VOLUME-8, ISSUE-9, SEPTEMBER-2019 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

General Surgery

A CASE SERIES OF NEUROENDOCRINE TUMOURS OF GI TRACT- A INCREASE INCIDENCE IN RECENT DAYS

Dr. Magesh Kumar. J*

Assistant professor, Department of General Surgery, Sree Balaji Medical College & Hospital, Bharath University, Chromepet, Chennai *Corresponding Author

P. Suresh Babu

Associate Professor Sree Balaji Medical College & Hospital, Bharath University, Chromepet, Chennai – 600044

K. S. Ravishankar

Professor & HOD, Department of General Surgery,Sree Balaji Medical College & Hospital, Bharath University, Chromepet, Chennai – 600044

ABSTRACT Gastric neuroendocrine carcinomas are rare and have a poor prognosis and the diagnostic criteria for this disease have recently changed. This is a case series of the case admitted in Sree Balaji medical college and hospital for a period of two year and to find out the incidence of the neuroendocrine tumor and its various modalities of presentation and its management.

KEYWORDS : Gastric Neuroendocrine Carcinoma, Sporadic Gastric

INTRODUCTION: Neuroendocrine carcinomas (NECs) of the stomach, although rare, deserve particular attention as they are aggressive and have an extremely poor prognosis [1–6]. In addition, the concept of this disease and its diagnostic criteria have been changed recently. The World Health Organization (WHO) proposed new diagnostic criteria in 2010 that mainly depend on the rate of cellular proliferation [7]. This is a case series of the case admitted in Sree Balaji medical college and hospital for a period of two year and to find out the incidence of the neuroendocrine tumor and its various modalities of presentation and its management

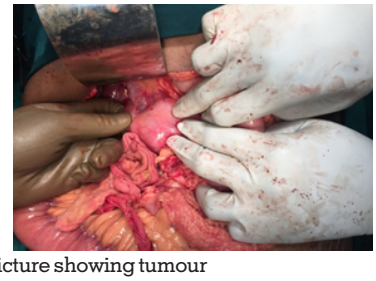
MATERIALS AND METHODOLOGY:

- This is a case series of the case admitted in sree balaji medical college and hospital for a period of two year and to find out the incidence of the neuroendocrine tumor and its various modalities of presentation and its management.
- Inclusion criteria
- All cases of NEC biopsy proven
- Exclusion criteria
- Associated with other malignancy
- After thorough clinical examination patient is examined systematically and necessary investigations sent such as USG abdomen, CECT andomen, MRI contrast

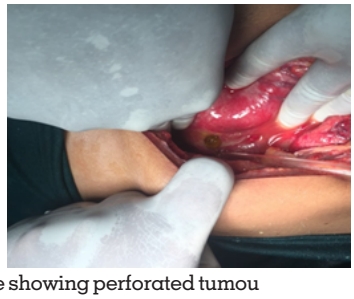
CASE SERIES

S no	Age and sex	Clinical presentation	Investigations	treatment
1	60/F	Non- specific abdominal pain	UGI scopy – Moderate dysplasia consequent scopy biopsy leading to NEC	Total gastrectomy with GJ and JJ
2	50/M	Acute Pain Abdomen Features suggestive of gastric perforation	CECT – Gastric perforation with perigastric nodes (growth in pylorus)	Bilroth II surgery HPE - NEC
3	45/F	Dyspepsia for evaluation	UGI scopy revealed – polyp in the D1 Biopsy –NEC	Endoscopic removal of the polyp. Patient is in observation
4	45/M	Presenting with Gastric outlet obstruction	CECT, UGI revealed the pathology HPE - antral growth	Palliative gastrectomy with GJ and JJ
5	52/M	Rectal growth, Bleeding PR for evalauation	HPE proven – NEC	Pelvic evisceration with prostatectomy as it was infiltrating with ileal conduit.

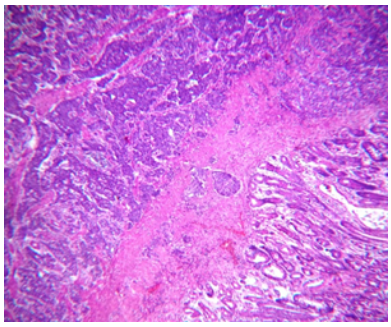
PICTURES:



