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Case series: Clinico-pathological studies of gastrointestinal neuroendocrine tumors (GI-NETs)

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ABSTRACT

Gastrointestinal neuroendocrine tumors (GI-NET) are one of the rarest cancers that occur with an annual global incidence of 2.5-5/100000 patients. Gastrointestinal NET is the second cancer that affects any individuals, after cancer of the colorectal region. Early identification and early intervention will prevent the mortality of individuals dying due to gastrointestinal neuroendocrine tumors. The main element of prevention is early identification; hence clinicians can identify the rarest cases and can receive enlighten insights to reduce the mortality due to the rarest diseases.

Keywords: gastrointestinal, gastrointestinal neuroendocrine tumors (GI-NeT), chromogranin A protein, neoplasia, neurofibromatosis, intra-arterial therapies, polypoid

INTRODUCTION

The neuroendocrine system is composed of nerve cells, along with gland cells. The neuroendocrine system secretes hormones and releases them into the bloodstream, and neuroendocrine tumors (NETs) are rare [1]. As per WHO 2019 classification, tumors in the intestine are classified as neuroendocrine tumors and tumor occurs in the epithelial tissues of the intestine. Another classification given to NETs is goblet cell adenocarcinomas [2].

Most of the NETs' growth is slow, but a few of the NETs are rapidly growing, and around 20% of the NETs are connected to hereditary genetics such as endocrine neoplasia and neurofibromatosis [3]. NETs in the intestinal regions are the rearrest form of tumors, and gastric NETs are divided into 3 types: type I is associated with autoimmune atrophic gastritis; type II is associated with gastric tumor/MEN-1; and (3) type III scattered with normal gastrin concentration. Type III Gastric NETs tend to appear larger and deeper more invasive than types I and II [4].

The incidences of GI-NETs have increased recently due to endoscopy, and proton-pump inhibitors, and excepts heterogenicity both clinically, and pathologically thus showing variation in endocrine activities, and also in cancerous cell growth [5,6]. The classifications of GI-NETs are based on the embryological origins of foregut, midgut, and hindgut GI-NETs [7]. Based on US national cancer registration, the annual GI-NET incidence was 3.6-3.9/100,000 population [8].

The study showed that the initial tumor resection without removing metastatic diseases has provided a longer survival in all their stages (hazard ratio: 0.38-0.66, P < 0, 01) [9]. Around 70% of the neuroendocrine tumor's disease burden can be cytoreduced, still, careful consideration is required for liver-involved neuroendocrine tumors [10]. Published data described that NET metastases especially liver involved respond effectively to intra-arterial therapies (IATs) [11].

Clinical presentation of case series

The case series patients with neuroendocrine tumor (NET) were presented to the hospital with main symptoms such as flushing diarrhea, abdominal pain, feeling tired, bloating, shakiness, and sudden weight loss.

Primary evaluation of case study patients

The primary evaluation of neuroendocrine tumor was evaluated by the blood test (CgA) and the test for CgA was positive for the 3 case series patients.

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Primary evaluation leading to the identification of rarest diseases - Gastrointestinal Neuroendocrine Tumors

After the primary evaluation by the CgA test, the case series patients were further undergoing biopsy tests to confirm the rarest disease Gastrointestinal Neuroendocrine Tumor (GI-NET). The histopathological biopsy from the patient showed chromogranin A protein as shown in Figure 1.

