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# The small neuroendocrine intestine tumor as the cause of acute gastrointestinal obstruction and diffuse peritonitis – case report

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**ABSTRACT**

NET is a group of mostly malignant neoplasms with neuroendocrine differentiation. NET tumors are usually located in the small bowel (sbNET), in most cases their symptoms are the non-specific and surgical treatment of this pathogenic lesions is usually planned. Currently used classification of this group of tumors was created World Health Organization and is based on the rank expression of the Ki-67 (the mitotic index), angioinvasion and size of the tumor. GEP-NETs (gastroenteropancreatic neuroendocrine tumors) are known for expressing specific extracellular markers, such as synaptophysin and chromogranin A (CgA), which are used in a diagnostic process and can be detected with immunohistochemistry methods. The occurrence of clinical symptoms only at the advanced stage of the tumor development explains a low rate of life expectancy. At present, surgical removal of the tumor is the most effective treatment method. This case report describes a 67-year-old female with acute symptoms of gastrointestinal obstruction, complicated with acute peritonitis, who was diagnosed with sbNET during an ad hoc treatment.

***Keywords*:** NET, tumor, cancer, GEP-NETs, surgery, oncology, intestinal obstruction

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**Abbreviations:**

NETs - neuroendocrine tumors, sbNET - small intestine neuroendocrine tumors, CgA - chormogranin A, 5-HIAA - 5-hydroxyindoleacetic acid, CT - computer tomography, MR - magnetic resonance, SSRS - stereotactic spinal radiosurgery, PET - positron emission tomography, USG - ultrasonography

## 1. INTRODUCTION

Neuroendocrine tumors (NETs) is a group of tumors which originate in the neuroendocrine system. The current incidence of this disease is 3 per 100,000 persons. During the years 1973-2004, a fourfold increase of morbidity has been noted. However, this may be a result of a progress in techniques used for medical diagnostics [1-3]. Typically, NETs are located within the gastrointestinal tract (approximately 30% of all cases) and in the pancreas. In addition to these locations, NET's can be found throughout the body due to the range of the neuroendocrine system [1, 4, 5].

The WHO classification specifies three grades of NET's differentiation. Grades G1 and G2 correspond to well-differentiated tumors, whereas G3 is a low-diversity tumors [6, 7]. Small intestine neuroendocrine tumors (SBNET) often give metastases to the liver, which are detected in about 30% of newly diagnosed patients. Primary tumors of the small intestine are often multifocal (25-44%) and small in diameter. Interestingly, metastasis of small intestine tumors to the liver are more common for G1 grade rather than in G2 or G3. For patients with metastases, the mean survival time is 56 months [8-12]. The five-year survival rate for patients diagnosed with NET is 67,2% [13, 14], as the tumor is often diagnosed late as its advanced stage.

Early diagnosis SBNET is difficult due to usually small tumor size, with non- specific clinical symptoms, such as:

- partial obstruction of the intestine (caused by local fibrosis associated with the hormonal activity of cancer cells),
- non-specific abdominal pain,
- bleeding from the gastrointestinal tract,
- carcinoid syndrome (which are most often the result of SBNET), appearing due to increased secretion of serotonin. Typical symptoms include skin redness, cyanosis and diarrhea. This syndrome is often related to the presence of hepatic metastates [4, 8, 15, 16].

The diagnostic process of SBNET group of tumors includes:

- biochemical tests assessing levels of chromogranin A (CgA) in serum and 5-hydroxyindole acetic acid (5-HIAA) in urine,
- imaging diagnostic methods: CT, MR, SSRS, PET, USG examination and capsule endoscopy,
- histopathological examination of tissue samples collected during surgery (the image of lobules and islands is often observed under the microscope; tabecula image is less common [13, 17-19],

Unfavorable prognostic factors include:

- high concentration of CgA in the blood serum,
- primary tumor with a diameter > 2 cm,
- high Ki67 proliferation rate,
- hormone-active products secreted by cancer cells, which indicate the stage and progression of the disease
- the presence of clinical symptoms depends on the size and location of the tumor [16].

