Acta Scientific Clinical Case Reports

Volume 1 Issue 8 September 2020

Case Report

Pancreatic Insulinoma - The Once in a Blue Moon Oncological Episode

Ismail Abdillahi Iltireh[1], Robleh Hassan Farah[2], Carlo Astini[3], Median Said[4], Christiane Osman Glele[5] and Divya Dhananjay Singh[1]*

[1]*Associate Surgeon, Department of General Surgery, Hospital Military Djibouti, Soudan*

[2]*Associate Surgeon of the Hospital Cheikho the Balballa, Djibouti, Soudan*

[3]*Visiting Surgeon, Department of General Surgery, Hospital Military Djibouti, Soudan*

[4]*Senior Consultant Anaesthesia, Department of Anaesthesia, Hospital Military Djibouti, Soudan*

[5]*Resident Anaesthetist, Department of Anaesthesia, Hospital Military Djibouti, Soudan*

***Corresponding Author:** Divya Dhananjay Singh, Associate Surgeon, Department of General Surgery, Hospital Military Djibouti.

Received: July 08, 2020

Published: August 12, 2020

Abstract

Insulinoma is primarily a pancreatic neuroendocrine tumour, known to be rare and benign, in 90% of cases, while 10% cases are developed in Multiple Endocrine Neoplasia patients.

The age of onset is 50 years, except for the malignant forms related to the MEN syndrome cases, where it appears between 20 and 40 years of age. The clinical findings and blood chemistry parameters coupled with the imaging techniques (Echo-endoscopy, CT, MRI) make it possible to locate the tumour in 80% of cases.

The treatment of choice is essentially surgical, such as enucleation or removal of part of the pancreas.

Keywords: Pancreas; Hypoglycemia; Endocrine Tumour; Neuroendocrine Tumour

Introduction

Insulinomas are a type of endocrine tumor of the pancreas that originates from the islets cells, with an incidence of 1 to 4 cases per million population [6]. Approximately 80% of insulinomas are isolated and benign and therefore can be resected in a radical manner if they are identified [4]. They are malignant in 4 to 14% of cases [7-10].

The median age of onset is 50 years, except in Multiple endocrine neoplasia (MEN) type 1 where it appears between 20 and 30 years of age.

The diagnosis is clinico-biological. A topographical assessment based on imaging to ascertain the exact location is necessary to guide the therapeutic procedure [2,3].

We report a case of insulinoma located in the tail of the pancreas.

Case Report

A 51-year-old patient, with no significant past history till date, presented to the Out-patient of the General Surgery Department with chief complaints of having hypoglycemic signs such as syncope and asthenia for 3 years, tremors, palpitations, sweating, hunger and nervousness which were preceded by signs of visual blurring and tingling of the upper limbs. These occured during fasting and between meals, unrelated to work effort, becoming more severe and more frequent gradually up until the present condition.

The frequency ranged from 2 to 3 episodes/day and improved on taking oral diet.

These episodes were confirmed by a venous blood sample with fasting blood glucose levels of 0.43 g/l. The patient had unquantified weight gain during these 3 years due to the regular and increased oral intake to relieve the symptoms time and again.

Investigations

In view of Whipple's triad (Symptoms occur during fasting, symptoms occur in the presence of hypoglycemia, Carbohydrate ingestion relieves the symptoms) a diagnosis of insulinoma was assumed and confirmed by the biochemical studies with the presence of a secretion of inappropriate amounts of insulin (40 mIU/l (2.6- 24.9)).

As part of the topographic assessment, an abdominal CT scan was initially performed, carried out in fine cuts with injection of the contrast medium with highlighting of an enhancing mass developed at the tail of the pancreas which was rounded in shape, iso dense measuring 32- 31 mm with an intense and homogeneous rise in the arterial phase.

Figure 1: Abdominal CT scan in axial section: lesion of the tail of the pancreas in the abdominal cavity, enhancing after injection of the contrast medium.

Figure 2: Abdominal CT scan in coronal reconstruction showing a lesion of the tail of the pancreas measuring 3 cm long axis.

In addition, it was ascertained that the assessment for multiple endocrine neoplasia type 1 (MEN 1) was Negative in this patient.

