Insulinoma: Diagnosis and Management on Two Observations
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Abstract

Insulinoma is an insulin-secreting pancreatic tumor responsible for hypoglycemia. It is a rare tumor that occurs in 1 to 4 persons / million in the population and represents 1 -2% of pancreatic tumors. The diagnosis is made by demonstrating, insulin secretion by measuring insulin levels and C-peptide in the presence of hypoglycemia and by demonstrating a pancreatic tumor by pancreatic CT and/or pancreatic MRI [5]. Surgical resection is the main modality for the treatment of insulinomas [1]. We report 2 observations of an insulinoma. A 47 year old patient, who consulted us for lipohypmie associated with cold sweats and hunger, occurring preferably in the morning between 6 and 7 o'clock. The blood sugar level taken at the time of the malaise was 0.35 g/l. Assessment performed: Insulinemia ↑: 701 pmol/l (18-173), Peptide C↑: 2,35 pmol/ml (0,3-1,4) in comparison with a hypoglycemia of 0.35 g/l. Abdominal MRI revealed a 16×16 mm nodule in the isthmus of the pancreas with poor vascularity compatible with an insulinoma. Observation 2: patient, 37 years, admitted for investigation and management of hypoglycemia ranging from 0.3 g/l occurring during physical activity. Workup performs: fasting test: peptide C↑: 3 ng/ml (1.1-1.47), insulinemia: 22.6 mUI/l (2.6-24.9) vs. hypoglycemia 0.50 g/l, insulin/glycemia ratio=0.45 (normal <0.3), turner index:113 (normal <50). Normal abdominal CT scan completed by pancreatic MRI: pancreatic nodule in the isthmic region of 13*8 mm compatible with an insulinoma. Octreoscan: a hyperfixing focus on an isodense region of 13*8 mm compatible with an insulinoma. Surgical management: enucleation. Favorable evolution marked by the disappearance of hypoglycemia.

Keywords: Insulinoma, pancreatic tumors, insulinemia, C-peptide, hypoglycemia, pancreatic MRI, Octreoscan, Surgical management

INTRODUCTION

Insulinoma is an insulin-secreting pancreatic tumor responsible for hypoglycemia. It is a rare tumor that occurs in 1 to 4 persons / million in the population and represents 1 -2% of pancreatic tumors. They can occur at any age and are equally distributed between the two sexes. 90% of insulinomas are benign and 90% are solitary tumors, 90% are of intra pancreatic location and 90% have a diameter < 2 cm [2-4]. The diagnosis is made by demonstrating insulin secretion by measuring insulin levels and C-peptide in the presence of hypoglycemia and by demonstrating a pancreatic tumor by pancreatic CT and/or pancreatic MRI [5]. Surgical resection is the main modality for the treatment of insulinomas [1]. We report 2 observations of an insulinoma.

OBSERVATION 1

A 47 year old patient, married, mother of 2 children, housewife, with no medical or surgical history, who consulted us for lipohypmie associated with cold sweats and hunger, occurring preferably in the morning between 6 and 7 o'clock, with the need to take sugar, and amendment of the signs after eating, which had been evolving for the last 9 months, without any disturbance of the consciousness. The patient reported a moderate weight gain, no pituitary tumor syndrome, no signs of hypersecretion or anteropituitary insufficiency, no notion of bone pain, no renal colic or stone emissions.

The blood sugar level taken at the time of the malaise was 0.35 g/l. The blood sugar levels taken over 3 days showed morning hypoglycaemia.

