Case Report
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Atypical Carcinomatosis of Intestinal Neuroendocrine Tumor: Case Report and Literature Review

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Abstract

Neuroendocrine tumours are rare and slow growing neoplasms. They can grow and occur anywhere in the human body; however, the gastrointestinal system is the most common site. In our article we discuss a case of a 38-year-old male patient, who is previously healthy, and presented to our hospital after been complaining of left Para-umbilical and suprapubic pain of few weeks' duration. CT abdomen pelvis with IV contrast was done in a peripheral hospital showing multiple abdominal cystic masses along with a variety of adenopathies of different sizes. Our general surgery team was consulted for surgical biopsy. Intra-op, the largest jejunal mass was identified, as well as, numerous abdominal adenopathies, mesenteric and peritoneal deposits suggestive of carcinomatosis. Pathology result came back conclusive of gastrointestinal neuroendocrine tumors.

Keywords

Neuroendocrine tumors • Gastrointestinal neuroendocrine carcinoma • Ki 67 • Peritoneal carcinomatosis

Introduction

Neuroendocrine Tumors (NET) are slow growing tumors with both neural and endocrine characteristics, which arise from the diffuse system of neuroendocrine cells [1]. They constitute only 0.5% of all malignant conditions and 2% of all malignant tumors of the gastrointestinal tract. The incidence and prevalence have been increasing in the last few decades possibly due to early stage detection, increased awareness and widespread use of endoscopy and imaging studies for various gastrointestinal diseases [2]. Most of neuroendocrine tumors are sporadic, only 10% are familial, arising as autosomal dominant inherited syndromes (VHL, MEN1-2, NF) [3].

As neuroendocrine cells are found everywhere in our body they can form in different organs. They are classified as foregut, midgut or hindgut according to the embryological origin. Foregut neuroendocrine tumors are tumors arising in the respiratory tract, thymus, thyroid, stomach, duodenum and pancreas. Midgut tumors develop in the small bowel, appendix, and ascending colon, while hindgut tumors appear in the transverse, descending colon, and rectum [4]. 55% of the neuroendocrine tumors are in the gastrointestinal tract while 25% in the bronchopulmonary system [5].

40% of neuroendocrine tumors can be functional depending on the excess of hormones (serotonin and substance P) and/or peptides (chromogranin and synaptophysin) secretion. Functional neuroendocrine tumors can cause symptoms such as flushing, secretory diarrhea and abdominal cramps while non-functional neuroendocrine tumors can grow undetected for years, causing symptoms in later stages due to mass effect, for instance intestinal bleeding or blockage. Chromogranin A (CgA) is elevated in both non-functioning and functioning NETs and is the most commonly used biomarker to assess the disease burden and monitor treatment response. Chromogranin A and synaptophysin are necessary for diagnostic confirmation but proliferative index of Ki-67 and mitotic index are essential for prognosis information [6].

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Gastrointestinal Neuroendocrine tumors with peritoneal carcinomatosis, is a very infrequent entity with scarce data on its prognostic factor and management approaches. Herewith, we report here a very rare case of a young patient with a high grade poorly differentiated neuroendocrine tumor of the small bowel with peritoneal carcinomatosis.

Case Report

This is a 38-year-old male patient previously healthy with no past medical or surgical history who presented to our hospital on February 3rd, 2021 for left para-umbilical and inguinal pain along with mild dysuria of few weeks' duration that has not improved on analgesics. Patient denies dermatologic flushing and diarrhea. CT abdomen pelvis with IV contrast was done showing a cystic 80 × 82 mm left flank mass (Figures 1-3), a heterogeneous 71 × 49 mm nodule in the cul-de-sac (Douglas) (Figures 4 and 5), along with multiple peritoneal nodules (Figure 6). Patient was admitted to our hospital for biopsy, however, radiology team refused to perform the procedure, due to the cystic nature of the nodule and the high possibility of an inconclusive result. So patient was planned to undergo surgery for proper excisional biopsy collection and assessment of small bowel mass, which is most likely inducing these abdominal complaints by mass effect.

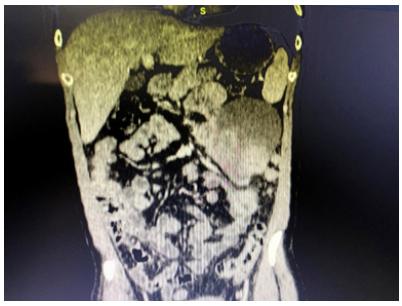

Figure 1. Cystic 80 × 81 mm left flank mass.

