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The Utility of 68Ga-DOTATOC PET/CT to Surface and Follow-up of Gastroenteropancreatic Neuroendocrine Tumors: A Case Report

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1. Abstract

Gastroenteropancreatic neuroendocrine tumors are characterized by specific tissue characteristics targeted by molecular imaging. Functional imaging is an important diagnostic tool because most NETs have high cell surface somatostatin receptor expression levels, which has a great impact on patient management, including better localization of occult tumors in the small intestine and pancreas as well as improved staging and restaging. We report the case of a male diagnosed with pancreatic neuroendocrine tumor, that during the follow-up a 68Ga-DOTATOC PET/CT scan revealed distant disease (bone and bowel), findings that conventional imaging did not reveal.

2. Case Description

A 52-year-old smoker male was referred to our endocrine Unit in 2017 following an incidental ultrasound finding of an asymptomatic nodule in the pancreatic body, initially diagnosed as a pancreatic neuroendocrine tumor. The patient underwent a CT scan, showing a hypervascular nodule, a neuroendocrine focal lesion in the pancreatic body of 28x20 mm diameter that produces discrete ectasia of the Wirsung duct in the pancreatic tail. The patient presented no symptoms related to neuroendocrine hormonal secretion and blood exams were normal. Somatostatin receptor imaging by SPECT did reveal and abnormal area of tracer accumulation in the pancreas body and 9th right posterior costal arch. The patient underwent corporocaudal pancreatectomy, splenectomy, and lymphadenectomy without cholecystectomy of the pancreatic body lesion, rendering consistent results with well-differentiated neuroendocrine tumors G1. In 2018, systematic treatment with somatostatin analogs was initiated.

In the postoperative course, new Somatostatin receptor imaging by SPECT continues to reveal a bone lesion with abnormal overexpression of somatostatin receptors in the 9th right posterior costal arch. In follow-up via external consultations, a 68Ga-DOTATOC PET/CT scan was performed. It brought to light an abnormal area of tracer accumulation in the terminal ileum and in the D9 costovertebral joint (Figure 1 and 2). The study was coupled with a colonoscopy and a computed tomography. The former did not detect pathological findings whereas the latter evidenced a doubtful nodular image of approximately 20 mm in the terminal ileum.

Since the suspicion of Metastatic Neuroendocrine Carcinoma remained significant, a biopsy was practiced on the right paravertebral subpleural nodule next to D9 costovertebral junction. This procedure surfaced a metastatic low-grade neuroendocrine tumor. In order to identify the origin of the abnormal area of tracer accumulation in the terminal ileum, a right hemicolectomy was carried out. The pathological finding was consistent with a well-differentiated G1 neuroendocrine tumor located in the terminal ileum, propagated up to the muscle layer, with the presence of

great mesenteric mass (> 20 mm) that metastases in seven local lymphatic ganglia, per PT2N2 classification.

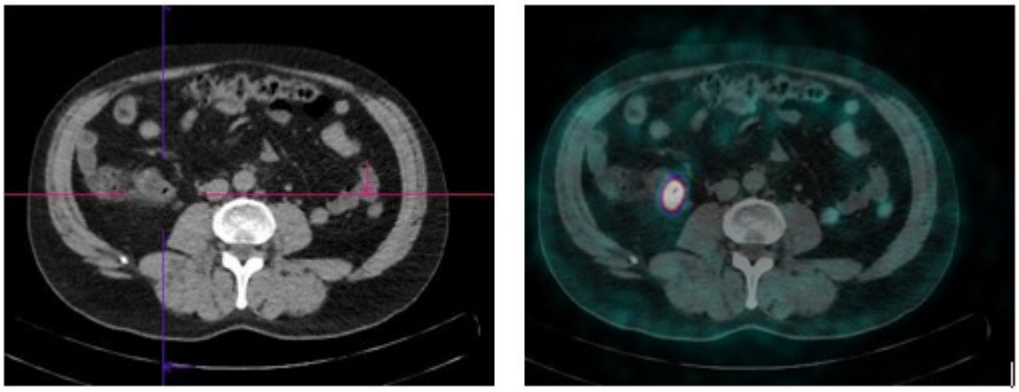

Figure 1: 68Ga-DOTATOC PET/CT scan. A computed tomography (CT) and B fused PET/CT:focal lesion with tracer accumulation is visible in the terminal ileum (SUVmax 21.87).

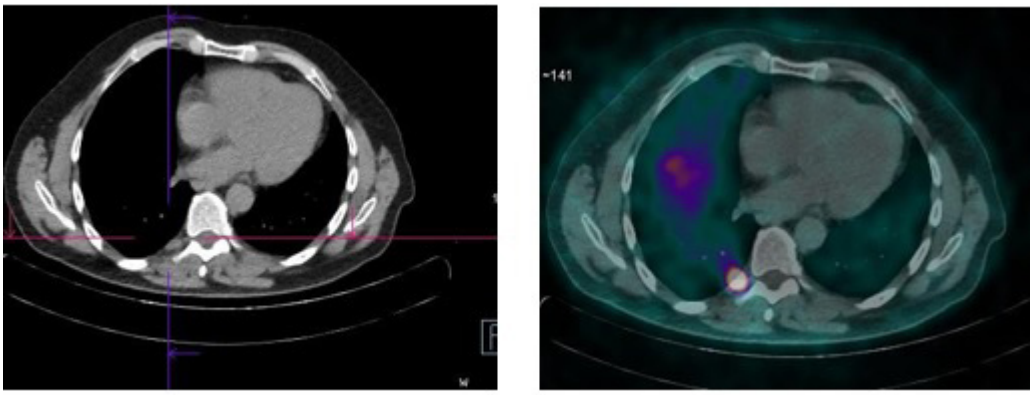

Figure 2: 68Ga-DOTATOC PET/CT scan. A computed tomography (CT) and B fused PET/CT:nodule with tracer accumulation is visible in the D9 costovertebral joint (SUVmax 16.26).

