

VIPoma Presenting With Obstructive Jaundice: A Case Report

Sim Yin Ng and Ken Seng Chiew

Medical Department, Hospital Sultan Ismail, Johor Bahru, Malaysia

Abstract

VIPoma is a rare pancreatic neuroendocrine tumor characterized by the overproduction of vasoactive intestinal peptide (VIP), typically manifesting as watery diarrhea, hypokalaemia and metabolic acidosis. Its presentation can be atypical, complicating diagnosis. We report the case of a 30-year-old male who initially presented with obstructive jaundice and fatigue, with imaging revealing a pancreatic head mass and liver metastases. Histopathological analysis confirmed a low-grade pancreatic neuroendocrine tumor. The clinical course was complicated by portal vein thrombosis and metastatic spread. Six months later, the patient developed persistent, refractory watery diarrhea with associated hypokalaemia. Elevated serum VIP levels and Gallium-68 DOTATATE positron-emission tomography and computed tomography (PET-CT) supported the diagnosis of VIPoma. Symptom resolution was achieved with subcutaneous octreotide, followed by transition to monthly long-acting release (LAR) octreotide. Approximately 60% of VIPoma cases are metastatic at the time of diagnosis, as demonstrated in this patient. The case highlighted the diagnostic challenges of VIPoma in the presence of atypical symptoms such as jaundice and absence of initial diarrhea. It also underscores the need for close multidisciplinary collaboration to determine the best course of action and to optimize patient outcomes.

Key words: VIPoma, diarrhea, pancreatic neuroendocrine tumor

INTRODUCTION

VIPoma is a rare neuroendocrine tumor (NET) that arises primarily in the pancreas but may also occur elsewhere in the gastrointestinal tract. It is most frequently associated with Verner-Morrison syndrome, characterized by the triad of profuse watery diarrhea, hypokalaemia and metabolic acidosis resulting from the overproduction of vasoactive intestinal peptide (VIP).¹ Although chronic diarrhea is the hallmark manifestation, presentation may be subtle or atypical, creating a diagnostic challenge.

We report a 30-year-old male who initially presented with obstructive jaundice and fatigue, suggestive of a primary hepatobiliary or gastrointestinal pathology. However, further investigation revealed a pancreatic mass, which was subsequently diagnosed as a VIP-secreting neuroendocrine tumor. His course was complicated by liver metastases and portal vein thrombosis. The case highlights the importance of a comprehensive diagnostic approach, including advanced imaging modalities and biochemical testing in patients with atypical presentations of pancreatic NETs. Early recognition and intervention in these complex cases significantly influence therapeutic strategies and patient prognosis.

CASE

A 30-year-old male presented with a 1-week history of progressive jaundice accompanied by dark-colored urine and pale stools. He denied any history of abdominal pain, nausea, or vomiting. He had no recent travel, alcohol use, or known liver disease, and his medical history was otherwise unremarkable. Laboratory results showed cholestatic jaundice (Table 1).

Hepatobiliary ultrasonography showed a well-defined hypoechoic lesion at the periportal region measuring 3.9 x 4.9 x 4.0 cm, with dilatation of the common bile duct and bilateral intrahepatic ducts. Computed tomography (CT) scan showed a suspected pancreatic carcinoma causing biliary obstruction, with abdominal lymph node and liver metastasis and portal vein thrombosis (Figure 1). Endoscopic ultrasound of the pancreas showed a hypoechoic lesion at the head of pancreas measuring 38 x 35 mm, causing upstream dilatation of the pancreatic duct and common bile duct. Endoscopic retrograde cholangiopancreatography (ERCP) with sphincterotomy and metal stenting was performed. Fine-needle biopsy demonstrated a low grade neuroendocrine tumor with mitosis rarely seen and a Ki67 index of 1% - 2% (Figure 2). The patient was referred to oncology to discuss further management but was lost to follow-up.

