PANCREATIC INSULINOMA. CASE REPORT AND REVIEW OF THE LITERATURE

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Abstract

Insulinoma is a rare pancreatic islet cell tumor, the most common cause of hypoglycemia related to endogenous hyperinsulinism. We present the case of an adult patient with pancreatic insulinoma. The patient presented to our clinic after prior hospitalizations in diabetes and psychiatry hospital units for repeated episodes of loss of consciousness, sweating and tonic-clonic seizures. Early detection of the cause is important for prompt initiation of therapy and to reduce symptoms. We describe our diagnostic and therapeutic strategies with references to previously published reports.

Keywords: insulinoma, endocrine carcinoma, syncopate, hypoglycemia, neuroendocrine tumor

Introduction

Pancreatic endocrine tumors are classified, according to the symptomatology, in secreting and nonsecreting tumors. The nonsecreting tumors (silent, in hormonal terms) represent about 50% of the total; they are followed by insulinomas - 25% and gastrinomas - 15% [1,2]. Insulinoma is a functional neuroendocrine tumor that secretes insulin. It may be associated with other endocrine glands tumors in the multiple endocrine neoplasia type I (MEN I) (parathyroid, pituitary, endocrine pancreas). The islet cell tumors are the most common cause of hypoglycemia resulting from endogenous hyperinsulinism. The male-to-female ratio for insulinomas is 2:3 [3]. No racial predilection appears to exist. The median age at diagnosis is about 47 years, except in insulinoma patients with MEN 1, in whom the median age is the mid-20's [4].

Case report

A 61-years old man known with hypertension and alcoholic steatohepatitis, presented on 26/03/2013 for syncopes, tonic-clonic seizures, sweating, anxiety. Alcohol consumption had been stopped 2 months before the onset of the symptoms, according to the patient and his relatives statements.

In the patient medical history we found an emergency admission on 20/02/2013 for psychomotor agitation, episodes of loss of consciousness with tonic-clonic seizures, delirium of mixed etiology (alcohol and hypoglycemia), tremor of the upper limbs, sweating, disorientation in time and space, important hypoprosexia, fixing and evocation hypoamnesia, insomnia. Blood tests evidenced 41 mg/dl hypoglicemia, hyperkaliemia, twice the normal values of lactate dehydrogenase (LDH). The cranial computed tomography (CT) did not reveal any damage except an old ischemic millimetric lesion and a degree of atrophy.

The patient was admitted to the Diabetes, Nutritional and Metabolic Diseases Clinic for suspected insulinoma. The abdominal CT revealed no pathological changes in the abdominal organs, no lymph node changes. Due to his agitation, seizures, and delirium, the symptoms were interpreted as alcohol withdrawal and he was transferred to the Department of Psychiatry. During hospitalization the blood glucose fasting levels were found again between 30 and 50 mg/dl. The neurologist interpreted the old ischemic lesion shown on the CT as possibly due to hypoxic damage caused by severe hypoglycemia. The patient was discharged with the diagnosis of complicated withdrawal seizures, chronic alcohol dependence, history of disabling ischemic stroke in the left carotid territory, with recommendation for hospitalization in a medical clinic.

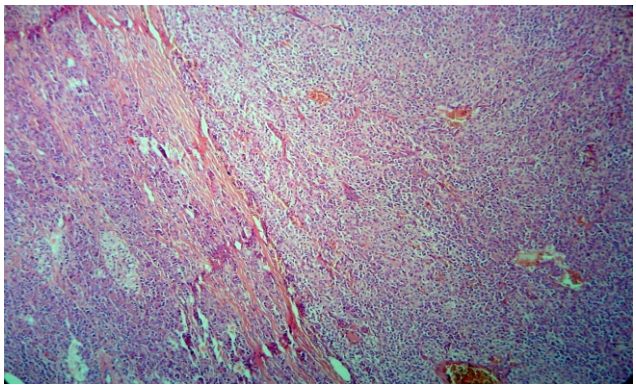

Figure 1. The edge of the tumor (hematoxylin eosin reaction). On the left side the pancreas, on the right side the tumor.

The patient presented in our clinic for further investigation on 27/02/2013. The following were determined: the C peptide, insulinemia and glycated hemoglobin,

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which were normal and did not support the diagnosis of insulinoma. HbsAg was found positive. Abdominal ultrasonography revealed no changes in abdominal organs. In conclusion, hypoglycemia was attributed to the alcohol consumption and the patient was released on 03/04/2013.

