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Pancreatic Insulinoma: Diagnosis and Surgical Management

Habibi Soufiane[1*], Ezzaki Houda[1], Souiki Tarik[1], Ibn Majdoub Karim[1], Toughrai Imane[1], Habibi Sanae[2], Ouahabi Hanane[2], Mazaz Khalid[1]

[1]Department of General and Visceral Surgery, Hassan II University Hospital of Fez, 30050, Fez, Morocco
[2]Department of Endocrinology, Diabetology and Metabolic Diseases, Hassan II University Hospital of Fez, Morocco

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***Corresponding author:** Habibi Soufiane
Department of General and Visceral Surgery, Hassan II University Hospital of Fez, 30050, Fez, Morocco

Abstract **Case Report**

Insulinoma is the most common endocrine tumor of the pancreas. Over 90% of the insulinomas are benign and single, and can be cured by simple excision. Depending on the location, insulinomas can be enucleated, might require partial or distal pancreatectomy or pancreaticoduodenectomy. We report a case of an insulinoma successfully treated by surgical intervention. The management of insulinoma involves the diagnosis, localization of the tumor and treatment.

Keywords: Pancreatic Insulinoma, Enucleation, Pancreas.

INTRODUCTION

The pancreas makes insulin, which helps keep your blood sugar level balanced. Tumors on your pancreas, called insulinomas, make extra insulin more than your body can use. This causes blood sugar levels to drop too low. These tumors are rare and usually do not spread to other parts of your body. We report a case of an insulinoma successfully treated by surgical intervention.

PRESENTATION OF CASE

We present the case of a 37-year-old male, presented to our hospital with a history of loss of consciousness for an unknown duration. At presentation, his random blood glucose (RBG) was 1.6mmol/litre (normal range 3.7-6.1mmol/litre). The hypoglycemia was corrected with an intravenous bolus of 50% dextrose, followed by an infusion of 5% dextrose. The patient regained consciousness after the treatment but became unresponsive approximately 8 hours later.

He had a 1-year history of recurrent episodes of loss of consciousness, confusion, seizures, and bizarre behaviour. Symptom onset was during periods of fasting, often in the mornings, and resolved after food intake. Additionally, there was polyphagia with significant weight gain.

CLINICAL FINDINGS

The patient's vital signs were within normal limits and she had a BMI of 27.7 kg/m2 (height 170cm, weight 80kg). Systemic examination was normal.

CT-scan

The CT demonstrated a 2.2 cm by 3.3 cm well-circumscribed hypodense tumour in the body region of the pancreas, and a 2cm by 1.8 cm well-circumscribed hypodense tumeur in the uncinate process, with no lesions suggestive of lymph node involvement or metastases noted in other organs.

Biology

Peptide C: 3.06 pmol/ml (0.37-1.47) Insuline: 235.4 pmol/l (17.8-173) Turner indice: 678 > 150.

Pathology

Pathology report: macroscopically, the tumours were nodular, well-circumscribed, encapsulated and measured 2.2cm and 2 in diameter. The cut surfaces were hemorrhagic. Microscopically, a monotonous population of medium-sized round to oval cells were observed. The tumour cells were arranged in solid nests and acini. The nuclei were centralized, had inconspicuous nucleoli and with salt and pepper chromatin. The cytoplasm was eosinophilic and moderately abundant. No atypia and mitoses were noted. The tumours were highly vascularized. Lymphovascular invasion was not evident. Immunohistochemically, the cells were positive for neuroendocrine markers. Well-differentiated

neuroendocrine tumours were diagnosed histologically (WHO grade 1).

Surgery

Caudal pancreatectomy and Enucleation of the second pancreatic tumour were done with 24-hour postoperative monitoring in the intensive care unit (ICU). The patient was discharged home following an unremarkable postoperative period and a multidisciplinary team review with complete resolution of his pre-surgery symptoms.

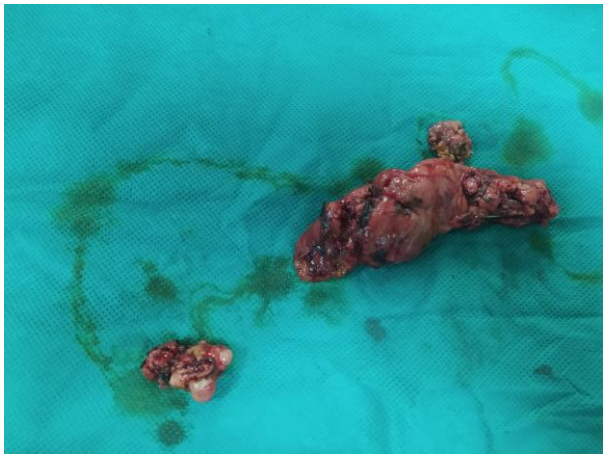

Figure 1: caudal pancreatectomy and the enucleation pieces

DISCUSSION

An insulinoma is a rare functional pancreatic neuroendocrine tumour that is usually sporadic and solitary [1]. They are insulin-secreting tumors of pancreatic origin that cause neuroglycopenia symptoms and uncontrolled symptoadrenal activity, and hypoglycemia [2]. Insulinomas occur in 1-4 people per million in the general population and represent 1%-2% of all pancreatic neoplasms [3]. Insulinomas can occur at any age and have an equal gender distribution [3, 4].