Table 1. Summary of investigations during first presentation

Investigations	Results	Unit	Normal range
Renal profile			
Urea	2.4	mmol/L	3.2-8.2
Creatinine	57	mmol/L	49-90
Sodium	136	mmol/L	136-145
Potassium	4.2	mmol/L	3.4-4.5
Calcium	2.4	mmol/L	1.5-3.0
Phosphate	0.9	mmol/L	0.8-1.7
Magnesium	1.0	mmol/L	0.66-1.07
Chloride	103	mmol/L	98-107
Liver function tests			
Total bilirubin	277.9	μmol/L	3-19
Direct bilirubin	205	μmol/L	0-5
Alkaline phosphatase	742	U/L	46-116
Gamma-glutamyl transferase	612	U/L	12-73
Alanine transaminase	69	U/L	10-49
Aspartate transaminase	51	U/L	0-34
Albumin	50	g/L	32-48
Tumor markers			
Carbohydrate Antigen 19.9 (CA19.9)	4.0	U/mL	0-37
Carcinoembryonic Antigen (CEA)	1.0	ng/mL	<5

Table 2. Summary of investigations during second admission

Investigations	Results	Unit	Normal range
Renal profile			
Urea	4.1	mmol/L	3.2-8.2
Creatinine	74	mmol/L	49-90
Sodium	144	mmol/L	136-145
Potassium	1.5	mmol/L	3.4-4.5
Calcium	2.3	mmol/L	1.5-3.0
Phosphate	0.8	mmol/L	0.8-1.7
Magnesium	1.0	mmol/L	0.66-1.07
Chloride	108	mmol/L	98-107
Liver function tests			
Total bilirubin	19.4	μmol/L	3-19
Alkaline phosphatase	126	U/L	46-116
Alanine transaminase	15	U/L	10-49
Aspartate transaminase	27	U/L	0-34
Others			
Serum VIP	211	pg/mL	<86
24-hour urine 5 HIAA	12.96	μmol/L/day	3.66-42.89
Serum chromogranin A	96	ug/L	<101
Stool Ova and cyst	Negative		
Stool culture and sensitivity	No growth		

Six months later, he was readmitted with a 2-week history of diarrhea. He reported frequent episodes of watery stools (5-6 times a day) over the past week, accompanied by muscle weakness, fatigue, and unintentional weight loss of approximately 8 kg over the past month. His diarrhea was continuous and had worsened over the past several days. He denied fever, abdominal pain, or intake of any new medications. On examination, he was mildly dehydrated, with dry mucous membranes and a reduced skin turgor. There was mild epigastric tenderness but no palpable masses.

Laboratory testing showed resolution of cholestasis but severe refractory hypokalaemia despite 3 days of intravenous potassium replacement (Table 2). There were normal calcium levels and a mildly elevated chloride level which is atypical as VIPomas are often associated with hypochlorhaemia due to bicarbonate loss. Stool

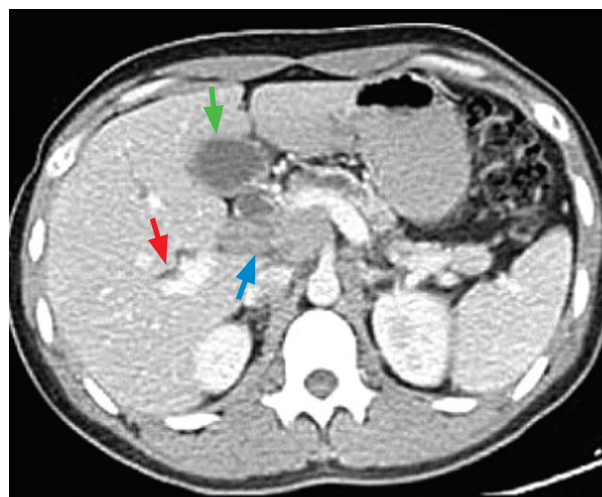


Figure 1. CT abdomen showed an ill-defined hypodense mass at pancreatic head measuring about 3.0 x 3.5 x 4.2 cm (blue arrow) with distended gallbladder (green arrow) and dilated intrahepatic duct (red arrow).

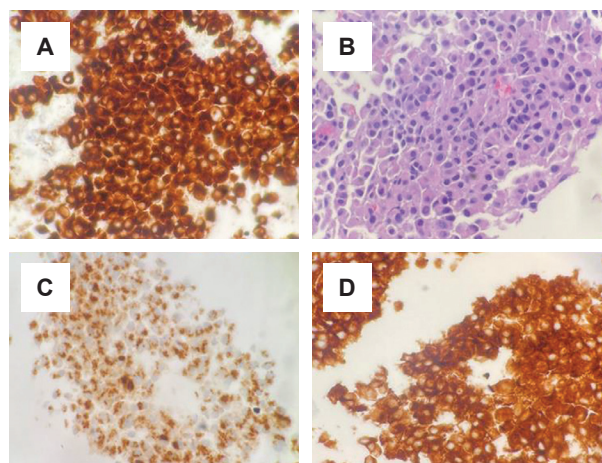


Figure 2. FNB head of pancreas: Scanty tumor tissue with neuroendocrine differentiation (A) cytokeratin stain (ck ae1/ae3, 400x); (B) H&E stain (400x); (C) Chromogranin A stain (400x); (D) Synaptophysin stain (400x).