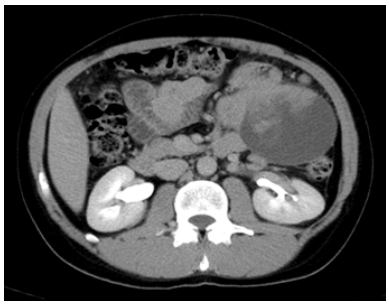

Figure 2. Cystic 80 × 82 mm left flank mass.

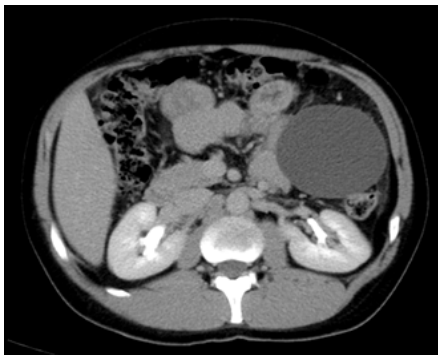

Figure 3. Cystic 80 × 83 mm left flank mass.

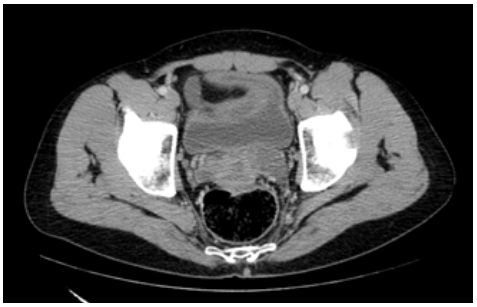

Figure 4. A heterogeneous 71 × 48 mm nodule in the cul- de- sac de doughlas.

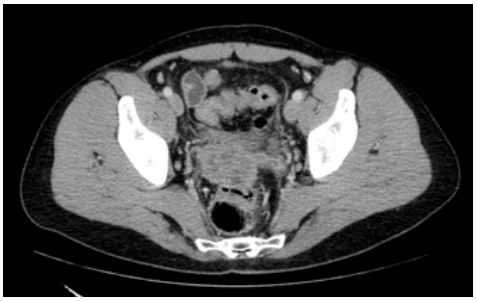

Figure 5. A heterogeneous 71 × 49 mm nodule in the cul- de- sac de doughlas.

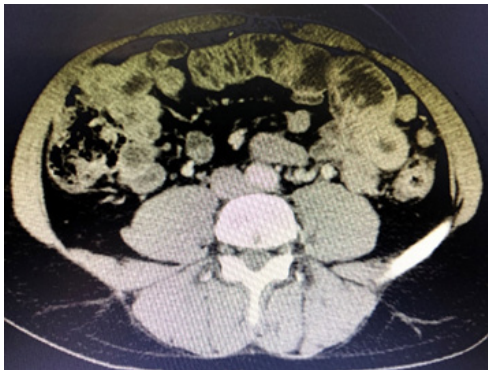

Figure 6. Multiple peritoneal nodules.

Midline laparotomy incision was done to access the abdomen, where copious peritoneal nodules of variable sizes were identified (Figures 7 and 8). Multiple mesenteric lesions and peritoneal deposits encountered, multiple biopsies retrieved and sent for frozen section, but result was inconclusive and pathologists required further testing with immunohistochemistry for proper diagnosis. The 80 x 82 mm Jejunal mass invading the sub mucosal layer was identified (Figures 9 and 10), and decision was taken for enterectomy and a primary hand sewn anastomosis. As for the pelvic mass, it was found to be adherent to the ureter at the uretero-vesicular junction and the bladder, impossible to dissect it off, so it was retained.

10 days later frozen biopsy result showed that resection margins were clear of lesions, however, specimen was positive for Anti- Cytokeratin, Synaptophysin, Vimentin, and Ki 67 with greater than 50 mit/HPF, and negative for Anti- chromogranin.

These findings led to the diagnosis of a high grade gastrointestinal neuroendocrine carcinoma.

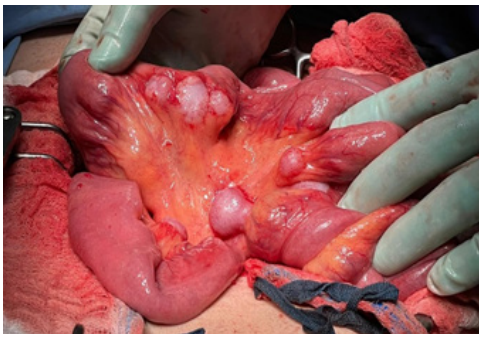

Figure 7. Copious mesenteric peritoneal nodules of variable sizes.

