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Management Challenge in a Young Patient With Insulinoma: Case Report

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Case Report

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Abstract

Introduction.

Insulinoma is a rare functional pancreatic neuroendocrine tumour that typically presents as a solitary, benign, and sporadic lesion, although it can be associated with multiple endocrine neoplasia type 1. Clinical manifestations result from intermittent insulin secretion and recurrent hypoglycemic episodes, particularly during fasting or physical exertion. Whipple's triad remains the diagnostic standard, with neuroglycopenic symptoms such as confusion, loss of consciousness, seizures, behavioural disturbances, amnesia, asthenia, and weakness being the most severe. Surgical intervention offers the only potentially curative treatment, with the approach determined by tumour location and size. Enucleation is recommended for small tumours that do not involve the main pancreatic duct, whereas pancreatic resection is commonly performed in other cases. The Whipple procedure is reserved for larger tumours located in the pancreatic head or for cases where malignancy is suspected.

Case presentation.

We present the case of a 32-year-old man with a one-year history of asthenia who underwent Whipple surgery. This case underscores the importance of considering metabolic etiologies in young patients to facilitate timely treatment and effective management of complications.

Conclusions.

Early diagnosis of insulinoma is critical in young patients presenting with neuroglycopenic symptoms, as delayed identification and management can adversely impact prognosis. Biliary stenosis following pancreatoduodenectomy is a common complication. This complication occurs more frequently in individuals with preoperative small-diameter bile ducts and in male patients. Biliary stenosis after pancreatoduodenectomy can be managed effectively with less invasive procedures such as endoscopic retrograde cholangiopancreatography or cholangioplasty.

INTRODUCTION

Insulinoma is a functional pancreatic neuroendocrine tumour (PanNET) with a rare incidence, presenting an annual rate of 1 to 4 cases per million worldwide. Approximately 90% of cases are solitary, benign, and sporadic tumours, while 5% to 10% are associated with multiple endocrine neoplasia type 1 (MEN1) (1–3). Clinical presentation is directly related to autonomous insulin secretion that is not suppressed during hypoglycemia, resulting in recurrent episodes, particularly during fasting or physical exercise (4). As the brain relies primarily on glucose as an energy source, neuroglycopenic manifestations are typically the most severe and include confusion, loss of consciousness, seizures, behavioural disturbances, amnesia, asthenia, and weakness. The Whipple triad remains the gold standard for

diagnosis and includes symptoms of hypoglycemia, low serum glucose during symptoms, and relief following glucose administration (5). Surgical intervention is the preferred treatment for localised insulinomas (6).

This report describes a 32-year-old male who experienced asthenia for one year before the underlying cause was identified and subsequently underwent surgical treatment. The case underscores the importance of considering metabolic etiologies in young patients and emphasises the necessity of timely intervention and appropriate management of complications to achieve disease resolution.

CASE REPORT

A 32-year-old male with no significant medical history presented with asthenia, blurred vision, muscle weakness, and recurrent diaphoresis for one year. Symptom relief was achieved through the consumption of carbohydrate-rich foods, which contributed to delayed medical consultation. Subsequently, the patient experienced a loss of consciousness at work and was admitted to the emergency department. On examination, he regained consciousness and exhibited anxiety and confusion, with no neurological deficits or palpable masses identified. Initial laboratory findings were as follows: haemoglobin 15 mg/dL, leukocytes $7x10^3$, cholesterol 155 mg/dL, glucose 83 mg/dL, triglycerides 321 mg/dL, creatinine 0.70 mg/dL, TGO 113, and TGP 30. During hospitalisation, another episode of loss of consciousness occurred without tonic-clonic movements; glucose was 30 mg/dL and was rapidly corrected with intravenous administration of six ampoules of 33% dextrose. Serum insulin was measured at 80 µU/mL.

Given suspicion for insulinoma, contrast-enhanced computed tomography of the chest, abdomen, and pelvis was performed, revealing a lesion visible on the arterial and portal phases without evidence of adenopathy or secondary disease (Fig. 1). Additional contrast-enhanced abdominal magnetic resonance imaging identified a 19 x 12 mm lesion in the pancreatic head, characterised by regular, partially lobulated borders, a mixed but predominantly intermediate signal, and faint peripheral enhancement in the venous and late phases. No lymphadenopathy or masses were observed in the retroperitoneum (Fig. 1).

