# Case Report

## Unusual Presentation of Gastric Neuroendocrine Tumour

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## Abstract

Gastric neuroendocrine tumors (NETs) develop from neuroendocrine cells. Gastric NETs are usually discovered as submucosal lesions during upper gastrointestinal endoscopy. NETs are graded into 3 types based on mitosis and Ki-67 index. We describe a case of upper GastroIntestinal Bleeding which was diagnosed to be a well differentiated type III neuroendocrine tumor of the stomach.

Key Words: Neuroendocrine tumor, GI bleeding, Endoscopy

## Introduction

Neuroendocrine tumours previously mentioned as NETs are now described collectively under a term called Gastroenteropancreatic Neuroendocrine tumours (GEPNETs). They originate in the enterochromaffin cells located in the gastrointestinal (GI) tract. NETs are subdivided into foregut (gastric, duodenal and pancreatic) midgut (jejunal, ileal, cecal) and hindgut (distal colic and rectal)[1] Most common site of origin is ileum, followed by the rectum and the appendix[2,3]. Recent accepted nomenclature is by primary tumour site not by embryologic origin.

Gastric neuroendocrine tumours comprise less than 1% of all gastric tumours [4]. Depending on clinical presentation and histological findings, three types exist. Type I is associated with enterochromaffin like (ECL) cells hyperplasia, hypergastrinemia, achlorhydria and chronic atrophic gastritis with or without pernicious anemia[5] Type II is associated with Zollinger-Ellison syndrome (ZES) and multiple endocrine neoplasia (MEN-1) syndrome. Type III tumors are large, solitary, sporadic and invasive in nature[5].

They are usually asymptomatic or present with various upper abdominal symptoms of pain abdomen, bleeding and anemia. We describe a case of a large type III neuroendocrine tumor of the stomach.

## Case Report

A 39 year old female presented with moderate hematemesis followed by malena and generalized weakness. There was no previous history of blood vomiting, pain abdomen or distension. On physical examination she was obese with BMI of 48kg/m$^2$ and mild pallor was present, Vitals were normal. Laboratory findings reveal Hemoglobin of 8.6 gm/dl, otherwise normal.

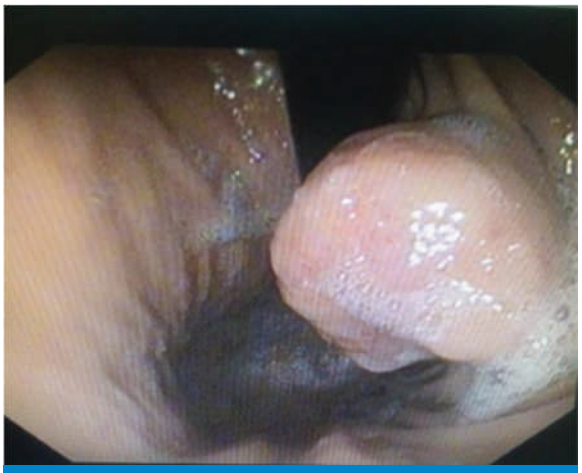

**Fig 1** : Upper GI endoscopy

Upper GI endoscopy (Fig 1) showed a (2 cm x 3 cm), globular, submucosal lesion with blood spot, 5cm below the esophago gastric junction in proximal body, along the greater curve. A possibility of Bleeding gastrointestinal stromal tumor (GIST) was kept and Endoscopic Ultrasound (EUS) was planned.

EUS(Fig 2) done with radial array echo endoscope showed a Single large mass lesion of 2.5 x 2.2cm in anterior wall along greater curve in proximal stomach with surface ulceration and no active bleeding, it appeared to be arising from submucosal layer and able to delineate the third and fourth layer clearly, hence the diagnosis of neuroendocrine tumour of stomach was made.

CT abdomen (Fig 3) showed no evidence of regional lymphadenopathy or distant organ metastasis. Patient did not depict any clinical evidence of carcinoid syndrome.

