CARCINOID TUMOUR CASE STUDY

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INTRODUCTION

Carcinoid tumours originate in the cells of the neuroendocrine system. They have been classified according to their embryologic site of origin, such that foregut carcinoids start in the lungs, bronchi or stomach; midgut carcinoids start in the small intestine, appendix, or proximal large bowel; and hindgut carcinoid tumors start in the distal colon or rectum.[1] The appendix presents the most frequent site of carcinoid tumours followed by the rectum, ileum, lungs, bronchi, and stomach.[2] These neoplasms characteristically present in patients 50 to 60 years of age.[3]

Carcinoid tumours contain many neurosecretory granules responsible for the synthesis, storage, and release of substances, including serotonin, histamine, prostaglandins, kallikrein, bradykinins, substance P, gastrin, corticotrophin (ACTH), and neuron-specific enolase.[4] The most prominent of these substances is serotonin (5-hydroxytryptamine) which is degraded into 5-hydroxyindoleacetic acid (5-HIAA), which in turn is excreted in the urine. Initially, the lungs and liver metabolize many of the substances secreted by carcinoid tumours, consequently preventing their release into the systemic circulation until metastases develop.[5] When they are finally released into the systemic circulation, 5-hydroxytryptamine can elicit symptoms of the so-called carcinoid syndrome.[6] This syndrome occurs in less than 10% of patients, and its most characteristic clinical manifestations include cutaneous flushing (face, neck, upper chest) and diarrhea.[7]

CASE REPORT

A 70-year-old Caucasian male was referred to our gastrointestinal endoscopy clinic due to persistent GI bleeding. At the time of his first visit on April 21st, 2008, the patient did not mention any additional symptoms and no irregular bowel movements. His body weight had been steady throughout the last three to four months and he maintained a healthy appetite. According to the patient, ten days before his first visit to our clinic, he complained of muscle pains, and was administered NSAIDs. The next day, he noticed fresh blood in his stool and complained general weakness.

From his **past history** we were informed about a laparoscopic cholecystectomy performed two years previously. His father had died from lung cancer. He was a non-smoker, social drinker and stated no known allergies.

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Clinical examination revealed normal vital signs as well as no abnormalities in other organ systems. Abdominal examination was normal and lymph nodes were not palpable. Digital rectal exam (DRE) was positive for fresh blood.

Laboratory investigations showed elevated ESR, CRP, GGT, GPT as well as increased serum urea and creatinine levels.

The patient was urgently admitted to Apollonio Private Hospital where he underwent a total colonoscopy with biopsy and gastroscopy with CLO, which revealed no abnormalities and no active bleeding sites from the stomach and colon. When capsule endoscopy was performed an actively bleeding polypoid lesion situated at the ileocecal area was discovered.

The patient failed to follow-up until his second visit one year later. Laboratory investigations were performed again and showed elevated levels of total cholesterol, triglycerides, LDL cholesterol, GGT, as well as increased serum urea and creatinine levels. Further kidney function tests such as elevated eGFR indicated kidney failure. Repeated upper gastrointestinal endoscopy and colonoscopy were normal. The patient underwent capsule endoscopy once again where active bleeding from the ileum was established and the suspicion for submucosal tumour was raised (Fig. 1).