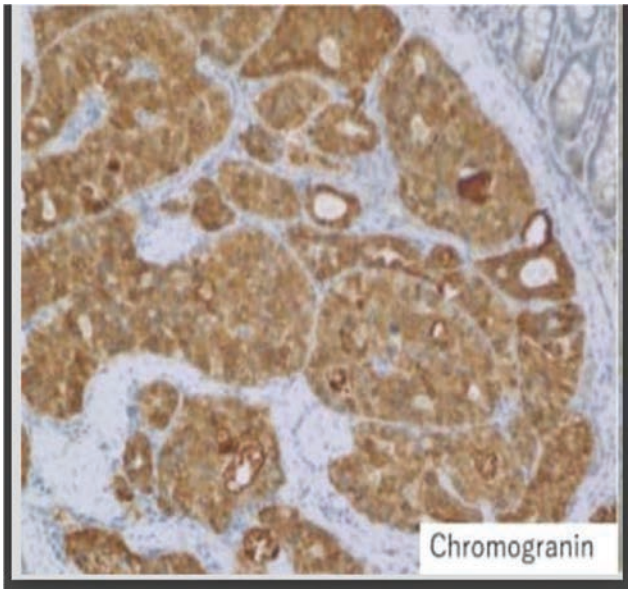

FIGURE 1. Chromogranin A protein in Gastrointestinal Neuroendocrine Tumor patient

Confirmative evaluation identification of rarest diseases - GI-NET tissue biopsy - synaptophysin, and eosin immunohistochemistry

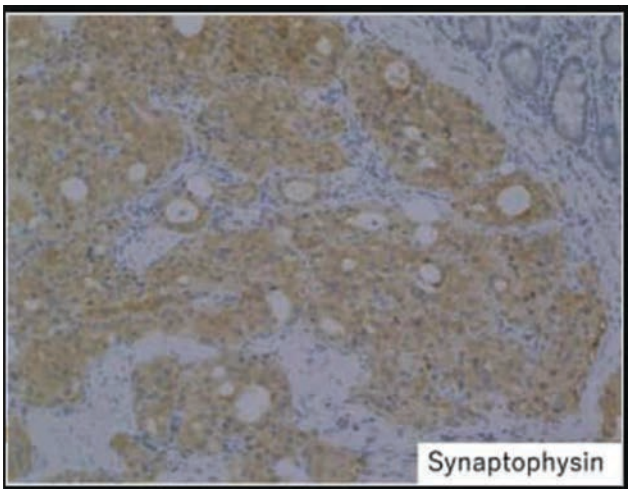

FIGURE 2. Tissue biopsy - synaptophysin-Gastrointestinal Neuroendocrine Tumor

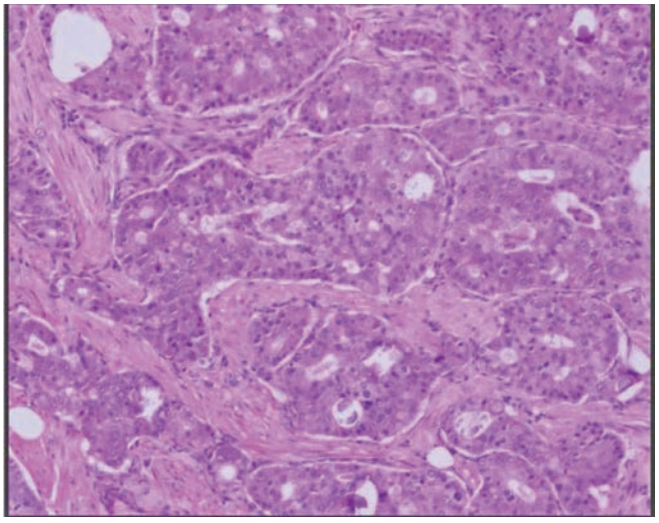

FIGURE 3. Chromogranin A protein in Neuroendocrine Tumor patient in eosin staining

