Surg. Gastroenterol. Oncol. 2024;29(2):140-144 DOI: 10.21614/sgo-670

Neuroendocrine Neoplasms of the Colon and Rectum

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ABSTRACT

Introduction: Neuroendocrine neoplasms (NENs) originate from neuroendocrine cells diffusing throughout the body. They are a heterogeneous group of tumors with neuroendocrine function and malignant potential. They manifest themselves in various and complex clinical manifestation and localization, mostly affecting the GIT(gastrointestinal tract), the pancreas (GEP) and the bronchopulmonary system. The incidence of colon and rectum NEN (r-NEN) tumors has increased significantly over the last decade, partly as a result of improved diagnostic methods. Most commonly they are highly differentiated tumors with small size and good prognosis. Most of them are non-functioning and the diagnosis is made in advanced stages when the patients develop clinical symptoms from the GIT-anemia, hematochezia, obsruction. The rectal NENs represent 1-2% of all rectal tumors.
Methods: We report a retrospective cohort single center study of patients diagnosed with NENs who underwent surgical interventions in our department between 2010-2022.
Results: 32 patients (19 women and 13 men) participated in the study. The locations of the neuroendocrine tumors were: colon and rectum - 9 patients, small intestine - 6 patients, stomach - 4 patients, pancreas - 7 patients, adrenal glands - 2 patients, liver metastases - 4 patients. The histological type was: neuroendocrine tumor – 27, Insulinoma – 3, pheochromocytoma – 2.
Conclusions: R- NENs and small bowel NENs are the most frequent NENs of the digestive system. Their incidence has hugely increased due to widespread use of endoscopic screening for colorectal cancer. Highly differentiated rectal tumors (< 2 cm) are indicated for endoscopic resection. Tumors larger than 2 cm are suggested for surgical resection with higher risk for distant metastases. The best results in the treatment of NETs are achieved in highly specialized centers, with the participation of endoscopists and surgeons.
Key words: rectal neuroendocrine tumors, neuroendocrine neoplasms, endoscopic submucosal resection, surgery

INTRODUCTION

Neuroendocrine tumors (NETs) or neuroendocrine neoplasms (NENs) are a heterogeneous group of tumors with neuroendocrine function and malignant potential. The first description of a neuroendocrine tumor was in 1867 when Theodor Langhans described a polyp of the small intestine that appeared poorly differentiated on histology but without evidence of invasion (1). In 1907 Oberdorfner described these tumors of the small intestine that appeared

Received: 04.04.2024
Accepted: 10.06.2024

histologically malignant but acted clinically benign (2).

In 1963, Williams and Sandler broadened the term carcinoid to include other functional tumors with similar clinical and biochemical findings and categorized carcinoid tumors by embryologic origin. The foregut carcinoid tumors include those arising from the bronchus, stomach, pancreas, and proximal to the mid-duodenum. Midgut carcinoids arise in the mid-duodenum, jejunum, ileum, and mid-transverse colon. Hindgut carcinoids arise from the descending colon and rectum (3-5). NENs develop slowly and asymptomatically or with nonspecific symptoms, which are determined by the localization of the tumor process and could be: abdominal pain, obstruction, nausea, vomiting, bleeding, jaundice.

Capella et al. recommended replacing the term "carcinoid" with "neuroendocrine tumor" to describe tumors originating from neuroendocrine cells which exist at the neuronal and endocrine interface and are defined by their secretory products (6).

The term neuroendocrine neoplasm includes well-differentiated NETs and poorly-differentiated neuro-endocrine carcinomas (NECs)(7).

METHODS

Thirty-two patients with NENs were admitted in Second Department of Surgery between 2010-2022 presented with abdominal pain, ileus, jaundice and hematochesia. All patients signed an inform consent approved by our hospital. After imaging procedures: ultrasound, X-ray, and CT scan and fibrocolonoscopy the patients were operated. The specimens were sent for pathomorphological and immunohistochemical examination by protocol. Diagnosis was established after the histological results.

Statistical analisys

Microsoft Excel 2019 and SPSS (Statistical Package for Social Science) v16.0 software products were applied in connection with data processing. The level of significance was set at < 0.05.

