Clinical Case No. 16

55-year-old female

Family medical history: negative

Past medical history:

Cholecystectomy for gallstones
Nissen - Rossetti fundoplication for GERD
Habitual constipation treated with laxatives

Recent medical history

Approximately ten years after the last surgery for GERD, the patient, until then extremely constipated and a habitual user of laxatives, began to complain of increasingly intense diarrhea, with numerous evacuations each day. Her family doctor found no signs of abdominal disease on physical examination. Laxatives were obviously suspended, also due to the suspicion of abuse of the agents by a somewhat psychologically unstable subject. Antidiarrheal agents, intestinal disinfectants and dietary measures were prescribed.

Diarrheal symptoms showed no signs of diminishing; rather, evacuations became increasingly more numerous.

The family doctor became increasingly concerned with his patient's unbearable intestinal disturbance, which inevitably impacted negatively on cenestesis and sleep, not to mention the severe asthenia, adynamia, and weight loss (also owing to dietary restrictions). He thus ordered a series of diagnostic examinations.

Preliminary diagnostic examinations

Stool examinations:

Qualitative characteristics: watery, no blood or other noteworthy signs
Functional examinations: indifferent
Parasitological examination: negative
Coproculture: no contribution for pathogenicity

Blood tests:

Hypochromic anemia
Low grade hyperglycemia
Hypopotassemia
Hypercalcemia
No contribution from other examinations

The poor diagnostic specificity of clinical and laboratory findings, together with the persistence of symptoms despite the therapeutic measures taken and the worsening of the patient's physical conditions as a result of dehydration phenomena and electrolyte alterations, prompted the patient's hospitalization in gastroenterology.

Hospitalization in Gastroenterology

The first measures taken were aimed at correcting the fluid and electrolytic imbalance.

On clinical examination the patient appeared dehydrated and cachexic, with diffuse abdominal pain, serious asthenia, muscle cramps, cardiac arrhythmia, massive watery diarrhea.

Laboratory tests show hypokalemia, hypophosphatemia, hypercalcemia, hypomagnesemia, moderate hyperglycemia - metabolic acidosis.

Possibilities of differential diagnoses were discussed, namely:

Crohn's disease,
ulcerative colitis (CUC),
disease (also neoplastic) of the right colon

but none of these were confirmed by the following examinations:

colonoscopy - negative
CT enema - negative

Ultimately, a diagnosis - albeit preliminary - was reached with the following examinations:

Tomographic ultrasound (Fig. 1)
Endoscopic ultrasound (Fig. 2)
Double contrast CT (Fig.3)

which revealed a nodular formation in the tail of the pancreas.

