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Case Report

Successful Surgery of a Pancreatic Insulinoma Misdiagnosed as a Neuropsychiatric Disorder for 9 Years: A Case Report

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Abstract

Insulinoma is a rare functional pancreatic neuroendocrine tumour that is usually sporadic and solitary. It can have a varied presentation. Neuroglycopenic manifestations of hypoglycemia due to insuline hypersecretion can mimic neurological or psychiatric disorders, thus often a diagnosis and treatment delay. Insulinoma is a potentially curable condition, but it can be fatal if left unrecognized. We report a case of A 45-year-old woman who had a 9-year delay before diagnosing insulinoma after being initially assessed with anxiety–depressive disorder. The case report below provides a detailed review of the diagnosis, tumour localization, and the successful surgical intervention implemented for the patient.

Keywords: Insulinoma, Hypoglycemia, Neuropsychiatric symptoms, Diagnosis delay.

INTRODUCTION

Insulinomas are hormone-producing pancreatic neuroendocrine neoplasms with an estimated incidence of 1 to 4 cases per million per year. Most insulinomas present with the Whipple triad: which is the presence of hypoglycemic symptoms, documented hypoglycemia and resolution of the hypoglycemic symptoms after glucose administration [1]. Some cases are however misdiagnosed in outpatient clinics as neurological or psychiatric disorder, such as epilepsy [2], stroke [3], and hysteria [4]. Despite of the tumor's size, its insulin secretion is a major cause of hypoglycemic brain lesions and cognitive impairment. For single solitary insulinomas, curative surgical excision remains the treatment of choice, but it can be fatal if left unrecognized.

CASE PRESENTATION

A 45-year-old non diabetic woman was referred for the evaluation of hypoglycemic symptoms. She had been experiencing for about 9 years, episodes of profound intermittent asthenia associated with excessive sweating, blurriness of vision, Dizziness Mixed anxiety–depressive disorder without any episode of consciousness loss, or seizures.

She noticed that these symptoms occur mostly in the morning and disappear after having breakfast.

She has consulted two general practitioners who had misdiagnosed hypoglycemia, and considered it to be a neurotic disorder. She was treated with anxiolytics, which was discontinued due to persistence of the symptoms. The physicians did not investigate the possibility of hypoglycemia, partly because her HbA1c level 4,60% was within normal range.

During a routine consultation, a gynaecologist who was measuring capillary blood glucose systematically for all her patients, identified incidentally a hypoglycemia in our patient and referred her to an endocrinologist.

Screening for sulfonylurea, anti-insulin antibodies and anti-insulin receptor antibodies couldn't be performed because of lack of ressources. Renal and hepatic function tests were Normal.

Morning cortisol at 8 a.m was 15,37ug/dl.

There was no need for a fasting test. Concomittent with a blood glucose of 0,43g/l identified in counsultation, a blood sample was taken and showed:

Insuline: 10,79uUI/ml; **C- Peptide:** 2,86ng/ml; **Insuline/peptide C index**: 0,08 (less than 1), confirming hyperinsulinemic hypoglycemia.

Abdominal CT scan showed no abnormalities. Then, she had been referred to our center for further etiological localization. An abdominal magnetic resonance imaging (MRI) has showed nodular formation of the pancreatic isthmic region measuring 16*18 mm, solidocystic, multiloculated, with fine septa, lobulated contours, hyposignal T1, heterogeneous T2 hypersignal, slightly enhanced after injection of contrast, bringing to mind in the first place a neuroendocrine tumour of an insulinoma. **(Figure 1).**

Biological screening for MEN1 was negative.

Surgical resection of the tumor corrected her glucose levels as well as eliminated the insulinoma neuropsychiatric symptoms with a follow-up of 06 months after surgery.

Pathological examination showed that the tumor was positive for (chromogranin A, synaptophysin and insulin.)

