

Sporadic Duodenal Gastrinoma causing Zollinger Ellison Syndrome – A Rare Case Report

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ABSTRACT

Introduction: Gastrinoma is a rare gastrin secreting neuroendocrine tumor. Clinical manifestations are nonspecific gastrointestinal (GI) symptoms or as Zollinger Ellison Syndrome (ZES) which often delays the diagnosis in majority of patients. Hence a high clinical index of suspicion is warranted in patients who present with nonspecific GI symptoms to rule out gastrinoma.

Case report: We report a case of 55 year old female who presented with long standing dyspepsia and chronic diarrhoea and was diagnosed with Sporadic Duodenal Gastrinoma on detailed evaluation. She was treated with surgical resection and pathologically diagnosed as well differentiated neuroendocrine tumor, Gastrinoma – grade I after IHC analysis. Patient was relieved of her symptoms and became eugastrinemic after surgery.

Conclusion: Any patient with refractory dyspepsia associated with long standing non specific abdominal symptoms should be evaluated for Gastrinoma and treated accordingly to avoid misdiagnosis and complications in the long run.

Keywords: Gastrinoma, Duodenum, Zollinger Ellison syndrome, Neuroendocrine.

INTRODUCTION

ZES is a clinical syndrome due to the ectopic secretion of gastrin by a neuroendocrine tumor (gastrinoma), located primarily in the duodenum (60%-80%) or pancreas (10%-40%), resulting in gastric acid hypersecretion, which if left untreated results in refractory peptic ulcer disease, severe gastroesophageal reflux disease, diarrhea and finally death, primarily due to the complications of the refractory peptic ulcer disease.¹⁻³ First described by Zollinger and Ellison together in 1955⁴ gastrinoma is one of the rare causes of refractory dyspepsia. The incidence of ZES is rare, ranging from 0.1 to 3 per million in the population each year.⁵⁻⁷ Sporadic occurrence is noted in around 80% of gastrinomas, while approximately 20–30% are found along with Multiple Endocrine Neoplasia Type 1 (MEN-1) syndrome.⁷

Gastrinoma should be ruled out in any patient with dyspeptic symptoms not responding to conventional management with proton pump inhibitors or who have relapse of symptoms immediately once medications are stopped. Evaluation includes an Esophagogastroduodenoscopy and Fasting serum Gastrin assay. Modern imaging like CECT and DOTANOC PET CT has helped in the exact localisation of the lesions and for preoperative planning of the treatment. If feasible all patients with Gastrinomas, should be offered surgical resection in view of relatively high incidence of malignant pathology.

CASE REPORT

A 55 year old female presented to our Gastroenterology OPD with complaints of chronic diarrhoea and dyspepsia of 5 years duration. She had undergone Laparoscopic Cholecystectomy for biliary symptoms around 5 years back elsewhere. Her examination otherwise revealed no abnormal clinical findings.

She was evaluated with Gastroduodenoscopy and Colonoscopy which revealed pangastritis with gastric and duodenal erosions and normal mucosal findings respectively. She was treated initially with proton pump inhibitors (PPIs) to which she responded. However on discontinuing proton pump inhibitors her symptoms recurred. Her fasting Serum Gastrin level showed mild elevation to 234 pg/ml (Normal 13.00 – 115.00 pg/ml). Hence she underwent CECT Abdomen evaluation to rule out any neuroendocrine lesion and it revealed an isodense arterial phase homogeneously enhancing lesion measuring 1.6 x 1.3 cm noted along the medial and superior wall of the first part of duodenum just distal to the pylorus. No extramural extension, regional lymphadenopathy or metastatic liver lesions noted. Later she underwent a 68 Ga- DOTANOC PET CT evaluation which revealed an abnormal uptake in the enhancing lesion in first part of duodenum. (Fig.1). No other abnormal focal/ diffuse 68 Ga- DOTANOC uptake noted elsewhere. Possibility of MEN-I was ruled out by evaluating serum calcium levels, hormonal levels. Probable diagnosis of sporadic duodenal gastrinoma was made and she was advised surgical resection. Intraoperatively around 1.5 x 1.5 cm nodular lesion was noted along the superior and posterior aspect of the duodenum, just distal to pylorus. After extensive Kocherisation and lesser sac evaluation, head of pancreas, uncinate process and adjacent area were palpated to rule

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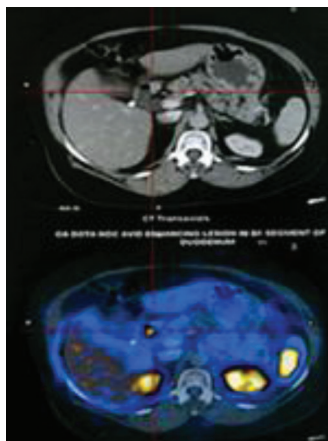