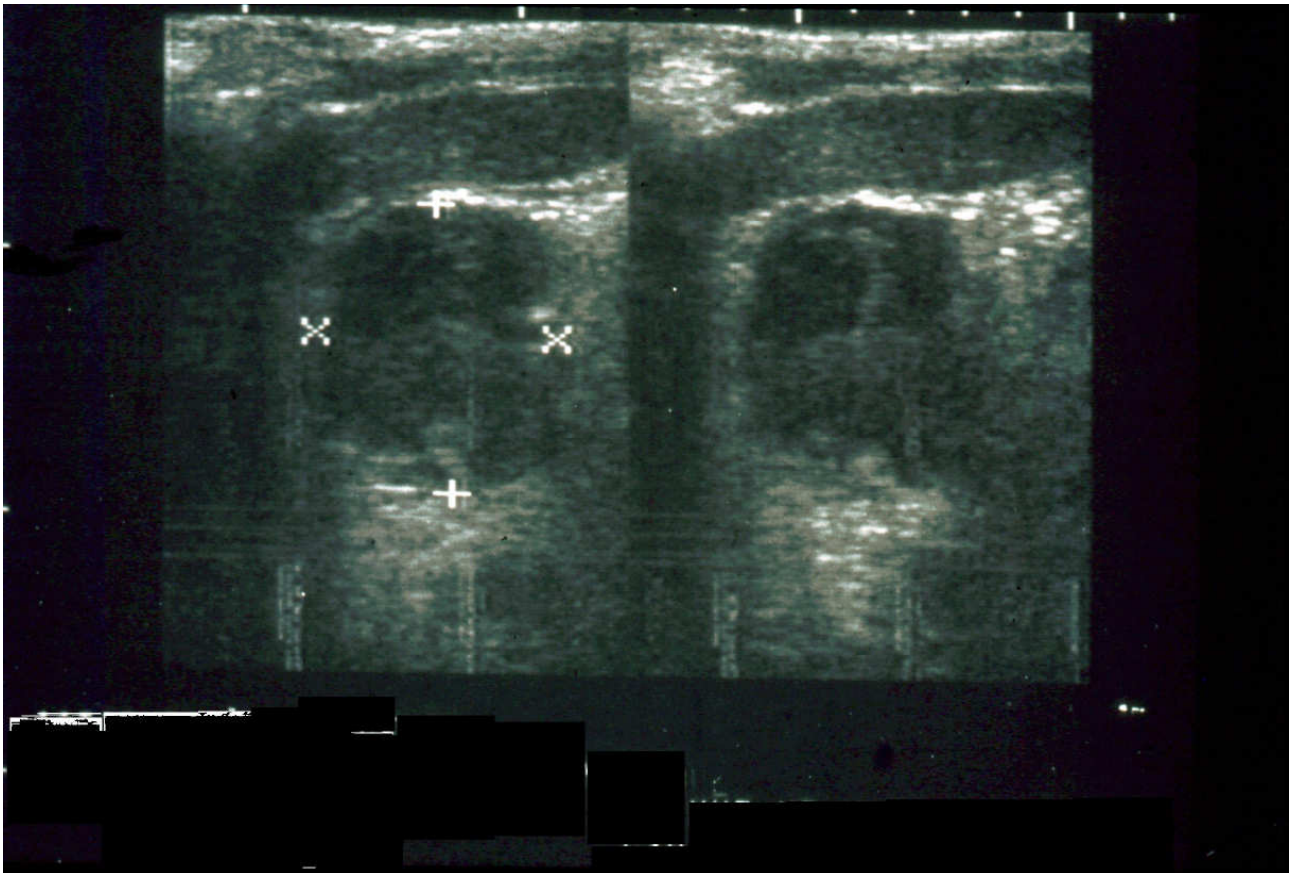

Fig. 1

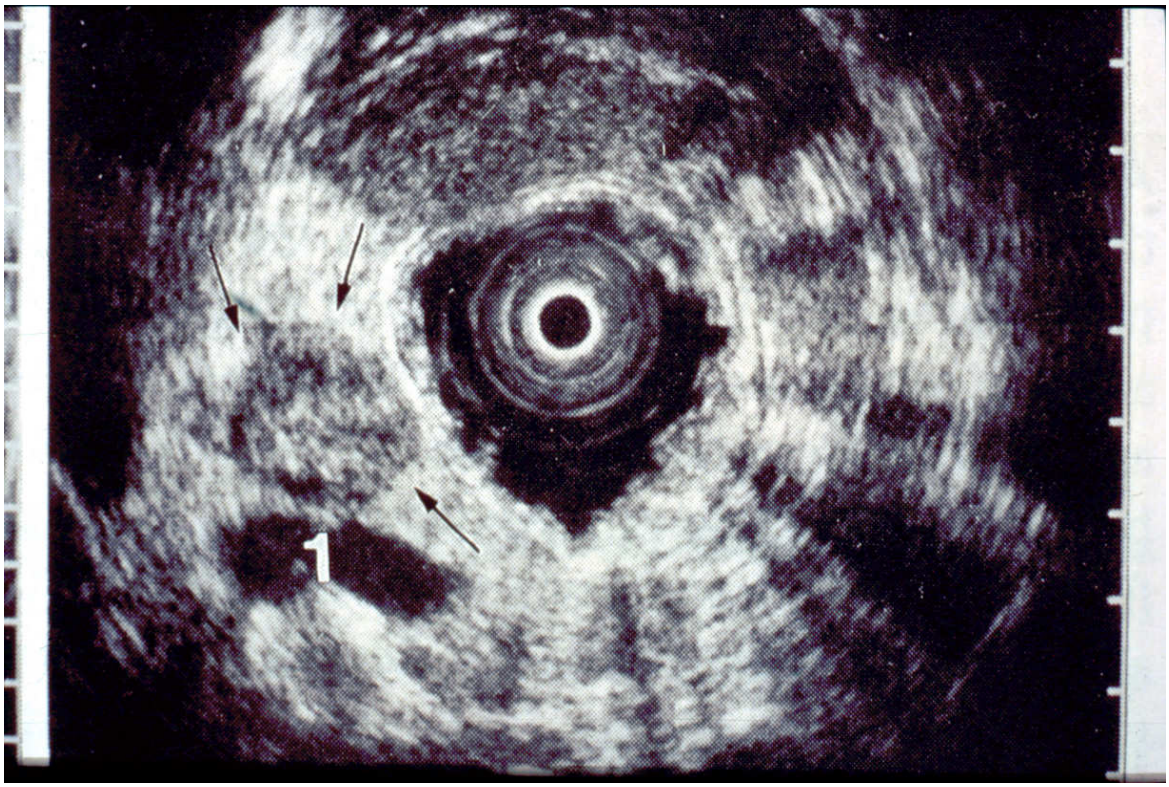

Fig. 2

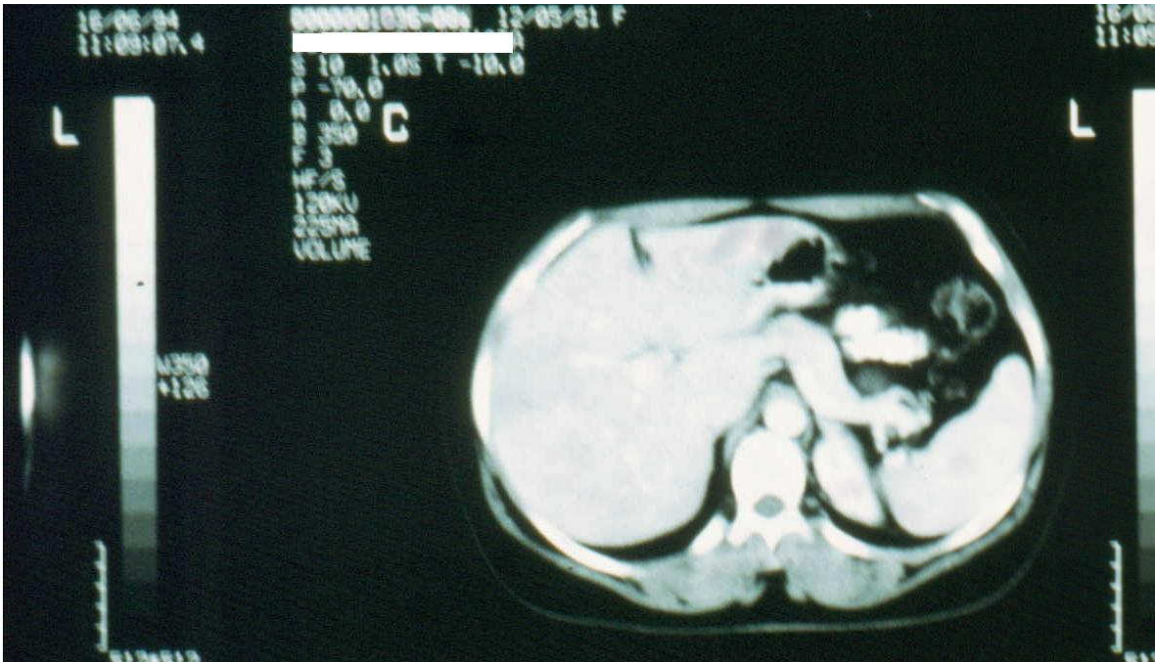

Fig. 3

At this point gastroenterologists were able to formulate a convincing diagnostic alternative, whose confirmation was achieved through the following results:

- elevated serum levels of Vasoactive Intestinal Peptide (VIP) and chromogranin;
- selective detection of the nodule on somatostatin receptor scintigraphy (SRS).

The diagnosis was thus made of **pancreatic cholera**, Verner-Morrison syndrome - secondary to **VIPoma of the tail of the pancreas**

The patient was transferred to our Division for surgical treatment.