studies excluded infectious causes, and 24-hour urine 5-hydroxyindoleacetic acid (5-HIAA) was normal. Following endocrinology referral, subcutaneous octreotide was initiated and titrated up to 100 mcg thrice a day, resulting in resolution of symptoms and hypokalaemia within 24 hours.

A fasting serum VIP sample obtained before treatment was elevated at 211 pg/mL (normal range <86 pg/mL). PET-CT with Gallium-68 DOTATATE showed a large focal DOTA-octreotide uptake over an ill-defined hypodense lesion at the pancreatic head and portal hepatic lymph node (maximum standardized uptake value, 19.09) measuring 3.34 x 3.06 x 5.51 cm with multifocal uptake in abdominopelvic lymph nodes and both hepatic lobes (Figure 3). In the setting of watery diarrhea, hypokalaemia, elevated VIP level, the PET CT results supported the diagnosis of VIPoma.

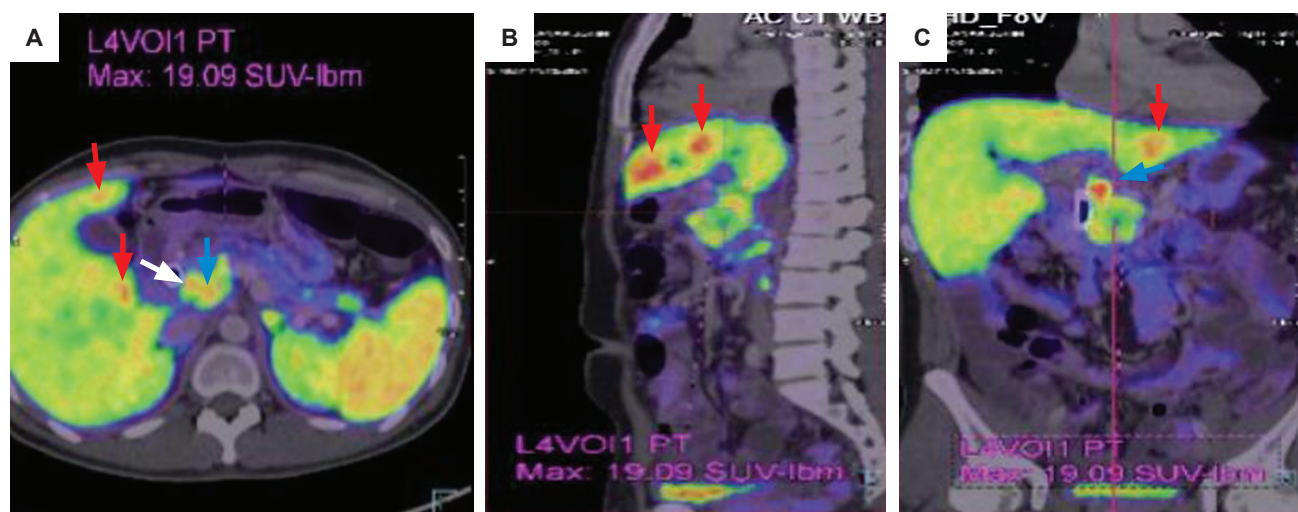


Figure 3. Gallium-68 DOTATATE PET-CT images show somatostatin receptor–expressing lesions: **(A)** adjacent porta hepatis lymph nodes (*white arrows*); **(A, B and C)** multiple lesions in both hepatic lobes (*red arrows*); and **(A and C)** a large focal lesion in the pancreatic head (*blue arrow*).

He was then transitioned to long-acting release (LAR) octreotide 20 mg monthly, with an overlap period for symptom control. A multidisciplinary team comprising hepatobiliary surgeons, oncologists, and endocrinologists concluded that curative surgery was not feasible due to metastases and vascular involvement. He remains clinically stable and asymptomatic on octreotide LAR, at subsequent clinic visits and reports satisfaction with the current treatment outcome.

