NEUROENDOCRINE TUMOR OF COLON WITH COLOCOLONIC INTUSSUSCEPTION – RARE TUMOR WITH RARE PRESENTATION – A CASE REPORT

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ABSTRACT :

Introduction: Neuroendocrine tumors (NET) of the colon are uncommon compared to colorectal adenocarcinoma. Few reports have been made of NET of the colon and sigmoid colon that presents with peritonitis and large bowel obstruction. Case presentation: A 35 year old female came with features of intestinal obstruction. Patient underwent exploratory laparotomy and a colocolonic intussusception at splenic flexure with perforations in proximal bowel were found, so Extended right hemicolectomy was done which on cut section showed 2x2cm polypoidal growth as lead point . Specimen histopathology of the descending colon showed neuroendocrine carcinoma features. Clinical outcome was very poor. Conclusion: Neuroendocrine tumors of colon are uncommon comprising <1% of colorectal cancers . Prognosis is poor because mostly metastatic at time of presentation.

Keywords: Neuroendocrine tumor, Colorectal cancer, Peritonitis, Colocolonic intussusception

INTRODUCTION

Neuroendocrine carcinoma (NEC) of the large intestine and rectum is an uncommon type of neuroendocrine tumor (NET) that accounts for <1% of all colorectal cancer. The clinical development of NEC includes very destructive and aggressive growth, followed by rapid spread; it is accompanied by a significant tendency to metastasis. These cause serious health problems, such as colonic obstruction and perforation results in a poor prognosis. The incidence of NETs has increased, probably due to improved diagnosis. Surgical resection appears as an effective approach. 3-year overall survival (OS) was estimated to be 5%–27%, and response to chemotherapy was reported as the only predictive factor in patients with metastasis. Because of its aggressive nature and high recurrence rate of the NEC, adjuvant chemotherapy constitutes a critical part of the treatment and significantly improves survival.

Intussusceptions in adult patients represents 5% of all intussusceptions and 1-5% of bowel obstructions in adults. It is caused by well established pathological mechanisms such as carcinoma , polyps, diverticula, stenosis or benign neoplasms. Colonic intussusception is a rare cause of intestinal obstruction in adults, with an incidence of 2-3 cases/1000000/year and is usually diagnosed in the 5th-6th decades of life, with identical incidence in men and women . It is caused by a malignant lesion in about 70% of cases in adults and therefore attempts to reduce the intussusception are contraindicated.

CASE REPORT

A 35 year old female came with abdominal distension, bilious vomiting and non passage of stools for 5 days. She had h/o ATT intake for abdominal Kochs. On examination tachycardia, tachypnea with abdominal distension and absent bowel sounds. Xray abdomen reveals multiple air fluid levels. On exploration a colocolonic intussusception at splenic flexure with 2x0.5 cm perforation just proximal to intussusception and 2 perforations on hepatic flexure were found, Extended right hemicolectomy was done which on cut section showed 2x2cm polypoidal growth as lead point. On Post operative day 1 due to gangrenous stoma reexploration was done and gangrenous ileal segment was resected. End Ileostomy was made and a vascular thrombus found at the root of mesentery of SMA.

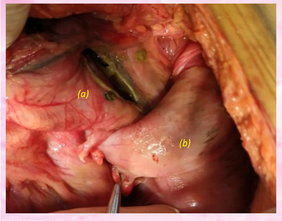


FIGURE 1 *Introperative image showing splenic flexure(a) as intussusceptum and descending colon(b) as intussuscipiens and perforation in splenic Flexure flexure (arrow)*



FIGURE 2
POST OPERATIVE DAY 1 ON RE-EXPLORATION SMALL BOWEL UPTO 170 CM LENGTH OF ILEUM FOUND GANGRENOUS INCLUDING THE STROMA

