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Bronchospasm Complicating A Small Intestine Neuroendocrine Tumor Resection: A Case Report

BACHAR Amine, JAMALEDDINE Khalid, ELABBASSI Taoufik, LEFRIYEKH Mohamed Rachid

Department of general surgery, IBN ROCHD University hospital of Casablanca, Casablanca, Morocco

*Correspondence: BACHAR Amine

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Abstract

Small intestinal neuroendocrine tumors (SI-NETs) are rare neoplasms with increasing incidence, known for their diverse clinical presentations and potential hormonal complications. We present the case of a 65-year-old male with a history of chronic smoking and alcoholism, who presented with right iliac fossa pain, liquid diarrhea, and weight loss. Imaging revealed a neuroendocrine tumor of the small intestine, and the patient underwent surgical resection. However, postoperatively, he developed respiratory distress suggestive of bronchospasm, requiring intensive care management. Histopathological analysis confirmed a well-differentiated neuroendocrine tumor, Grade 2. This case underscores the importance of early recognition and management of hemodynamic complications following surgical resection of SI-NETs. Preoperative assessment for carcinoid syndrome and optimization of cardiac function are crucial to minimize perioperative risks. Surgical resection with meticulous attention to complete tumor removal and mesenteric dissection remains the mainstay of treatment for SI-NETs. Further research is needed to refine perioperative management strategies and improve long-term outcomes for patients with SI-NETs.

Key Words: Small intestinal neuroendocrine tumors, SI-NETs, carcinoid syndrome, bronchospasm, surgical resection, perioperative management.

INTRODUCTION

Small intestinal neuroendocrine tumors (SI-NETs) are the most common small bowel tumors. The annual incidence of SI-NETs has increased lasting recent decades and was in 2003 around 1/100,000 [1]. They are recognized for their ability to produce histamin, serotonin and bradykinins; which may cause mesenteric fibrosis and the carcinoid syndrome, consisting of flush, frequent diarrhea, and, in advanced cases, right-sided heart failure and tricuspid valvulopathy [2].

Indeed, NETs of the small intestine are the most common causes of the carcinoid syndrome that oc-

curs in 20–30% of patients with liver metastases from these NET. The classical (typical) carcinoid syndrome is usually characterized by cutaneous flushing, gut hypermobility with diarrhea and bronchospasm with wheezing and shortness of breath [4], it is this latter we will be discussing in this work.

In contrast to small bowel adenocarcinoma, SI-NETs are also known for their advantageous survival, with 5- 10- and 15-year overall survival rates of 80%, 54%, and 36%, respectively [3].

AIM OF THE ARTICLE:

We discuss here the case of a sixty five years old male patient admitted and operated for a small intestine neuroendocrine tumor having presented hemodynamic complications after tumor resection.

PRESENTATION OF CASE

We present the case of a 65-year-old male patient, a chronic smoker and alcoholic, who has been experiencing right iliac fossa pain for 03 months, described as heaviness, along with liquid diarrhea of up to 5 stools per day, with a general state of deterioration and a weight loss of 06 kilograms in 03 months.

Clinical examination reveals a patient in fairly good general condition, stable, with no particular findings on cardiorespiratory auscultation, a soft abdomen, and a rectal examination without particularities.

An abdominal CT scan reveals a tissue process with endoluminal budding subsenosant measuring 32.9x31.5 mm at the level of the terminal ileum with mesenteric densification, suggestive of a neuroendocrine tumor of the small intestine (figure 1).

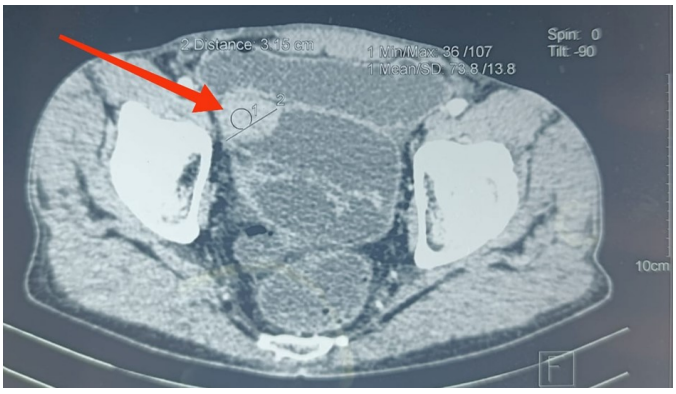

Figure 1: a CT scan slide showing the tumor (arrow)

A chromogranin A assay was performed, returning positive at 122 ng/ml, while ACE and CA19.9 assays were negative.