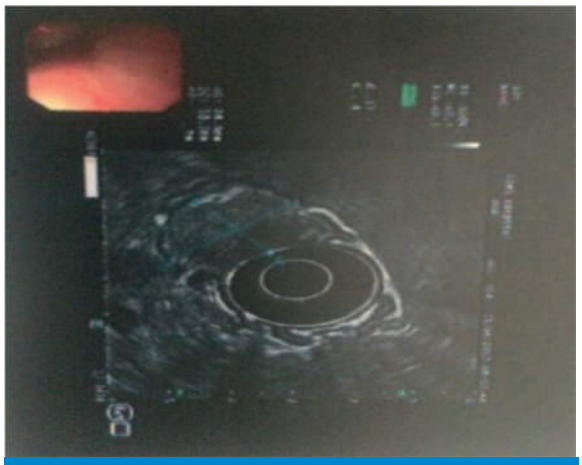

**Fig 2** : EUS image

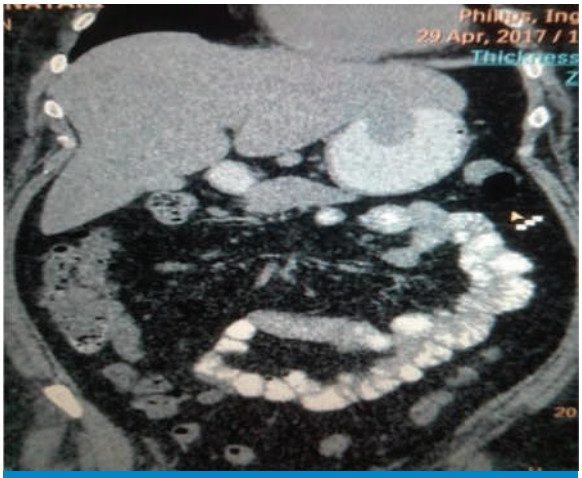

**Fig 3** : A well defined endophytic, isodense, enhancing lesion seen in fundus.

After careful evaluation, patient was referred to surgeon and planned for surgery. An open surgery with partial gastrectomy was done and a segment measuring 6x 3 cm was sent as gross specimen (Fig 4).

Negative margins were confirmed by frozen section. Cut surface showed a lobular mass measuring 3x2x2 cm with mucosal ulcerations. Resected margins were free of tumor cells with no vascular and perineural invasion.

