

Rare Occurrence Of Hypergastrinemia due to Thoracic Neuroendocrine Tumor: Detection and Characterization by ^{68}Ga -DOTATATE PET-CT

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Keywords: HYPERGASTRINEMIA; THORACIC NEUROENDOCRINE TUMOUR; ^{68}Ga -DOTATATE PET-CT

Short running title: **^{68}Ga -DOTATATE PET-CT in Hypergastrinemia**

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ABSTRACT

Hypergastrinemia is a prominent feature of a segment of gastroenteropancreatic neuroendocrine tumours, the gastrinomas, mostly occurring in the gastrinoma triangle. Hypergastrinemia due to a thoracic NET is a very rare occurrence with paucity of literature elucidating the same. We report a case of thoracic NET who had initially presented with symptoms of peptic ulcer disease of 3 years duration. On evaluation, the fasting serum gastrin levels were raised. Conventional imaging modalities and endoscopic evaluation did not identify the location of possible gastrinoma or any other mass in the abdomen. In view of hypergastrinemia, somatostatin receptor (SSTR) targeted imaging with ^{68}Ga -DOTATATE PET/CT was undertaken which showed a SSTR expressing paravertebral para-aortic mass (next to thoracic aorta) in the left lung. The mass was excised and the histopathology was suggestive of metastatic neuroendocrine tumour (Mib1 labeling index of 2%). The present case underscores the importance of ^{68}Ga -DOTATATE PET-CT in both detecting and characterizing the causative lesion missed on ceCT, that was not easily amenable to a biopsy.

INTRODUCTION

Neuroendocrine tumours (NET) are tumours arising from the neuroendocrine cells, which are the peptide and amine producing cells dispersed throughout the body. Gastrinomas are a type of NET which secretes the hormone gastrin leading to hypergastrinemia. The most common site of these gastrinomas (more than 80%) is the gastrinoma triangle, bounded by the cystic and common bile duct superiorly, the second and third portions of the duodenum inferiorly and the neck and body of the pancreas medially. Clinically, hypergastrinemia causes increase in the gastric acid secretion and the symptoms of gastrinoma are associated with peptic ulcer disease, diarrhoea and reflux esophagitis. Dyspepsia, haemorrhage and abdominal pain are related to

hyperacidity (1). Hypergastrinemia is a rare occurrence in cases of thoracic NETs. There are very few reports supporting the same in the literature.

CASE REPORT

A 44 years old male, initially presented with history of hyperacidity, recurrent diarrhoea and vomiting since 3 years. He was continuously being treated with proton pump inhibitors which relieved him of the symptoms for a short duration and recurrence following discontinuation of medications. Multidetector CT (MDCT) of abdomen done previously showed diffuse wall thickening with enhancement of gastric rugae in the fundus and body regions of the stomach. Incidental horse shoe kidney was also detected. Upper and lower GI endoscopy and the biopsy from the stomach was repeatedly negative for malignancy. The only positive finding for OGDscopy was esophagitis, thick folds and duodenitis. Fasting serum gastrin level was raised (674 ng/ml). The local reference range for serum gastrin level is 13-115 pg/ml.

The patient was referred for SSTR targeted imaging for suspected gastrinoma. The ⁶⁸Ga-DOTATATE scan showed a solitary focus of uptake and SSTR expression in the para-aortic mass in the left lung (Fig 1 left panel and 2). A review of the previous done CT was undertaken: the lower chest sections of the CT (Fig 1 right panel) showed a para-aortic mass near the thoracic descending aorta in the left lung, which was incidentally missed. The para-aortic mass was excised by video assisted thoracoscopic surgery (VATS) and the histopathology was suggestive of neuroendocrine tumour (Mib1 labeling index of 2 %) with immunohistochemistry positive for synaptophysin, chromogranin and CD 56. At this follow-up point (one and half month post surgery), the patient is being observed with next follow-up at 3 months.

DISCUSSION

Hypergastrinemia is a condition with raised fasting serum gastrin levels. The most common cause of hypergastrinemia is gastrinoma, a type of neuroendocrine tumour. Gastrinomas causing the Zollinger–Ellison syndrome are almost exclusively located in the abdomen, primarily in the duodenum or pancreas, and rarely in the stomach, mesentery, spleen, liver and ovaries. In 10-50% of cases, gastrinomas cannot be located in the abdomen even after

careful abdominal exploration. Though most missed gastrinomas are present in the duodenum or pancreas, the present case shows that extra-abdominal cause is possible.

Hypergastrinemia is rarely encountered in a thoracic NET. It has been reported in rare cases of cardiac gastrinoma (2, 3), cases of bronchoalveolar carcinoids associated with MEN 1 Syndrome (4), non small cell carcinoma of lung (5) and in association with diffuse idiopathic neuroendocrine cell hyperplasia in the lungs (DIPNECH) (6).

