Use of ^{68}Ga DOTATATE, a new molecular imaging agent, for neuroendocrine tumors

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ABSTRACT

Neuroendocrine tumors (NET), such as insulinomas and carcinoid tumors, can be challenging to diagnose since patients often present with vague symptoms. Adding to the challenge, these tumors are often occult on typical cross-sectional imaging modalities. Because of these challenges, there has been an increase in the utilization of radiopharmaceuticals that take advantage of specific receptors expressed by NET. Among the multiple radiopharmaceuticals that can be used, ^{68}Ga DOTATATE is emerging as the most sensitive and specific imaging agent. We present a case where ^{68}Ga DOTATATE was used to diagnose a well-differentiated neuroendocrine tumor.

KEYWORDS Carcinoid; ^{68}Ga DOTATATE; F-18 fludeoxyglucose; neuroendocrine tumors; positron emission tomography/computed tomography

Neuroendocrine tumors (NETs) can be difficult to diagnose, both clinically and radiographically, often until the disease has progressed to the point of causing systemic symptoms or secondary pathology due to mass effect. As a result of these diagnostic shortcomings, emerging nuclear imaging techniques have been increasingly studied and have been shown to be more sensitive and specific than conventional imaging such as computed tomography (CT) and magnetic resonance imaging (MRI) for the diagnosis of NETs.

CASE DESCRIPTION

A 74-year-old man presented with abdominal pain, and an ultrasound showed cholelithiasis but no findings for acute cholecystitis. CT of the abdomen and pelvis with intravenous and oral contrast showed a small, partially calcified mass in the right lower quadrant mesentery and a small filling defect in his distal small bowel (*Figure 1a*). These findings raised suspicion for carcinoid tumor. Imaging with ^{68}Ga DOTATATE PET-CT scan showed avid tracer uptake within a focal mass within the terminal ileum that corresponded to the soft tissue mass with calcified deposits and intraluminal filling defect on the previous CT abdomen and pelvis (*Figure 1b*). This was presumed to be the primary lesion, as no other lesion was identified within the imaged

body. The calcified mesenteric mass and the small bowel mass were resected, and surgical pathology showed well-differentiated neuroendocrine tumor, grade I. The patient did well postoperatively.

DISCUSSION

^{68}Ga DOTATATE scan utilizes the radionuclide gallium-68, which is then attached to a somatostatin receptor analog. Because NETs such as carcinoid tumors,

Figure 1. (a) Coronal CT image showing an intraluminal mass within the distal small bowel (arrow). (b) Coronal ^{68}Ga DOTATATE PET-CT image showing moderately intense uptake that corresponds to the intraluminal mass (arrow) present on the patient's presenting CT scan. This proved to be a primary NET of the terminal ileum.

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Received August 15, 2019; Revised October 3, 2019; Accepted October 7, 2019.

Figure 2. Additional example of a patient with NET. (a) A transaxial CT image showing mass-like fullness in the body of the pancreas (arrow). (b) Transaxial F-18 FDG PET-CT at the level of the pancreas. The soft tissue mass has very little activity (arrow). (c) The ^{68}Ga DOTATATE transaxial image showing avid uptake in the body of the pancreas (arrow).

particularly those that are well differentiated, typically have a large amount of somatostatin receptors, a ^{68}Ga DOTATATE scan is well suited to identify them.¹ Some authors have concluded that ^{68}Ga DOTATATE is so effective in detecting somatostatin receptor-positive tumors that it is nearly as accurate as the gold standard—biopsy.² As is the case in all molecular imaging, knowledge of the normal biodistribution of the radiotracer used is essential to identifying lesions.

Several additional nuclear scans that have been around for many years can aid in the diagnosis of NET; however, these are less effective than the newer ^{68}Ga DOTATATE.^{3,4} Octreoscan (^{111}In -pentetreotide) and F-18 FDG PET-CT can both identify NETs, but have less favorable radiation dosimetry, take longer to complete, have more overlap with normal physiologic background activity which makes the images harder to interpret, and, most importantly, are less sensitive and specific than ^{68}Ga DOTATATE (Figure 2). In addition, ^{68}Ga DOTATATE has been shown to have higher sensitivity in identifying metastatic bone disease when compared to F-18 FDG PET-CT.^{3–5} In recent studies, the utilization of ^{68}Ga DOTATATE for diagnosis and follow-up has also been shown to result in significant alterations in management of NETs.

Ki-67 is a histologic marker for cellular proliferation and correlates with the degree of differentiation of NET. There is an inverse relationship such that the lower the amount of cellular proliferation, the more somatostatin receptors are present. As such, the lower the Ki-67 level, the more activity is seen within the tumor on ^{68}Ga DOTATATE scans (as ^{68}Ga DOTATATE binds somatostatin receptors). A radiographic scoring system, called the Krenning Scoring System, can be used for ^{68}Ga DOTATATE scans and is based on the amount of tumor uptake when compared to normal biodistribution. Patients with low Ki-67 and high ^{68}Ga DOTATATE activity tumors can be considered for peptide receptor radionuclide therapy with therapeutic radiopharmaceuticals such as Lutetium-177.

In addition to identifying NETs, ^{68}Ga DOTATATE scans can be of benefit in other tumors expressing somatostatin receptors. Other tumors that can be imaged by ^{68}Ga DOTATATE include pheochromocytomas, paragangliomas, neuroblastomas, meningiomas, mesenchymal tumors causing oncogenic osteomalacia, medullary thyroid cancer, Merkel cell carcinoma, esthesioneuroblastoma, and small cell lung cancer.¹

^{68}Ga DOTATATE PET/CT has emerged as the standard molecular imaging study for neuroendocrine tumors given its higher sensitivity and specificity compared with other molecular imaging tests including Octreoscan and F-18 FDG PET-CT as well as its impact on clinical management, including earlier curative surgery.

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