A surgical resection of the small intestine, removal of nearby lymph nodes and mesentery is the treatment of choice for SBNET tumors [3, 13]. During laparotomy, the condition of the jejunum and ileum should be carefully assessed. Post-operative follow-up examinations include biochemical tests (CgA and 5-hydroxyindoleacetic acid concentration in serum), physical examination, CT scans and if necessary - somatostatin receptor scintigraphy. The follow up should be performed every 6-12 months for G1 and G2 tumors, and every 3 months for G3 tumors. The tests should be carried out until the end of the patient's life [5].

## 2. CASE REPORT

65-years-old female patient, as a matter of urgency, was admitted to the ward on 9$^{th}$ December 2017 due to obstruction of the gastrointestinal tract and diffuse peritonitis.

The following non-specific clinical symptoms were observed for 2 days:

- lack of appetite,
- empty bouncing,
- girdle pain in the upper right abdomen pain,
- vomiting with stomach contents - up to 12 times per day,
- flatulence, lack of stool

Above ailments lasted for two days before hospitalization, the patient was consulted twice during this period and treated conservatively.

Physical examination revealed:

- constant girdle pain and positive Blumberg’s syndrome during shallow palpation in the upper right abdomen and umbilical region,
- metalic peristalitis, especially in the upper epigastrum,
- abdominal guarding,
- umbilical hernia.

Interview revealed that the patient has been treated chronically for type 2 diabetes, hypertension, dyslipidemia and obesity. The patient denied any surgical procedures in the past. No family burden with neoplasms was confirmed.

On admission to the surgery, ER interview and physical examination were carried out along with additional X-rays examination of abdomen and thorax. X-rays imaging revealed attributes of small intestine obstruction. The ultrasonographic examination of pelvis and abdomen was performed using the Logic 200 device with 3.5 MHz Convex head. USG revealed

that the intestinal walls are thickened and their peristalsis is impaired, also the fluid was found in in recto-uterine pouch.

**Table 1.** Results of performed laboratory blood tests.

| **Performed laboratory tests** | **Results [norms]** |
|---|---|
| WBC (White Blood Cells) | 4710 /µ |
| Erythrocytes | 5,18 mln/µl |
| HBG (Hemoglobine) | 17,1 g/dl |
| PLT (Thrombocytes) | 27,9 % |
| Sodium in serum | 136.85 mmol/I |
| Potassium in serum | 4.19 mmol/l |
| Amylase | 49.54 U/l |
| Amylase in urine | 418.75 U/l |
| Creatinine | 111.32 µmol/l (higher) [21-80 µmol/l] |
| eGFR(Glomerular Filtration Rate) | 42.65 ml/min/1,73 $cm^2$ |
| Serum glucose | 13,76 mmol/l (higher) [3,90-5,50 mmol/l] |
| CRP (C-reactive protein) | 80.39 mg/l (higher) [0-5 mg/l] |
| AST | 12,1 U/l |
| ALT | 26,5 U/l |
| Alkaine phospatase | 57,06 µmol/l |
| GGT (Gamma-glutamyltransferaze) | 21,06 U/l |
| CK (Creatine Kinase) | 55 U/l |

| | |
|---|---|
| CK-MB activity | 23,5 U/l |
| HBs antigen | Negative |
| INR (International Normalized Ratio) | 1,05 |
| PR (Protrombine Ratio) | 95 % |
| tPT (Protrombine Time) | 11,9 s |
| APTT | 30,5 s |

**Table 2.** Results of performed laboratory urine tests.

| **URINE** | | |
|---|---|---|
| **Performed tests** | | **Results** |
| Urinalysis | Specific gravity | 1,030 kg/l |
| | Ketones | absent |
| | Urobilinogen | slightly raised |
| | Bilirubin | absent |
| | Nitrites | absent |
| | Proteins | 0,3 g/l |
| | Blood | absent |
| | Leukocytes | present |
| Urinary sediment | Squamous cell epithelium | numerous |
| | Leukocytes | 3-5 |

| | | |
|---|---|---|
| | Bacteria | numerous |
| | Mucus band | numerous |
| Bilirubin in urine | | negative |
| Amylase in urine | | 418.75 U/l |