Diagnosis

Insulinomas are the most common cause of hypoglycemia related to endogenous hyperinsulinism. The episodic nature of the hypoglycemic attack is due to the intermittent secretion of insulin by the tumor [8]. Common autonomic symptoms of an insulinoma include diaphroresis, tremor, and palpitations, neuroglycopenic symptoms like confusion, behavioral changes, personality changes, visual disturbances, seizures and coma [5].

The classical diagnosis of insulinoma depends on satisfying the criteria of Whipple's triad, which remains the cornerstone of the screening process: hypoglycemia (plasma glucose < 50 mg/dL); [5, 6] neuroglycopenic symptoms [5]; and prompt relief of symptoms following the administration of glucose [6].

The gold standard for biochemical diagnosis remains measurement of plasma glucose, insulin, C-peptide, and proinsulin during a 72-h fast. This prolonged fasting test can detect up to 99% of insulinomas [5-7]. Delays in the diagnosis of insulinoma are common because the symptoms usually precede detection of a tumor and there may be misattribution of the symptoms to psychiatric, cardiac, or neurological disorders [8]. Once a diagnosis of insulinoma is considered, it is important that patients are managed in a timely and safe manner.

Classical diagnosis
Hypoglycemia (plasma glucose < 50 mg/dL)
Neuroglycopenic symptoms
Prompt relief of symptoms following the administration of glucose
Present consensus
At the time of hypoglycemia during a 72-h fasting test:
5 mIU/L (36 pmol/L) insulin threshold
0.6 ng/mL (0.2 nmol/L) C-peptide threshold
Insulin/C-peptide ratio < 1.0
20 pmol/L proinsulin cut-off level
Absence of sulfonylurea (metabolites) in the plasma or urine

Figure 2: Diagnosis of insulinoma [27]

Surgical Techniques

Surgical resection is the gold standard treatment modality for insulinomas, and it's primordial for the surgeon to detect the localization of the tumor before surgery. Furthermore, intraoperative manual palpation of the pancreas by an experienced surgeon and intraoperative ultrasonography are both sensitive methods to localize insulinomas [8].

The type of surgical resection is based on the tumor location and the distance to the main pancreatic duct [9].

- Distal pancreatectomy is defined as a pancreatectomy with pancreatic resection at the level of the isthmus [10].
- Caudal pancreatectomy, on the other hand, which is considered parenchyma sparing pancreatectomy, was defined as a pancreatectomy with pancreatic resection on the left side of the isthmus [10,11].
- Enucleation and parenchyma-sparing pancreatectomy (central pancreatectomy, resection of the uncinate process, and caudalpancreatectomy) is preferred whenever possible [11,12].

During surgery, pancreatic exploration after mobilization of the transverse colon root is first performed through visual inspection and surgical ultrasonography to confirm the tumor location [8,12].

SURGICAL MANAGEMENT

PREOPERATIVE

Control of hypoglycemia preoperatively is mandatory. The patient must apply some lifestyle changes such as eating frequent mixed-carbohydrate meals, and reducing exercise that will increase overall metabolic requirements [13]. The patient should be admitted the day before surgery and placed on an intravenous dextrose infusion so as to not develop hypoglycemia while fasting [14].

INTRAOPERATIVE

If the tumour is preoperatively localized, enucleation or pancreatic resection may be performed in a minimally invasive way. In a nonlocalized tumour with sporadic insulinoma, surgical exploration is indicated [15]. Close communication with the anesthesia team is paramount. Blood sugars should be monitored closely throughout the case, in 15-min intervals to detect intraoperative hypoglycemia [16]. The IV dextrose infusion can be stopped once the tumor is removed, and blood sugars continue to be carefully monitored [17].

As most of these tumors are intrapancreatic, intraoperative ultrasound (IOUS) is mandatory. Full mobilization of the pancreas is required to perform IOUS adequately [18]. IOUS alone has been shown to identify up to 90% of insulinomas even without palpation [19]. It also allows identification of the relationship of the tumor to vital structures, including the pancreatic duct, splenic vessels, common bile duct, and superior mesenteric vessels [20]. Manual palpation alone also has an approximately 90% sensitivity in localization, with tumors in the tail and body easier to palpate than those located in the head of the pancreas or uncinate process. When manual palpation and IOUS are using in conjunction, this combination can virtually identify 100% of insulinomas [21].

