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**Life-threatening diarrhea and acute renal failure secondary to pancreatic VIPoma treated by surgery: a clinical case**

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**ABSTRACT**

Pancreatic neuroendocrine tumors represent less than 5% of all pancreatic tumors. They are a heterogeneous group of neoplasms with a diverse behavior and prognosis. Pancreatic vasoactive intestinal polypeptide tumor (VIPoma) is an exceptional tumor within this group due to its low incidence.

The presence of pancreatic VIPoma should be clinically suspected in all patients with watery diarrhea, particularly when accompanied by a loss of potassium and bicarbonate and a pancreatic mass on imaging. There are other pathologies with similar symptoms; therefore, a correct differential diagnosis with an adequate treatment is essential for its management.

We present the case of a 46-year-old patient who developed a prerenal kidney failure secondary to severe watery diarrhea after a diagnosis of pancreatic VIPoma. Thus, a resection was performed as the patient was rapidly deteriorating and required an

intervention.

**Key words:** VIPoma. Pancreas. Neuroendocrine tumors. Renal insufficiency. Diarrhea.

## INTRODUCTION

VIPoma is a very rare neuroendocrine tumor that produces the vasoactive intestinal polypeptide (VIP) hormone, which is mainly secreted in the gastrointestinal tract and pancreas. VIP is a neurotransmitter that inhibits gastric secretion and stimulates glucagon, insulin and somatostatin secretion. These actions lead to a secretory diarrhea, hypokalemia and dehydration (1). We present the clinical case of a 46-year-old patient who was evaluated in the Emergency Room due to persistent diarrhea and prerenal kidney failure. The patient was subsequently diagnosed with pancreatic VIPoma and underwent a surgical resection.

## CASE REPORT

A 46-year-old morbidly obese male presented to Emergency Room with a poor performance status associated with 30-40 watery diarrhea per day. The physical examination was anodyne. An analytical study identified acute kidney failure (urea 82 mg/dl and creatinine 4.06 mg/dl), hyponatremia (127 mmol/l), hypokalemia (3.4 mmol/l), hypercalcemia (11.9 mmol/l) and metabolic acidosis (pH 7.09, HCO<sub>3</sub> 7.1 mmol). An ultrasound identified a solid and heterogeneous mass of 11 cm, which seemed dependent on the minor gastric curvature. The patient was admitted due to these findings in order to perform a complete study.

Complementary tests identified VIP > 405 pg/ml (< 100) and glucagon 1,064 pg/ml (25-250). Computed tomography (CT) and magnetic resonance imaging (MRI) showed a mass in the pancreatic body of 13 x 13 cm, without infiltration (Fig. 1). OctreoScan® observed an area with increased uptake on gastric topography (Fig. 2). Fine needle aspiration puncture (FNAP) identified a well-differentiated neuroendocrine tumor with a positive immunohistochemistry for synaptophysin, chromogranin A and a Ki 67 index of < 2%.

Despite treatment with octeotride, admission to the Intensive Care Unit was required due to an increased number of depositions associated with progressive renal function impairment. Surgery was performed due to the diagnosis of a VIPoma that caused clinical repercussions, which could not be controlled with medical treatment. Intraoperatively, a large tumor was observed on the pancreas and gastric posterior wall, measuring 16 x 17 cm. A distal splenopancreatectomy was performed with a section at the level of the pancreatic neck with a 60 mm SEAM-GUARD® endoGIA™ (Fig. 3).

The patient evolved favorably, the intestinal transit normalized and he was discharged on the eighth postoperative day. The histopathology analysis showed a neuroendocrine tumor without perineural or vascular infiltration and free margins. Nine lymph nodes were resected and none were affected. The disease stage was pT2N0MX.

## **DISCUSSION**

A hormone-secreting neuroendocrine tumor should be suspected due to the clinical scenario of profuse watery diarrhea of more than one liter per day, dehydration, hypokalemia and metabolic acidosis (2). The difficult management is based on the low clinical suspicion due to the incidence and the rapid clinical deterioration in this case. A rapid hydroelectric replenishment and treatment with octreotide is crucial to avoid an acute renal failure, as in our patient.