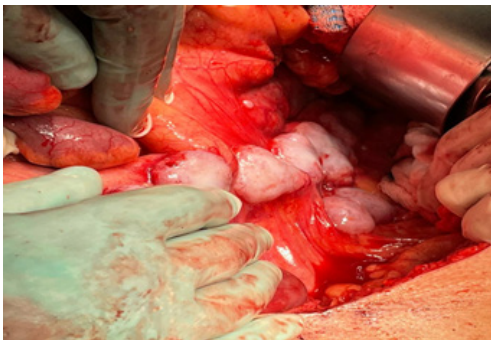

Figure 8. Copious mesenteric peritoneal nodules of variable sizes.

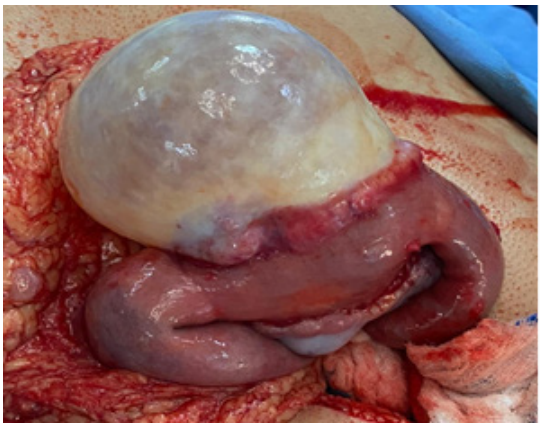

Figure 9. 80 × 81 mm Jejunal mass invading the sub mucosal layer.

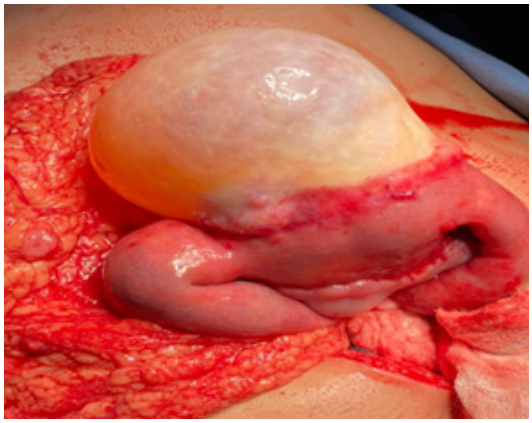

Figure 10. 80 × 82 mm Jejunal mass invading the sub mucosal layer.

Discussion

Neuroendocrine neoplasms are infrequent slow epithelial tumors with various sites of occurrence primarily in the gastrointestinal tract, making up around 0.5% of all malignancies and 2% of all GI neoplasms. Gastrointestinal neuroendocrine neoplasms mostly occur in the small intestines (46%) [1,2].

The TNM classification of malignant tumors is also applied to GI NETs. According to the new classification, the presence of mesenteric neoplastic mass greater than 2cm in maximum diameter corresponds to N2 category, even if lymph node metastasis is not documented. Also, the new M1 category (distant metastasis) contains 3 sub-categories, namely hepatic metastasis only (M1a), extra hepatic metastasis only (M1b) and hepatic and extra hepatic metastases (M1c) [7,8].

Moreover, in 2017, the World Health Organization updated the classification of NET. The histologic grading is centered on mitotic index and Ki-67 index.

For the well differentiated neuroendocrine neoplasms: NET grade 1: ki-67<3% and mitotic index/10 HPF <2, NET grade 2: ki-67 3-20% and mitotic index/10 HPF 2-20, NET grade 3: Ki-67>20% and mitotic index/10 HPF>20.

Poorly differentiated neuroendocrine neoplasm is NEC grade 3: Ki-67>20% and mitotic index /10 HPF>20 divided into small cell type and large cell type.

In our case, and as per the TNM classification, our patient would be staged as M1b, due to the presence of multiple enlarged lymph nodes in the absence of any hepatic metastasis. Furthermore, immunohistochemistry studies came back positive for Ki 67 with greater than 50 mitotic index/10 HPF. Both, conclusive of a bad prognosis poorly differentiated neuroendocrine tumor.

The poor prognostic factors have also been identified: male gender, age>50 years, jejuno-ileal localization, tumor size ≥ 2 cm, tumor depth (presence of symptoms upon discovery (such as carcinoid syndrome) and distant metastases [9]. Depending on the presence or absence of metastases, 5-year survival rates are respectively of 47% and 73% [10]. All of the above factors are met in our case except for that of carcinoid tumors, due to the absence of facial flushing and diarrhea upon diagnosis. However, all of the rest are suggestive of a bad prognosis [11].

