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FIRST-LINE USE OF DOTATATE-177LUTETIUM THERAPY IN THE TREATMENT OF NEUROENDOCRINE TUMOR OF THE PANCREAS: CASE SERIES

Gabriela El Haje Lobo Rocha
Núcleos Radiologia e Medicina Nuclear

Marian Beatrice Lourenço Martins
Núcleos Radiologia e Medicina Nuclear

Janaína França de Magalhães Souto
Núcleos Radiologia e Medicina Nuclear

Pedro Fernando de Melo Cavalcante
Núcleos Radiologia e Medicina Nuclear

Marcelo do Vale Gomes
Núcleos Radiologia e Medicina Nuclear

Ênio de Freitas Gomes
Núcleos Radiologia e Medicina Nuclear

Bruno Galafassi Ghini
Núcleos Radiologia e Medicina Nuclear

Murilo Buso
Núcleos Radiologia e Medicina Nuclear

Paulo Bergerot
Núcleos Radiologia e Medicina Nuclear

Gustavo do Vale Gomes.
Núcleos Radiologia e Medicina Nuclear

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INTRODUCTION

Neuroendocrine tumors (NET) of the pancreas are a heterogeneous and rare group of neoplasms, corresponding to 1% to 2% of primary pancreatic tumors. Although most present indolent behavior, metastases are not infrequent and reduce overall survival. Complete surgical resection is the treatment of choice, although not all patients are eligible. In this scenario, there are other therapeutic options, such as radionuclide therapy, whose effectiveness in neoadjuvance has been demonstrated in the literature. We report a series of 3 cases of patients with pancreatic NET treated with somatostatin analogue labeled with Lutetium-177 (DOTA-177Lu) or peptide radionuclide receptor therapy (PRRT) as first line.

REPORTS

Female, 33 years old, with a large tumor involving the head of the pancreas and the proximal portion of the duodenum; Biopsy revealed adenocarcinoid tumor of the pancreas. Abdominal CT showed inoperability, in addition to liver implants. Scintigraphy with somatostatin analogue showed the presence of marked expression of receptors in the primary tumor and secondary lesions. Male, 37 years old, diagnosed with NET of inoperable pancreas. After multidisciplinary discussion and review of the literature, we opted for PRRT (according to the Rotterdam protocol) in the first line with neoadjuvant intention in both cases, with good initial response, tumor reduction and the possibility of a surgical approach. In the first case, the liver implants were no longer identified. The patients underwent pathologically confirmed complete tumor resection and currently have no evidence of disease. Female, 67 years old, with radiological suspicion of NET of the body of the pancreas. PET-DOTA showed a single lesion with high expression of somatostatin receptors. Upon refusal of biopsy and surgery and negative PET-FDG, it was suggested that PRRT be performed in the first line. MRI after 4 doses of 150 mCi of DOTA-177Lu no longer showed the primary lesion. He has been disease-free for 2 years.

DISCUSSION

PRRT is known to be effective in NET with high expression of somatostatin receptors, and the use of DOTA-177Lu as a second or third line of treatment in these cases is well established. As a first-line therapy for pancreatic tumors, its use has been demonstrated in the literature with high efficacy in tumor reduction, making surgical and curative approaches possible, as well as controlling symptoms, making it an interesting neoadjuvant therapeutic strategy, especially in locally advanced and inoperable.

FINAL COMMENTS

In the first two cases, in which neoadjuvant PRRT was used, there was a good clinical response and tumor reduction, allowing surgery. In the third case, there was a complete radiological response to date. Patients showed good tolerance to the treatment, with no evidence of renal or hematological toxicity, suggesting that the therapy can be used upfront in occasional cases of resectable and unresectable localized disease.

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PSC- High-grade (G3; Ki-67 index >20 percent) tumors were considered equivalent to poorly differentiated carcinomas. However, it became apparent that not all G3 tumors were poorly differentiated and that some tumors, particularly those with a Ki-67 index in the 20 to 55 percent range, had relatively well-differentiated histology, relatively good prognosis (compared with poorly differentiated carcinomas), and relatively poor response to platinum-based chemotherapy. Therefore, the 2017 WHO classification of pancreatic NENs (table 1) includes a NET G3 category (Ki-67 >20 percent) that must be distinguished from the poorly differentiated pancreatic NEC category.

2017 World Health Organization (WHO) classification and grading of pancreatic neuroendocrine neoplasms (PanNENs)

Classification/grade	Ki-67 proliferation index* (percent)	Mitotic index*
Well-differentiated PanNENs: Pancreatic neuroendocrine tumours (PanNETs)		
PanNET G1	<3	<2
PanNET G2	3 to 20	2 to 20
PanNET G3	>20	>20
Poorly differentiated PanNENs: Pancreatic neuroendocrine carcinomas (PanNECs)		
PanNEC (G3)	>20	>20
Small cell type		
Large cell type		
Mixed neuroendocrine-non-neuroendocrine neoplasm		

* The Ki-67 proliferation index is based on the evaluation of ≥500 cells in areas of higher nuclear labelling (so-called hotspots). The mitotic index is based on the evaluation of mitoses in 50 high-power fields (0.2 mm^2 each) in areas of higher density, and is expressed as mitoses per 10 high-power fields (2.0 mm^2). The final grade is determined based on whichever index (Ki-67 or mitotic) places the tumour in the highest grade category. For assessing Ki-67, casual visual estimation (eyeballing) is not recommended; manual counting using printed images is advocated.