The patient underwent surgery after pre-anesthetic consultation and normal cardiac evaluation. An open surgery was performed consisting of ileocecal resection carrying the mass 10 cm from the ileocecal junction with ileocolic anastomosis. Exploration did not reveal retracted mesentery, nor hepatic metastases, nor carcinosis nodules.

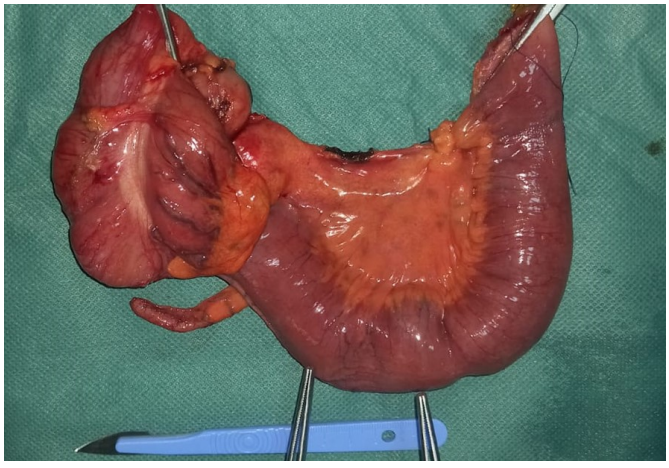

Figure 2: A picture of the specimen before its opening.

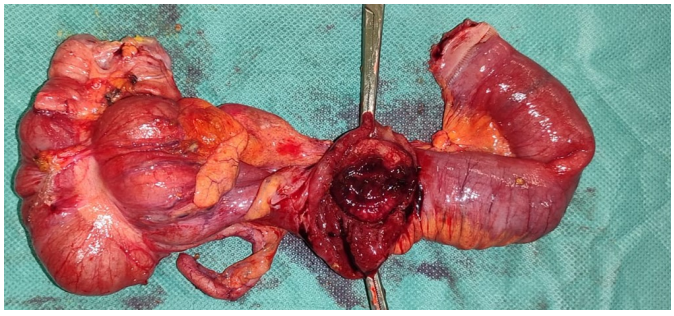

Figure 3: A picture of the specimen after its opening.

However, intraoperatively and following surgical resection, the patient presented with respiratory distress, with oxygen saturation at 76% and wheezing in both lung fields. The diagnosis of bronchospasm was made, even in the absence of hepatic metastases without alarming cardiac signs. The patient's condition was managed with octreotide and he was hospitalized in intensive care for 03 days.

Postoperative recovery was uneventful, with resumption of feeding on the 4th postoperative day and discharge on the 6th postoperative day.

In the histopathological and immunohistochemistral study, markers for chromogranin, synaptophysin, anti-Synaptophysin antibody, and CD56 were positive. The Ki67 index was 20%. The diagnosis made was that of a well-differentiated neuroendocrine tumor, Grade 2, according to the WHO classification.

DISCUSSION:

Small intestinal neuroendocrine tumors (siNETs), originally described as carcinoid tumors by Oberndorfer in 1907, derive from serotonin-producing enterochromaffin cells and present with an incidence of approximately 0.67–0.81/100,000/year.[4]

Frequently they present with nonspecific symptoms (abdominal pain or weight loss) while 20–30% of patients with liver metastases develop carcinoid syndrome due to serotonin or tachykinin production. Occasionally, complications due to carcinoid fibrosis leading to mesenteric fibrosis and carcinoid heart disease (CHD), where right heart valve lesions may predominate the clinical presentation, while carcinoid crisis is a life-threatening condition characterized by excessive flushing, bronchospasm and hemodynamic instability that has to be urgently diagnosed and treated.[5]

Which matches our patient's case presentation who's history of diarrhea and weight loss orientated the diagnosis.