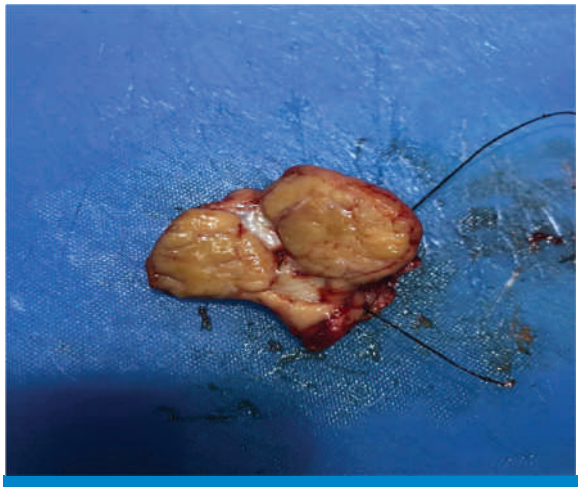

**Fig 4** : Gross specimen

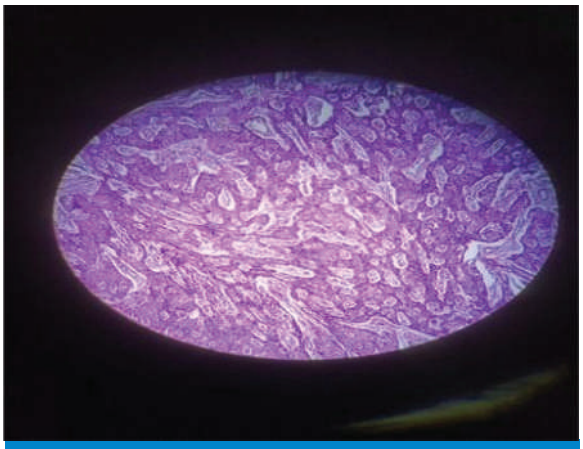

**Fig 5** : Nests, trabaculae, ribbons of large Neuroendocrine cells

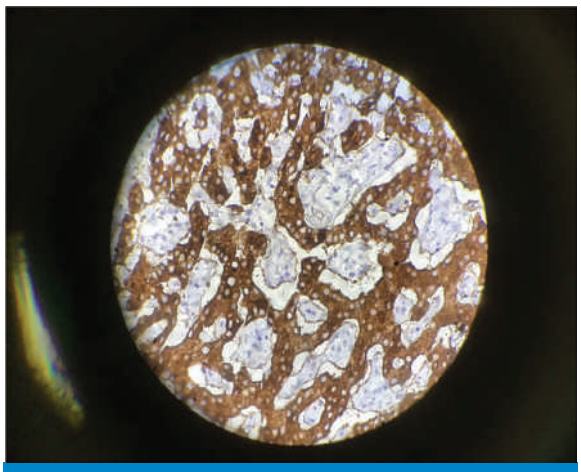

**Fig 6** : Synaptophysin and Chromogranin shows bright membranous positivity

Histopathology of the mass showed a well differentiated gastric neuroendocrine tumor (Fig 5), invading muscularis propria which stained positive for synaptophysin and chromogranin A (Fig 6) with background chronic gastritis.

A diagnosis of large solitary type III gastric carcinoid with low grade malignant potential of Grade–G1(Mitosis < 2 /10 hpf, Ki 67 <= 2%) as per modified WHO grading system and TNM Stage of T2 was made. Patient remained stable in post operative period and advised to follow up with 68Ga-DOTATATE PET/CT after six months[6].

## Discussion

NETs are explained by two major classifications, the WHO and American Joint Committee on Cancer. The 2010 WHO classification is based on number of mitosis and the Ki67 index shown in Table 1. The 2009 American Joint Committee on Cancer/Union for International Cancer Control(AJCC/UICC) classification system uses tumor invasion, number of lymph nodes affected and metastases (TNM).

Due to increase in screening endoscopies, incidence has increased[7] to 1–2 cases per 100,000 population per year with a female predominance.

| WHO(2010)and ENETS Nomenclature | GRADE | Mitotic Count | Ki – 67 Index (%) | Cell Type |
|---|---|---|---|---|
| NET | G1 | <2mitosis/10HPF | <2 | -- |
| NET | G2 | 2-20 mitosis/10HPF | 3-20 | -- |
| Neuroendocrine carcinoma (NEC) | G3 | >20 Mitosis/10HPF | >20 | Large v/s small cell |

Ref : ENETS - European Neuroendocrine Tumour Society

**Table 1 -** WHO classification of NETS

In type I GNETs, atrophic gastritis because of autoimmune etiology or related to H.pylori causes destruction of parietal cells, responsible for hypergastrinemia[8]. Type 1 tumors are multifocal, having size less than 2 cm, located in fundus or body.

Patients with gastric NET suspicion should be evaluated with serum chromogranin A level and gastrin levels to rule out hyper-gastrinemia. On endoscopy gastric NETs are found incidentally when dyspeptic symptoms or anemia are evaluated. Biopsies of normal appearing mucosa also helps to rule out atrophic gastritis. To assess depth in lesions of more than 2 cm Endoscopic ultrasound (EUS) should be done[9]. An Octreotide scan and FDG-PET scan are still more sensitive when symptoms of carcinoid syndrome are present.

It is important to consider Gastric NETs while evaluating any gastric polyp. Gastric NETs may present with Gastro-intestinal bleeding and anemia. The early diagnosis of these rare tumors makes a difference if they are having high malignant tendency.

Grade determines the prognosis. NET G1 is having good prognosis with high 5 year survival. NET G2 is aggressive but favourable prognosis. NET G3 are already invasive at initial diagnosis. The overall 5 year survival for all gastric NETs is 49%.

In Neuroendocrine carcinoma (NEC) prognosis is poor as malignant potential is high. NET less then 1cm can be removed by endoscopic means, However risk of recurrence exists. NEC requires extensive surgery[10]. Liver metastasis requires treatment with somatostatin analogues, hepatic artery embolisation, radiotherapy or chemoembolisation. The adjuvant chemotherapy for NEC is cisplatinum based chemotherapy[11].

Our patient, had no distant metastasis and was treated with partial gastrectomy, although theoretical risk of recurrence still exists. This case is reported for its rarity of the site and unusual presentation.

## Conclusion

Treatment of GEPNETs includes team-based approach, using multiple tools to improve outcomes.

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