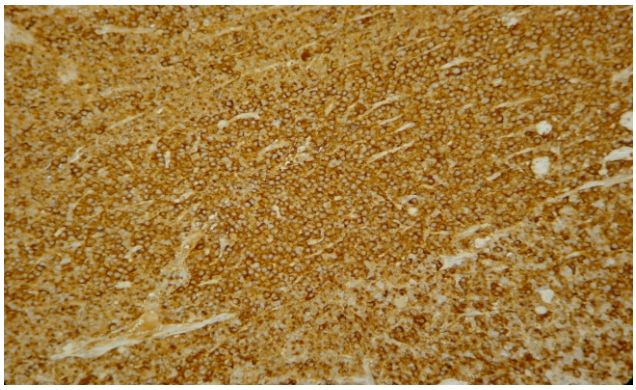

Figure 2. Immunohistochemical reaction for chromogranin.

After a month, on 26/03/2013, the patient came back for persistent symptoms. Blood tests showed 39 to 59 mg/dl glucose levels and mixed dyslipidemia, carbohydrate antigen (CA)19-9 was normal, the other analyses were normal. We decided to repeat the abdominal magnetic resonance imaging (MRI) with contrast, and we discovered a 21 mm hypervascular tumor of the pancreatic uncinate process, suggesting, as first hypothesis, an endocrine tumor and peripancreatic millimetre lymph nodes. We transferred the patient to the surgery department, where the uncinate process tumor was excised and peripancreatic lymph nodes were biopsied.

The histopathological appearance (Fig.1) pleaded for a well differentiated endocrine carcinoma. The pathology report showed that the chromogranin A immunohistochemical reaction (Fig. 2) was positive and Ki-67 proliferation index (Fig. 3) was positive in 5-6% of tumor cells (nuclear expression), findings that were supporting the diagnosis of neuroendocrine tumor. The low levels of Ki-67 immunoreactivity is an indicator of good prognosis [5]. Based on the result of the histopathological examinations, corroborated with the imaging and intraoperative exploration, the tumor stage was as pT3N0Mx.

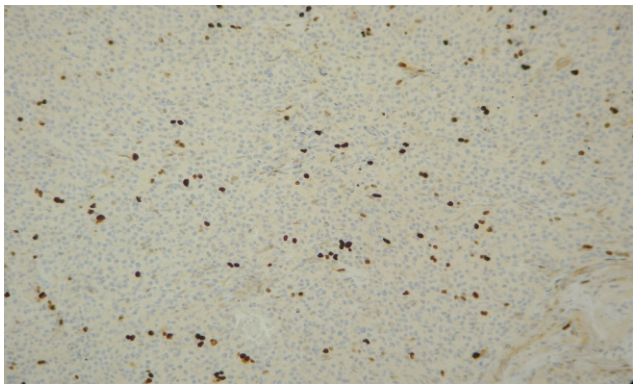

Figure 3. Anti-Ki67 antibody stain (nuclear expression).

The postoperative evolution of the patient was favorable. Insulinemia and glycemia after one month were normal. The patient is undergoing chemotherapy.

Discution

Most insulinomas are solitary and benign. The "rule of 10" states that 10% are multiple, 10% are malignant, 10% are associated with MEN1, and 10% are ectopic. Insulinomas are associated with MEN 1 in 5% of patients and it is estimated that 21% of patients with MEN1 develop insulinomas [4,6]. The incidence is 3-10 cases per million people per year. Once surgically removed, the insulinomas occurring in this autosomal dominant syndrome have a higher risk of relapse [7].

Long-term survival of patients with insulinoma is generally excellent; it is considered that approximately 90-95% of insulinomas have benign histological behavior, so healing with dissaperance of symptomatology after complete resection is the rule [4]. Recurrences were observed in 5.4% of cases in a series of 120 patients with benign insulinomas, over a period of 4-17 years. In these cases surgical intervention was performed [8]. Long-term survival is possible in malignant insulinomas, especially in cases strictly localized to the pancreas and with good response to adjuvant chemotherapy; median disease-free survival after curative resection is estimated at 5 years [4]. The median survival after disease recurrence is only 19 months.

Conclusion

The diagnosis of insulinoma often comes from a hunch, from the impossibility of highlighting the cause of repeated hypoglycemia in an apparently healthy patient. But for diagnostic certainty, patient follow-up and repeated analysis are necessary. Proper management for timely treatment of a patient with insulinoma involves complex medical teamwork consisting of physicians from various specialties: endocrinology, internal medicine, surgery, pathology, medical imaging, oncology and, like in our case, psychiatry.

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