International Surgery Journal
*Lourenço R et al. Int Surg J. 2023 Sep;10(9):1518-1521*
http://www.ijsurgery.com
pISSN 2349-3305 | eISSN 2349-2902

DOI: https://dx.doi.org/10.18203/2349-2902.isj20232644

**Case Report**

# Severe gastroenteritis as presentation of a neuroendocrine tumor of pancreas

**Rita Lourenço*, Teresa Santos, Ana C. Carvalho, Ricardo Moreira, Jorge Magalhães, Catarina Longras, André Magalhães, Diana Matos, Rui Pinto, Carlos Alpoim**

Department of General Surgery, Hospital Senhora da Oliveira, Guimarães, Portugal

**Received:** 16 August 2023
**Received:** 21 August 2023
**Accepted:** 24 August 2023

***Correspondence:**
Dr. Rita Lourenço,
E-mail: ritalourencog@gmail.com



## ABSTRACT

Pancreatic neuroendocrine tumors (PanNETs) are a very rare entity, corresponding to 1-2% of all pancreatic neoplasms, although incidence and prevalence are rising. According to hormonal production, they can be functional or nonfunctional, leading to a subset of symptoms. A 45-year-old man, came to our emergency department complaining of vomiting and profuse non-bloody diarrhea for a week, with asthenia and no improvement with medication. He presented with diminished muscular strength and severe electrolytic changes with electrocardiographic repercussion. Patient was admitted to our intensive care unit (ICU) for hypovolemic and distributive shock due to a severe gastroenteritis. Further research studies were carried out which have shown a nodular structure of 5x4cm in the pancreas tail on computed tomography scan. A biopsy was made, and a histopathological exam revealed a pancreatic well differentiated neuroendocrine tumor. Hormonal analysis showed an elevation on vasoactive intestinal polypeptide (VIP). On $^{68}$Ga-DOTA-NOC PET/CT, there were 2 nodular lesions with anomalous overexpression of somatostatin receptors, one in the pancreatic tail near splenic hilum and another in the pancreatic head. Patient underwent a total pancreaticoduodenectomy with en bloc splenectomy. Postoperative period was uneventful. Mostly, this kind of pancreatic neuroendocrine tumors are indolent, but till 39% can have an aggressive course, so they have variable prognosis.

**Keywords:** PanNET, Severe gastroenteritis, VIP, Pancreaticoduodenectomy

## INTRODUCTION

Pancreatic neuroendocrine tumors (PanNET) are rare neoplasms of endocrine tissue, known as islet cell tumors, arising from stem cells in pancreatic ductal epithelial cells. They account for fewer than 3 percent of all pancreatic tumors and have an incidence of ≤1 case per 100,000 individuals per year.[1] According to hormone secretion and clinical manifestations, they can be classified as functional or nonfunctional, with 50% to 75% being nonfunctional and asymptomatic.[1]

Functional pancreatic neuroendocrine tumors are termed after the hormone they hypersecret and resulting clinical syndrome. Insulinomas are panNET with insulin hyperproduction leading to episodic hypoglycemia; Gastrinomas present with gastrin hyperproduction and Zollinger-Ellison syndrome (only 20% to 25% arise from pancreas); Glucagonomas has glucagon hyperproduction and glucagonoma syndrome. Somatostatinomas shows somatostatin hyperproduction, abdominal pain and weight loss; and VIPomas are panNET with vasoactive intestinal polypeptide (VIP) hyperproduction and VIPoma syndrome.[2]

VIPoma is a very rare neuroendocrine tumor, with an incidence of 1 in a million individuals per year and appears between 30 and 50 years of age.[3] In the adult, 90% arise from pancreas and it can be malignant in 40% to 70% of cases. Usually, they are isolated tumors, but in 5% of cases, they are part of multiple endocrine neoplasia syndrome type 1 (MEN 1) and occur in association with pituitary and parathyroid tumors, gastrinoma or other tumors. MEN 1 syndrome (or Werner syndrome) is clinically defined as the occurrence of 2 or more of these tumors.[4-6] PanNET occurring in patients with MEN 1 syndrome are usually multiple.