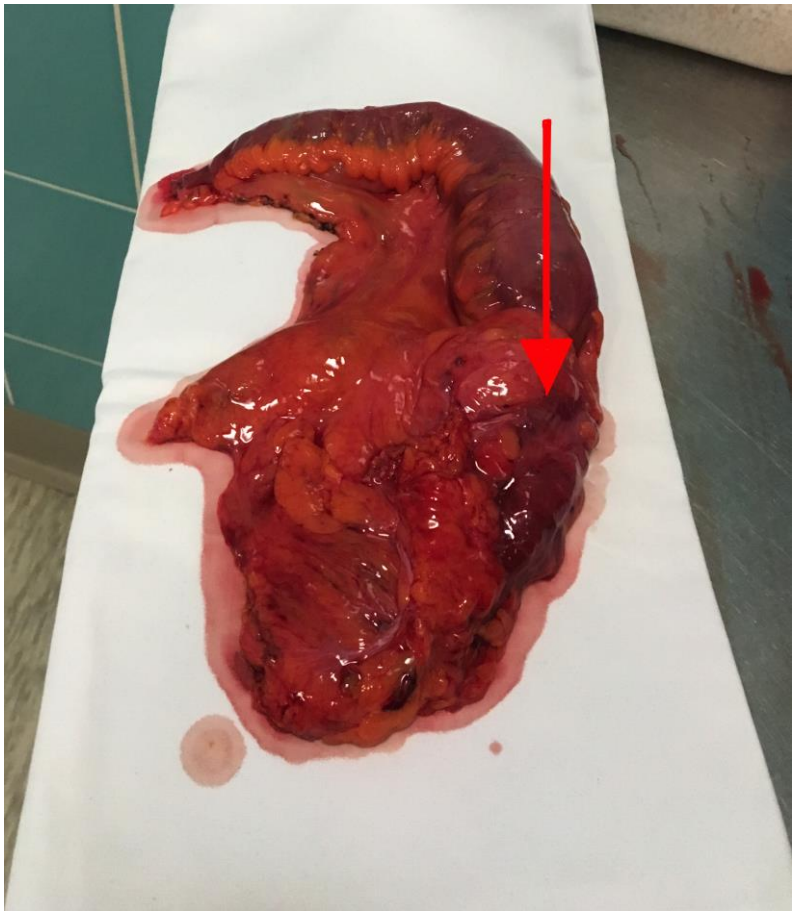

**Figure 1.** A photo of a neuroendocrine tumor narrowing the luminal diameter of the small intestine (indicated by the red arrow).

The assessment of the rest abdominal organs was difficult due to distended intestinal loops. Patient's serum was tested for C-reactive protein and the value raised to 80.39 mg/l (reference range 0-5 mg/l). Other observed abnormalities included increased values of creatinine 111.32 μmol/l (reference value 21-80 μmol/l) and plasma glucose 13.76 mmol/l (standard 3.90-5.5 mmol/l).

On the basis of the general clinical picture, a diagnosis of peritonitis in the course of obstruction of the upper gastrointestinal tract was made, and as a result, the urgent surgery for life indications was recommended. The patient was operated on the day of admission to the Department of General Surgery.