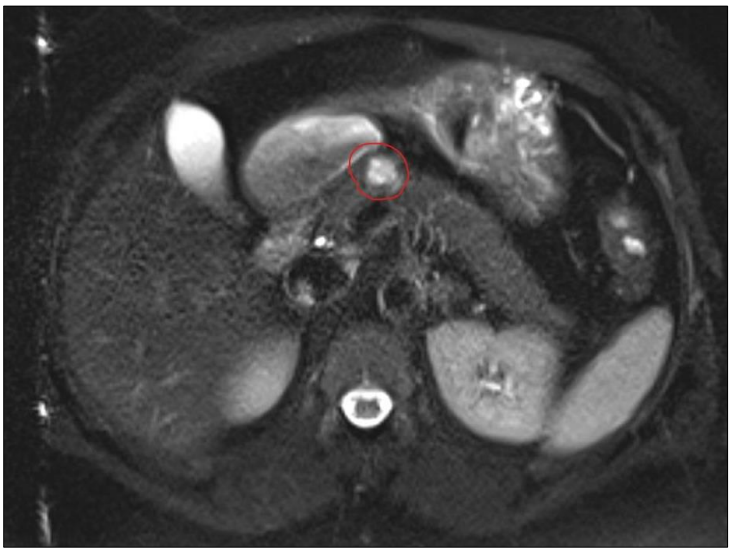

Figure 1A: MRI, axial view of the tumour

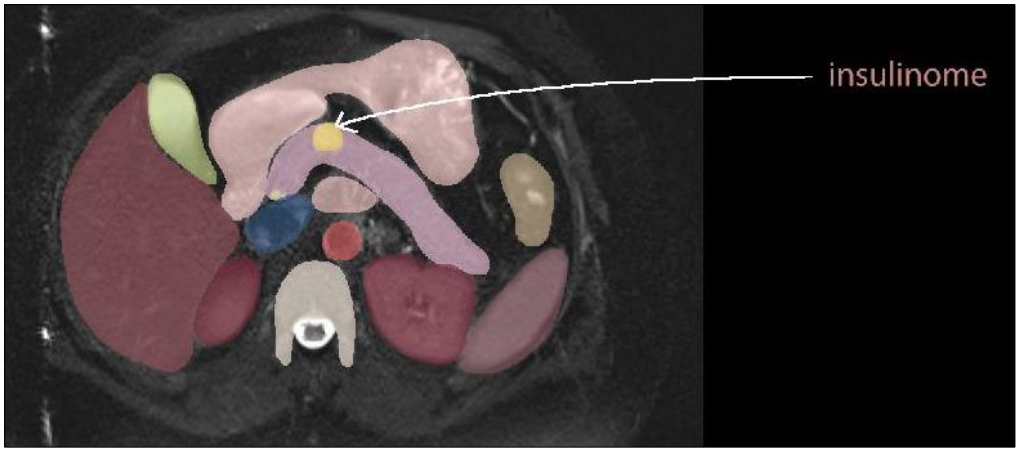

Figure 1B: MRI image schematic reconstruction

DISCUSSION

Hypoglycemic symptoms can be classified as neuroglycopenic and neurogenic symptoms. The former occur as a result of central nervous system glucose deprivation, while the latter are due to autonomic nervous system discharge caused by hypoglycemia.

Neuroglycopenic manifestations appear as various neuropsychiatric symptoms (NPS), such as confusion, weakness, dizziness, fainting, convulsion, and visual disturbances. Patients can present with a combination of various neuropsychiatric symptoms (NPS), which can mimic neurological and psychiatric disorders.

An international survey of 1928 patients with NETs (Neuroendocrine tumors) reported a mean delay of 52 months between symptom onset and diagnosis. According to the study, patients see an average of 6 different health care providers before receiving the correct diagnosis [5].

Insulinomas are the most common functioning endocrine neoplasm of the pancreas. As clinical

manifestations are non-specific, diagnosing an insulinoma is challenging. Some cases can present with neuroglycopenic symptoms suggesting neuropsychiatric disorders, delaying diagnosis and treatment [6].

A chinese study was performed to characterize NPS of the patients with insulinoma from a regional clinical center. Among 42 patients with insulinoma, 25 patients with NPS were initially misdiagnosed as having a neurological or psychiatric disease. Most (64%) of NPS cases were not diagnosed correctly until 12 months after the first consultation. In patients with NPS that remained undiagnosed for at least 5 years, the most frequent symptoms were confusion, convulsion, and visual disturbances. Twelve cases of NPS were initially misdiagnosed as epilepsy and 3 of them showed epileptiform discharges on electroencephalography [7].

Following Biochemical confirmation of hyperinsulinism using a supervised 72-hour fasting test with plasma glucose, insulin, C-peptide, and proinsulin (if available) level measurements; the next step is tumour localization and exclusion or confirmation of metastatic disease by CT to guide therapeutic protocol and surgical procedures. Conventional computed tomography CT is still the preferred initial localization modality followed by Endoscopic UltraSound (EUS) or magnetic resonance imaging (MRI) for indolent, localized insulinomas.

Abdominal Ultrasound and Conventional computed tomography (CT) have respectively a sensitivity ranging from (0-39%) and (22 à 43%). Helical CT is slightly more performant with a sensitivity ranging from (15 to 64%). This sensitivity falls from 40% for lesions 3 cm to just 21% for tumors less than 1 cm in size. A clear improvement has recently been made by the biphasic helical scanner which, thanks to its high resolution and the thin sections it offers, enables tumor detection during the arterial phase, when contrast with the healthy parenchyma. Its sensitivity reaches 94%.

In our case, due to the lack of recent technological ressources in the radiological center where the first CT has been performed, as it failed to localize the tumor, we decided to opt for MRI as another non-invasive topographic imaging tool. MRI is much more sensitive in the detection of insulinomas even small tumors comparatively to Abdominal US and CT. Its sensitivity ranges from 85 to 95%. Insulinomas generally present as a T1-hyposignal formation with intense enhancement after gadolinium injection, and hypersignal in T2 [8, 9].

For single solitary insulinomas, curative surgical excision remains the treatment of choice, with cure rates ranging from 77 to 100%. 90% of insulinomas are benign, solitary, and small (less than 2 cm in diameter) therefore pancreas-sparing techniques like enucleation and partial pancreatectomy are preferred. This can be done via an open or laparoscopic approach. The extent of surgery is dependent on the tumour's location and its malignant potential [5].

Medical options such as: Diazoxide, calcium channel blockers, propranolol, glucocorticoids and somatostatin analogues; exist for pre-operative control of serum glucose levels, patients not fit to tolerate anaesthesia or those with uncontrolled metastatic disease.

Patients diagnosed with benign insulinomas have an excellent prognosis, all returning to normal life after treatment.

Our patient had being managed before surgery with intravenous glucose infusions, without need for other medical options. She underwent a successful laparotomic abdominal surgery with a tumor enucleation, with normalisation of blood glucose levels and disappearance of neuropsychiatrc symptoms according to a 6 months follow up after the surgery.

CONCLUSION

It is, therefore, important for physicians to be aware that insulinomas can manifest as neuroglycopenic symptoms and to consider the possibility of hypoglycemia by careful medical interview and if available Continous Glucose Monitoring, especially when patients suspected of psychiatric disorders do not show the expected response to antipsychotic drugs.

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