



Research Article

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Enucleation of Pancreatic Insulinomas with the use of Intraoperative Ultrasonography

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Abstract

Tumor-induced hypoglycaemia is very rare, usually caused by a pancreatic beta cell tumor (insulinoma). Symptoms caused by inappropriate insulin secretion usually occur during fasting periods, they can be neurogenic or neuroglycopenic. The diagnosis usually takes up to 2-years, this is biochemical with imaging support. The only curative treatment for an insulinoma is surgical resection (enucleation or partial pancreatectomy).

Objective: To show our experience in the diagnosis and treatment of insulinomas, mentioning diagnostic methods and location with Intraoperative Ultrasonography.

Method: A retrospective analysis of five patients treated at the Clinical Hospital of the University of Chile between 2006 and 2015 was performed.

Results: The average age was 49.2 years (SD 28). The average time between the onset of symptoms and diagnosis was 3.1 years. An imaging study was performed in all patients, with CT of the abdomen and pelvis, identifying a single tumor in all cases with an average size of 1.24 cm (SD 0.26 cm).

Conclusion: Insulinoma should be suspected for symptomatic hypoglycemia, especially in non-diabetic patients. The use of ultrasonography allows to precisely orient the dissection avoiding pancreatic complications and the presence of remnants that could recur. Intraoperative US allows successful enucleation, avoiding morbid resections.

Keywords

Insulinoma, Ultrasonography, Enucleation

Introduction

Tumor-induced hypoglycaemia is very rare, being caused in most cases by a pancreatic beta-cell tumor (insulinoma). Insulinoma are the most frequent functioning pancreatic neuroendocrine tumors (25%). However, their overall incidence is 4/million inhabitants/year [1]. They usually appear during the fifth decade of life, predominantly in females (60%). Most are single and benign (87%), but may be multiple in 7% of cases, and malignant in 6% of patients. It is very important to remember that they can occur in the context of hereditary pathologies such as MEN [2].

Symptoms caused by inappropriate insulin secretion occur most frequently during periods of fasting, and can appear at

any time of the day. These can be neurogenic, such as hunger, diaphoresis, paresthesia, palpitations, sweating, anxiety and tumor [1,3] or neuroglycopenic, such as confusion, altered

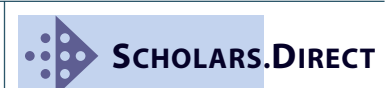
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mental status, behavioral changes, seizures, confusion and coma [4]. A Clinical sign that should raise suspicion of insulinoma is weight gain as a result of frequent feeding to avoid symptoms of hypoglycaemia [1].

The aim of this study is to show our experience in diagnosis and treatment of insulinomas, mentioning diagnostic methods and localization with Intraoperative Ultrasonography (US IOp).

Material and Methods

A retrospective analysis of five patients treated at the Clinical Hospital, Universidad de Chile between 2006 and 2015 was performed (Table 1).

Surgical protocol: Bilateral subcostal laparotomy. Wide Kocher maneuver, exposure of the entire pancreas. Intraoperative ultrasonography to identify the lesion, location and relationship with the duct of Wirsung. Careful blunt dissection and hemostasis with ligatures. Enucleation. Real time ultrasonographic control. Ex situ control of the lesion to compare size and characteristics. US IOp review of pancreas for remaining lesions.

Results

Five patients were included, 4 females and 1 male, with a mean age of 49.2-years (SD 28-years).

The average time between the onset of symptoms and diagnosis was 3.1-years (SD 4.9 years). Among the symptoms, the most frequent was hypoglycaemia, occurring in 4/5 patients, two patients, 3/F and 5/H presented neuroglupenic

symptoms, manifesting with an episode of lipotimia and confusional syndrome respectively (Table 2).

An imaging study was performed in all patients with CT of the abdomen and pelvis, a single tumor was identified, with an average of 1.24 ± 0.23 cm, 2 were located in the head of the pancreas, 2 in the neck and 1 in the uncinete process.