A multidisciplinary team evaluated the case and determined that surgical intervention was warranted. Cephalic pancreatoduodenectomy was performed with end-to-side pancreatojejunal and biliojejunal anastomoses, as well as Roux-en-Y reconstruction. Intraoperatively, a 2 x 2 cm tumour was palpated in the pancreatic head, exhibiting irregular borders and a firm, mobile consistency, without involvement of adjacent structures or adenopathy. The Wirsung duct measured 10 mm, and the common bile duct measured 8 mm. The patient tolerated the procedure; however, on postoperative day four, choluria and cutaneous and conjunctival jaundice developed. Laboratory analysis revealed a total bilirubin of 15 mg/dL. Stenosis of the bilioenteric anastomosis was suspected, and cholangioresonance demonstrated a right hepatic duct of 12.4 mm, left hepatic duct of 13.7 mm, common hepatic duct of 12.1 mm, and intrahepatic bile duct dilation secondary to anastomotic stenosis (Fig. 2).

After further evaluation, conservative management with percutaneous cholangioplasty was chosen (Fig. 3). The procedure was successful, resulting in clinical improvement and a reduction in bilirubin levels (total bilirubin 1.4 mg/dL, direct bilirubin 0.26 mg/dL, indirect bilirubin 1.14 mg/dL). The patient was subsequently discharged in stable condition, tolerating a diet without complications.

At outpatient follow-up, pathology results were obtained. Macroscopically, a nodular lesion measuring 2 x 1.7 x 2 cm was identified in the pancreatic head, located 0.5 cm from the surgical margin and without involvement of the Wirsung duct. Microscopic analysis demonstrated a well-differentiated neuroendocrine tumour, with 1 mitosis per 2 mm², Ki-67 index of 2%, unifocal, and no evidence of lymphovascular or perineural invasion or tumour necrosis. All surgical margins exceeded 0.5 cm. All 25 regional lymph nodes were negative for malignancy. Immunohistochemistry showed positivity for synaptophysin and chromogranin, and negativity for CK7, EMA, and CGA (Fig. 4). The postoperative diagnosis was well-differentiated neuroendocrine neoplasia, pT1N0M0, stage I. The patient continues with periodic follow-up, with no evidence of recurrence or secondary disease. There have been no reports of asthenia, diaphoresis, signs of hypoglycemia, or alterations in quality of life.

DISCUSSION

Although insulinomas are rare, they remain the most prevalent type of functioning PanNET, accounting for 25% of endocrine pancreatic tumours and being the primary cause of hyperinsulinemic hypoglycemia (8, 9). Approximately 90% of cases are solitary and sporadic, with peak incidence occurring in the fifth decade of life and a slight female predominance. In contrast, patients with multiple endocrine neoplasia type 1 (MEN1) typically present at a younger age (8). The mean size of insulinomas is 1.5 cm; 24% measure less than 1 cm, 42% measure 1 to 3 cm, 30% measure 2 to 3 cm, and 4% exceed 3 cm. Malignancy is defined by the presence of metastases, primarily in lymph nodes and the liver (10, 11).

This case exemplifies the diagnostic and therapeutic challenges associated with atypical symptom presentation. The 12-month delay in diagnosis aligns with literature indicating that such delays can extend for years due to the non-specific nature of symptoms. In this instance, the delay was attributed to frequent consumption of glucose-rich foods to alleviate asthenia, which postponed medical consultation. Furthermore, the absence of initial endocrine testing suggests that the clinical presentation may deviate from typical expectations.

Unprovoked and sporadic hypoglycemia is pathognomonic for insulinoma, reflecting the tumour's intermittent insulin secretion. Predominant symptoms include autonomic manifestations such as palpitations, irritability, and diaphoresis, as well as neurological symptoms including confusion, behavioural disturbances, and amnesia. The gold standard for biochemical detection of insulinoma is the measurement of plasma insulin, C-peptide, and proinsulin during hypoglycemic episodes (8, 9).