Gibril et al in their report (2) presented a case of a cardiac gastrinoma in a patient who had presented with abdominal pain and had raised fasting gastrin levels. Conventional imaging modalities failed to localise an intra-abdominal mass while MRI was suggestive of a cardiac mass. Echocardiography with Doppler study and cardiac catheterisation localised a left ventricular wall mass. The mass could not be biopsied, however was positive in somatostatin receptor imaging undertaken with [111In-DTPA-DPhe1] octreotide. The patient died due to other comorbidities and on autopsy the cardiac mass was found out to be neuroendocrine tumour staining positive for gastrin, chromogranin and synaptophysin.

MEN1 syndrome is an autosomal dominant syndrome associated with tumours of pituitary, pancreas and parathyroid. Bronchopulmonary carcinoids are very rare. In a study carried out for incidence of bronchopulmonary carcinoids in MEN 1 syndrome patients, the incidence was found to be 5% (4) and hypergastrinemia was common in patients with the pulmonary nodules as compared to the other patients.

Conclusion:

Thus, the present case illustrates the importance of ^{68}Ga -DOTATATE PET-CT in detecting a lesion that was missed on the ceCT. Additionally important is the fact that even if it had not been missed, it would be impossible to characterize this mass a neuroendocrine tumor based on CT alone and underscores the importance of somatostatin receptor based PET imaging.

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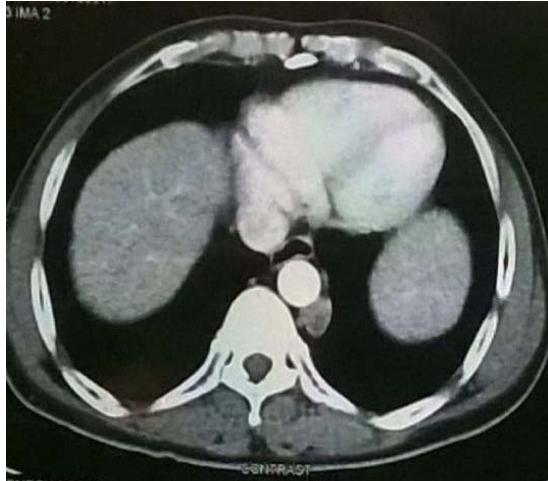


Figure 1A



Figure 1B

Figure 1A: MDCT abdomen showing the para-aortic paravertebral mass in the lower chest section, which was not reported in the abdominal ceCT report. **Figure 1B.** ^{68}Ga -DOTATATE PET-CT transaxial slice demonstrating the paravertebral paraortic mass showing avid tracer uptake.

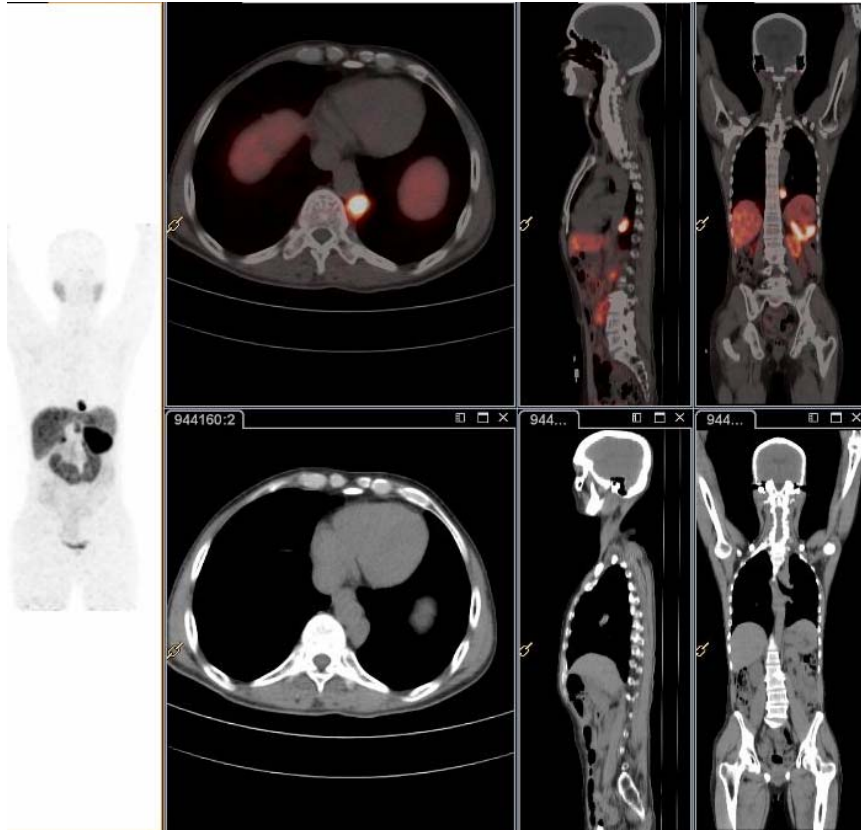


Figure 2

Figure 2: ^{68}Ga -DOTATATE non-contrast PET-CT (MIP and 3 plane images) showing a solitary focus of uptake and SSTR expression in the paravertebral paraaortic mass in the left lung indicating SSTR expression, rest of the whole body survey being unremarkable.