Surgical Operation
Laparotomy - The neoformation (Fig. 4), evident in the tail of the pancreas, measured approximately 5 cm., was well-encapsulated, and showed no signs that hinted at malignancy. Caudal resection of the pancreas.

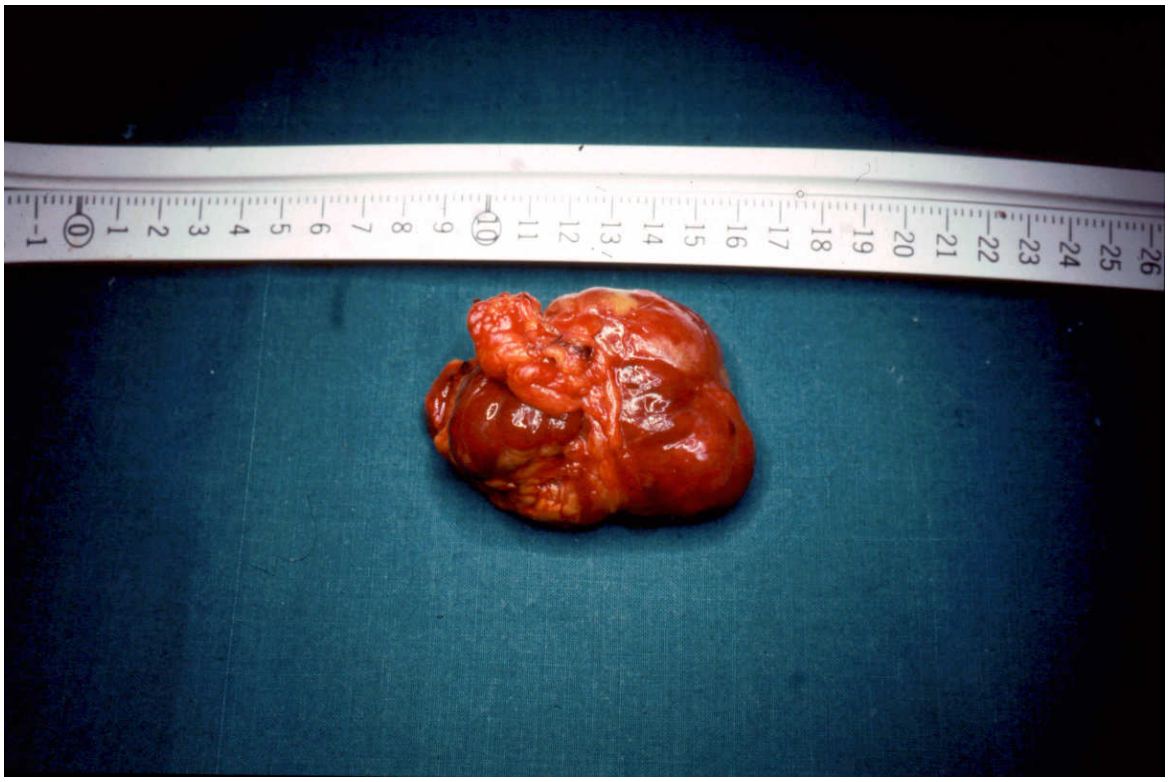

Fig. 4

Pathologic Anatomy - microscopic (Fig. 5)
Histological and immunohistochemical studies confirmed the diagnosis of neuroendocrine tumor (VIPoma) without apparent signs of malignancy.