Insulinomas are almost exclusively located in the pancreas, although insulin-secreting ectopic tumours have been reported (12, 13). Imaging modalities such as ultrasound, computed tomography (CT), and magnetic resonance imaging (MRI) demonstrate sensitivities ranging from 70% to 85%; therefore, a

negative result does not exclude the diagnosis (6). These tumours are hypervascular and exhibit increased enhancement during the arterial phase on both CT and MRI. Endoscopic ultrasound, despite being invasive, achieves a detection rate of 70% to 95% and is preferred when conventional imaging is inconclusive. However, its effectiveness is limited for evaluating the distal body or tail of the pancreas (37%-60%) (8, 9, 14).

In certain cases, preoperative tumor localization remains unsuccessful despite advances in diagnostic techniques, necessitating surgery without precise knowledge of tumour location. Manual palpation of the pancreas by an experienced surgeon yields a sensitivity ranging from 42% to 95%, and the tumour may occasionally be found in a location different from that indicated by prior imaging studies (15, 16).

Surgical intervention remains the only potentially curative treatment for insulinoma, making accurate tumour localisation essential. Reported cure rates range from 77% to 100%, with the choice of surgical procedure determined by tumour location and size (17). Enucleation is recommended for small tumours not involving the main pancreatic duct, while left pancreatic resection is commonly performed in approximately 90% of cases. In cases involving large tumours in the pancreatic head or suspected malignancy, the Whipple procedure or pylorus-preserving pancreatoduodenectomy may be indicated. Minimally invasive approaches are suitable options, although they limit tactile feedback, which is a disadvantage in patients with uncertain tumour localisation (6, 18–20).

The laparoscopic approach is most frequently employed and is indicated for superficial tumours that do not involve the pancreatic vessels or bile duct, with a reported conversion rate of 17% (19). Complication rates are similar to those observed in other pancreatic surgeries, ranging from 45% to 52%. In the present case, the primary complication was stenosis of the hepatic-jejunal anastomosis, likely related to the small duct diameter, which complicates the procedure and increases the risk of stenosis. Most Whipple or pancreatoduodenectomy (PD) procedures are performed for ductal carcinomas of the pancreas, distal bile duct cancer, and ampulla of Vater cancer, conditions typically associated with bile duct dilation that facilitates more efficient anastomosis.

PD is a highly invasive procedure that previously carried a mortality rate of up to 5% before 2000; this rate has since decreased to 1%. Despite this improvement, complications such as pancreatic fistula, surgical site infection, and delayed gastric emptying remain prevalent. The incidence of hepatic-jejunal stenosis following PD ranges from 2.6% to 10.1% and is influenced by factors including the anastomosis method and technique, suture material, and surgical approach (21–25). This stenosis is typically managed with percutaneous cholangioplasty or endoscopic retrograde cholangiopancreatography (ERCP), which reduces the need for reoperation and minimises patient morbidity (26, 27).

Early-age presentation necessitates evaluation for MEN-1, which requires lifelong surveillance for associated tumours in the parathyroid and pituitary glands, as well as screening of first-degree relatives. The oncological prognosis for surgically treated, well-differentiated PanNETs is excellent, with cure rates exceeding 95%. The primary long-term concern is the risk of neurological sequelae; however, substantial improvement and complete recovery following surgery have been documented (6, 28, 29).

One limitation of this study is that the preoperative bile duct diameter could only be assessed intraoperatively, as prior imaging did not allow measurement. Another limitation concerns the hepatic-jejunostomy technique, which was performed using an 8-mm diameter; despite the use of appropriate suture material, stenosis developed. Further research is needed to determine whether bile duct stenosis is associated with the anastomosis method, particularly in patients with small bile duct diameters.

CONCLUSION

Early diagnosis of insulinoma is critical in young patients presenting with neuroglycopenic symptoms, as delayed identification and management can adversely impact prognosis. Considering hypoglycemia in the differential diagnosis enables timely intervention and enhances clinical outcomes. Biliary stenosis following pancreatoduodenectomy is a common complication that imposes a substantial burden on patients. This complication occurs more frequently in individuals with preoperative small-diameter bile ducts and in male patients. Currently, biliary stenosis after pancreatoduodenectomy can be managed effectively with less invasive procedures such as endoscopic retrograde cholangiopancreatography (ERCP) or cholangioplasty.

