sella turcica and infiltrating surrounding tissues. The clinical and hormonal work-up showed no abnormality in the activity of the pituitary gland, indicating non-functioning PitNET (NF-PitNET). Two transsphenoidal resections were conducted in 2008, but they were incomplete (Fig. 1). Postoperative histopathological examination demonstrated a gonadotroph type of NF-PitNET with a Ki-67 index of 3%. In the follow-up MRI in 2010, local progression was observed at approximately 20%. Scintigraphy using [^{99m}Tc] Tc-HYNIC-TATE showed overexpression of somatostatin receptors (SSTRs), especially subtype 2 (SSTR2) within the adenoma (Krenning score: 3) (Fig. 2). Based on this finding, long-acting somatostatin analogue (SSA) treatment was initiated. Additionally, a patient has been qualified for experimental RLT with [^{177}Lu] Lu-DOTATATE due to local expansion. The patient received 3 doses of 7.4 GBq each, without any reported side effects. Post-therapeutic imaging performed 6 months after treatment revealed stable disease (SD) based on RECIST 1.1 criteria. Since then, the patient has remained under regular medical care, and now his condition is good and stable. He continues the SSA treatment (octreotide LAR). Annual

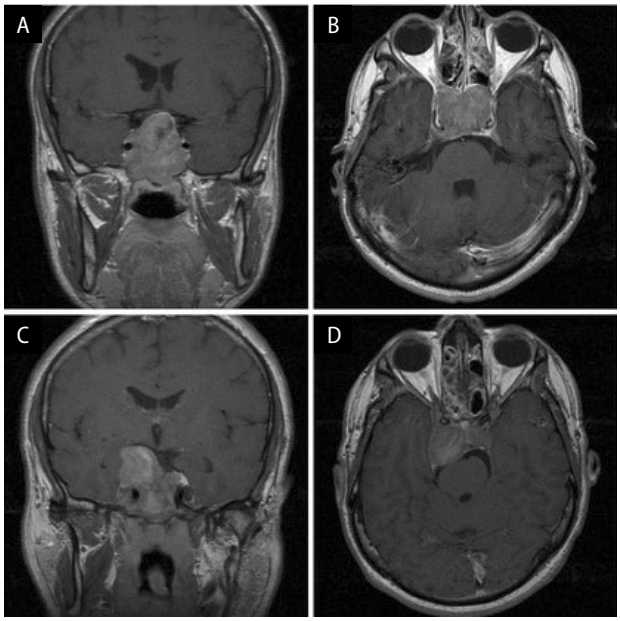

Figure 1. *Magnetic resonance imaging (MRI) of the brain.* **A, B**. *Initial brain MRI (02.2007).* **C, D**. *Brain MRI after surgical interventions (09.2009)*

dr n. med. Dorota Brodowska-Kania, Military Institute of Medicine, Department of Endocrinology and Isotope Therapy, Szaserów 128, 04–349 Warsaw, Poland, tel/fax: +48 261 816 110; e-mail: dbrodowska-kania@wim.mil.pl

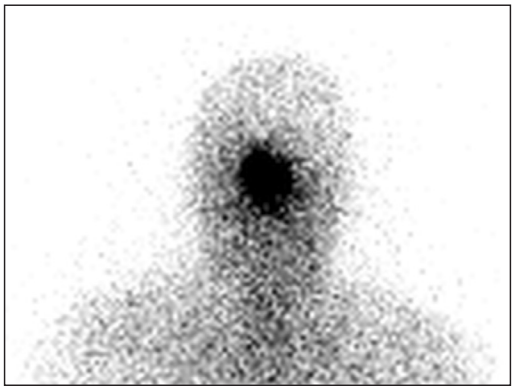

Figure 2. *Scintigraphy using [^{99m}Tc] Tc-HYNIC-TATE showing overexpression of somatostatin receptors (SSTRs) within the pituitary neuroendocrine tumour (PitNET)*

follow-up MRI scans have consistently demonstrated SD up to now, even 12 years after the RLT (Fig. 3).

RLT is a therapeutic option for treating neoplasms with an overexpression of SSTR. The therapy delivers cytotoxic radiation selectively, using a radionuclide linked to a somatostatin receptor ligand that binds to SSTRs on the cell surface. SSTR2 is the primary target of RLT, and its presence on tumour cells must be confirmed before the treatment. RLT is primarily used for treating gastroenteropancreatic neuroendocrine tumours. Still, its clinical application has expanded recently to other neoplasms with high expression of SSTR, such as primary brain tumours, paragangliomas, or thyroid cancer [3]. Furthermore, SSTRs were shown to be expressed in PitNETs, suggesting the potential efficacy of the therapy for these tumours [4].