The most common dissemination sites include the liver (in 50%-60% of patients), distant lymph nodes (20%-30%), lungs (3%-5%) and bones (1%-6%). Unfortunately, the effect of peritoneal carcinomatosis on prognosis of GI NET has not been solely studied due to the impact and medical concentration of liver metastasis itself. However, a study has shown that peritoneal carcinomatosis has a poor prognosis overall (5-year survival rate 52% vs. 32%) [12]. Moreover, revisions have shown that resection of primary tumor combined with excision of loco-regional peritoneal lesions when possible yields a symptomatic relief and survival benefit, but even more importantly, in some cases enables physicians to focus secondarily on treatment options for liver metastasis. Nevertheless, this aggressive surgical treatment is advised when R0/R1 resection is expected [12]. Nevertheless, scientists have decided to follow the Peritoneal Cancer Index (PCI), which was initially introduced by Jacquet and Sugar baker for carcinomatosis of colorectal cancer [13]. It is a quantitative index ranging from 0 to 39 that evaluates both cancer distribution and cancer implant size throughout the abdomen and the pelvis, in order to predict the possibility, beneficence, and efficacy of Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy (CRS-HIPEC). Preoperative assessment using imaging has not been considered to be accurate, and instead scientists recommend the PCI to be determined during laparotomy by 2 experienced surgeons. During which, surgeons would inspect the size of peritoneal carcinomatosis and their distribution within the 13 abdominal-pelvic regions. Implants are given a score of 0 through 3 (LS-0 to LS-3). LS-0 in the absence of implants in that specific region. Visible up to 0.5 cm in greatest diameter are scored as LS-1. LS-2 describes nodules larger than 0.5 cm and up to 5 cm. Finally, implants 5 cm or greater in diameter are scored as LS-3 [13-15]. The total PCI is calculated by adding all 13 regions. The PCI index, beyond which CRS-HIPEC would be contraindicated, hence suggestive of a bad prognosis, is considered to be 20 [13-15].

Alternative treatment options for NETs are the following: 1) Surgical excision, which is curative yet rarely done, compared to ablation that is more often considered. 2) Radiofrequency ablation /embolization, chemoembolization/radio embolization; irradiation, external (bone, brain metastasis)/tumor targeted, radioactive therapy; 3) medical therapy: Chemotherapy, biological treatment (somatostatin analogs, a-Interferon, m-TOR inhibitors, VEGF R inhibitors, Other TKI's) [16].

Small bowel NET has a diverse prognosis and treatment options based on location and severity of disease, however, a complete oncologic resection of primary tumors and mesenteric adenopathy is the definitive solution. In general, the median overall survival for all patients is 8.4 years, and surgically resected tumors have a significantly improved 5-year survival rate compared to unresected ones (75% vs. 28% respectively) [14]. Metastasis most commonly occur to the liver and are usually numerous and bilobar. Outcomes vary based on extent of liver metastasis, but tumor along with liver resection, when possible, showed great survival benefit (5-year survival rate 73% vs. 29%) [12].

In our case, (Figure 11) the patient had an extensive peritoneal carcinomatosis with numerous lesions hindering possible surgical excision. Hence, the patient was planned to undergo chemotherapy instead. Follow up with radiologic imaging is planned for possible surgical excision later on in case of response.

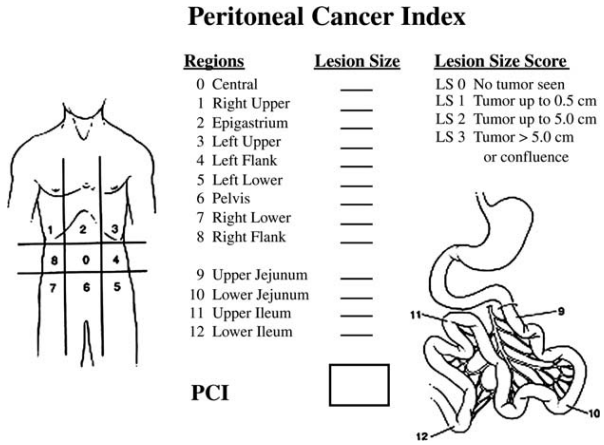

Figure 11. Peritoneal carcinomatosis with numerous lesions.

Conclusion

Gastrointestinal neuroendocrine neoplasms are rare tumors with diverse prognosis and treatment options depending on their location, size, and extension of metastasis at diagnosis. Peritoneal carcinomatosis is very infrequent, with very limited data on its effect on prognosis and treatment approaches.

Acknowledgement

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Conflict of Interests

The authors report no conflict of interest.

Informed Consent

An informed consent was signed by the patient to authorize access in his medical records and for the completion of this work.

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