Pancreatic neuroendocrine tumors (PNET) account for less than 5% of all pancreatic tumors and can present as nonfunctioning and functioning PNETs. The second group includes the pancreatic VIPoma and its incidence is < 1 case/10,000,000 inhabitants/year. It originates in the non- $\beta$  cells of the pancreatic islets that produce vasoactive intestinal peptide (3). They are usually isolated tumors, larger than 3 cm in diameter and are located in the tail of the pancreas in 70% of cases (4). Five per cent of these tumors form part of the multiple endocrine neoplasia syndrome type 1 (MEN1). The case presented here is a 46-year-old patient with a large isolated lesion, located in the body of the pancreas.

These tumors produce the Verner-Morrison clinical syndrome, pancreatic cholera or watery diarrhea hypokaliemia achlorhydria (WDHA) (1). This syndrome is characterized by severe watery diarrhea with a loss of bicarbonate and potassium, which in turn gives rise to hypovolemia with hypokalemia and metabolic acidosis. It is associated with hypochlorhydria or achlorhydria in 75% of cases. Clinical history and VIP values higher than 200 pg/ml leads to a diagnosis (5). The main imaging techniques used for the diagnosis and follow-up of PNETs are ultrasound, CT, MRI or even OctreoScan® (6). Endoscopic ultrasound has a higher sensitivity than CT and MRI (92 and 93%, respectively) to visualize smaller tumors. In our case, CT and MRI allowed us to specify the tumor size and location. Endoscopic ultrasound was also performed, which allowed samples to be obtained via FNAP and helped to plan the surgical strategy. The study was completed with an OctreoScan®, whose sensitivity depends on the density of somatostatin receptors of the tumor cells where the radioisotope is fixed (7).

Surgical treatment for functioning PNETs will depend on the control of symptoms, tumor size, location and the degree of malignancy. The World Health Organization recommends surgery for all functioning PNETs with localized disease, regardless of the size. The type of surgery operation depends on tumor location and tumor size. A standard pancreatic resection, such as pancreatoduodenectomy or distal pancreatectomy, can be performed. However, parenchyma-sparing surgery, such as enucleation of a tumor, is also an option. The latter approach preserves a greater amount of pancreatic tissue and is indicated for tumors smaller than 2 cm and for stages I-II. Standard surgery has a lower rate of pancreatic fistulas compared to a conserving surgery, although there is a poorer endocrine and exocrine function (8). In our patient, parenchyma-sparing surgery could not be performed due to the large size of the tumor and the location in the body-tail. Thus, a distal splenopancreatectomy was performed.

The rate of malignancy ranges between 40 and 95% and therefore, lymphadenectomy is advisable given the risk of functioning ganglion metastases. Tumor size (> 4 cm), degree of differentiation and radiological suspicion of lymph node involvement are considered as independent predictors of lymph node metastasis (9). The aim for locally advanced VIPomas is to achieve an R0 resection, or at least a 90% reduction of the

tumor mass (10).

VIPoma is a very rare variant of pancreatic neuroendocrine tumors. Elevated serum levels of VIP associated with the characteristic clinical condition are essential to obtain a diagnosis. Specific medical tests are important when a VIPoma is suspected in order to obtain a correct diagnosis. The curative treatment of choice is a surgical resection for functioning neuroendocrine tumors with localized disease.

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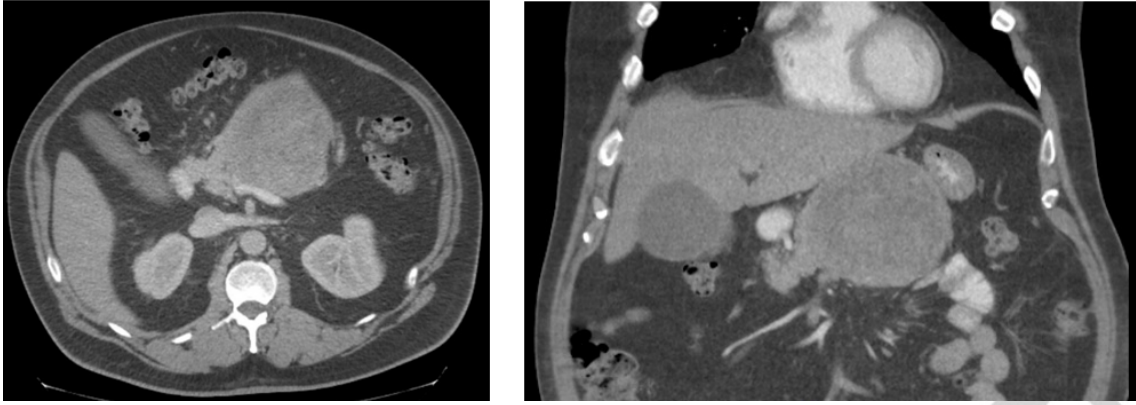