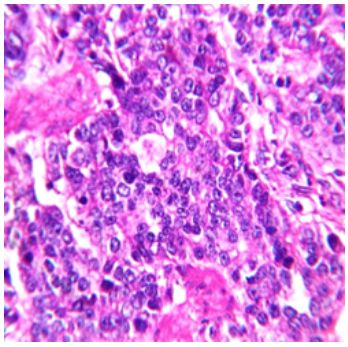
Intra op picture showing tumour



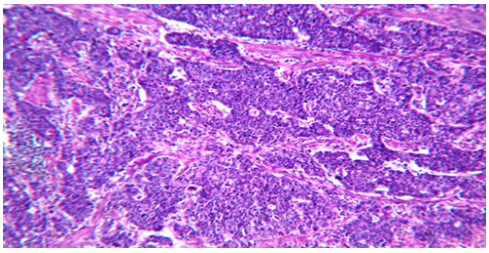
Intraop picture showing perforated tumou



Slide showing normal mucosa &tumour site



Salt and pepper nuclei appearenace



Peripheral palisading of cells

For all the mentioned cases immunohistochemistry helped in finalising the diagnosis.the patients are still in followup stusy and doing well.still larger scale of study is in progress.

DISCUSSION:

Neuroendocrine neoplasm (NEN) is an epithelial neoplasm with predominant neuroendocrine differentiation and is an uncommon tumor with multiple sites of occurrence [5]. NENs are commonly divided by origin as located in the foregut (lung, bronchus, stomach or duodenum), midgut (jejunum, ileum, appendix or proximal colon) and hindgut (distal colon or rectum). The percentage of foregut cases is 34%, midgut 30% and hindgut 36% [6]. Gastric neuroendocrine neoplasms (NENs) embrace a group of tumors that exhibit a spectrum of histopathologic variations, ranging from clearly benign tumors to highly malignant ones. Recently, the concept of this disease and its diagnostic criteria have been changed. In the 2010 WHO criteria, NENs of the stomach are defined as neoplasms with neuroendocrine differentiation, including neuroendocrine tumors (NETs) and NECs arising in the stomach [7].

Synonyms for gastric NETs include carcinoid, well-differentiated endocrine tumor/ carcinomas, and enterochromaffin-like cell NETs, and synonyms for NECs include poorly differentiated endocrine carcinomas and small cell and large cell endocrine carcinomas. NENs are classified into NET G1 (carcinoid) and G2, NECs, mixed adenoneuroendocrine carcinomas, enterochromaffin cells, serotonin-producing NETs, and gastrin-producing NETs [7].

Gastric NEN is classified into neuroendocrine tumor (NET), neuroendocrine carcinoma (NEC), mixed adenoneuroendocrine carcinoma, enterochromaffin cells, serotonin-producing NETs and gastrinproducing NETs. NETs include NET G1 (carcinoid) and NET G2 (well-differentiated neuroendocrine tumor/carcinoma). NECs include NEC G3 (poorly differentiated neuroendocrine carcinoma small cell type/large cell type) [4]. NEN is positive for synaptophysin and chromogranina [7].

NEN is classified based on the level of cellular proliferation, including the mitotic and Ki-67 indices [4]. In our case, the mitotic index was 16/10 HPF and the Ki-67 labeling index was 26%-50%. Thus, she was diagnosed with NEC. We suspected jumping metastasis from the main lesion to the proximal margin. In the Japanese Classification of Gastric Carcinoma, NENs are classified into carcinoid tumors and endocrine carcinomas (small cell type and large cell type) [8]. Although the prevalence of gastric NENs has recently risen, they are thought to be relatively rare tumors that account for less than 1% of all gastric tumors [9]. In general, the majority of these tumors are NETs, whose courses are indolent and not life threatening. Concerning NETs, more than 100 years have passed since Oberndorfer proposed the term "carcinoid" in 1907 [10]. In 1993, Rindi et al. advocated a classification system with three subtypes of gastric carcinoid tumors according to the clinicopathological features [1], and this classification system is reflected in the 2010 WHO criteria.