VIPoma syndrome happens when vasoactive intestinal polypeptide is hypersecreted by the tumor and binds to receptors on intestinal epithelial cells leading to secretion of sodium, chloride, potassium and water into intestinal lumen. This results in profuse watery diarrhea, dehydration, muscle weakness, hypokalemia and achlorhydria (WDHA syndrome).[7]

## CASE REPORT

A 45-year-old man, came to our emergency department complaining about watery diarrhea five times per day, estimated average volume loss of nearly 2.5–3 l/day, with no blood or mucus, since two weeks before and worsening muscle weakness. No response to medical treatment (loperamide and probiotics) was achieved. He had no cohabitants with those symptoms, no food intoxication, and no recent travel to tropical areas.

As pathological background, one year before, he had a parathyroidectomy for parathyroid adenoma with hyperparathyroidism and several hipercalcemia events. He also had nephrolithiasis and a previous severe gastroenteritis needing hospital stay. As family background, his father had hyperparathyroidism and his sister had a pituitary adenoma and acromegaly.

On physical examination in emergency department, he was lethargic, had signs of dehydration and objectively a decreased overall muscle strength.

Blood tests showed hypercalcemia, hypernatremia and a severe hipokalemia (1.33 mEq/l) with electrocardiographic changes such as ST depression, T wave inversion and QT prolongation. He also had metabolic acidosis on arterial blood gas, hypotension and tachycardia (HR 130 bpm).

Given the risk of severe dysrhythmia and hypovolemic shock, he was admitted to our intensive care unit. He developed an acute respiratory distress syndrome (ARDS) requiring invasive ventilation. Fluid and electrolyte replacements were done as well as initial inotropic support.

Contrast-enhanced computed tomography (CT) scan showed a nodular structure of 53×43 mm, with peripheral enhancement and a cystic area measuring 35×30 mm in its central portion, apparently in continuity with pancreatic tail, contacting the splenic hilum and gastric fundus, not being able to exclude invasion of splenic vein. No metastases were recognized.

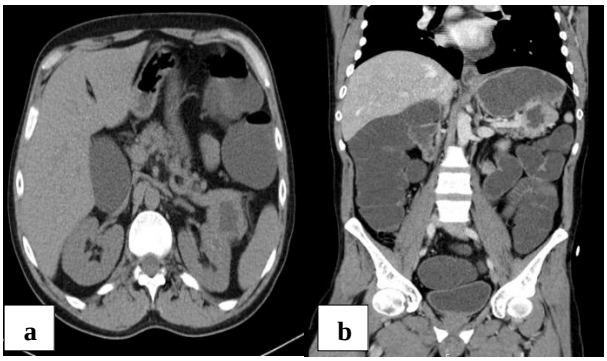


**Figure 1: (a) and (b) Contrast-enhanced computed tomography (CT) scan showing a nodular structure in pancreatic tail (axial and coronal section, respectively).**

Patient presented improvement during hospital stay being discharged three weeks later.

To complete disease investigation, a biopsy to the pancreatic tail lesion was made which demonstrated a well differentiated neuroendocrine tumor (grade 2). As we were suspecting a functional panNET, biochemical testing was performed, and an elevated VIP appeared (126 pg/ml) leading to diagnosis of a VIPoma.

Given his pathological and family background, we assumed a clinical diagnosis of MEN 1 syndrome. A transthoracic echocardiogram was made and showed no alterations. A cerebral magnetic resonance imaging (MRI) had no evidence of pituitary tumor. Other biochemical testing was taken for insulin, calcitonin, growth hormone, gastrin and indole acetic acid (5-HIAA) and there were no changes.

A $^{68}$Ga-DOTA-NOC PET/CT showed abnormal overexpression of somatostatin receptors in a nodular structure in pancreatic tail and in another nodular structure in the head of the pancreas.

He had a preoperative trivalent vaccine (*pneumococcus*, *haemophilus influenzae b* and *meningococcal* group C) as splenectomy would probably have to be done.

Our patient had a total pancreaticoduodenectomy with concomitant splenectomy and regional lymph node dissection. Postoperative period was uneventful.