Fig. 1. Axial and coronal CT plane.

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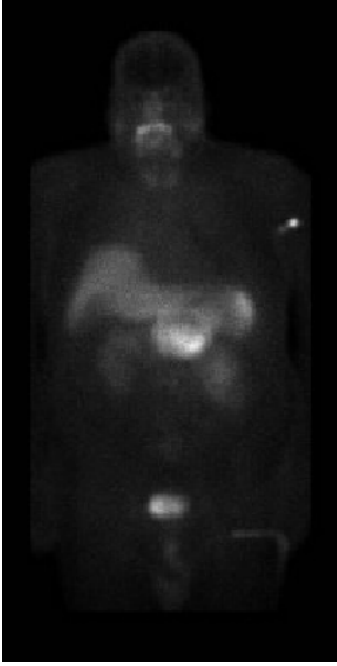


Fig. 2. OctreoScan®.

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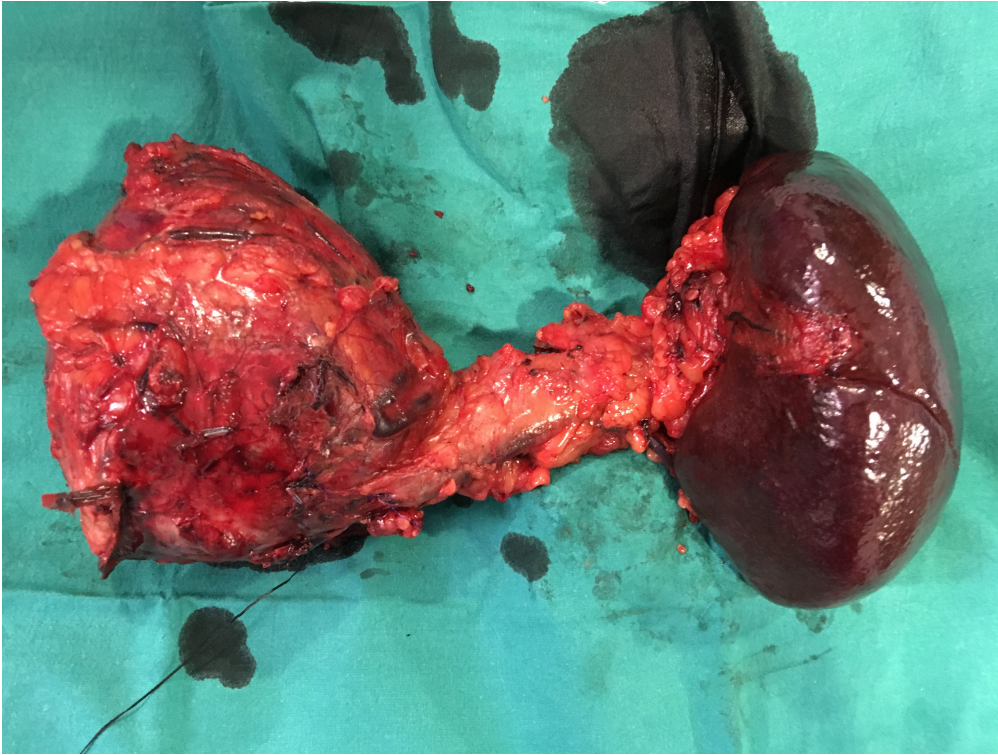


Fig. 3. Surgical specimen.

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