Table-1: 3-day fasting blood glucose at time discomfort

<table>
<thead>
<tr>
<th>Date</th>
<th>Glucose Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>13/01/2021</td>
<td>7am capillary glucose 0.66 g/l</td>
</tr>
<tr>
<td>14/01/2021</td>
<td>7am capillary glucose 0.35 g/l</td>
</tr>
<tr>
<td>15/01/2021</td>
<td>4am capillary glucose 0.46 g/l</td>
</tr>
</tbody>
</table>

Examination at the time of admission:
conscious patient, SG: 15/15, GC= 1.31 g/l post-lunch, HR= 97 bpm; FR = 18 cpm, Weight = 75 kg; Height = 158 cm; BMI = 30.4 kg/m2; TDT= 100 cm, Intertiguous last right foot space.

Assessment performed: Insulinemia ↑ : 701 pmol/l (18 -173), Peptide C ↑ : 2.35 pmol/ml (0.3-1.4) in comparison with a hypoglycemia at 0.35 g/l.

Multiple neoplasia type 1 workup:
Hypophysigram: FSH; 2 IU/L, LH: 1.5 IU/L, Estradiol: 130.8 ng/L, Cortisol: 8.16 μg/dl, TSH: 1.29 mui/l, T4L: 13 pmol/l, Prol: 8.16 ng/ml, Phosphocalcium balance: Ca: 98 mg/l, Albumin: 43.2 g/l, Phosphorus: 45 mg/l, Vit D: 7.64 ng/ml, PTH: 25.5 Pg/ml.

Management: surgical enucleation by laparotomy of the nodule at the level of the isthmus of the pancreas 2x2 cm of firm consistency and posterior development and removal of the hepatic nodule of segment III of the liver of about 0.3 cm with resection margin of about 1 cm and correction of vitamin D deficiency.

Histological examination in favor: morphological and immunohistochemical appearance of a pancreatic localization of a grade II neuroendocrine tumor of 1.8 cm long axis (WHO 2017) with healthy surgical resection limits of 2 mm. Simple operative follow-up and favorable evolution with disappearance of hypoglycemia.

**OBSERVATION 2**

Patient, 37 years old, married, father of 2 children, jeweller, without particular medical and surgical history admitted for investigation and management of hypoglycemia ranging from 0.3 g/l occurring during physical activity, usually at the end of the day and away from meals with sometimes loss of consciousness associated with hypotensive malaise and significant asthenia with improvement of the symptomatology after re-sugaring, all evolving in a context of weight gain of 18 kg over 1 year and a half, with fronto-temporal headaches, Decreased visual acuity for 2 years.

Objective admission examination: Patient conscious. GC= 1.09 g/l, BP= 130/75 mmHg, HR= 82 bpm, FC= 18 cpm, Weight = 78 kg; Height = 176 cm; BMI = 25.18 kg/m, Abdominal fire point scar, Palpable thyroid not increasing in volume.

Workup performs: fasting test: peptide C↑: 3 ng/ml (1.1-1.47), insulinemia: 22.6 mUI/l (2.6-24.9) vs. hypoglycemia 0.50 g/l, insulin/glycemia ratio=0.45 (normal <0.3), turner index:113 (normal <50). Normal abdominal CT scan completed by pancreatic MRI: pancreatic nodule in the isthmic region of 13x8 mm compatible with an insulinoma. Octreoscan: a hyperfixing focus on an isodense nodule of the head-neck junction of the pancreas measuring approximately 12x13 mm compatible with an insulinoma.

