Case Report

Multiple episodes of hypoglycemia secondary to an insulinoma: case report


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ABSTRACT

Within the group of pancreatic neuroendocrine tumors, insulinomas are the most frequent functioning tumors, representing 42% with an annual incidence of 0.4 cases per 100,000 inhabitants and exhibiting poor survival of less than 5 years. We report the case of a 57-year-old male with episodes of hypoglycemia of one year of evolution. Abdominal computed tomography reported a 3.5×3.6 cm mass in the neck of the pancreas. Surgery is the mainstay of treatment for insulinomas. Different studies have shown that the presence of these tumors is more frequent in patients undergoing post-mortem examinations. Diagnosis is usually late due to non-specific symptoms and is clinically based on the "Whipple's triad", as well as imaging and laboratory studies. Surgery is the mainstay of treatment for insulinomas. The minimally invasive procedure is an effective modality due to its benefits, however, it continues to be below conventional surgical management. In addition, the study of an intraoperative ultrasound helps to preserve the largest viable pancreatic tissue to avoid later complications.

Keywords: Insulinoma, Neuroendocrine tumor, Hypoglycemia, Laparoscopy

INTRODUCTION

Neuroendocrine tumors are a heterogeneous group of neoplasms that originate in the neuroendocrine cells of the gastrointestinal tract, pancreas, lungs, ovaries, thyroid, pituitary and adrenal glands.1 During the year 2000, the incidence of these tumors was estimated to be 100,000 age-adjusted tumors per year of age in the United States population.2 These tumors occur in 1 to 4 persons per million of the general population and account for 1% to 2% of pancreatic neoplasms.3 However, several autopsy studies have shown that the presence of these tumors is more frequent (0.8%-10%) in patients undergoing post-mortem examinations.4,5 Pancreatic neuroendocrine tumors occur frequently in patients between the sixth and seventh decade of life, being diagnosed at a more advanced clinical stage and exhibiting a poor survival of less than 5 years (<40%).6 On the other hand, insulinomas are the most frequent functioning pancreatic neuroendocrine tumors with an estimated annual incidence of 0.4 cases per 100,000 inhabitants.7 In this paper we present the case of an insulinoma with the aim of explaining our management and updating information in the literature.

CASE REPORT

A 57-year-old male with pathological history of hypertension, began a year earlier when he reported multiple episodes of asthenia, adynamia and nausea, which worsened prior to hospitalization due to hypoglycemia. Symptomatic medical treatment was given and a study protocol was initiated with triple-contrast computed tomography (CT) scan of the abdomen (October 2022), reporting a mass of 3.5×3.6 cm in the neck of the pancreas with contrast enhancement (Figure 1), suggestive of insulinoma as well as serum insulin extension studies of 33.7 uIU/ml (241.80 pmol/l) and C-peptide 5.3 ng/ml.

(1,754.30 pmol/l) (October 2022) in conjunction with clinical symptoms, integrating a presumptive diagnosis of insulinoma. He starts a study protocol by general surgery outpatient clinic in our institution (February 2023) without referring new hospitalizations or events of serious neurological alterations, requesting glycosylated hemoglobin 4.54%, PRO-BNP 10 pg/ml, serum insulin 75.5 uIU/mlR (541.71 pmol/l), and C-peptide 6.53 ng/ml (2,161.43 pmol/l) (February 2023).

He was admitted to our hospital unit on 06 February 2023. Laparoscopic distal pancreatectomy (Figure 2) was performed on 08 February 2023 and a Blake type drainage was placed in the surgical site. During the procedure a transoperative ultrasound was performed to delimit the lesion site and preserve as much tissue as possible. A sample of the body and tail of the pancreas was sent to pathology (Figure 3). The definitive histopathological report describes: macroscopic specimen of 13.5×5×2.5 cm, weight 65 grams, gridded surface, elastic and light brown; multiple cuts identify in the body a well delimited and encapsulated tumor measuring 1.7×1.2 cm reddish, hemorrhagic, fleshy appearance and soft consistency; the rest of the parenchyma finely separte, light brown and soft. Definitive diagnosis: Neuroendocrine neoplasm of low grade of malignancy with resection borders free of neoplasm (Figure 4).