CT or MRI can be helpful for the detection of the primary tumor and probable metastatic lesions while colonoscopy can detect tumors located in the terminal ileum. Serum Chromogranin A is a useful marker for the diagnosis and follow up of siNETs, while urine 5-hydroxy indole acetic acid (5-HIAA), a product of the metabolism of serotonin, has 100% sensitivity and 85–90% specificity for detecting carcinoid syndrome [6] , our patient benefited from CT scan imaging and serum Chromogranin A at the time of the diagnosis.

Resection of the primary tumor and locoregional lymph node metastases along the superior mesenteric root and around the mesentery results in improved survival of patients with siNETs.[7]

Perioperative management of SINETs patients requires preparation for the possibility of carcinoid crisis. Surgeons should maintain a low threshold for obtaining a preoperative echocardiogram in any SINETs patient with high serotonin levels or history concerning for carcinoid heart disease. Those with significant tricuspid or pulmonic valve disease must have this corrected prior to treatment of abdominal disease.[10]

Even without carcinoid heart disease, sudden hemodynamic instability or cardiovascular collapse due to carcinoid syndrome can occur, even in pa-

tients without clear symptoms of hormonal overproduction.87 Reported rates of perioperative carcinoid crisis range widely from 3% to 35%. [11,12,13,14]

However, since it may ameliorate carcinoid crisis symptoms [13,14], it has been recommended to provide octreotide at 100 mcg/hr throughout the case in addition to remaining ready to give additional fluids and vasopressors if necessary (preferably vasopressin or phenylephrine rather than epinephrine). Octreotide infusions are then weaned postsurgically by 25 mcg/hr every 8 hours. Postoperative venous thromboembolism prophylaxis follows standard treatment after major surgery. Extended homegoing prophylaxis may not be required, as rates of deep vein thrombosis and pulmonary embolism were lower for SINETs resections than those for other abdominal malignancies in a national retrospective database (1.7 vs 2.4%, $P < 0.05$).[15]

To develop even more, the anesthesia should follow a clear path, the diagnosis being generally made at the stage of the anesthesia consultation, the interrogation seeks the existence of a clinical carcinoid syndrome and its biological impact (hydroelectrolyte disorders, malabsorption...), while the complete examination supplemented by a cardiac echocardiography verifies the valvular status and the right and left ventricular function. In the presence of clinical carcinoid syndrome, preoperative preparation of patients with somatostatin analogs results in the disappearance of diarrhea and a significant reduction in the frequency and duration of flushing episodes. Additionally, it decreases the risk of perioperative carcinoid crises. Two agents are used, octreotide (Sandostatin®) and lanreotide (Somatuline LP®).[16,17,18,19]

Octreotide, the first available molecule for about fifteen years, inhibits the release of various mediators and their effects on target cells. With a half-life of 100 minutes, it is well suited for perioperative administration. Lanreotide, administered subcutaneously every 15 days (30 mg), lanreotide autogel, and octreotide LP (one injection per month) are more manageable for patients at home. Premedication includes an anxiolytic (as stress alone can trigger a carcinoid crisis), an H2 antagonist for antisecretory purposes, and an injection of octreotide one hour before surgery. Anesthetic induction will avoid histamine-releasing neuromuscular blockers (such as atracurium, mivacurium) as histamine release can also trigger a carcinoid crisis. Regardless of the chosen opioid, it will be administered at a high dose to block reactivity to painful stimuli. Maintenance includes a combination of a hypnotic, an opioid, and a neuromuscular blocker as per surgical requirements. Monitoring should include continuous invasive arterial pressure monitoring at a minimum. Cardiac output monitoring is recommended only for patients with tricuspid or pulmonary valve heart involvement or, more rarely, left heart involvement. Estimation of the depth of anesthesia using EEG parameters such as BIS appears very useful in cases of hypotension to differentiate between anesthetic overdose and vasodilation due to mediator secretion or in cases of hypertensive crisis to distinguish inadequate anesthesia from vasoconstriction induced by these same mediators. [20,21,22]

According to the released mediators (such as serotonin or bradykinin-histamine-kallikrein), this crisis can manifest as a hypertensive surge, hypotension, which can lead to circulatory arrest, or bronchospasm.