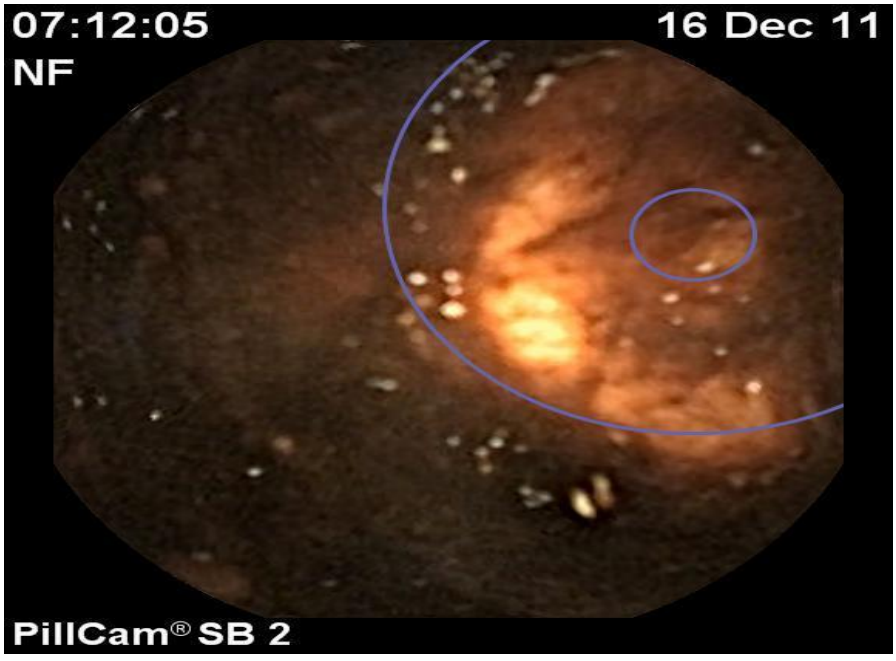

Figure 1

CT enteroclysis was performed to rule out Meckel's diverticulum, and a CT angiogram excluded angiodysplasia. Still, abdominal and pelvic CT revealed a 2 cm hypervascular lesion of the ileum associated with one enlarged lymph node near the bleeding point (Fig. 2).

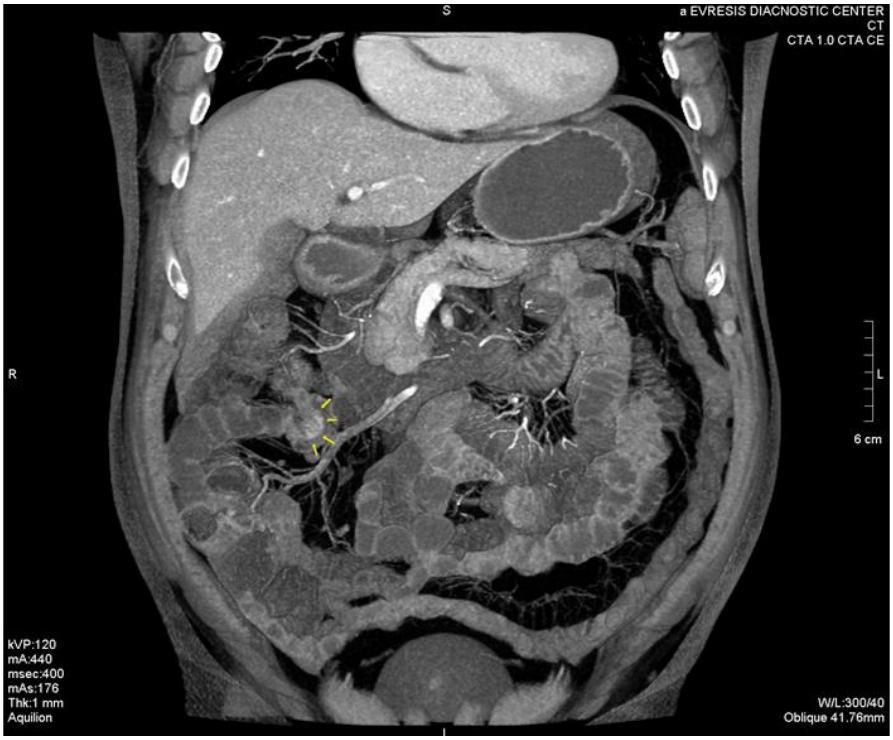

Figure 2

Consequent to the findings mentioned above, we decided to proceed with laparotomy during which intraoperative endoscopy of the small intestine was carried out.

The **macroscopical examination** revealed an ulcerated tumour 2 cm in size which was infiltrating the wall of the ileum. Proximal to the tumour, a 2.5 cm lymph node was noticeable (Fig. 3).