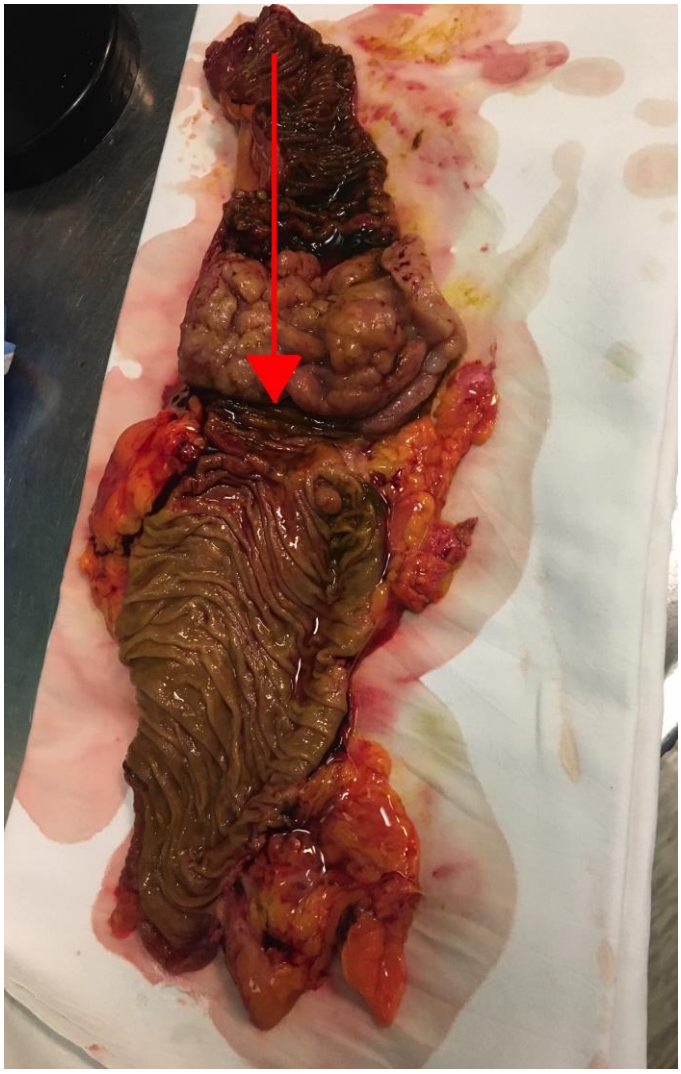

**Figure 2.** A photo of a NET narrowing the luminal diameter of the small intestine (indicated by the red arrow).

## 3. DESCRIPTION OF THE SURGICAL PROCEDURE

### 3. 1. Performed procedures

Exploratory Laparotomy. Decompression of the small intestine. Partial resection of the jejunum with the tumor. End-to-end jejuno-jejunal anastomosis. Excision of tumors of the right lobe of the liver segment 8. Excision the tumor of the uterine fundus. Drainage of the peritoneal cavity. Umbilical hernia repair.

### 3. 2. Description of the procedure

The midsection was performed. In the peritoneal cavity turbid liquid of about half a liter of volume was found and it was sucked out and taken for microbial analysis. The jejunum was found distended, filled with fluid content, strongly bloodshot. In the mesentery of the intestines a noticeable thrombosis of venous vessels was detected. Mucosa (found about 1.5cm from the Treitz's ligament) presented the appearance of neoplasm. Additionally, numerous enlarged mesenteric lymph nodes and jejunum were visible. In order to exclude metastatic lesions, the peritoneal cavity and the Lesser sac were opened and inspected. Other organs had a normal appearance, except for the detected nodule diameter of 1 cm in the uterus bottom (which was excised for histopathological examination) and three nodules of the right lobe of the liver - most likely liver cysts up to 2 cm in diameter. The jejunum was decompressed by shifting the content into the stomach and suction. Around 80 cm of jejunum with the tumor, which was previously causing total ileus obstruction, was excised. The mesenteric jejunum was dissected extensively in this section along with numerous lymph nodes. Stumps of the intestine were sutured together with the end-to-end method. The intestines were located back to their natural position. A drain was inserted into a pouch of Douglas and hemostasis was checked. Additionaly, the surgical fixation of umbilical hernia was performed. The closure of abdomen was performed layer by layer and the wound was closed. Dressing material and surgical instruments were counted and their correct number after the surgery was confirmed.