DISCUSSION

VIPoma, a rare pancreatic neuroendocrine tumor (pNET), presents a diagnostic challenge due to its often atypical and subtle clinical presentation. The classic syndrome associated with VIPoma, Verner-Morrison syndrome, is characterized by severe watery diarrhea, hypokalaemia, and metabolic acidosis caused by the excessive secretion of vasoactive intestinal peptide (VIP).¹ Symptoms at diagnosis are often varied and dependent in part on the site of tumors and also on whether the tumors are functioning in nature, which may cause significant delays in diagnosis.²

A recent systematic review of 65 patients with VIPoma reported that watery diarrhea was present in only 54.5% of cases at initial presentation, indicating that a substantial proportion of patients may lack the classic symptoms early in the disease course.³ Furthermore, despite advanced disease, our patient's serum vasoactive intestinal peptide (VIP) concentration was only modestly elevated at 211 pg/mL when diarrhea developed, compared with the median serum VIP level of 636 pg/mL reported in the systematic review.³ It is therefore plausible that the patient's VIP concentration was even lower at initial presentation and below the threshold required to induce clinically significant secretory diarrhea. The subsequent onset of diarrhea may have reflected progressive tumor growth and/or increased hormonal secretory activity over time. Although serial VIP

measurements were unavailable to confirm this hypothesis, this explanation is consistent with the patient's clinical course and highlights the potential variability in the timing and severity of symptom development in VIPoma.

In approximately 60 to 80% of all VIPoma cases described to date, the patient presented with metastases at the initial VIPoma diagnosis.⁴ The propensity for early metastasis underscores the importance of careful staging and imaging techniques. The metastases most commonly occur in the liver, lymph nodes, bones, and kidney.⁵ Additionally, the presence of portal vein thrombosis in advanced cases can significantly complicate the clinical picture, leading to further diagnostic uncertainty. Portal vein involvement may contribute to worsening prognosis by causing portal hypertension, gastrointestinal bleeding, and ascites.⁶

Radiologic imaging plays a critical role in both the diagnosis and management of VIPomas.⁷ Somatostatin receptor scintigraphy (SRS), a sensitive imaging modality for neuroendocrine tumors, has become a cornerstone in localizing the primary tumor and identifying metastatic sites.⁸ Somatostatin analogues, such as octreotide, bind to the somatostatin receptors on the tumor cells, allowing for detailed visualization of the tumor's location and metastatic spread. In combination with computed tomography and magnetic resonance imaging, these imaging modalities offer a comprehensive assessment of the tumor's extent, guiding both surgical and non-surgical treatment strategies. In this case, somatostatin receptor scintigraphy confirmed the presence of a pancreatic mass and liver metastases, confirming the diagnosis of a metastatic VIPoma.

Surgical resection remains the mainstay of therapy for localized VIPomas.⁹ However, metastatic disease requires a multidisciplinary approach. Somatostatin analogues, particularly octreotide, effectively control diarrhea and electrolyte disturbances by inhibiting VIP secretion, which

can improve the quality of life in patients with advanced disease.¹⁰ Octreotide has also been shown to reduce tumor burden in some cases. Long-acting formulations of octreotide provide sustained symptom relief and improve treatment adherence, making them a preferred treatment option for many patients.

Overall, the diagnosis and management of VIPomas require a high degree of clinical suspicion, especially in patients with atypical presentations. Elevated serum VIP levels, in conjunction with imaging techniques such as somatostatin receptor scintigraphy, are crucial for confirming the diagnosis and guiding treatment decisions. Early diagnosis, combined with appropriate imaging and treatment, can dramatically enhance patient outcomes and quality of life.

CONCLUSION

This case illustrates VIPoma presenting with obstructive jaundice prior to the usual presentation of watery diarrhea and hypokalaemia. The delayed onset of diarrhea reinforces the need to consider functioning NETs in patients with pancreatic masses, even when characteristic symptoms are initially absent.

Management can be additionally challenging with metastatic disease. A multidisciplinary approach is essential to optimize care and therapeutic decision-making.

Ethical Consideration

Patient's consent was obtained before submission of the manuscript.

Statement of Authorship

All authors certified fulfillment of ICMJE authorship criteria.

CRedit Author Statement

SYN: Conceptualization, Writing – original draft preparation, Visualization, Project administration; **KSC:** Conceptualization, Writing – review and editing, Visualization, Supervision.

Data Availability Statement

No datasets were generated or analyzed for this study.