RESULTS

The patients with rNEN will be considered and compared with other patients with NEN.

Imaging procedures were performed to all of the patients with NEN shown on *figs. 1, 2*.

Colonoscopy was done on seven patients, gastroscopy on 4 patients. In three patients the

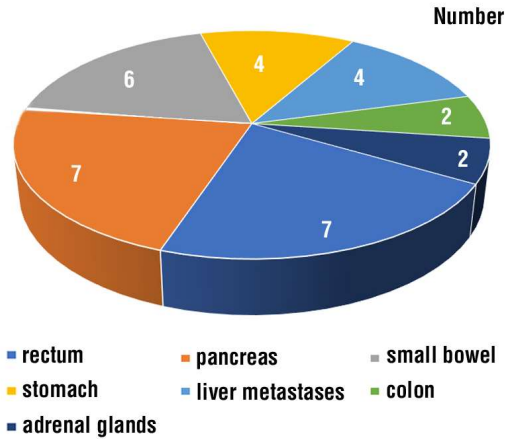

Figure 1 - Location of the NEN in the abdominal cavity

colonoscopy revealed a full (complete) obstruction at rectum level between 7 and 12 cm from the anal line. In two patients, at the level of the ascending colon tumor, a formation was located with image of recent bleeding and insignificant bleeding after biopsy. Two of the patients were operated in emergency because of a clinical presentation of few days' ileus proven by the X-ray and CT scan. A Hartmann procedure was made and liver biopsy was taken. The CT scan showed a presence of metastases in both patients with rectal NEN and in the patients with colonic NEN. The other patients were admitted in the clinic for elective surgery. Immunohistochemical study finding out that tumor cells show cytoplasmic expression of Chromogranin A, Synaptophysin, and negative TTF1; Ki67 < 2% (*fig. 3*).

Discussion: In 2010, the WHO classification defined this group of tumors as NEN - neuroendocrine neoplasms and divided them into neuroendocrine tumors and carcinomas (8).