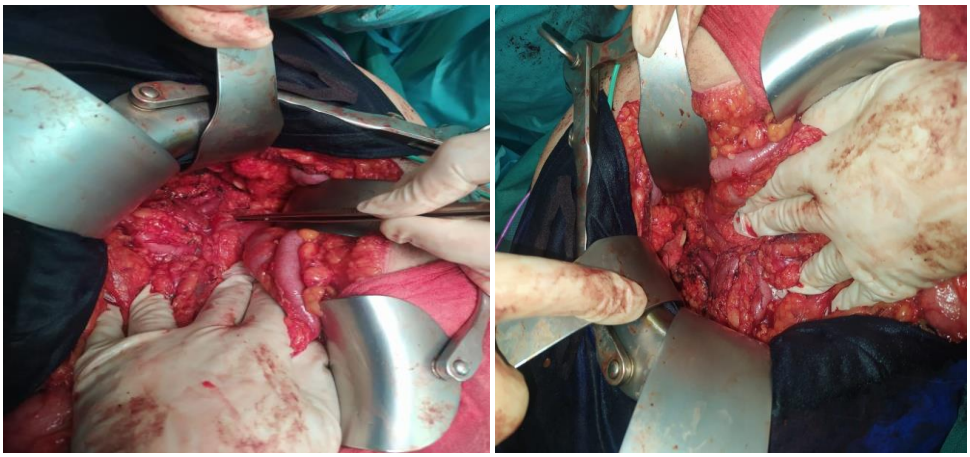

Figure 3: per operative view showing the pancreatic insulinomas.

POSTOPERATIVE

In postoperative, we still should check frequently for any hypoglycemia. Often, patients will experience a short period of rebound hyperglycemia, which can be managed without additional administration of insulin [22]. Postoperative complications from the actual pancreatic surgery include formation of pseudocyst, pancreatitis, intraabdominal abscess, development of diabetes, and pancreatic fistula [23, 24, 25].

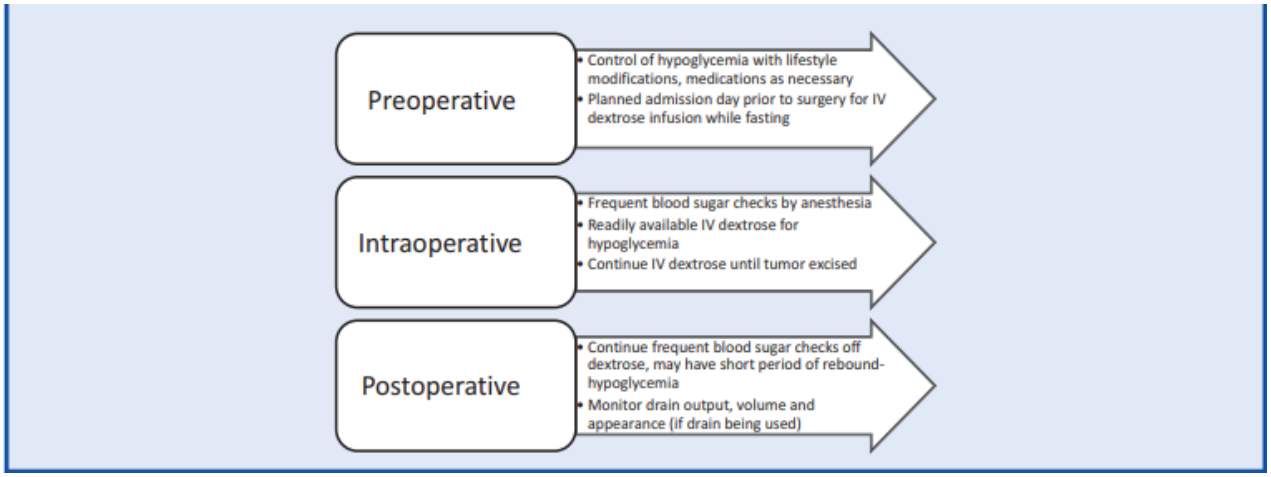

Figure 4: Management for patients with insulinoma preparing for resection [26]

CONCLUSION

Once the hormonal diagnosis of organic hypoglycemia has been confirmed by a 72 h fasting test, the main challenge for the surgeon is to accurately determine the tumor location. The second challenge is to define the best surgical strategy with regard to the type of resection (formal pancreatectomy vs. parenchyma-sparing pancreatectomy) and the surgical approach (laparotomy vs. laparoscopy). The final objective is to decrease the perioperative morbidity and minimize the late functional consequences of surgery.

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