Declarations

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Ethics Approval: The Ethics Committee of the Virgen de la Puerta EsSalud High Complexity Hospital approved this study.

Consent to Participate: Written informed consent was obtained from the patient.

Written Consent for publication: The patient provided written informed consent approving the publication of this case report and any accompanying images.

Availability of data and material: Not applicable.

Code availability: Not applicable.

Authors' Contributions: All authors have contributed, read, and approved the final manuscript for submission.

José Richard Tenazoa Villalobos: Patient Care and Manuscript Writing. Final Approval

Edgar Fermín Yan-Quiroz: Patient care and manuscript writing. Final review.

Olga Mercedes Viviana Burgos García and Gladys Llerena Cobián: Manuscript review and proportion of pathology images.

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Figures

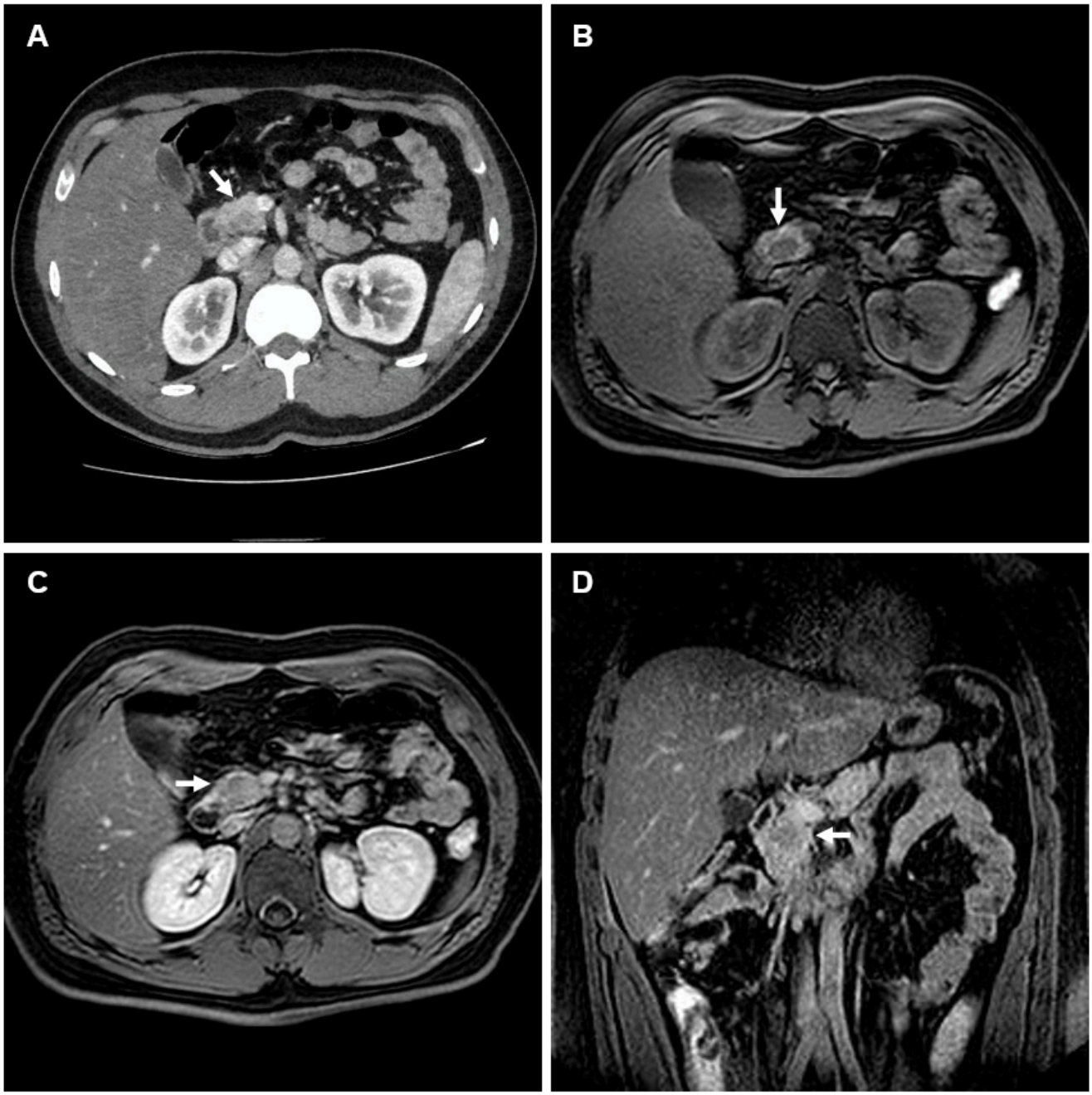


Figure 1

(A) Contrast-enhanced abdominal tomography, cross-sectional view, showing a hypodense lesion measuring 16 mm in the uncinate process of the pancreas (arrow). **(B, C) Contrast-enhanced abdominal MRI, cross-sectional views. (D) Coronal view.** The arrow indicates a 19 mm lesion in the head of the pancreas with regular and lobulated margins.

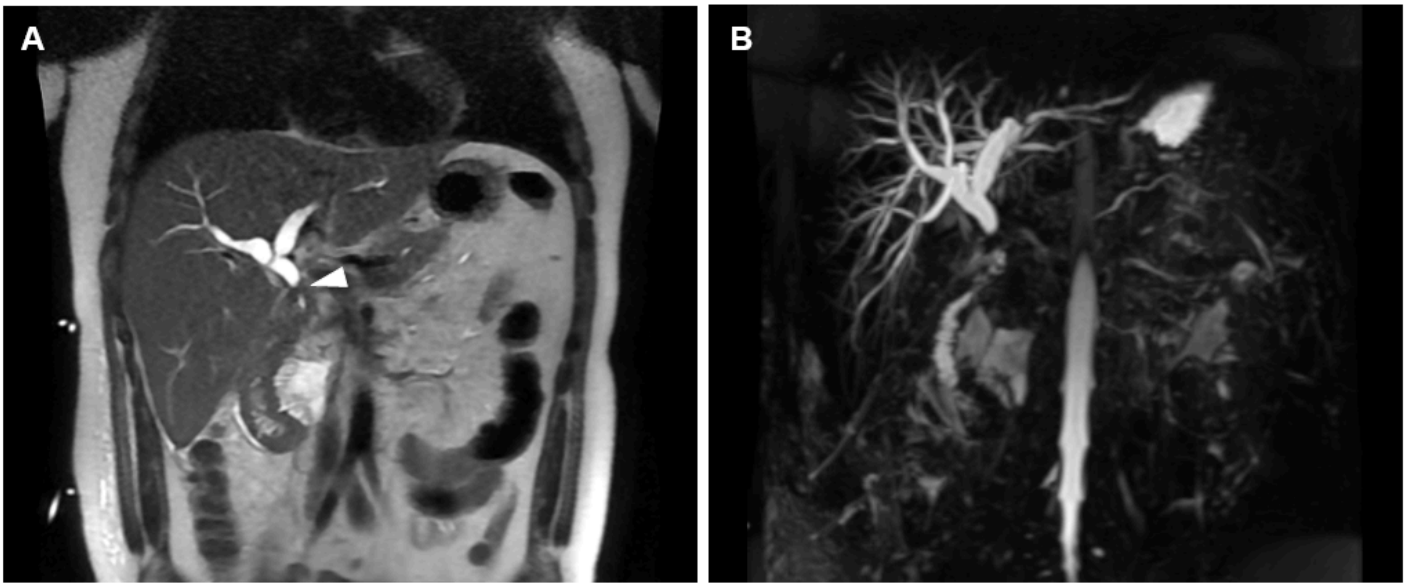


Figure 2

Postoperative contrasted cholangioresonance. A. A stenosis is observed at the level of the bilioenteric anastomosis (arrowhead), resulting in **B.** dilation of the intrahepatic bile duct.