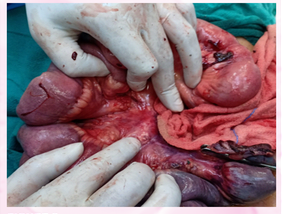


FIGURE 3
INDEX FINGER OF RIGHT HAND POINT AT THE VASCULAR THROMBUS AT THE MESENTERY INVOLVING SUPERIOR MESENTERIC ARTERY CAUSING



FIGURE 4
LINE OF DEMARCATION BETWEEN HEALTHY AND UNHEALTHY BOWEL AND THE PROXIMAL EXTENT OF INVOLVEMENT OF PROXIMAL ILEUM

Histopathology report suggests of small cell neuroendocrine carcinoma with presence of vascular emboli (positive for EMA,CD56, Synaptophysin , chromogranin)

DISCUSSION

NETs can be cancerous or benign; if NETs are malignant, the tumor has the potential to metastasize, although the tumor itself grows very slowly. Symptoms tend to be vague and nonspecific, and these symptoms are often related to the mass effects of the tumor. These can include vague abdominal colic, abdominal distention, weight loss, bleeding, obstruction, and constipation. However, the majority of the patients have no symptoms. Non-functional tumors can cause symptoms such as abdominal colic (68–78%), weight loss (32–50%), jaundice due to biliary obstruction or metastasis (21–50%), or vomiting (36%). There may also be nonspecific local effects of the tumor. For example, fibrosis from carcinoid tumors may cause obstruction from adhesions or stricture of the intestinal lumen, hydronephrosis, and subsequent renal failure, or mesenteric ischemia from constriction of the mesenteric vessels. The pathogenesis of this fibrosis is poorly recognized. About 10% of patients with NETs will experience carcinoid syndrome

NETs are derived from the so-called Kulchitsky or enterochromaffin cells of the gut, found throughout the intestinal tract within the crypts of Lieberkühns. They are also known as APUDomas. They elaborate substances like norepinephrine, dopamine, histamine, VIP, substance P, ACTH, growth hormone, glucagon, PP, gastrin, and serotonin. Grade 3 NETs are mostly small cell carcinomas(poorly differentiated). The majority occur in the GIT(54.5%) followed by lung and bronchus (30.1%), pancreas (2.3%), ovarian (1.2%), biliary (1.1%), and head and neck (0.4%). Within GIT, carcinoids occur predominately in the small intestine (44.7%) followed by rectum (19.6%), appendix (16.7%), colon (10.6%), and stomach (7.2%) Within the colon,sigmoid (35.7%), followed by rectosigmoid junction (26.7%), ascending colon (20.8%), transverse colon (9.2%), and descending colon (9.0%). Small cell Carcinoma presents 0.1% to 1% of all gastrointestinal (GI) malignancies commonest primary site is the rectum, followed by the cecum and sigmoid colon.biliary (1.1%), and head and neck (0.4%). Within GIT, carcinoids occur predominately in the small intestine (44.7%) followed by rectum (19.6%), appendix (16.7%), colon (10.6%), and stomach (7.2%) Within the colon,sigmoid (35.7%), followed by rectosigmoid junction (26.7%), ascending colon (20.8%), transverse colon (9.2%), and descending colon (9.0%). Small cell Carcinoma presents 0.1% to 1% of all gastrointestinal (GI) malignancies commonest primary site is the rectum, followed by the cecum and sigmoid colon.

Patients with suspected NETs should undergo biochemical evaluation. Traditionally, several plasma, serum, and urine markers have been evaluated as predictors of tumor progression in NETs, including 5-hydroxy indole acetic acid (5-HIAA), chromogranin A (CgA), serotonin, neuron- specific enolase (NSE), neurokinin A, E-cadherin, or neuropeptide K. Currently, CgA and 5-HIAA are commonly used in the clinical routine for diagnosing and following up with patients with NETs. NSE and CgA for detecting NETs and as indicators of tumor development and response to therapy. NSE has varying sensitivity (32%) and high specificity (100%) as a serum marker.