Differential diagnosis

A differential diagnosis of Primary islet-cell hyperplasia, non-insulinoma pancreatogenous hypoglycemia syndrome and Insulinoma was made.

Treatment

A distal subtotal pancreatic resection was performed in our patient. Removing the mass at the tail and a part of the body of the pancreas without splenectomy by bi-subcostal laparotomy (Figure 3).

Figure 3: 3 cm long axis lesion on the tail of the pancreas corresponding to the lesion radiologically described.

We cut up the surgical specimen after we put it in formaldehyde, the mass appears clearly in this figure.

Figure 4: Rounded mass at the tail of the pancreas (after formalin).

Anatomopathological study of the surgical specimen confirmed the neuroendocrine nature of the tumor.

It was well differentiated, classified as grade 2 according to the WHO 2010 classification. The resection limits were healthy (Figure 4).

Figure 5: Tumour proliferation infiltrating the pancreatic parenchyma, arranged in nests and in clumps; the tumor cells are monomorphic

Outcome and follow-up

The post-operational sequelae was marked by the total disappearance of hypoglycaemia. The patient was discharged at Day 11 postoperatively.

The anatomopathological study of the surgical specimen was in favour of an insulinoma. of high grade with uncertain prognosis.

Discussion

Pancreatic Insulinoma (PI) is a neuroendocrine tumour responsible for the secretion of excessive and inappropriate amounts of insulin leading to hypoglycemic events. This is a rare tumour which is confirmed by the fact that most case reports estimate an incidence of less than 1 to 4 cases per million [5]. However, this is the most common functional endocrine tumour of the pancreas, it is often isolated and generally benign, small in size (90% are less than 2 cm and 30% less than 1 cm).

In our patient the length was bigger and measured about 3 cm.

The tumour sometimes occurs in (5% to 10% of cases) in the context of a multiple endocrine neoplasia type 1 (MEN 1), where it is multiple, associating endocrine tumours of the pancreas, parathyroid, anterior pituitary gland, pancreas, parathyroid gland adrenal cortex, thymus, or bronchial tubes [1].

No such association was found in our patient.

The tumour is rarely found in the elderly and children, the average age of onset of insulinoma is 50 years with a female predominance [5].

The diagnostic delay is relatively long due to the lack of clinical specificity, of about 12 to 18 months on average [7], reaching 3 years in our patient.

Symptoms include those of hypoglycemia on fasting and onset of hypoglycemia in between meals, asthenia, blurred vision, dizziness, headaches, cold sweats that can be as severe and trouble with consciousness. Our patient's clinical picture was typically made up of the Whipple's triad.

The biological diagnosis of insulinoma is easily made with the ascertaining of hypoglycemia with high insulin levels in blood and C-peptide levels. In doubtful cases, an extended glucose test up to 72 hours can be proposed.

Topographical diagnosis faces many difficulties, the tumour being in small in general, measuring less than 1 cm in 24% of cases and 1 to 2 cm in 42% cases [8]. It was easily located in our patient because it was about 3cm long.

However, recent advances in scanning (multi-slice thin-section strips), imaging by magnetic resonance, excellent results of echo endoscopy and scintigraphy to somatostatin (Octreo- scan), have provided renewed interest in the preoperative identification of insulinoma.

However, two examinations dominate this stage: the endoscopic echo may reveal small, clearly infracentimetric lesions in the pancreas, or even millimetre-sized lesions in the duodenal wall.

In rare cases of malignant insulinoma, endoscopic ultrasound can reveal peripancreatic adenopathies allowing the clinician to have a differential diagnosis of malignant tumour from the outset. The fine section CT scan of the pancreas, with early arterial slices, had allowed to visualize the tumor in our patient, whose sensitivity reaches 80% according to the latest studies [3,6].

Prior to the therapeutic management of endocrine pancreatic tumors, identification of poly- endocrinopathy, type MEN I, is indis-

pensable since its identification would in any case lead to a different surgical strategy [10].

There is no specific biochemical marker for MEN 1 (E.g. calcitonin in EOD II).

However, family history, multifocality of tumors and especially the detection of hyperparathyroidism, even if it is latent with the correlation of blood calcium levels, with levels of intact parathormone, make it possible to confirm the diagnosis [11].

The therapeutic objective is twofold: the control of hormonal secretions and the removal of the hormone tumor [12].