A carcinoid crisis can be triggered by intubation, tumor manipulation, pain, and sometimes has no apparent triggering factor. The manifestations of a carcinoid crisis are generally resolved with the administration of octreotide (Sandostatin) with an onset of action within a few minutes. It is imperative to ensure the immediate availability of this medication before any intervention in a patient with a carcinoid tumor, even if they are being managed for another procedure. Recommended doses range from 50 to 200 mg as a renewable intravenous bolus or continuous infusion at a rate of 100 to 300 mg/hour. Boluses should be injected slowly to avoid bradycardia or conduction disturbances.

Additionally, the incidence of these crises is reduced by the use of octreotide as premedication (100 to 200 mg subcutaneously) or intraoperative infusion. The main difficulty lies in associating the clinical disturbance with a carcinoid crisis:

- Hypotension can be caused by hypovolemia or anesthetic overdose. Close monitoring of blood loss, vascular filling to maintain normovolemia, and adjustment of anesthesia depth using EEG bispectral index generally help avoid this trap. In case of doubt, a diagnostic test with octreotide may be recommended. However, it should be noted that catecholamines are not recommended as they stimulate serotonin release and can worsen hypotension.
- Hypertension may be induced by surgical pain stimulation if not adequately associated with analgesia. It may be attributed to a carcinoid crisis when it does not occur with increased analgesia depth.
- Bronchospasm is more commonly associated with a carcinoid crisis because it is a rare complication in anesthesia outside of an asthma or COPD context or inadequate analgesia level. It is preferable to treat it initially with a test dose of octreotide to confirm this mechanism.

Furthermore, hyperglycemia may be pronounced especially after pre- and perioperative treatment with octreotide. Its treatment is symptomatic. [19,20,23,24,25]

When the resection has not been complete, the postoperative release of mediators from residual tumors can be responsible for episodes of hypotension or bronchospasm. This may justify, on one hand, postoperative monitoring in the intensive care unit and, on the other hand, the continuation of octreotide infusion followed by gradual discontinuation after the disappearance of any clinical signs.

Surgery of the primary site, whether laparoscopic or open, must include thorough and careful palpation of the entire bowel length. Primary SINETs occur most commonly in the ileum and are often small. After identifying all tumors, segmental resection of the affected bowel includes adequate margins to include the associated mesentery [10]

Mesenteric resection includes the blood supply and associated lymph nodes up to the level of where the segmental branch vessels come off the superior mesenteric artery (SMA) and vein (SMV). Bulky involved nodes are carefully dissected from larger mesenteric vessels when possible without endangering the SMV/SMA. Large nodal metastases frequently produce fibrosis and foreshortening of the mesentery. Although this adds difficulty to the dissection,fibrosis and bulky nodal disease also contribute to obstructive or intestinal ischemic symptoms if left in place.[10]

In patients with liver metastases surgery should still

be attempted with a curative intent or as a palliative method to prevent complications attributed to tumor mass or reduce hormone related symptoms.[6] However, a recent retrospective study that included 363 asymptomatic patients with stage IV siNENs showed that prophylactic locoregional surgery resulted to no significant survival advantage while delayed surgery was associated with fewer reoperations for intestinal obstruction.[8]

Median OS after valve replacement varies between 6 and 11 years.[9]

CONCLUSION:

In conclusion, small intestinal neuroendocrine tumors (SI-NETs) pose diagnostic and therapeutic challenges due to their varied clinical presentations and potential for hormonal complications. Our case highlights the importance of early recognition and management of hemodynamic complications, such as bronchospasm, following surgical resection of SI -NETs. Preoperative preparation, including assessment for carcinoid syndrome and optimization of cardiac function, is essential to minimize perioperative risks. Surgical resection remains the mainstay of treatment for SI-NETs, with careful attention to complete tumor removal and mesenteric dissection. Postoperative surveillance and management of residual disease are crucial for optimizing long-term outcomes. Further research is needed to refine perioperative management strategies and improve survival outcomes for patients with SI-NETs.

PROVENANCE AND PEER REVIEW:

Not commissioned, externally peer reviewed.

CONSENT

As per international standard or university standard, patient(s) written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

CONFLICTS INTERESTS

Authors have declared that no competing interests exist.

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