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Case Report

Ga-68 DOTATATE PET/CT in a patient with Zollinger-Ellison syndrome ☆,☆☆

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ABSTRACT

This case report follows a 70-year-old male patient with Zollinger-Ellison syndrome undergoing computed tomography (CT) for weight loss and surveillance of bilateral adrenal nodules. Incidentally, diffuse gastric and duodenal wall thickening was noted on CT. The patient underwent esophagogastroduodenoscopy with biopsy results showing well-differentiated neuroendocrine tumors (NET) in the stomach and duodenum. Subsequent imaging with gallium-68 DOTATATE PET/CT showed intense tracer uptake in the stomach and proximal duodenum with liver and regional nodal metastases around the superior mesenteric artery. This case outlines the utility of Ga-68 DOTATATE PET/CT in diagnosing, localizing, and staging NET such as gastrinomas.

Introduction

Zollinger-Ellison (ZE) syndrome is a disease characterized by neuroendocrine tumors typically located in the duodenum or pancreas that hyper-secretes gastrin leading to refractory peptic ulcer disease (PUD). The syndrome is typically diagnosed in patients with refractory PUD and an established elevated level of gastrin at baseline or after stimulation. Tumor localization is traditionally performed by endoscopy followed by imaging such as computed tomography (CT), magnetic resonance imaging (MRI), or positron emission tomography (PET) scan. These imaging modalities often have nonspecific findings, therefore requiring nuclear medicine studies for better localization. The following case reports the utilization of Ga-68 DOTATATE PET/CT in identifying, localizing, and staging neuroendocrine tumors such as gastrinomas.

Case report

A 70-year-old male patient with a past medical history of ZE syndrome underwent an abdominal CT for surveillance and screening after complaining of new unintentional weight loss. The CT scan showed diffuse and heterogeneously enhancing gastric mural thickening (Fig. 1B), which was more conspicuous compared to prior studies. Given these findings, the

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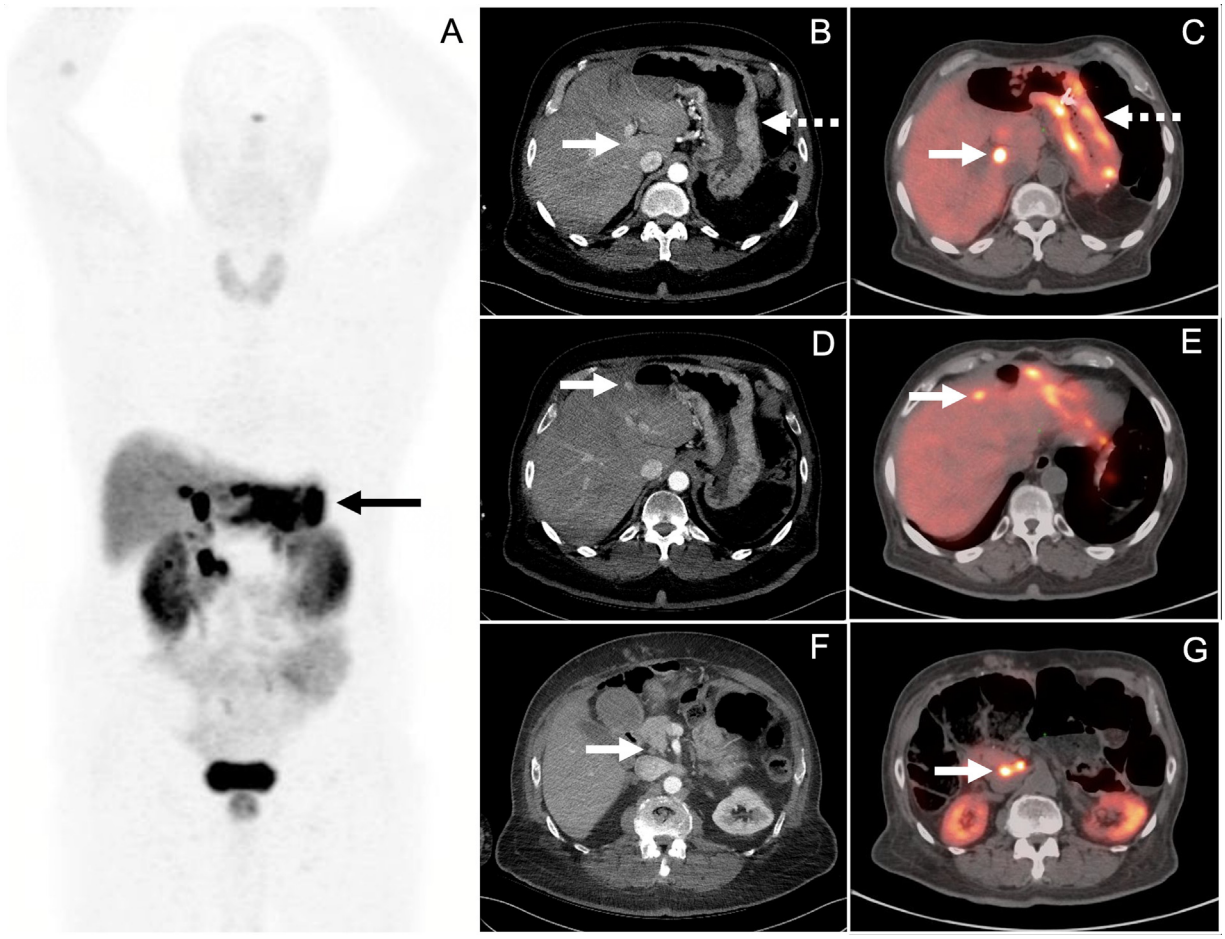