Abdominal MRI revealed a 16x16 mm nodule in the isthmus of the pancreas with poor vascularity compatible with an insulinoma.
Insulinoma is an insulin-secreting pancreatic tumor responsible for hypoglycemia. It is a rare tumor that occurs in 1 to 4 persons / million in the population and represents 1 - 2% of pancreatic tumors [1]. It can occur at any age (average age 47 years) in both men and women [6]. These insulinomas secrete insulin, of course, but also, concomitantly, in 95% of cases, pro-insulin. Severe neuroglycopenic manifestations (psychiatric disorders, neurological deficits, seizures, coma, etc.) typically occur on an empty stomach, in the morning or at a distance from a meal (more than 5 hours afterwards) and/or during physical effort [7]. Symptoms rapidly subside with the intake of fasting sugars (or with the injection of a serum glucose solution in case of coma). The Whipple triad associating hypoglycemia and neuroglycopenic signs corrected by the administration of carbohydrates is suggestive of insulinoma [6]. Hormonally, a blood glucose level below 0.45 g/l (2.5 mmol/l) concomitant with an insulin level greater than or equal to 3 mU/l (≥ 18 pmol/l) and a C-peptide greater than or equal to 0.6 ng/ml is highly suggestive of an insulinoma, hypoglycemia is obtained spontaneously or during a young person's test [5]. A German team recently proposed to use the amended insulin/glucose ratio, i.e. the ratio [blood insulin (pmol/l)]/[blood glucose - 1.7 mmol/l] [6]. For these authors, the amended insulin/glucose ratio, at a threshold of 53.6 (pmol/l)/(mmol/l) or 3 (mU/l)/(mmol/l), giving a positive predictive value (PPV) of 98% and a negative predictive value (NPV) of 99% [6]. The diagnosis of localization is based on pancreatic CT and/or MRI scans, which can reveal the insulinoma, sometimes immediately. 60-75% of insulinomas are smaller than 1.5 cm in diameter. About 40% are even smaller than 1 cm and may not exceed 2 cm in diameter [1-5]. The examination of choice for localization of an insulinoma is echo-endoscopy, Somatostatin-labeled analogue scintigraphy (Octreoscan®) can be used if MRI and CT are inconclusive [1, 5]. Typically, insulinomas are benign, in its sporadic form they present as solitary, benign lesions [5], within the framework of multiple endocrine neoplasia type 1 (MEN1), they are multifocal [7]. MEN-1 is characterized by the association, in the same patient or in related subjects of the same family, of a primary hyperparathyroidism by adenoma and/or hyperplasia, a pancreatic or duodenal endocrine tumor and/or a pituitary adenoma. The disease is most often inherited with autosomal dominant transmission occurring as a result of inactivating mutations in the MEN1 gene located on chromosome 11 [9,10]. The treatment of insulinoma is usually surgical by resection of the tumor and offers the only chance of cure. The choice of the operative technique depends on the location of the tumor, the number, and its size [1, 5, 7]. Resection of the tumor can be enucleation, partial or middle pancreatectomy [1, 7]. Other therapeutic options that can be used in case of non-operable, non-localized or malignant insulinoma are: octreotide injection, endoscopically guided alcohol ablation, radiofrequency ablation, and embolization [1]. Pathologically, in 2017 omns classifies pancreatic neuroendocrine tumors into 5 grades with the following characteristics: G1 neuroendocrine tumor: Well-differentiated morphology Mitotic index <2 and Ki-67 index <3%; G2 neuroendocrine tumor: Well-differentiated morphology, Mitotic index 2-20 and/or Ki-67 index 3-20%; G3 neuroendocrine tumor: Well-differentiated morphology, Mitotic index >20 and/or Ki-67 index >20%; neuroendocrine carcinoma: Poorly differentiated morphology, large cell type, small cell types, mitotic
index >20 and/or Ki 67 index >20%; Mixed neuroendocrine- non-neuroendocrine tumor (Mixed NEuroendocrine non-neuroendocrine Neoplasm [MiNEN]) [11]. The prognosis of insulinomas depends on the 2017 WHO classification. G1, 2, 3 tumors have better prognosis [12].

CONCLUSION

Insulinomas are the most frequent neuroendocrine tumors of the pancreas and are responsible for hypoglycemia related to endogenous hyperinsulinism. The image is the key examination to localization. More than 90% of insulinomas are benign and small solitary tumors well encapsulated. Surgical resection is the treatment of choice and offers the chance of cure; medical treatment and other therapies are reserved for non-localized and or malignant tumors. The prognosis depends on the classification of pancreatic neuroendocrine tumors WHO 2017.

REFERENCE