3. Discussion

This case portrays a patient with a focal lesion located in the pancreatic body, incidentally found by ultrasound scan as a neuroendocrine tumor in line with a positive reading of somatostatin receptor according to SPECT imaging. Then the follow-up 68Ga- DOTATOC PET/CT scan revealed an abnormal area of tracer accumulation in the terminal ileum and in D9 costovertebral joint, findings otherwise traced as either irrelevant or of doubtful significance via other complementary tests. Gastroenteropancreatic Neuroendocrine Tumors (GEP-NETs) constitute a heterogeneous group of diseases that stems from cells belonging to the endocrine system, distributed mainly through the gastroenteropancreatic tract [1]. These are classified according to the World Health Organization into grades 1 to 3 [2] in accordance with the Ki-67 proliferation index and mitotic count: Hence, well-differentiated GEP- NETs are sorted out either as G1 or G2 [1], leaving all poorly differentiated Neuroendocrine Carcinomas (NEC) within G3 [2]. GEP-NETs have specific tissue characteristics targeted by molecular imaging. These include expression of receptors, especially somatostatin subtype 2 (SSTR2) but also Glucagon-Like Peptide-1 (GLP-1R), insulinotropic peptide (GIPR), capacity for Amine Precursor Uptake Decarboxylation (APUD), and often low glucose turnover [2] as well. Somatostatin is a small cyclic neuropeptide found in neurons and endocrine cells throughout the brain, peripheral neurons, endocrine pancreas, and gastrointestinal tract [3]. Conventional anatomical imaging modalities in NET such as Computed Tomography (CT), Magnetic Resonance Imaging (MRI), and Endoscopic Ultrasound (EUS), constitute the radiological workhorses for abdominal imaging in general and are also relevant in patients for the detection of the primary tumor, staging, and evaluation of treatment response [4]. Molecular imaging techniques, especially with PET tracers, have a great impact on patient management, including better localization of occult tumors in the small intestine and pancreas as well as improved staging and restaging [2]. Functional imaging with radiopharmaceuticals is an important diagnostic tool because most NETs have high cell surface somatostatin receptor expression levels [5]. Gallium-68 (Ga68) DOTA-peptide positron emission tomography/computed tomography (68Ga- PET/CT) has therefore emerged as the best nuclear medicine tool for the diagnosis and staging of gastro-entero-pancreatic neoplasms [4]. A systematic review and meta-analysis of 68Ga-DOTATATE and similar somatostatin PET imaging analogs by Geijer and Breimer demonstrated a pooled sensitivity and specificity for these imaging agents of 0.93 (95% CI, 0.91–0.94) and 0.96 (95% CI, 0.95– 0.98) respectively, with the area under the summary receiver operating characteristic curve of 0.976 [5]. It is a salient characteristic of NET patients to cope for many years with the widespread disease while receiving multiple treatments. Changes in treatment strategy

are nearly always based on clinical or imaging-based signs of progression [6]. Thus, high performance in the detection of any new lesions is of great value in these patients [6].

With regards to staging and restaging in conjunction with theranostics, a direct comparison of SSTR PET/CT and whole-body multiphase MRI in patients with NETs/NECs (G1-G3) shows higher sensitivity and specificity of the former over the latter [2]. A comparison of overall lesion-based detection rates for metastatic involvement shows again a slightly higher accuracy for SSTR PET/CT. Organ-based detection rates, however, significantly differ with the superiority of SSTR PET/CT for lymph node and pulmonary lesions and superiority of MRI for liver and bone metastases [2].

SSTR PET/CT constitutes in such cases, the most accurate imaging modality for staging and restaging of patients with GEP-NETs (G1 and G2), showing additionally great impact on patient management. These findings are consistent with other recent series that have assessed the impact of Ga-68 dotatate PET/CT on the management of NETs [7].

In a European prospective study of 131 patients with NETs, Sadowski et al. posited Ga- 68 dotatate PET/CT imaging changed management in 33% of patients and identified occult primaries in 29% of patients [7]. Similarly, Hoffman et al. reported a series of 59 patients with NETs and found 47% of them experienced management changes, most frequently by rendering candidates for surgical resection through identifying an occult primary and by directing patients with unrespectable metastatic disease toward systemic therapy [6]. Crown, et al. supported the use of Ga-68 dotatate PET/CT in the care of patients with both early and advanced stage NETs, especially in patients with small bowel NETs that are referred for surgical resection [7]. This clinical case exemplifies the goodness of imaging follow up on these patients, where the molecular diagnose showed greater sensitivity and specificity compared to other conventional techniques, and its impact on clinical management will translate into improved outcomes and increased survival. Furthermore, to providing precise localization of disease, Ga-68 dotatate PET/CT has been shown to provide quantitative information regarding SSTR expression which can inform the use of therapies targeting the SSTR [7]. Yet, new innovations such as SSTR PET/MRI, radiolabeled SSTR antagonists and glucagon-like peptide-1 receptor (GLP-1R) agonists might further improve imaging of GEP-NETs [1].

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