Histopathological examination of specimen found five intrapancreatic neuroendocrine tumors, World Health Organization (WHO) grade 2, between 0.8 and 6.8 cm, World Health Organization (WHO) grade 2 without

lymphovascular or perineural invasion. There were no metastases on sixteen removed lymph nodes and no intersected margins. Proliferative index (Ki-67) was <3% and CAM5.2, synaptophysin and chromogranin A were positive on immunohistochemical study. It was a T3(m) N0 M0, stage II according to the American Joint Committee on Cancer (AJCC).

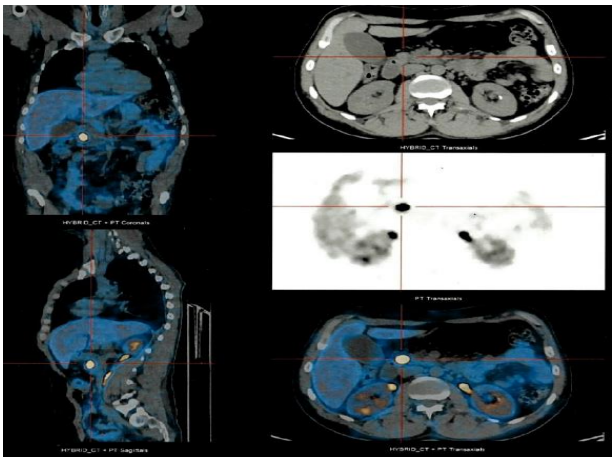

**Figure 2: $^{68}$Ga-DOTA-NOC PET/CT showing a nodular structure in pancreatic head overexpressing somatostatin receptors.**

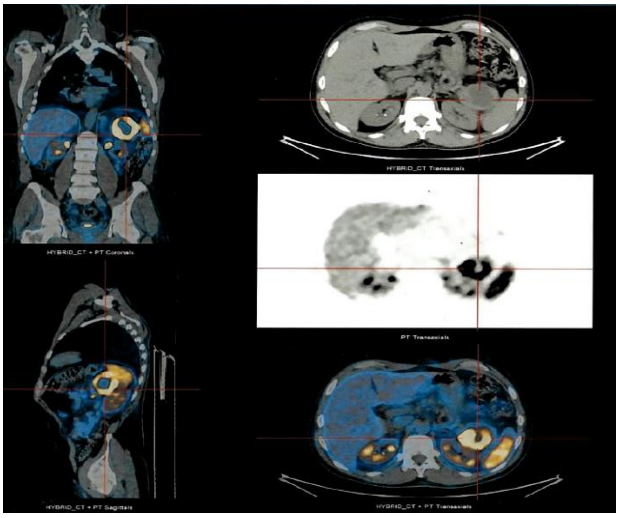

**Figure 3: $^{68}$Ga-DOTA-NOC PET/CT showing a bigger nodular structure in pancreatic tail (60×45 mm), also overexpressing somatostatin receptors.**

A genetic testing was performed and revealed a MEN 1 gene variant of indeterminate meaning.

Patient maintains endocrinology and surgery follow-up appointments, significant symptomatic relief, insulin controlled diabetes and no evidence of disease recurrence.

## DISCUSSION

Pancreatic neuroendocrine tumors are rare tumors of endocrine pancreatic tissue and VIPoma area even rarer. Well differentiated panNET are indolent malignancies but can cause life-threatening changes as seen in this case report of a functional panNET.

Diagnosis of a VIPoma is usually delayed and more than half of patients are already metastasized at diagnosis. As so, MEN 1 syndrome is a rare autosomal-dominant inherited disorder and requires a high index of suspicion also leading to frequently delayed diagnosis. In our case report, prompt investigation for panNET and MEN 1 syndrome was done, and diagnosis was easier as he had multiple nodular structures on pancreas, a severe watery diarrhea and suspicious personal and family background.[6-8]

Contrast-enhanced CT scan or MRI are appropriate for cross-sectional imaging as evaluation with somatostatin receptor imaging to assess receptor status and disease extent. $^{68}$Ga-DOTA-NOC PET/CT, a somatostatin receptor imaging, is more sensitive and specific than conventional imaging as CT scan and it was essential for correct surgical approach because it accurately showed the disease extent namely multifocality, that was missed on CT scan. Because of that, a pancreaticoduodenectomy was done, instead of a distal pancreatectomy, leading to diagnosis of five panNETs on histopathological examination.