On this background, Gilligan et al. advocated a treatment algorithm for gastric carcinoid tumors, including the above-mentioned subtypes as well as the size and number of tumors [11]. Recently, less invasive therapeutic options, such as endoscopic resection of the tumor, have been reported for small NETs [12]. NECs of the stomach are also rare, representing less than 10% of gastric NENs [2, 13], and such rarity has made it difficult to understand precisely their biological nature and to establish optimal treatment options. The NEC of our case was a difficult diagnosis to establish, and the immunohistochemistry played a major role. Microscopically, the patient's tumor was uniform in shape and arranged in small microtubular structures (rosette-like arrangement) to form solid nests, with medium-sized, round-to-cuboid-shaped tumor cells on hematoxylin and eosin staining. Onimmunohistochemistry, the tumors are usually positive for synaptophysin and neuronal-specific enolase, but are rarely positive for the chromograninA staining observed in our patient. In the 2010 WHO criteria, NENs are classified into NETs or NECs on the basis of the level of cellular proliferation, including the mitotic and Ki-67 indices. The mitotic index was 46/10HPF and the Ki-67 labeling index was 70–80% in our case, so he was diagnosed as NEC. Lymphatic invasion was widely observed and lymph node involvement was seen in many nodes, suggesting the high-grade malignant nature of this tumor and showing the compatibility of the diagnosis. Aggressive surgery and chemotherapy should be considered for any NEC [3].Gastric NEN is classified into neuroendocrine tumor (NET), neuroendocrine carcinoma (NEC), mixed adenoneuroendocrine carcinoma, enterochromaffin cells, serotonin-producing NETs and gastrinproducing NETs. NETs include NET G1 (carcinoid) and NET G2 (well-differentiated neuroendocrine tumor/carcinoma). NECs include NEC G3 (poorly differentiated neuroendocrine carcinoma small cell type/large cell type) [4]. NEN is positive for synaptophysin and chromograninA [7]. NEN is classified based on the level of cellular proliferation, including the mitotic and Ki-67 indices [4]. In our case, the mitotic index was 16/10 HPF and the Ki-67 labeling index was 26%-50%. Thus, she was diagnosed with NEC. We suspected jumping metastasis from the main lesion to the proximal margin. Gastric NEN has different prognoses

and treatments depending on type. The prognosis of NET G1 is good and the 5 year survival rate is high. NET G2 has a favorable prognosis but is aggressive. NEC has the highest malignant potential but the 5 year survival rate is 75%-80%; however, the prognosis is poor. NET can be removed by endoscopic resection, whereas NEC requires surgical resection and lymph node dissection [8]. The best choice adjuvant chemotherapy for NEC is cisplatinum-based chemotherapy [9]. However, in this case we used a 5FU oral agent because of the patient's financial status and compliance. In conclusion, a neuroendocrine tumor can be removed by endoscopic resection but it must be a radical surgical resection in accordance with a malignant tumor, due to its aggressive tendency and high malignant potential.

DIAGNOSIS PROTOCOL

- 24 hr urinary measurement of 5HIAA
- Serum chromogranin A
- **NT** – proBNP (N-terminal pro-brain natriuretic peptide)-
- used in surveillance & as a prognostic marker.
- **CECT scan** – investigation of choice – solid mass with spiculated borders & radiating surrounding strands that is associated with linear strands within the mesenteric fat & kinking of the bowel
- **MRI** – useful in liver metastasis
- **Nuclear imaging** - somatostatin receptor positivity – identification of extra abdominal metastatic disease or in cases where primary cannot be identified by CT scan.
- **Ga-DOTATATE PET/CT** – localize primary tumor in patients with neuroendocrine metastasis of unknown origin & to define the extent of metastatic disease .
- **PET scan using F-DOPA(dihydroxyphenylalanine)** - used in identifing NETs

MEDICAL AND SURGICAL TREATMENT:

- Multidisciplinary
- Surgical debulking, hepatic artery embolization, chemoembolization, or radioembolization and medical therapy
- Treatment of patients with small bowel NET – based on tumor size, site & presence or absence of metastatic disease.
- Lesion < 1cm with no evidence of regional LN metastasis – segmental intestinal resection.
- Lesion > 1cm, multiple tumors or with regional LN metastasis , regardless of size of primary tumor – wide excision of bowel & mesentery needed.
- Lesion of terminal ileum – right hemicolectomy.
- Small duodenal tumors- locally excised , whereas more extensive tumors needs pancreatoduodenectomy.
- Liver metastasis – trans arterial chemoembolization or arterial embolization.
- **OCTREOTIDE & LANREOTIDE & PASIREOTIDE** – relieves symptoms
- **PEPTIDE RECEPTOR RADIONUCLIDE THERAPY YTTRIUM & LEUTICIUM ISOTOPES** conjugated with somatostatin analogues – advanced NETs
- **INTERFERON ALPHA &PEGYLATED INTERFERON ALPHA-2b** – cell cycle inhibition at G1/S & antiangiogenesis effects through downregulation of VEGF.
- **CYTOTOXIC CHEMOTHERAPY**- STREPTOZOTOCIN, 5FU & CYCLOPHOSPHAMIDE – well differentiated & metastatic NETs.
- **KETANSERIN & CYPROHEPTADINE** – controls symptoms.
- **TELOTRISTAT ETIPRATE** – inhibits serotonin synthesis.
- **BEVACIZUMAB** – inhibits angiogenesis.
- Targeting of multiple signaling pathways is a treatment strategy that may provide better tumor control & overcome resistance mechanisms involved with targeting of a single pathway.

CONCLUSION

we described a case series of sporadic NEC. An adequate description of NECs should be globally and historically discussed in relation to the real manifestation of this tumor group, considering the evaluation of the Consensus Conference. The diagnosis and treatment of these tumors should be evaluated in large clinical studies.

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