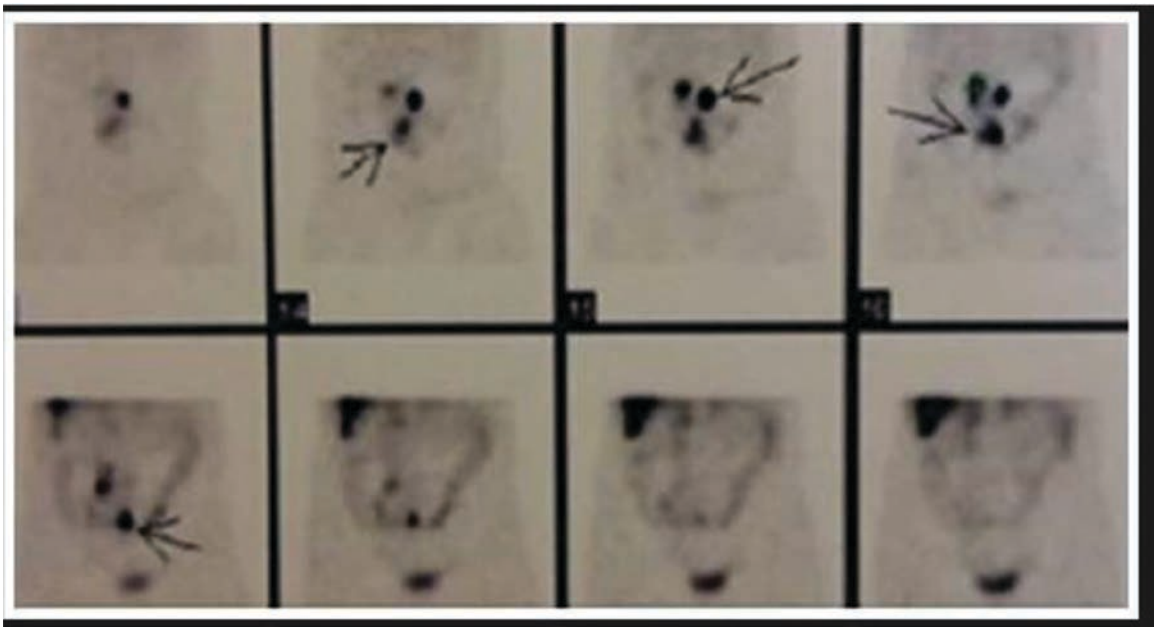

FIGURE 4. Chromogranin A protein in small intestinal NET- Neuroendocrine Tumor

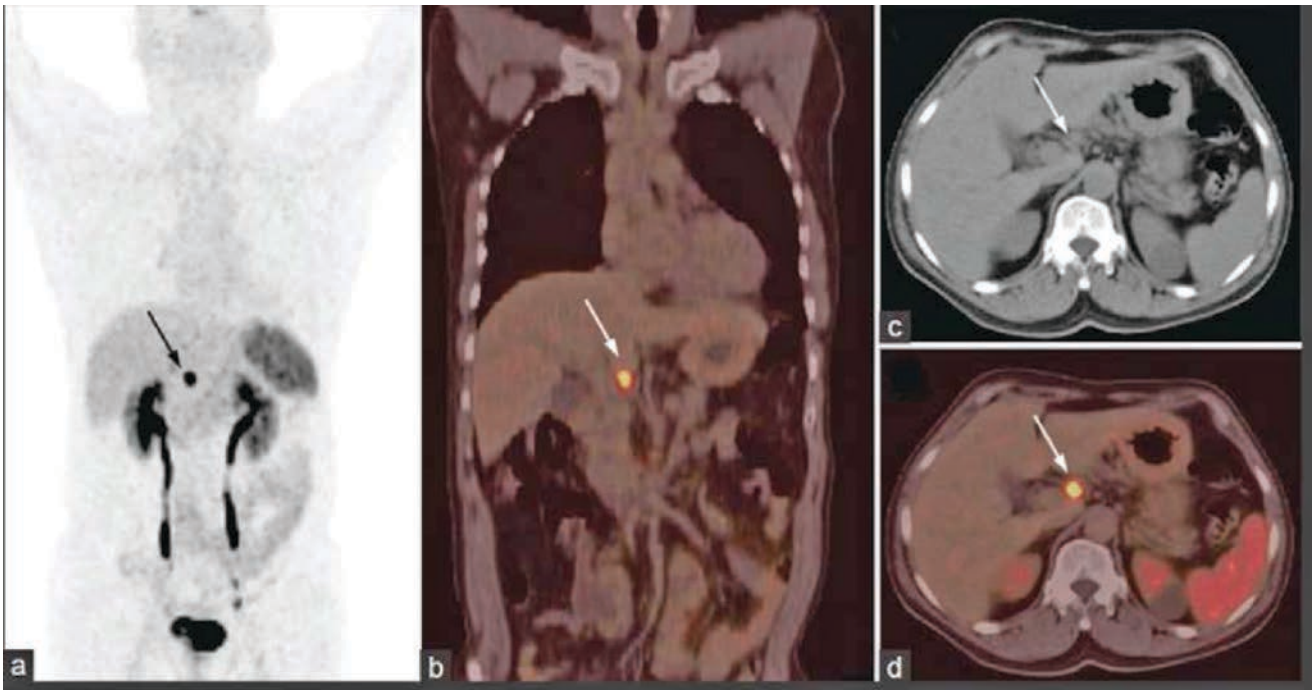

FIGURE 5. Confirmation of chromogranin A proteins confirming Gastrointestinal Neuroendocrine Tumor

The histopathological examination of the case series patient's biopsy showed chromogranin A proteins in synaptophysin as shown in Figure 2.

The histopathological examination of case series impression from the biopsy was featured in favor of neuroendocrine tumors, and IHL markers by eosin staining and illustrated in Figure 3.

The zoomed image of the histopathological examination of the case series showed chromogranin A protein illustrated in Figure 4.

Confirmative evaluation identification of rarest diseases - GI-NET CT - Confirmation of chromogranin A proteins proving Gastrointestinal Neuroendocrine Tumor

The confirmation of the case series was proved by CT and illustrated in Figure 5.

Case differentiation

The characteristics of the Gastrointestinal Neuroendocrine Tumor in the 3 patients of the case series were different, and their case characteristics were tabulated in Table 1.

DISCUSSION

GI-NETs are the rarest tumors, and R-NETs are the rarest NETs, and the incidence rate was 0.17% [12]. Duodenal neuroendocrine tumors are sporadic aggressive tumors that present with abdominal pain, bleeding in the intestine, nausea, vomiting, and polypoid that will be visible by endoscopy, in our case series of 3 patients, we found one of the patients had duodenal endocrine tumor [13].

Juhlin presented a case of anal GI-NET, C. C et al., and in their study, the case study patient was a 37-year-old male, in our case series, we found our case study patient was a 44-year-old female indicating that indiscrimination of genders, the anal GI-NET incidence was found [14].