In all cases, laparotomy was performed with bilateral subcostal approach, performing enucleation with fine dissection under intraoperative ultrasonographic imaging (location and real-time control of Wirsung's duct). A single tumor was evidenced in all cases, with an average size of 1.3 cm (E.D. 0.35 cm). Partial pancreatectomy was not performed in any case. The average surgical time was 210 minutes (D.E. 53 minutes). Dextrose 10% infusion and serial hemoglucotest control were maintained during the operation. In all cases the rapid biopsy was reported as insulinoma (Figure 1).

Regarding complications, one patient (1/F) presented with a small intra-abdominal collection during the postoperative period, which did not require intervention (Table 3).

Discussion

Because of its rarity, the diagnosis of insulinoma usually takes up to 2-years from the onset of symptoms. In our case the average time from symptom onset to diagnosis was 3-years. In patients presenting Whipple's triad (symptoms of hypoglycaemia with decreased glycemia that reverts with glucose intake), a biochemical diagnosis of insulinoma can be made by confirming that there is hyperinsulinism associated with the episode according to the following

Table 1: Description of cases symptoms, tumor characteristics and insulin requirements.

Patient	Age (year)	Symptoms	Δ Symptom-Diagnosis (days)	Location	TC size (cm)	Piece size (cm)	Insulin requirement (days)
1/F	25	Hypoglycemia	733	Uncinate process	1.4	1.5	4
2/F	59	Hypoglycemia	4322	Pancreatic head	1.2	1	2
3/F	66	Hypoglycemia lipotimias	198	Neck pancreas	1.6	1.8	2
4/F	15	Hypoglycemia	67	Pancreatic head	1	1.2	5
5/H	81	Confusional Syndrome	383	Collared collars	1	1	3
Average	49.2		1140.6		1.24	1.3	3.2

Table 2: Time of presentation of symptoms and diagnosis. Tumoral size and perioperative glycemic levels.

Parameter	Average	Minimum	Maximum
Age (years)	49.2	15	81
Time between onset of symptoms and diagnosis (days)	1140	67	4322
Glycemia on admission (mg/dL)	28	15	35
Insulinemia at admission (uU/mL)	23.03	7.7	36
Parameter	Average	Minimum	Maximum
Time between diagnosis and surgery (days)	26.4	4	62
Tumour size (cm)	1.3	1	1.8
Surgical time (minutes)	210	150	285
Preoperative Glycemia (mg/dL)	77.8	52	104
Intraoperative Glycemia (mg/dL)	141.8	130	152

Table 3: Postoperative Glycemic levels, hospital stay and insuline requirements.

Minimal Postoperative Glycemia (mg/dL)	89.2	80	100
Maximal postoperative glycemia (mg/dL)	202.2	180	220
Time in hospital (days)	15.6	7	26
Insulin requirement (U/day)	3	2	4
Insulin requirement (days)	3,2	2	5

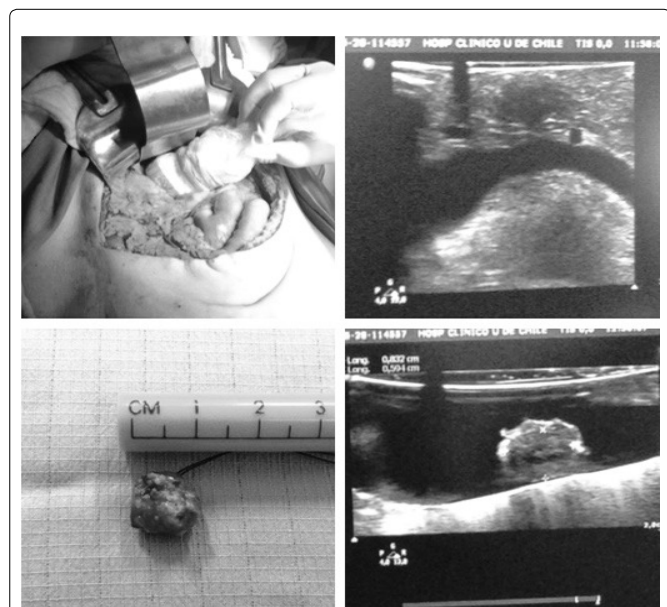


Figure 1: Intraoperative ultrasonography identificación steps and *ex situ* control of the resected lesion. Upper left: Position of transducer over pancreas, Upper right: Real-time. Identification of tumor lesion and wirsung's duct during dissection. Lower left: excised lesion and Lower right: *ex-situ* confirmation of lesion visualized intraoperatively.

