

Enucleation of Pancreatic Proinsulinoma: Case Report

Categorie: Endocrine tumours and neoplasia

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Introduction:

Functional islet beta-cell tumours represent 1%-2% of all pancreatic neoplasms. Diagnosing this type of tumour is often challenging because they present unspecific clinical features overlapping more common syndromes. Diagnosis involves expensive testing, so, establishing Whipple's triad and excluding causes of exogenous hyperinsulinemia is crucial before initiating investigation. Surgical resection is the primary treatment modality, so, accurate localization of the tumor is important, as it enables more conservative interventions.

Objective:

To report a rare case of a proinsulinoma highlighting diagnostic, localization and treatment challenges.

Case Report:

A 47-year-old woman was sent to the endocrinology department for evaluation of suspected spontaneous hypoglycaemia. She wasn't taking any medications and reported no other medical problems. Her profession wasn't unrelated to health care. For 2 years she had had adrenergic/neuroglycopenic symptoms that relieved rapidly after ingestion of simple carbohydrate-containing food. She had gained 20 kg/2 years. Symptoms aggravated with time, with weekly frequency and incapacitation for work in last 6 months. Fractionated-diet, excluding simple carbohydrates, failed to improve symptoms. The patient was taught how to use a glucose meter to measure capillary blood glucose (BMT) and instructed to do a diary, that include meals content and BMT during symptoms. The diary revealed hypoglycaemias with values under 50mg/dL associated with neuroglycopenia and without a predictable pattern.

A mixed meal test was programmed at the Day Care Hospital, that wasn't carried out because the patient presented at 9 p.m. with neuroglycopenia, after 13 hours of fast. Laboratorial investigation confirmed endogenous "hyperinsulinism" (Fig.1): venous glucose - 37 mg/dL, unsuppressed peptide C (2.3 ng/mL), Serum β -hydroxybutyrate levels at lower end of normal range (0.07 mmol/L), and after administration of 1 mg of glucagon, glucose levels increased 35 mg/dL. Autoimmunity was negative as were serum sulfonylurea levels. Insulinemia drop to levels within normal range (3.6 uUI/mL), proinsulinemia was nine times the normal range (47.3 pmol/L). So we concluded that endogenous hyperinsulinism was secondary to autonomous proinsulin production ("pro-insulinoma").