### 3. 3. Postoperative diagnosis

The ileal tumor was most likely cancerous. Suspected metastases to the mesenteric lymph nodes. Mechanical intestine obstruction occurred as a consequence. Peritoneal inflammation. Umbilical hernia accreta. Pelvic floor tumor. Cyst of the right lobe of the liver.

During the postoperative period no further complications, (neither general nor local) were observed. The patient was discharged to home in good condition.

### 3. 4. The result of histopathological examination of samples

Material collected intraoperatively and taken from small intestine revealed a neuroendocrine tumor with a diameter of 1.8 cm (NET) - IM 1/10 HPF. The result of the histochemical examination described tumor in its G1 stage. Markers tested in this case included CgA chromogranin result (+), Ki67 result (+) 1%, synaptophysin result (+). Metastasis was found in 3 of the 14 lymph nodes collected during the operation procedure. Tumor infiltrated the mucosa, submucosa, muscular and submucosal walls of the small intestine. The lesion was assessed as locally advanced.

## 4. DISCUSSION

Clinical symptoms commonly reported by patients' diagnosed with neuroendocrine tumor of jejunum and ileum include bowel obstruction and pain in the abdominal area. Similar symptoms have been described in this case study. In some rare cases bleeding from gastrointestinal tract (15%) or diarrhea might occur. The duodenal NETs tend to be asymptomatic and are usually diagnosed during other examination, however the large mass of the tumor might result in clinical symptoms [20, 21]. According to the patient's relation, the

symptoms of partial obstruction occurs 2 days ago - the patient was trying to treated herself with home methods. Patient reported to the hospital lately, when the obstruction was complete.

SBNET are usually diagnosed in their advanced stage, when metastases occurs in lymph nodes, which was the case in our patient [20, 21].

The occurrence of the metastates is an important factor in treatment plan and expected outcome. Neuroendocrine tumors' metastases typically localise in liver (75-80% of cases). In case of sbNET metastases to liver have been reported in 20% of patients and are usually detected as multiply lesions of different size. In such cases, resection of the liver is not recommended if primary location of the tumor was not found and excised, but if its a adequate treatment - excision is the best way of treatment [22-25]. In our patient, metastases in liver were suspected therefore a resection of this lesion was recommended. Further tests confirmed that the lesion was benign (cyst). In our patient, the proliferation rate of Ki67 was low and carcinoid syndrome did not occur. High Ki67 proliferation rate and carcinoid syndrome, according to the literature, are unfavorable prognostic factors [16].

According to the literature, on the majority of the patients with NET tumor, surgery is carried out on a scheduled basis - like in case described below.

Antoniadou et al., described a case of 60-years-old female patient who was admitted to the hospital with clinical symptoms present for 20 days prior to the admission. Symptoms involved vomiting, crampy abdominal pain, and diarrhea. Range of tests was performed, including CT scans, gastrointestinal endoscopy, blood tests, and tumor markers assay (CEA). The patient was diagnosed with recurrent partial obstruction of intestine and discharged with recommendation of future investigation in Gastrointestinal Department. However, patient's condition become worse. The diagnosis of a complete obstruction of intestine was made. An exploratory laparotomy revealed 4 tumors in small intestine, (size between 7 and 20 mm), which caused the obstruction [26]. A minority of patient with was admitted with acute symptoms and require immediate surgical treatment, during which tissue samples are collected and become the basis of which the final diagnosis is made - following situation for example was described by Mentzoros et al [27,28].

## 5. CONCLUSIONS

Neuroendocrine tumors are a rare form of neoplasms, and usually occurs in small bowel. Clinical symptoms are often non-specific and lead to diagnosis being made relatively late. Treatment of the advanced tumor is challenging, surgical treatment requires an excision of lesion with a larger margin of healthy tissue, which is currently a most effective treatment. It is worth to emphasize that patients with neuroendocrine neoplasm may be admitted to ER and an emergency surgery might be required for example due to intestinal obstruction complicated by peritonitis.

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