In our patient, high expression of SSTRs in the tumour was detected, enabling the administration of SSA therapy as well as experimental RLT. To our knowledge, this is the first reported case of a patient with NF-PitNET who underwent RLT, with subsequent long-term follow-up confirming disease stabilisation. Other available reports include 30 cases of various types of PitNETs treated with RLT. Among these cases, 30% achieved stable disease, and 18% showed a partial response, suggesting a favourable outcome in nearly 50% [2]. The response rate is comparable to other available therapeutic options for patients with aggressive PitNETs, such as temozolomide and other systemic therapies [2,4]. Therefore, after confirming high SSTR expression in the lesion, RLT could be considered an effective and safe option for patients with aggressive PitNETs. However, further clinical research is necessary to better understand and finally establish the role of RLT in the treatment of these tumours.

Ethics statement

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

Author contributions

Conception of the article — D.B-K., M.S., G.K.; design of the article — D.B-K., M.S., N.O., A.D., M.K.; acquisition of data, analysis and interpretation of data — D.B-K, M.S, N.O, A.D, M.K, writing of the manuscript — D.B-K., N.O., final approval — M.S, G.K.

Conflict of interest

The authors declare no conflict of interest.

References

1. Raverot G, Burman P, McCormack A, et al. European Society of Endocrinology. European Society of Endocrinology Clinical Practice Guidelines for the management of aggressive pituitary tumours and carcinomas. Eur J Endocrinol. 2018; 178(1): G1–G24, doi: 10.1530/EJE-17-0796, indexed in Pubmed: 29046323.
2. Nakano-Tateno T, Lau KJ, Wang J, et al. Multimodal Non-Surgical Treatments of Aggressive Pituitary Tumors. Front Endocrinol (Lausanne). 2021; 12: 624686, doi: 10.3389/fendo.2021.624686, indexed in Pubmed: 33841328.
3. Harris PE, Zhernosekov K. The evolution of PRRT for the treatment of neuroendocrine tumors; What comes next? Front Endocrinol (Lausanne). 2022; 13: 941832, doi: 10.3389/fendo.2022.941832, indexed in Pubmed: 36387893.
4. Marques P. The Effects of Peptide Receptor Radionuclide Therapy on the Neoplastic and Normal Pituitary. Cancers (Basel). 2023; 15(10), doi: 10.3390/cancers15102710, indexed in Pubmed: 37345047.

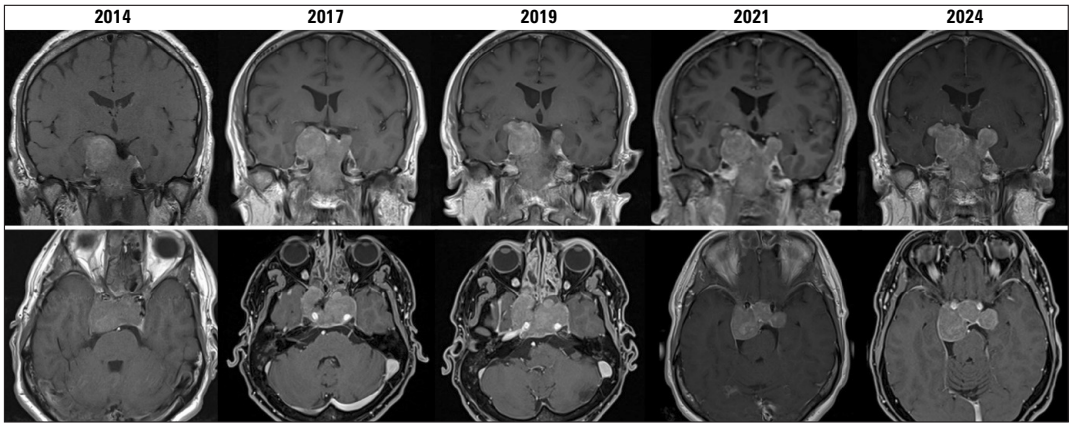

Figure 3. *Regularly performed magnetic resonance imaging (MRI) scans showing disease stabilisation*