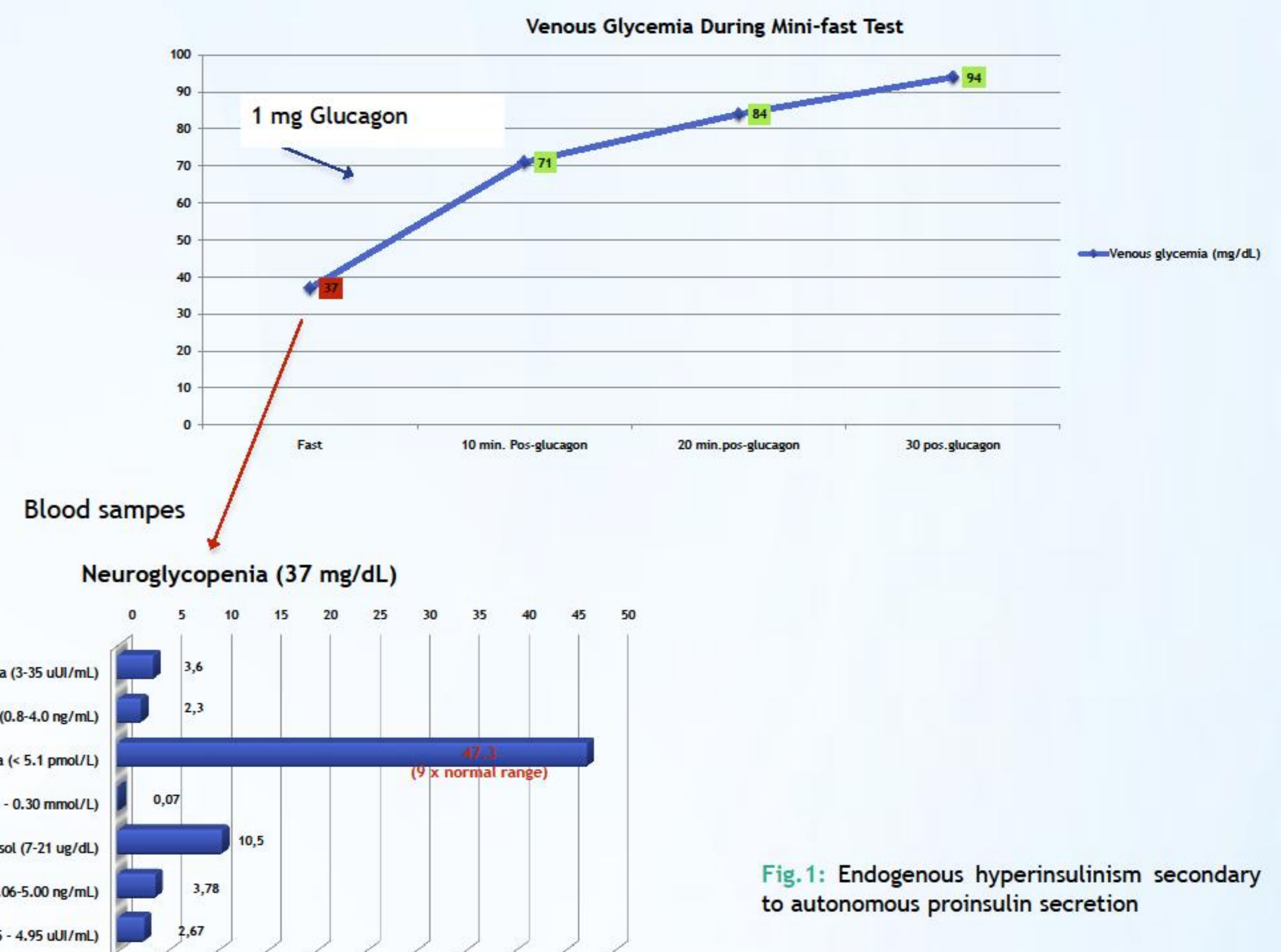


Fig. 1: Endogenous hyperinsulinism secondary to autonomous proinsulin secretion

The following exams were performed on the patient:

- Ultrasound and a CT scan with contrast, which showed a single oval nodule with 17x13 mm in relation to the duodenal part of the head of the pancreas with rapid clearance of the contrast, unidentifiable in portal phase or late acquisitions.

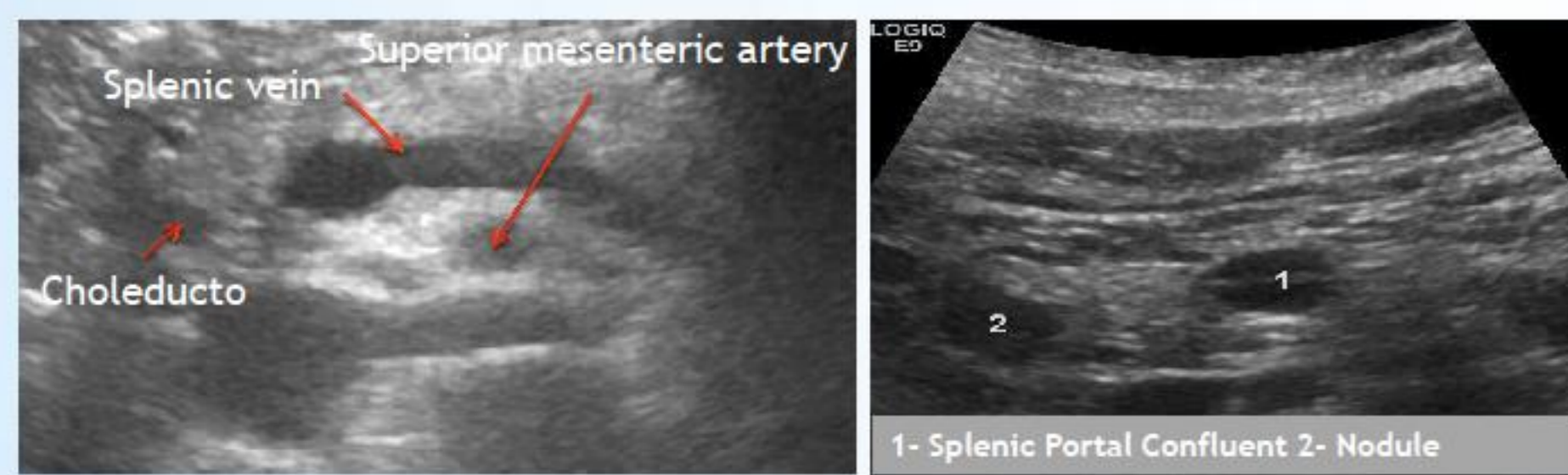


Fig. 2: Transabdominal Ultrasound
A. Pancreas
B. Nodule located at the pancreas head, homogeneously hypoechoic, with distinct margins.