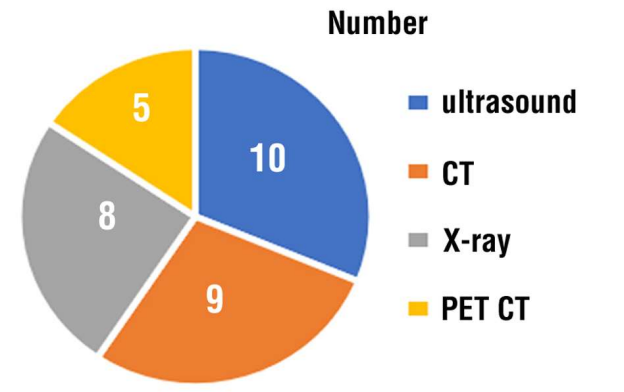

Figure 2 - Imaging procedures

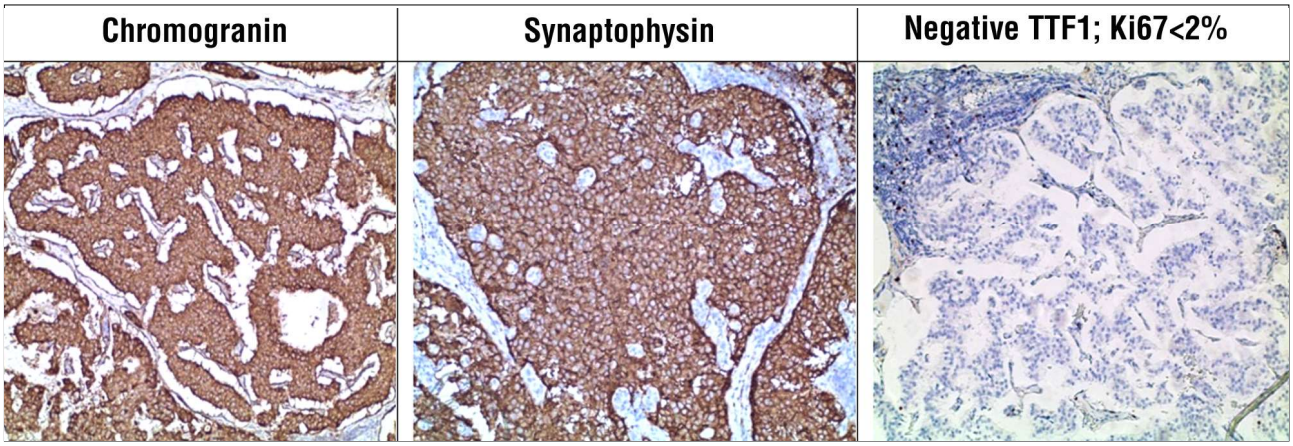

Figure 3 - Cytoplasmic expression

Neuroendocrine tumors of the gastro-entero-pancreatic system have different components, clinical manifestations and prognostic indexes according to their anatomical locations, which requires different diagnostic and therapeutic strategies (4).

In order to achieve the most optimal prognosis, both TNM and WHO classification are applied at the same time, increasing specificity and sensitivity of the index (9).

The reasons for these characteristics are associated with the following factors: neuroendocrine cells are produced by immature stem cells and the cancer cells themselves can release certain substances that stimulate growth, proliferation and dissemination of the tumor cells.

The rectum takes second place (27.4%) after the small intestine in NETs of GIT (4,10). In most cases, r-NETs are asymptomatic and are diagnosed incidentally during FCS. Less commonly, r-NETs may present themselves with anal discomfort, rectal bleeding, and lower dyspeptic syndrome (11). Most r-NETs which arise from neuroendocrine epithelial cells appear as small round polypoid lesions characterized by smooth, normal or yellow-stained mucosa, with a round pit shape /Kudo classification type I/, or invisible vessels as described by Sano as type I (12,13). R-NETs are found between 4 and 10 cm above the dentate line, along the anterior or lateral wall of the rectum (14).

A comprehensive literature search of PubMed, MEDLINE of Collected Reviews was performed to identify all of the English language publications related to neuroendocrine tumors in the abdominal cavity in 2001 to 2022. The subject of most publications is a literature review of data, long-term results and systemic management based without presenting their own patients with NENs, except one Chinese study describing the treatment in 58 patients in three medical centers (15). Furthermore these researches are separated by the location of the NENs, pancreas, (16-19) small intestine (20-25) and rectum (5, 26-31).

Our study showed that seven of our patients with rNENs (77.8%) had symptoms typical for rectal cancer with (the) diagnosis being established after operation and immunochemistry of the specimen were performed. The other two patients (22.2%) were admitted and operated in emergency with a clinical presentation of ileus. Besides the enlarged large bowel, CT scan revealed the tumor and lymph nodes and the presence of liver metastases. During the Hartmann procedure a biopsy was taken from the liver. Histopathology form both the tumor and the metastases confirmed the diagnosis of a r-NEN and metastases from r-NEN. After the operation patients were subjected to chemotherapy. The patients with NEN of the small intestine were also admitted in emergency with a clinical presentation of ileus which was confirmed via X-ray and CT scan of the abdomen. We can say that all of the patients with NEN were admitted too late in surgery and all the modern techniques for early diagnosis couldn't be applied because the patients needed emergency surgical treatment in the first place. From other point of view the complaints of the patients were not specific and for that reason the medical personnel outside the hospital couldn't recognize the early symptoms of NEN. Suspicion of rNENs before their resection is very important from a clinical standpoint. The main goal is R0 resection and lymph node dissection.

CONCLUSION

Rectal NETs are among the most common NETs of the GI tract, along with small bowel NETs. Their incidence has increased significantly in the last few years due to the wide use of endoscopic screening for colorectal cancer and the improvement in endoscopic techniques. There is still an underestimation of the frequency and prevalence of these neoplasms as they are difficult to be diagnosed by the endoscopist.

The diagnosis and treatment of NETs is a multidisciplinary process. The surgical treatment of NETs should be discussed in carefully selected patients with functional tumors, especially in the cases when they can be safely removed.

Conflict of interests

The authors have no conflict of interests to declare.

Funding

No funding or financial assistance was received by the authors.

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