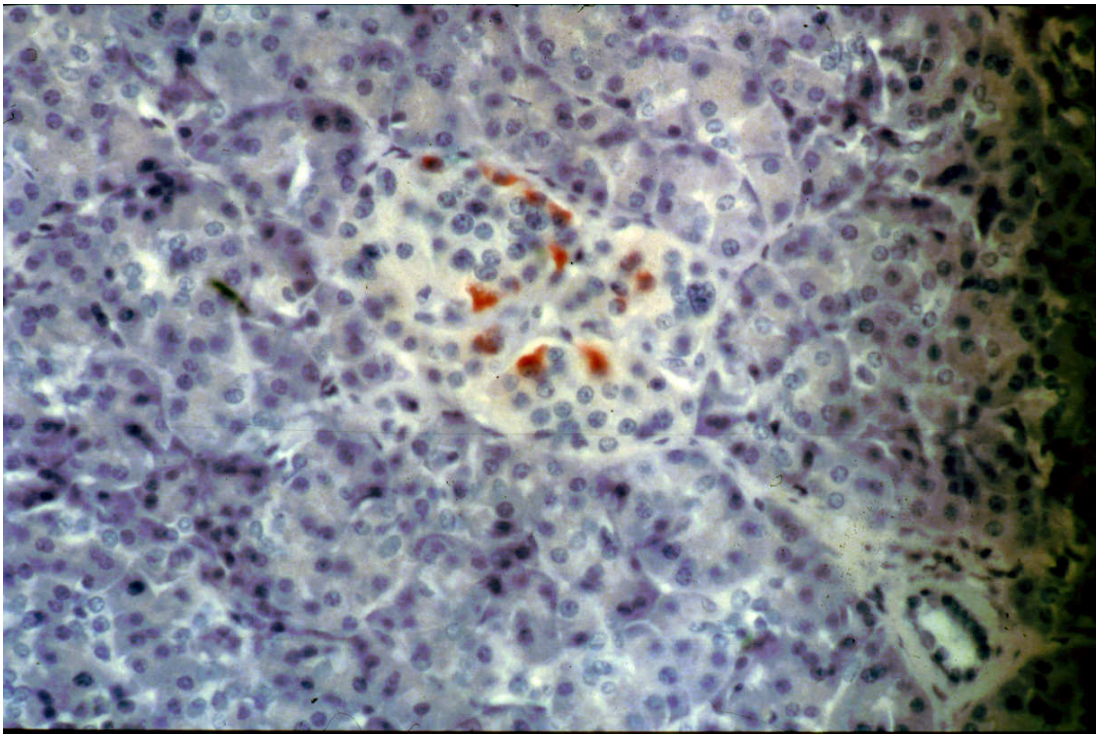

Fig. 5

Postoperative course - regular

Outcome was characterized by the disappearance of diarrheal symptoms and swift restoration of humoral, metabolic and psychological conditions.

Follow-up at long-term revealed no signs of correlated disease or particular sequelae.

Remarks

Given its rarity, encountering this neuroendocrine pancreatic tumor is exceptional. Unsurprisingly, the syndrome that it produces tends to create - as in the present case - diagnostic difficulties. Diarrheal symptoms are in themselves not always easily and immediately interpretable from an etiopathogenic standpoint. Moreover, the absence of any reference to well-known causes of diarrhea (enterocolitis, Crohn's disease, CUC, etc.) make diagnosis all the more difficult if this seldom-seen disease is not taken into account.

In our case the procedures implemented first by the patient's family doctor and second by attending gastroenterologists were exemplary. The first measures addressed the reestablishment of the patient's fluid and electrolyte balance, above all the correction of the potassium loss. Only instrumental and serological means defined the diagnosis. The patient's swift transfer to surgery obviated the treatment of diarrhea with somatostatin or derivatives (octreotides), which are otherwise indicated if the disorder cannot be resolved (advanced malignant forms).

In the case described here the neoplastic cause of the syndrome was in a favorable position (tail of the pancreas), both for diagnosis by means of imaging localization and for surgical treatment. A mini-invasive video-assisted laparoscopic approach could have been attempted with relative ease; however, the previous operations on the upper abdomen and the need (given the patient's poor conditions) for intervention as expeditious as possible prompted an open approach.

The tumor's relatively modest dimensions, its well-delimited macroscopic appearance and encapsulation, and the absence of signs indicative of malignity, were findings that led us to believe (with all due reservations dictated by the case) that the tumor was benign in nature. VIPomas, in fact, have a malignancy rate of over 50%. Our pathologists had ruled out the reliability of perioperative cryostat sections, both for the type of lesion and for its macroscopic features, as well as pre- or intraoperative fine needle aspiration, which as a rule is unreliable for neuroendocrine tumors. Histologic and immunohistologic tests, beyond confirming the diagnosis, excluded with considerable approximation the malignant nature of the lesion. Indeed, it's well-known that with neuroendocrine tumors histology by itself is not always a failsafe means to evince malignity, which is proven only by the size of the neoplastic mass and/or by infiltrating characteristics and long-term manifestations.

Long-term follow up confirmed the benign nature of the lesion.