Non-contributory immune-histochemistry: chromogranin, synaptophysin, mck ki67. The score for risk of pancreatic fistula was calculated as 8 points (28.1%), high risk of pancreatic fistula. During his postoperative period, the patient reported significant clinical improvement, denying symptoms related to hypoglycemia, and continued with quantification of Blake type drainage with improvement in its characteristics and volume. Control studies were requested showing fasting serum glucose of 107 mg/dl, PRO-BNP 129 pg/ml, serum insulin 21.1 uIU/ml (151.39 pmol/l) and C-peptide 2.2 ng/ml (728.20 pmol/l) (February 2023). Medical discharge was decided after clinical improvement on the eighth day of in-hospital stay and sixth day post-surgery.

**DISCUSSION**

Neuroendocrine tumors can be classified as functional when associated with clinical syndromes and non-functional when no clinical syndrome is present. Functional tumors can secrete a variety of peptide hormones including insulin, gastrin, glucagon, and vasoactive intestinal peptide, among others. Within this classification, insulinomas constitute 42%, gastrinomas 24%, glucagonomas 14%, VIPomas 10%, somatostatinomas 6%, and the remaining neoplasms are...
very rare. Insulinoma commonly presents as a solitary benign tumor; however, a mutation in chromosome 11q13 can be present, associating with multiple endocrine neoplasia type 1 in most cases. Similarly, up to 10% of insulinomas can be part of multiple endocrine neoplasia syndrome type 1. Most insulinomas are single tumors smaller than 2 centimeters in diameter, occurring with the same frequency in all anatomical sites of the pancreas, and only 8% exceed 5 cm in diameter. Clinical diagnosis is based on the “Whipple’s Triad”, described by Allen Whipple in 1930, which consists of: symptoms caused by hypoglycemia, low serum glucose levels during these previous episodes, and improvement of symptoms after administration and normalization of glucose. Multiple imaging studies such as abdominal ultrasound, endoscopic ultrasound, magnetic resonance imaging, and computed tomography have been used for its diagnosis, presenting sensitivities of 0-66%, 80-90%, >92%, and 94.4% respectively. Current plasma criteria for the presence of an insulinoma include a plasma glucose ≤45 mg/dl with concurrent plasma insulin ≥6 U/ml, C-peptide ≥0.6 ng/ml (0.2 nmol/l), and proinsulin ≥5 pmol/l. It has been established that a proinsulin concentration >22 pmol/l at the end of a 48-hour fast is sensitive, specific, and highly suggestive of the presence of an insulin-producing tumor. The treatment of choice for functional insulinoma is surgery, and although laparoscopy was initiated in 1996, it currently continues to lag behind conventional surgical management (open surgery), with 14.1% laparoscopic, 83.3% open and 2.6% medical management (open surgery), with 14.1% laparoscopic, 83.3% open and 2.6% medical management. In patients who are not candidates for or refuse surgical management, conservative measures such as diet modification and pharmacological agents can be used. The most frequent complications of the surgical procedure are pancreatic fistula and stenosis of the main pancreatic duct.

The diagnosis of malignancy for this tumor is with the presence of metastasis, with liver and lymph nodes being the most frequent sites. It is considered that after tumor resection, the patient has been cured. After the surgical procedure, follow-up is recommended for 3, 6, and 12 months and then annually.

CONCLUSION

Insulinoma is a rare pancreatic tumor that causes multiple episodes of hypoglycemia in affected patients. The difficulty in diagnosing insulinomas lies in the localization of the tumors, which is also key to surgical success. Surgery is the mainstay of insulinoma treatment. The minimally invasive procedure is an effective treatment modality when the tumor is correctly identified in its anatomy. In addition, the study of a transoperative ultrasound helps to preserve as much viable pancreatic tissue as possible to avoid episodes of post-surgical hyperglycemia. The benefits of laparoscopic surgical management include faster recovery from pain, fewer surgical wounds or scars, and a brief resumption of the patient’s daily activities.

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