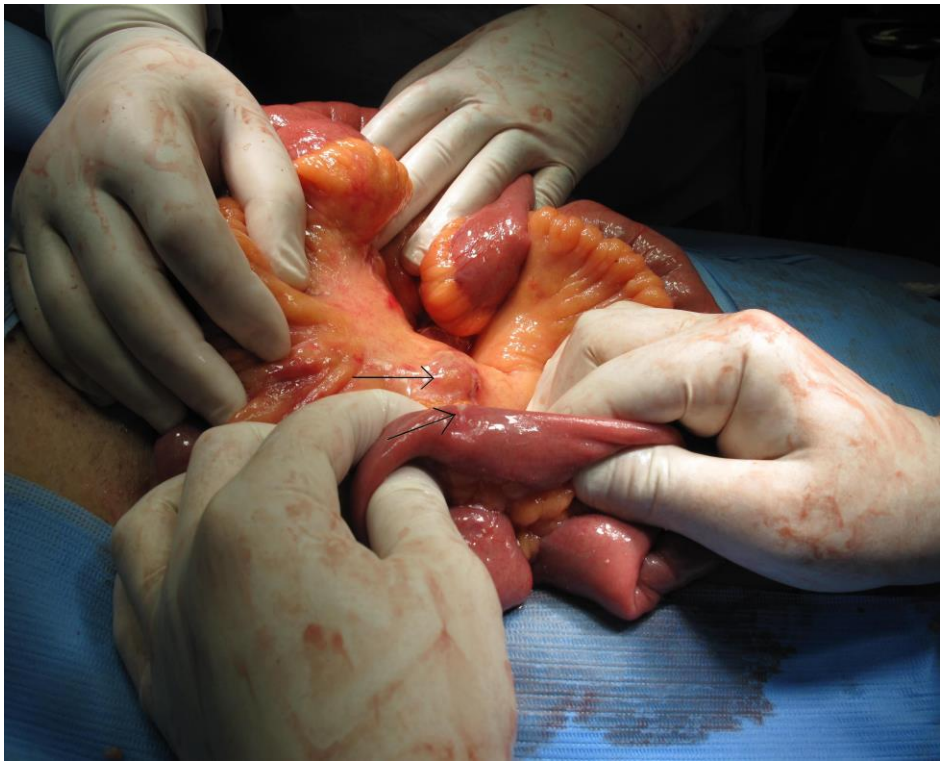
Figure 3

Microscopical examination revealed the following:

- **Type of tumour**: classic type neuroendocrine neoplasm (NEC) composed of uniformly rounded small cells arranged in solid nests with rare mitoses embedded within dense fibrous stroma.
- **Extent of invasion**: extending into the visceral peritoneum (T4).
- **Lymph nodes affected**: One proximal lymph node shows metastasis and three others are reactive.
- **Vascular, lymphatic and perineural invasion** are not present (V0).
- **Fibrous reaction** is of Grade II.
- The **proximal and distal edges** are clear.

The final **diagnosis** was serotonin producing carcinoid tumour of the ileum with metastasis to a single nearby lymph node.

DISCUSSION

Carcinoid tumours represent rare neoplasms with a slow rate of growth.[6] Symptoms present late in the course of the illness, are commonly vague, non-specific and organ related, thus causing long delays in diagnosis.[3] As can be seen from *Table 1*, symptoms can be either due to local tumour mass effects (invasion, intussusception, fibrous adhesions, hypermotility), the effects of tumour-engendered fibrosis or to the secretion of bioactive products by the neoplasm.[8] Most carcinoid tumours are discovered incidentally during surgery for other abdominal disorders.[7]

TABLE 1

Symptoms of Carcinoid Tumours by location:

Location	**Symptoms**
Lungs, bronchi and trachea	Recurrent pneumonia, cough, hemoptysis, chest pain
Stomach	Anemia, abdominal pain
Small intestine	Abdominal pain, small bowel obstruction
Appendix	Appendicitis caused by tumour presence or incidental discovery during other pelvic procedures
Colon	Pain, anorexia, weight loss
Rectum	Rectal bleeding, pain, constipation

From the investigations we performed on our patient, capsule endoscopy has proven to be an extremely valuable means of detecting the active site of bleeding in our patient.

As a sequence of investigations in cases with suspected carcinoid tumours we would recommend the following:

24-hour urinary excretion of 5-hydroxyindoleacetic acid (5-HIAA)

This test lacks the sensitivity and specificity for the diagnosis of carcinoid tumours because 5-HIAA may not be elevated in atypical carcinoids and can be elevated in other conditions such as tropical sprue, celiac disease, Whipple's disease, and small bowel obstruction, and can be caused by ingestion of foods high in serotonin, or certain medications.[9]

Serum analysis of Chromogranin A (CgA)

CgA analysis presents a specificity of approx. 95% and sensitivity for carcinoid tumours of approx. 80%. A 40% false-positive rate has been noted in patients with multiple myeloma.[10]

Localization Studies

Previous research suggests using combinations of imaging studies depending on the suspected site of the tumour.[11] As outlined in *Table 2*, carcinoid tumours can be localized using morphological, functional and other means:[7]

TABLE 2
Localizing studies in carcinoid tumours / the carcinoid syndrome:

Morphological:
- Transabdominal ultrasonography
- Endoscopy
- Endoscopic ultrasonography
- Capsule endoscopy
- Computerized tomography (CT)
- Magnetic resonance imaging (MRI)
- Selective abdominal angiography

Functional:
- ^{111}In-pentetreotice scintigraphy
- ^{123}(^{131}I)-metaiodobenzylguanidine (MIBG) scintigraphy
- Bone scintigraphy
- Positron emission tomography (PET)
- Intraoperative radionuclide probe

Miscellaneous:
- Echocardiography

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