Prognosis of VIPoma depends on tumor grading, staging and surgical resectability. A vast majority (60%) have already metastasized at the time of diagnosis as it can be seen in many case reports, but fortunately not on this one.[9,10] Surgery remains the gold standard of treatment and the only one potentially curative.

Our patient had a well differentiated, low-grade (Ki-67 <3%) pancreatic neuroendocrine tumor, with no distant metastases and a complete surgical resection (R0) which confers an excellent prognosis, some studies referring a 95% five-year survival rate.[10,11]

## CONCLUSION

We report a case of a VIPoma in a MEN 1 syndrome patient, highlighting the importance of a good personal and familial clinical history as well as the importance of $^{68}$Ga-DOTA-NOC PET/CT to evaluate disease extent and to properly prepare for surgery.

*Funding: No funding sources*
*Conflict of interest: None declared*
*Ethical approval: Not required*

## REFERENCES

1. Halfdanarson TR, Rubin J, Farnell MB, Grant CS, Petersen GM. Pancreatic endocrine neoplasms: epidemiology and prognosis of pancreatic endocrine tumors. Endocr Relat Cancer. 2008;15(2):409-27.

2. Klimstra DS. Nonductal neoplasms of the pancreas. Mod Pathol. 2007;20(1):S94.
3. Angelousi A, Koffas A, Grozinsky-Glasberg S, Gertner J, Kassi E, Alexandraki K, et al. Diagnostic and Management Challenges in Vasoactive Intestinal Peptide Secreting Tumors: A Series of 15 Patients. Pancreas. 2019;48(7):934-42.
4. Al-Salameh A, Cadiot G, Calender A, Goudet P, Chanson P. Clinical aspects of multiple endocrine neoplasia type 1. Nat Rev Endocrinol. 2021;17(4):207-24.
5. Thakker RV, Newey PJ, Walls GV, Bilezikian J, Dralle H, Ebeling PR, et al. Clinical practice guidelines for multiple endocrine neoplasia type 1 (MEN1). J Clin Endocrinol Metab. 2012;97(9):2990-3011.
6. Kouvaraki MA, Shapiro SE, Cote GJ, Lee JE, Yao JC, Waguespack SG, et al. Management of pancreatic endocrine tumors in multiple endocrine neoplasia type 1. World J Surg. 2006;30(5):643-53.
7. Schizas D, Mastoraki A, Bagias G, Patras R, Moris D, Lazaridis II, et al. Clinicopathological data and treatment modalities for pancreatic vipomas: a systematic review. J BUON. 2019;24(2):415-23.
8. Abu-Zaid A, Azzam A, Abudan Z, Algouhi A, Almana H, Amin T. Sporadic pancreatic vasoactive intestinal peptide-producing tumor (VIPoma) in a 47-year-old male. Hematol Oncol Stem Cell Ther. 2014;7(3):109-15.
9. Una Cidon E. Vasoactive intestinal peptide secreting tumor: An overview. World J Gastrointest Oncol. 2022;14(4):808-19.
10. Azizian A, König A, Hartmann A, Schuppert F, Seif Amir Hosseini A, Kitz J, et al. Surgical treatment of metastatic VIPoma: a case report. Therap Adv Gastroenterol. 2021;14:17562848211051132.
11. National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology. Fact sheet: Neuroendocrine and Adrenal Tumors, Version 1. 2023. Available at: https://www.nccn.org/guidelines/guidelines-detail?category=1&id= 1448. Accessed on 23 March 2023.
12. Sakurai M, Wakabayashi T, Kondo Y, Ikeda E, Watanabe K, Takei A, et al. A case of vasoactive intestinal peptide-secreting tumor (VIPoma) arising from MEN1 inactivation which recurred 15 years after the initial resection. Endocr J. 2023;70(6):573-9.

**Cite this article as:** Lourenço R, Santos T, Carvalho AC, Moreira R, Magalhães J, Longras C, et al. Severe gastroenteritis as presentation of a neuroendocrine tumour of pancreas. Int Surg J 2023;10:1518-21.