Author Disclosure

The authors declared no conflict of interest.

Funding Source

None.

References

- Karele EN. All you need to know about VIPoma: Review on the latest studies. *Presse Med.* 2024;53(2):104222. PMID: 38109967 DOI: 10.1016/j.lpm.2023.104222
- Basuroy R, Bouvier C, Ramage J, Sissons M, Srirajaskanthan R. Delays and routes to diagnosis of neuroendocrine tumors. *BMC Cancer.* 2018;18(1):1122. PMID: 30445941 PMCID: PMC6240263 DOI: 10.1186/s12885-018-5057-3
- Schizas D, Mastoraki A, Bagias G, et al. Clinicopathological data and treatment modalities for pancreatic VIPomas: A systematic review. *J BUON.* 2019;24(2):415-23. PMID: 31127985
- Azizian A, König A, Ghadimi M. Treatment options of metastatic and nonmetastatic VIPoma: A review. *Langenbecks Arch Surg.* 2022; 407(7):2629-36. PMID: 35931878 PMCID: PMC9640398 DOI: 10.1007/s00423-022-02620-7
- Helbing A, Menon G, Sandhu S, et al. VIPoma. In: *StatPearls*. StatPearls Publishing; Updated February 23, 2025. Bookshelf ID: NBK507698
- Boccatonda A, Gentilini S, Zanata E, Simion C, Serra C, Simioni P, et al. Portal vein thrombosis: State-of-the-art review. *J Clin Med.* 2024; 13(5):1517. PMID: 38592411 PMCID: PMC10932352 DOI: 10.3390/jcm13051517
- Bicci E, Cozzi D, Ferrari R, Grazzini G, Pradella S, Miele V. Pancreatic neuroendocrine tumors: Spectrum of imaging findings. *Gland Surg.* 2020;9(6):2215-24. PMID: 33447574 PMCID: PMC7804535 DOI: 10.21037/gs-20-537
- Park S, Parihar AS, Bodei L, Hope TA, Mallak N, Millo C, et al. Somatostatin receptor imaging and theranostics: Current practice and future prospects. *J Nucl Med.* 2021;62(10):1323-29. PMID: 34301785 PMCID: PMC9364764 DOI: 10.2967/jnumed.120.251512
- Brugel M, Walter T, Goichot B, et al. Efficacy of treatments for VIPoma: A GTE multicentric series. *Pancreatology.* 2021;21(8):1531-9. PMID: 34404601 DOI: 10.1016/j.pan.2021.08.001
- de Herder WW, Hofland J. Vasoactive intestinal peptide-secreting tumor (VIPoma). In: Feingold KR, Adler RA, Ahmed SF, et al., eds. *Endotext*. South Dartmouth (MA): MDText.com, Inc.; 2000-. Bookshelf ID: NBK278960/

Authors are required to accomplish, sign and submit scanned copies of the JAFES Author Form consisting of: (1) Authorship Certification, that authors contributed substantially to the work, that the manuscript has been read and approved by all authors, and that the requirements for authorship have been met by each author; (2) the Author Declaration, that the article represents original material that is not being considered for publication or has not been published or accepted for publication elsewhere, that the article does not infringe or violate any copyrights or intellectual property rights; that no references have been made to predatory/suspected predatory journals; and that use of artificial intelligence (AI) or AI-assisted technologies shall be declared to include the name of the AI tool or service used; (3) the Author Contribution Disclosure, which lists the specific contributions of authors; (4) the Author Publishing Agreement which retains author copyright, grants publishing and distribution rights to JAFES, and allows JAFES to apply and enforce an Attribution-Non-Commercial Creative Commons user license; and (5) the Conversion to Visual Abstracts (*optional for original articles only) to improve dissemination to practitioners and lay readers. Authors are also required to accomplish, sign, and submit the signed ICMJE form for Disclosure of Potential Conflicts of Interest. For original articles, authors are required to submit a scanned copy of the Ethics Review Approval of their research as well as registration in trial registries as appropriate. For manuscripts reporting data from studies involving animals, authors are required to submit a scanned copy of the Institutional Animal Care and Use Committee approval. For Case Reports or Series, and Images in Endocrinology, consent forms, are required for the publication of information about patients; otherwise, appropriate ethical clearance has been obtained from the institutional review board. Articles and any other material published in the JAFES represent the work of the author(s) and should not be construed to reflect the opinions of the Editors or the Publisher.