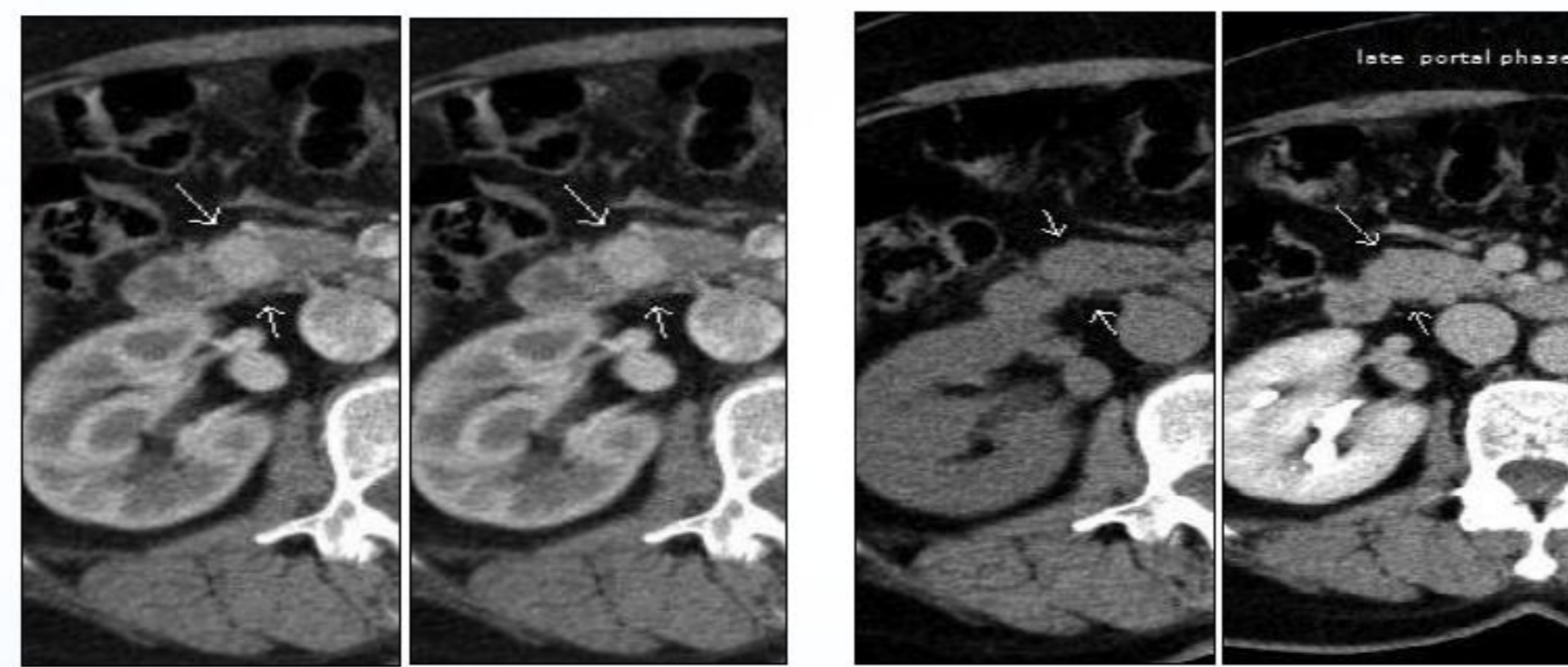


Fig. 3. A/B. Arterial phase
Fig. 3. C/D. Early and late portal phase
Fig. 3. Computed tomography with contrast
Nodule with greater enhancement than normal pancreas parenchyma during arterial and capillary phases (A/B), and rapid washout (C/D).

- Ecoendoscopy (Fig.4) characterized the nodule as hypoechoic, very vascularized and well-defined and excluded other lesions in the pancreas.