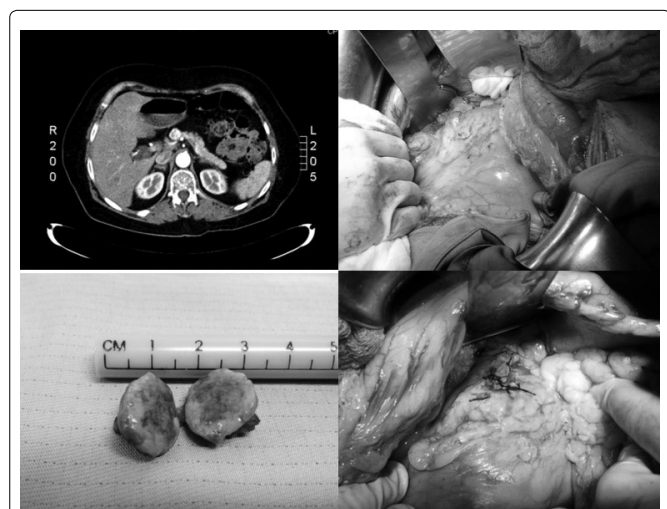


Figure 2: Preoperative and intraoperative identification, resected tumor and post-resection Surgical site.

criteria: fasting glycemia < 55 mg/dL, plasma insulin \geq 3 mU/mL, plasma C-peptide \geq 6 ng/mL, plasma proinsulin \geq 5 pmol/L, b-hydroxybutyrate \leq 2.7 mmol/L, glycemia change \geq 25 mg/dL after 30 minutes of EV glucagon administration, negative blood sulfonylureas study and absence of circulating anti-insulin antibodies. If we only have a history of episodes with compatible symptomatology, without an associated diagnostic laboratory [1], a prolonged fasting study (72h fasting) can be performed according to the protocol used in our series of patients to make the diagnosis (Figure 2).

Once the biochemical diagnosis has been made, the presence of the tumor must be confirmed by imaging; ultrasonography, tomography or magnetic resonance imaging can be used as localization methods. However, a negative imaging study does not rule out the presence of the tumor. In these cases, endosonography or laparoscopic ultrasound may be an option to confirm its presence and determine its location [5]. In our series, CT of the abdomen and pelvis was performed and was diagnostic in all patients.

The only curative treatment for an insulinoma is surgical resection, performing enucleation of the tumor or partial pancreatectomy. In most centers, it is performed by laparotomy, but in some centers, it is also performed laparoscopically, reporting similar morbidity [1].

In cases where the patient refuses surgery or is not a good candidate for it, medical treatment with frequent carbohydrate intake associated with the use of diazoxide (200-600 mg/day POV) or somatostatin analogues can be left [1].

Insulinoma are rare tumors, which should be suspected in symptomatic hypoglycaemia, especially fasting hypoglycaemia in non-diabetic patients, but their Clinical presentation follows a certain classic pattern. For this same reason, it is important that the index of suspicion for this pathology is high when faced with a non-diabetic patient presenting with hypoglycaemia, especially if it is fasting.

The diagnosis is biochemical, complementad by findings of pancreatic radiological tumor, usually unique.

The only curative treatment for insulinoma is complete resection [6]. In this retrospective study, we used the laparotomy approach with ultrasonography support, which allows us to better guide the dissection without causing pancreatic complications and in order not to leave remnants that could recur. In addition, in patients with head, neck or uncinete process location, intraoperative US allows successful enucleation, avoiding extensive resections such as pancreaticoduodenectomy or Whipple's operation.

Authors Declaration

There are no conflicts of interest in this review on the part of any of the authors. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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