In insulinoma, diazoxide (oral, 150 - 600 mg/d) is most often sufficient for the treatment of the tumour pre-operatively. In advanced forms or in case of diazoxide intolerance (edema resistant to thiazide diuretics, hirsutism, nausea), everolimus (5 - 10 mg/d) [13] or the analogs of somatostatin are used starting with a subcutaneous form [14]. Secretory control of advanced forms is achieved in approximately 50% of cases. of insulinomas on diazoxide or somatostatin analogues. Therefore, in the case of insulinoma, surgery and/or tumour reduction are systematically proposed [15].

The usual approach for an endocrine tumor of the pancreas requires a broad approach, first to explore the duodeno-pancreatic block and then the entire gland. In practice, the procedure involves either a supra-umbilical median incision extended by a few centimeters below the umbilicus downwards or a large bi-subcostal incision especially in cases of obesity, which is a frequent phenomenon in patients with insulinoma (due to compensating their hypoglycemia with insulin supplements and Repetitive feeds).

After visualizing and palpatory exploration of the gland, the intraoperative ultrasound scan is done for confirmation. It is most often used to confirm the data from the exploration and sometimes to detect a previously unnoticed lesion (10% of cases), or small, unknown multiple lesions, deeply embedded in the parenchyma, and to diagnose EOD I.

In the case of a small superficial adenoma (less than 2 cm), not adherent to the Wirsungs duct (ultrasound data), enucleation is the intervention of choice, which best allows to protect the pancreatic parenchyma and avoid postoperative diabetes [16]. Hemostasis of the enucleation chamber is achieved gradually by electrocoagulation. bipolar or by using small clips. After enucleation, the exploration is done to carefully check for a Wirsung breach or a leak in the pancreatic fluid.

During the entire procedure must be performed, from the anesthetic induction, monitoring peripheral blood glucose levels should be done every 10 minutes. This constant monitoring protects the patient from neuroglycopenia under general anaesthesia, which could lead to irreversible brain damage. Glucose infusion is stopped immediately after the tumour is removed, but the sharp rise in blood sugar can be delayed. From the start of the procedure, the peripheral insulin samples are taken. They are repeated 15 to 20 minutes after excision. The insulin level should have returned to normal with a half-life of 5 minutes [17].

Anatomo-pathologically, insulinomas do not have Cytoarchitectural features to differentiate them from other neuroendocrine tumours. The identification of malignant forms is not always easy and is based on the criteria on pathological data established by the WHO in 2010 [18].

Insulinoma is considered to be of uncertain prognosis if one of the criteria are the following: anatomopathological conditions: height greater than 2 cm or grade 2 according to the WHO 2010 classification or, vascular and/or peri-neural invasion or, presence of necrosis. It is considered benign if the above characteristics are absent.

The malignancy of insulinoma is asserted for tumours classified as grade 3 in the 2010 WHO classification or by the demonstration of a relapse, an extra-pancreatic or lymph node locoregional tumour extension or a remote tumour. In the case of insulinoma classified as benign, operated with R0 resection, no monitoring is required. proposed.

In cases of insulinoma classified as having an uncertain prognosis according to WHO 2010, although the value of the surveillance is not demonstrated, the latest studies propose to carry out 2 assessments (examination clinical and abdominal MRI) at 6 months and then annually for 5 - 10 years; then every 2 years thereafter every five years to life.

The merits of this strategy will have to be re-analysed after obtaining a sufficient cohort of patients being followed. This strategy should be proposed in particular for Incomplete excisions R1. In case of malignant insulinoma, two clinical and morphological assessments at 3 months are performed and then, if stable, repeated every 3 to 6 months [19].

Conclusion

The diagnosis of insulinoma is clinico-biological. The location of the tumor remains the most important step in the diagnosis which

may be more difficult if it is determined intraoperatively. The standard treatment is often enucleation by laparotomy or laparoscopy, but sometimes a large bi-subcoastal incision is used. followed by distal pancreatic resection reserved for insulinomas of the large sizes like ours about 3 cm and with malignant insulinomas or fitting into the frame. of an EOD 1. The 5-year survival rate for insulinoma is 97% and the factors for poor prognosis are malignancy and association with MEN 1.

Conflict of Interest

None declared.

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