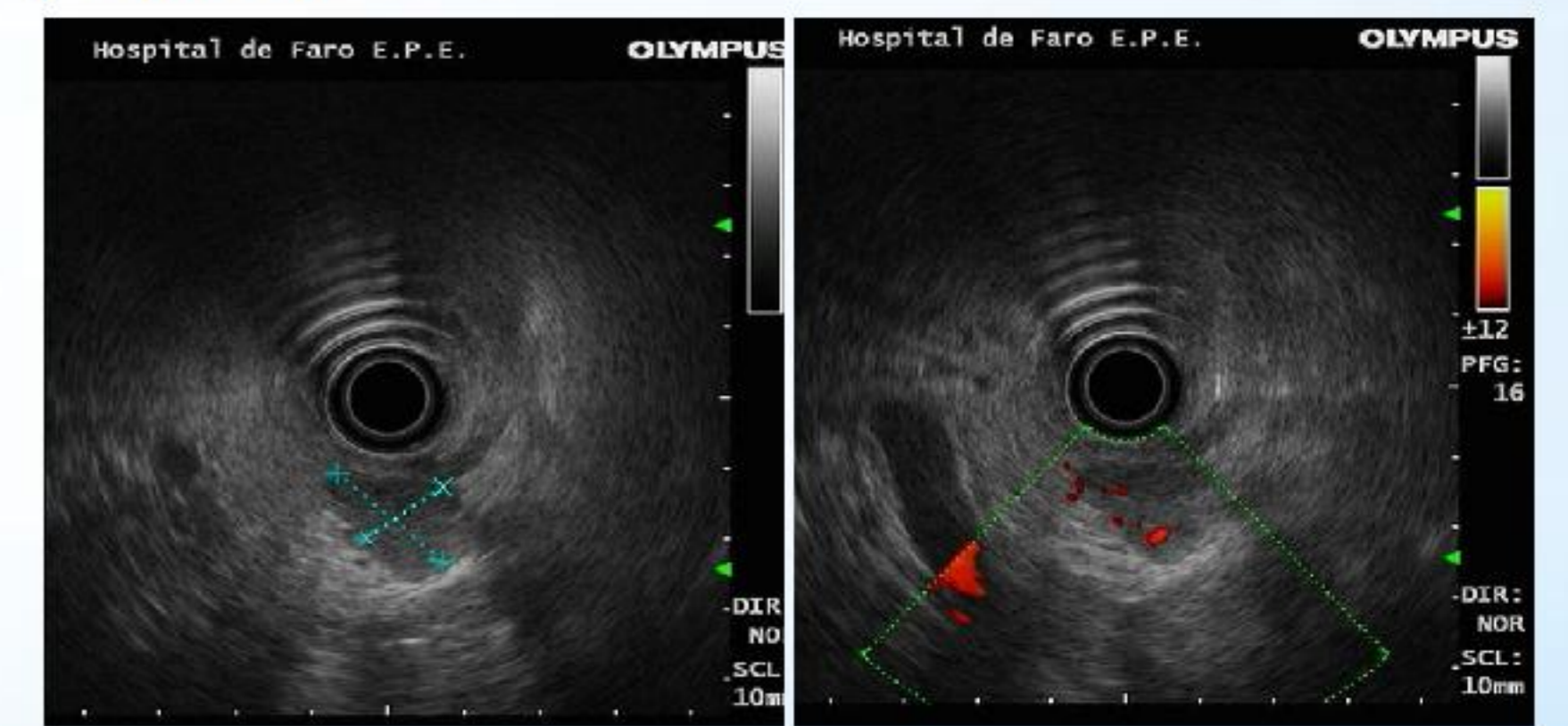


Fig. 4: Ecoendoscopy with Doppler. Nodule hypoechoic, very vascularized and well-defined

Given the nodule to be unique and with very suggestive features of proinsulinoma, it was decided not to perform aspiration cytology.

The patient started treatment with diazoxide while waiting for surgery. She developed maleolar edema during treatment.

In September of 2014, she underwent a tumor enucleation, without complications (Fig 5). In the postoperative period the patient resolve symptoms and hypoglycemia did not recur.

The histopathological study confirmed a low-grade neuroendocrine tumor with high reactivity to α -chromogranin and synaptophysin (Fig 6).

Seven month pos-surgery she didn't present hyperglycemia or diabetes mellitus.