Fig. 1 – (A) Whole body rotating (MIP—multiple intensity projection) image from patient's Ga-68 DOTATATE PET/CT show intense uptake in the stomach (black arrow) and other foci in the upper abdomen. B and C are CT and fused PET/CT images showing multifocal to diffuse uptake in the stomach corresponding to heterogeneously enhancing mural thickening (dashed arrow). There is also focal uptake in a subtly enhancing hepatic metastasis (solid arrow). Images D and E show focal uptake in a small enhancing hepatic metastasis (arrow). Images F and G show focal uptake in subcentimeter lymph nodes at the level of the SMA.

patient was scheduled for an esophagogastroduodenoscopy for direct visualization and tissue sampling, which revealed well-differentiated Grade 2 neuroendocrine tumors (NET) in the stomach and Grade 1 NET in the proximal duodenum. Serum gastrin level was elevated during this time at 4438 pg/mL (normal 0-100 pg/mL). A fasting gastrin level above 1000 pg/mL is diagnostic of ZE. The case was then discussed at tumor board and staging was completed with Ga-68 DOTATATE PET/CT.

About 5.4 mCi of gallium-68 DOTATATE was administered intravenously and images were acquired about 60 minutes later. A low-dose non-contrast–enhanced CT was acquired concomitantly for attenuation correction and anatomical localization. The PET/CT showed intense tracer uptake correlating with the areas of gastroduodenal thickening (Fig. 1C), consistent with a somatostatin receptor avid neuroendocrine tumor. Additionally, there was evidence of multiple liver metastases in the left lobe and hilum region, nodal metastases around the mesenteric root, and the duodenum (Figs. 1C, E, and G). After discussing these findings and the prognosis with the patient, he chose conservative therapy with octreotide injections rather than invasive surgery. Patient has since received one dose of the octreotide injection and has not returned for follow-up on symptoms due to hospitalization for pulmonary embolism.

Discussion

ZE syndrome is caused by the proliferation of gastrin cells forming so called "gastrinomas." The function of gastrin is to stimulate the parietal cells of the stomach to secrete hydrochloric acid for chemical digestion of food. With unopposed gastrin secretion, the walls of the stomach and intestines are unable to protect the intimal layer from erosion leading to PUD. Other symptoms commonly associated with ZE syndrome include chronic diarrhea and gastroesophageal reflux disease [1]. Although gastrinomas are typically slow growing, studies have seen 60%-90% are malignant

with metastases playing a significant role in patient survival [2].

Given the unopposed gastrin release in patients with ZE syndrome, they are often dependent on constant suppression of gastric acid by proton pump inhibitors (PPI). While this medication is typically necessary for management of the symptoms, it can sometimes make diagnosis challenging [3]. ZE, commonly associated with Multiple Endocrine Syndrome-1 (MEN1), is typically diagnosed in patients with refractory PUD with elevated gastrin levels. Diagnosing ZE syndrome via measurement of gastrin levels at baseline requires individuals to abstain from PPI use for at least 1 week [4]. It has been posited that widespread PPI use in these patients delays diagnosis and causes refractory symptoms. It has been shown that elevated fasting gastrin levels can be attributed to chronic PPI use or chronic atrophic gastritis [5].

Standard management depends on the extent of symptoms. Historically gastrectomy was the standard of care before the advent of H2 receptor antagonists and PPIs [2]. Although pharmacology is targeted at reducing the effects of excessive gastric acid secretion, some tumors require surgical management due to location and invasion into neighboring structures [6]. In patients with associated MEN1 syndrome, surgical management remains controversial due to unpredictable course and frequent metastases. Surgical resection is usually offered to prevent metastasis in patients with tumors larger than 2 cm, given that MEN1 patients with pancreatic tumors $\leq$2 cm have normal life expectancy [7].

Given the unreliability of gastrin assays as well as the importance of determining whether symptoms are due to ZE syndrome, novel imaging has shown promise as a tool for accurate diagnosis. While multiphasic CT and MRI have been useful tools for detecting large tumors and metastases, smaller tumors are more likely to be hidden using these modalities. CT has shown to detect tumors $>$1 cm, liver metastases and pancreatic head tumors with sensitivities and specificities of 59%-78% and 95%-98% respectively [4]. MRI has demonstrated sensitives and specificities of 25%-85% and 100%, respectively [4].

Newer imaging techniques utilizing somatostatin receptor radiolabeled analogs (SSR) such as Ga-68 DOTATATE are proven alternatives, especially for challenging cases [7]. The case discussed above demonstrates how Ga-68 DOTATATE PET/CT is a reliable and efficient imaging modality to diagnose and localize gastrinomas of varying sizes throughout the body. Combined Ga-68 PET/CT scans have shown sensitivities and specificity of 93% and 96%, respectively [8]. This modality has also shown to be more sensitive for well-differentiated NET than ^{111}In octreotide scintigraphy [9]. Another major benefit to SSR imaging is its utility in determining patient candidacy for peptide receptor radionuclide therapy [7]. Using the Krenning score, a system based on intensity and location of SSR uptake, patients are assessed if they would benefit from the treatment that involves targeting metastatic NETs using high-energy radiation. The most common somatostatin analog used for this therapy is Lu-177 DOTATATE [10]. For a patient similar to the one discussed here, peptide receptor radionuclide therapy could serve as a safe, approved alternative to surgery or conservative octreotide medical therapy [11].

Patient consent

A written informed consent was obtained from the patient for the publication of this case report.

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