TABLE 1. Case differentiation of case series of Gastrointestinal Neuroendocrine Tumor

Case characteristics	Case study patient-1	Case study patient-2	Case study patient-3
Age	72 years	46 years	44 years
Gender	Female	Male	Female
Position of Neuroendocrine Tumor in the intestine	Duodenum	Ileum with Lymph node	Anal region
Primary evaluation	Neoplasm is composed of epithelial cells arranged in nests, and tubules, round to oval with eosinophilic cytoplasm, and few congested vessels.	The hypoechoic lesion in both lobes of the liver largest measuring 3.6* 2.8 cm in seg II of the left lobe. Multiple rounded hypodense lesions in both lobes of the liver measuring 3.4* 3.3 cm.	Rectal mucosa with submucosa showing a neoplasm composed of nests, trabeculae, and organoid patterns of neoplastic cells having eosinophilic cytoplasm and nuclei exhibiting stripped chromatin.

An important and precise method of evaluating NET is PET, and CT imaging, in our case series, we confirmed our case series patients using tissue biopsy, and CT [15-17]. Even with the increased incidence of NETs, the survival of NET patients is increasing significantly due to the invention of medical imaging methods of diagnosis, which detects the tumor early leading to survival [18]. Studies are evident that early diagnosis of GI-NETs, and primary tumor resection than radiation therapy was found to be an effective intervention, and aids in increasing the survival rate in GI-NETs patients [19-21].

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Author's contribution:

First Author- Akilandeswari Alagan Ramasamy- Case series identification, approval

Corresponding Author - J Janifer Jasmine- Study design and preparation

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