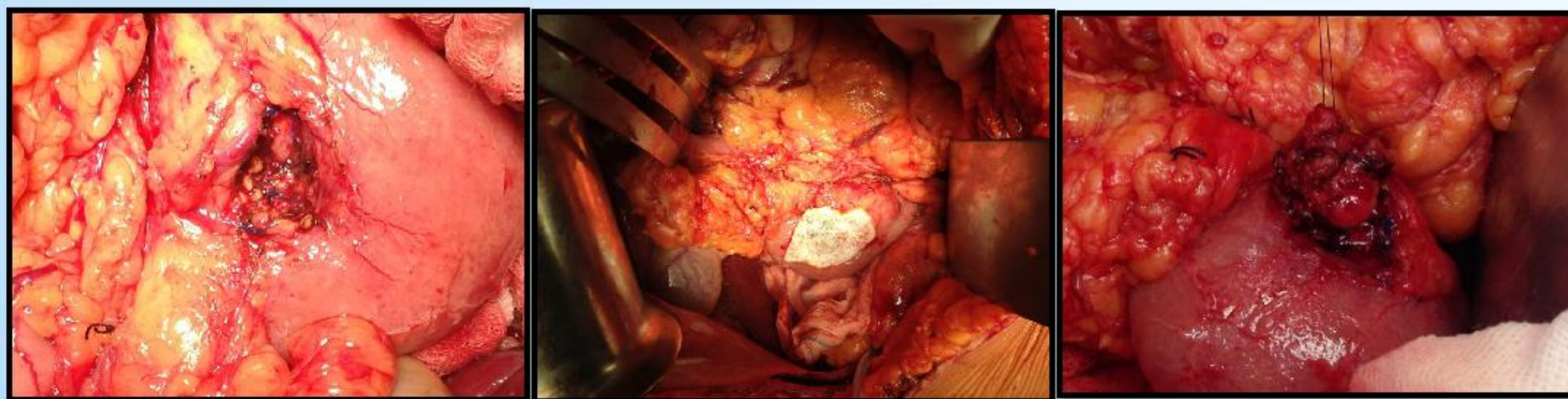
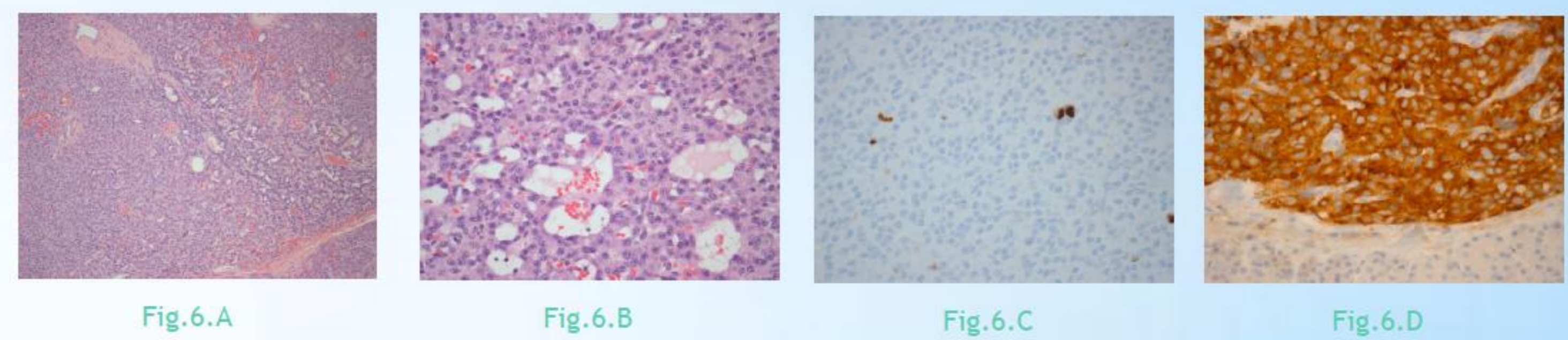


Fig. 5. Surgery. Tumor enucleation



Legend:

- Fig. 6.A. HE 10x: Low -power photomicrograph demonstrating a neuroendocrine tumor. The tumor shows solid, ribbonlike, and acinar growth patterns.
- Fig. 6.B. HE 40x: Higher magnification showing monomorphic cell, large nuclei and small nucleoli as well as inconspicuous cytoplasm and fine chromatin. Mitoses are rare.
- Fig. 6.C. Low antibody staining against Ki-67 (nuclear protein present during all active phases of cell cycle and absent from resting cells)
- Fig. 6.D. Intense staining against synaptophysin (cytoplasmic protein located in neurons and neuroendocrine tumors)

Conclusion:

The work-up of fasting hypoglycaemia is crucial because a wrong diagnosis can lead to unnecessary pancreatectomy or a missed pancreatic tumour. Localization is challenging so imaging studies should only take place once the diagnosis has been established. Highly specific serum insulin assay can difficult the diagnosis. As in these case, an enucleative approach minimizes the risk of developing pos-operative diabetes, leading to a favourable prognosis.