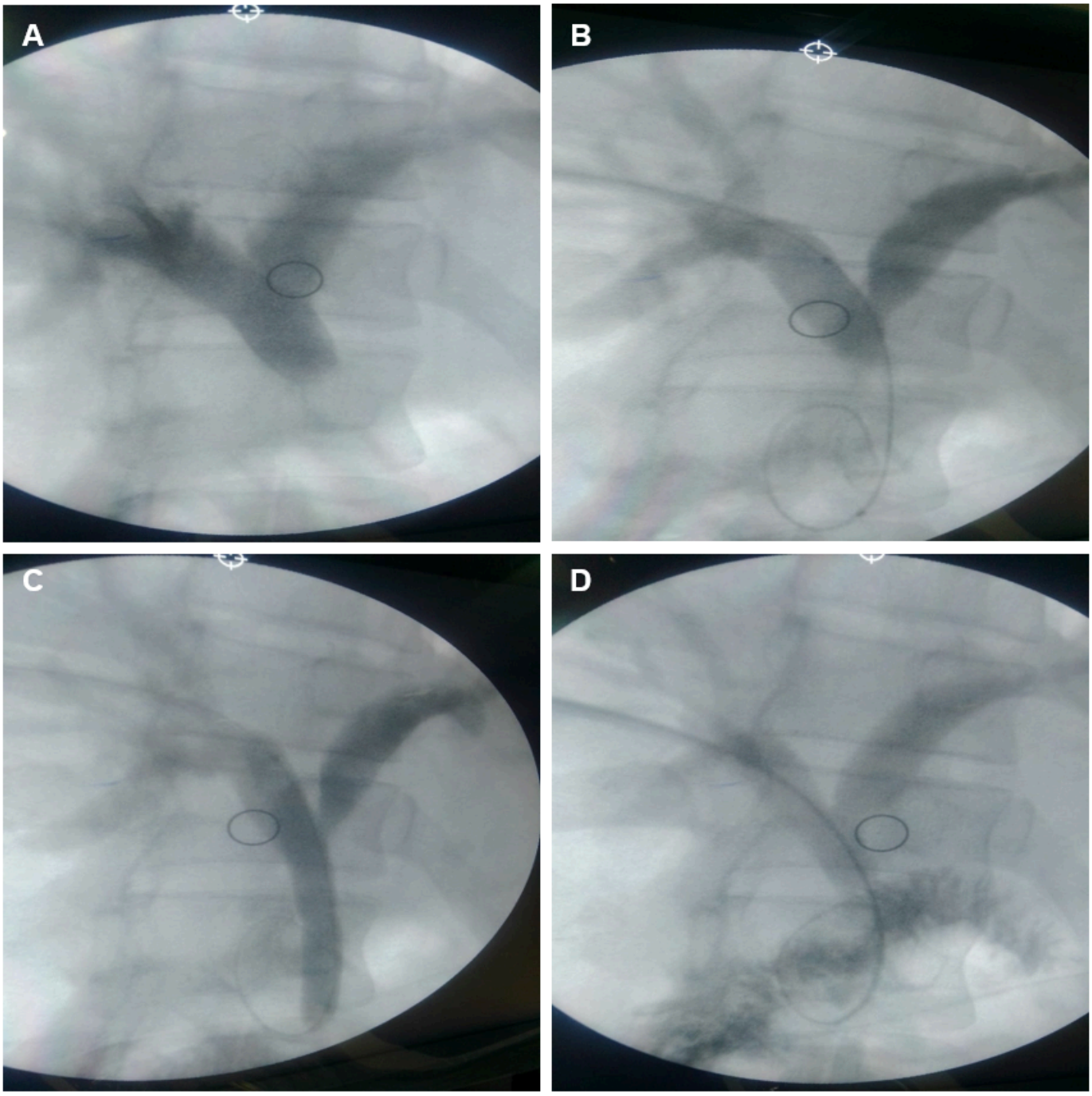


Figure 3

Percutaneous cholangioplasty. A. Dilation of the bile ducts. **B.** Stent placement traversing the biliojejunal stenosis and positioned within the intestine. **C.** Contrast instillation outlining the bile ducts. **D.** Successful transfer of contrast into the intestine.