Figure-1: 68 Ga-DOTANOC Scintigraphy showing abnormal uptake at the first part of duodenum

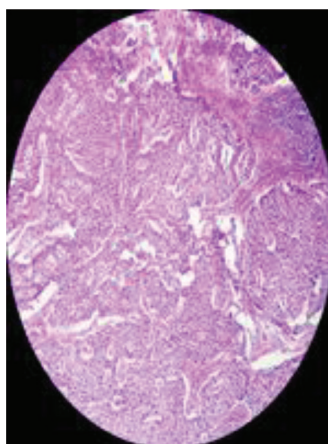


Figure-2: Trabecular pattern typical of neuroendocrine tumor

out any other similar nodules. First part of duodenum was mobilised partly from pancreas by dividing right gastric artery and branches from pancreaticoduodenal arcade to first part of duodenum. Resection of the nodular lesion along with 5 mm margin was done after duodenotomy along with sampling from retroduodenal and hepatoduodenal lymph nodes. Defect was closed transversely in single layer along with omental buttressing. Histopathological analysis showed trabecular histologic pattern, characteristic of neuroendocrine tumors with negative margins all around (Fig.2). Immunohistochemical analysis were positive for Chromogranin A. Remarkable improvement in clinical symptoms were noted after surgery.

DISCUSSION

Gastrinoma is the second most common functional neuroendocrine tumor of gastrointestinal tract, usually located in the Gastrinoma triangle. It is the second most common functional neuroendocrine tumor, usually located typically in the Gastrinoma triangle. Most common presentation is of sporadic nature (75%) and remaining as part of Multiple Endocrine Neoplasia Type 1 (MEN-1) syndrome. The presentation of ZES due to Gastrinoma is usually indistinguishable from ordinary peptic ulcer disease and in those patients with symptoms not related to peptic ulcer, i.e., diarrhoea, as their main complaint, the diagnosis

is often not even considered. A high index of suspicion is required, however, in patients with recurrent ulcers, multiple ulcers and in those with resistant or rapidly relapsing ulcers after conventional therapy to rule out gastrinoma. Two major treatment problems to be kept in mind when dealing with patients diagnosed with gastrinomas are: treatment must be directed at controlling the acid hypersecretion and because of high malignant potential of gastrinomas, treatment must be directed against the gastrinoma itself. Gastrinoma arising from pancreas are usually more aggressive and are more likely to metastasize to the lymph nodes, liver and bone than are duodenal tumors.

Once a clinical suspicion of Gastrinoma is made in view of refractory peptic ulcer disease and secretory diarrhoea along with elevated fasting serum gastrin level, imaging should be done to localize the disease and rule out metastatic lesions. Modern imaging investigations like 68 Ga DOTANOC scintigraphy helps in localisation of tumors.⁸ CT and MRI are both highly accurate in detecting lesions greater than 3 cm; however, accuracy decreases for tumors that are smaller than 2 cm in size (studies have reported around 42–56% sensitivity of CT scans and 25–83% sensitivity for MRI). Since Gastrinomas express somatostatin receptors, SRS scans can be utilized for tumor detection with a higher sensitivity than CT/MRI (reported to be around 80–85%). Of late EUS has also become an important tool in case of small tumors located in the pancreas. This emphasizes that the use of multiple imaging modalities, including SRS, may be imperative in the diagnosis of a gastrinoma.

Only curative management in case of gastrinoma is surgical resection. Fraker et al⁹ reported that gastrinoma patients administered conservative treatment exhibited a higher risk of liver metastasis (23%) compared with those who received surgery (3%). For gastrinoma located in the pancreas, enucleation is advised, while for gastrinomas of the duodenum, due to its possibility of multiple distribution, the duodenum should be lanced and the lesions resected. Importantly, lymph node dissection should be performed even if no primary tumor is identified due to the possibility that the primary tumor may have occurred in the (peripancreatic) lymph nodes. Lymph nodes along the celiac trunk and hepatic ligament should also should be dissected.

Conservative management is advised only in patients unfit for surgery or in case of widespread metastatic disease. Proton pump inhibitors are the mainstay of medical management for controlling the acid secretion. Though somatostatins like octreotide have been used, no therapeutic guidelines have been established regarding dosage and duration of treatment. Chemotherapy regimen are available in case of widespread metastatic disease, first line which includes combined therapy with streptozotocin and 5-fluorouracil or doxorubicin.¹⁰ Whether chemotherapy prolongs the survival is controversial and radiotherapy is usually not advised.

CONCLUSION

Gastrinoma being a rare disease can produce considerable morbidity and poor quality of life if misdiagnosed and left

untreated. Maintaining a high index of suspicion along with modern investigations helps in the diagnosis of Gastrinomas. Surgical resection is the only treatment which offers chance of complete cure, hence should be attempted whenever feasible.

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