Elevated levels of CgA serum have been associated with poorer prognosis. Increased circulating CgA levels are found in approximately 70% of NETs, both functional and non-functional—even in non-neoplastic cases, such as hepatic impairment, atrophic gastritis, and renal insufficiency. So it should not be relied upon in isolation as a diagnostic test

The most-commonly employed marker in patients suspected of having a carcinoid tumor is urinary 5-hydroxy indole acetic acid (5-HIAA). Serotonin is a neurotransmitter that is produced mainly in the brain but also in the bronchi and gastrointestinal tract; it is degraded in the liver, and its metabolite 5-HIAA is excreted through urine. Usually, 5-HIAA is only present in small amounts in the urine, but it can increase in carcinoid syndrome. The 5-HIAA sensitivity was seen to be 65–75% with a specificity of 100%

The European Neuroendocrine Tumor Society (ENETS) guidelines recommend using CT or MRI for patients with tumors larger than 10 mm in size and for recurrence and suspected metastasis to other organs. Colonoscopy and guided biopsy. FDG-PET has high-sensitivity to detect tumor, as well as high-proliferation, therefore it is precious to diagnose tumor with clinical feature of NEC.

WHO's classification (2019), NET is determined by histopathology and biological characteristics, including grading of tumor cells, size and location of primary tumors, a proliferation of tumor cell markers, local and vascular invasion, and production of active biological substances

Differentiation	Grade	GI – NET(excluding pancreas)
Well differentiated	Low Grade (G1)	<2 mitoses/10 HPF and/or <3% Ki-67 index
	Intermediate Grade (G2)	2–20 mitoses/10 HPF and/or 3–20% Ki-67 index
	High Grade (G3)	>20 mitoses/10 HPF and/or >20% Ki-67 index
Poorly differentiated	High Grade (G3)	>20 mitoses/10 HPF and/or >20% Ki-67 index

Lesions <2 cm may be excised endoscopically by polypectomy or endoscopic mucosal resection. In the case of incomplete resection or G3, an oncological resection should follow. Since the majority of tumours are in fact invasive through the muscularis propria and 1 2 cm, a localized colectomy with oncological resection of the lymph drainage is appropriate., they have overall poor prognosis, with 5-year survival rates of only 33–42%. If possible, radical surgery is the standard therapy for NETs. If there is locoregional or liver metastasis, debulking surgery can be performed, with the possibility of the tumor being removed at almost 90% . It is recommended to perform palliative surgery in the following clinical situations: in primary tumors with non-operable liver metastases (especially functional NETs), because symptoms correlate with neoplastic masses; if the primary tumor is localized in the small intestine, because it can cause intestinal obstruction; and in the context of surgery that allows for subsequent multimodal treatment

Resection of the GI-NET must be followed by adequate regional lymph node resection (including all palpable tumors, where feasible) and thorough exploration of the associated synchronous primary tumors (15%–30% incidence)

Within 3–12 months after the operation, it is necessary to perform GI-NET surveillance, which consists of history-taking and physical examination, biochemical marker examination (as clinically indicated), abdominal pelvic multiphasic CT or MRI (as clinically indicated), and chest CT with or without contrast (as clinically indicated).

The prognosis for patients with NETs varies according to the stage at diagnosis, the histologic classification, and the primary site of the tumor.

At present, early diagnosis followed by the surgical resection is the most favorable clinical course for better prognosis, and if impossible, careful making decision for chemotherapy and stenting for obstruction is significant. Adjuvant chemotherapy in G3/poorly differentiated tumours with incomplete resection. Furthermore, NEC with higher cell proliferation not only may cause the intestinal obstruction, but also the invasive growth to the surrounding organs, leading to the tumor rupture after stenting inside the tract, thus careful consideration is essential

CONCLUSION

Neuroendocrine tumors of colon are uncommon comprising <1% of colorectal cancers . Prognosis is poor because mostly metastatic at time of presentation.