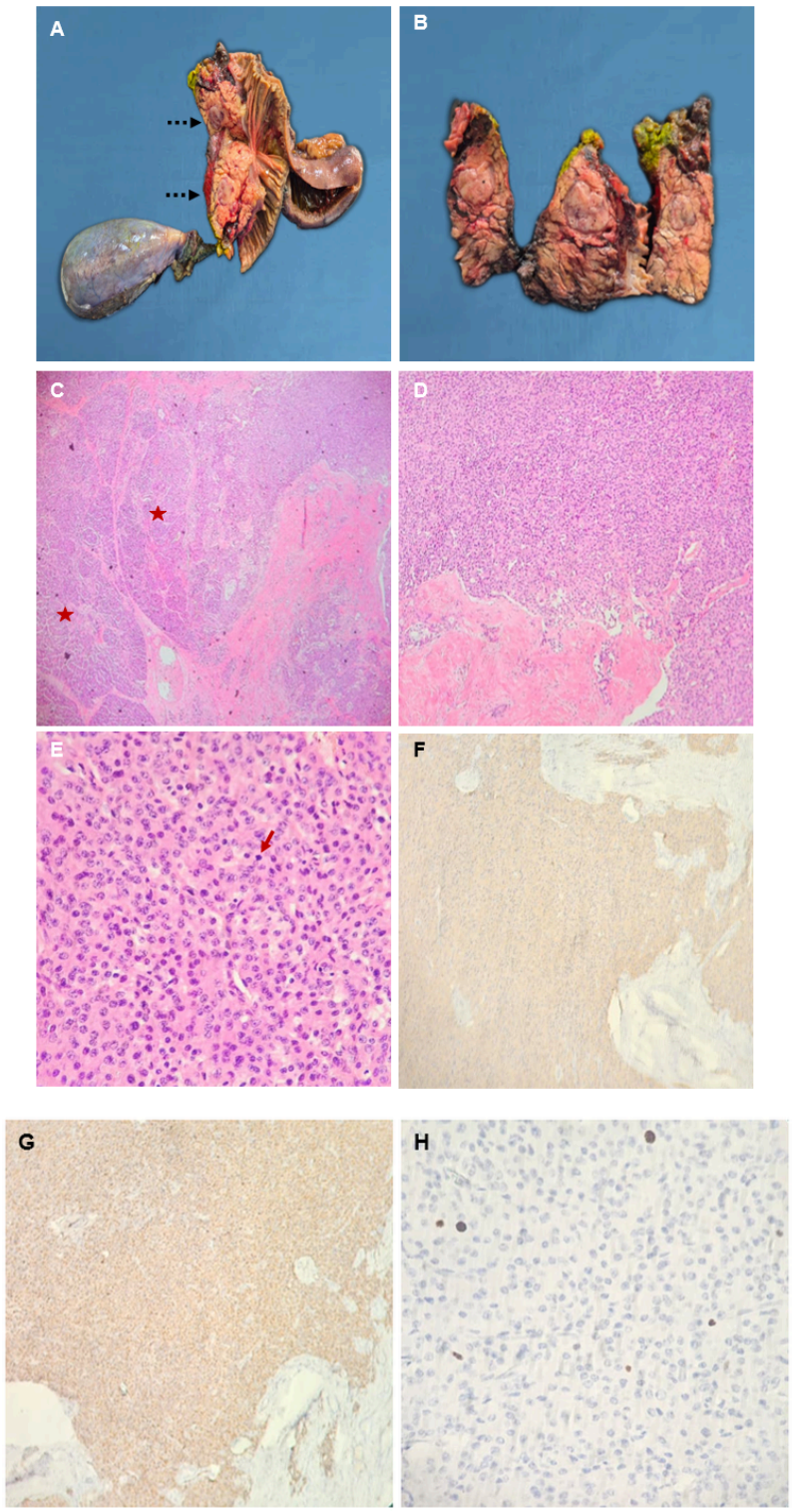


Figure 4

Macroscopy: A, B. Pearly, 2 cm tumour located in the head of the pancreas (dotted arrow), without involvement of the duct of Wirsung. **Microscopy: C. 4x, D. 10x.** Well-differentiated neuroendocrine neoplasm exhibiting solid architecture with glandular foci (star), composed of medium-sized, round, monomorphic cells displaying minimal atypia. **E.**Mitotic index: 1 mitosis per 2 mm². The arrow indicates a mitosis in prophase. Nuclei demonstrate coarse chromatin with a salt-and-pepper appearance.

Immunohistochemistry: **F.** Synaptophysin positive. **G.** Chromogranin positive. **H.** Ki-67 proliferation rate: 2%.