Letters to the Editor

Dementia solved with surgery: Report of a case

Dear Editor:

Insulinoma is the most frequent pancreatic neuroendocrine tumour, characterised by insulin secretion, and its key symptom is hypoglycaemia, with an incidence of 1–4 cases per million inhabitants. The typical presentation of insulinoma is Whipple’s triad: validated plasma blood sugar levels <50 mg/dl, symptoms consistent with hypoglycaemia and their resolution after glucose administration. Upon revision of the medical literature available in PubMed using the key words “dementia”, “insulinoma” and “Alzheimer’s disease”, we present the first case of cognitive impairment secondary to insulinoma in Europe and its resolution after surgical treatment.

The subject is a 61 year-old female brought to the Emergency Department due to hypoglycaemia of 20 mg/dl with impairment of the consciousness level and recovery after intravenous infusion of glucose at 50%. Acute disease was ruled out at that moment and after blood sugar levels stabilisation. The Endocrinology department was informed. She had high blood pressure treated with enalapril 5 mg, incipient Alzheimer type dementia (GDS 4, CDR 1) treated with galantamine 24 mg and hysterectomy for uterine fibroids. During the 2 previous years, she had experienced feeling of objects spinning, general discomfort and pallor after walking 30 min. She was assessed by the Cardiology Department, where the presence of a heart condition was ruled out. 15 months before her admission, she was assessed by the Neurology department due to failure to perform instrumental activities. A complete examination was carried out and she was diagnosed with Alzheimer type dementia. Treatment was initiated with 5 mg of donepezil, but after 4 months, it was discontinued due to night terrors and episodes of visual hallucinations, and changed to galantamine 24 mg. She reported episodes consistent with hypoglycaemia, for which she had never been examined before, predominantly during the morning, which resolved with fruits or sweets. For the last 2 years approximately, the symptoms appeared when the subject was resting or performing activities that required effort. She had gained 12 kg of weight in that time. She denied taking unsupervised medication, having insulin or hypoglycaemic drugs available, consuming toxic agents, having dietary transgressions, fasting and doing exhausting exercise. The examination showed only class II obesity. A fasting test was performed, and the results were consistent with endogenous hyperinsulinism. Sulfonyleurea detection was negative. Chromogranin A and neuron-specific enolase were normal. The abdominal CT scan and NMRI, the scintigram with somatostatin analogues and the PET–CT showed no evidence of injuries consistent with insulinoma. The pancreatic protocol CT scan in the ventral area of the body showed a hypervascularised image of 1.5 cm diameter and density alteration consistent with neuroendocrine tumour. The patient was assessed by hepatobiliary and pancreatic surgery, selecting elective surgery as the best option. The intraoperative ultrasound scan showed a hypoechoic image of 2 cm diameter, separated from the duct of Wirsung, in the pancreatic body. Tumour enucleation was performed. The intraoperative biopsy was consistent with insulinoma-like neuroendocrine tumour, confirmed in the definitive biopsy, with no data of malignancy in the piece. The study was completed to disregard diseases associated with the insulinoma, and it turned out to be negative.

Our patient had a benign insulinoma that appeared initially as cognitive deterioration consistent with Alzheimer type dementia. Weight gain occurs in 18% of the patients. Diagnosis delay is not unusual as the symptoms are frequently attributed to psychiatric, cardiac or neurological disease. The biochemical diagnosis of the insulinoma is carried out with the fasting test. Once it is done, the location diagnosis must be performed, as it is essential to differentiate between insulinoma and adult neuroendiosis. It can be performed through non-invasive (ultrasound scan, CT scan, NMRI, PET–CT and scintigram) or invasive (endoscopic ultrasound scan, arteriogram and selective venous catheterisation) tests. Most of them are intrapancreatic, unique and smaller than 2 cm. The preferred treatment for this condition is surgery. The selection of the procedure depends on the tumour mass, location, relation with neighbouring structures and pancreatic involvement. In patients at high surgical risk, other less invasive treatments are preferred, such as drugs (analogue of somatostatin, diazoxide), ablative treatment of the injury with alcohol, radiofrequency ablation or embolization. Regular reviews shall be carried out to rule out associated diseases or polyglindu lar syndrome. The patient was reassessed by the Neurology department 3 months after surgery and no data of cognitive impairment or failure were observed in the ordered tests. Nowadays, she’s subject to regular reviews and she continues asymptomatic.

References


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Autoimmune hypoglycemia syndrome associated with α lipoic acid consumption

Síndrome de hipoglucemia autoimmune asociado al consumo de ácido α lipoico

Dear Editor,

The insulin autoimmune syndrome (IAS) is a rare cause of endogenous hyperinsulism, characterised by fasting hypoglycaemia, postprandial hypoglycaemia or both, by very high levels of insulin and by positive anti-insulin autoantibodies (IAAs). It can be induced by certain drugs, especially those with sulfhydryl groups, which have been related to up to 50% of the cases. In particular, its onset can be triggered by the α lipoic acid (ALA), increasingly used during the last years as nutritional supplement.

The case of a Caucasian 55 year-old female referred for hypoglycaemia examination is presented. Allergy to iodinated contrast was the only relevant history; no use of habitual medication was reported. She had a 2-month case history characterised by adrenergic and neuroglycopenic symptoms, both in fasting and postprandial states, that resolved after food intake, and a 2 kg weight gain (weight 53 kg, body mass index [BMI] 21 kg/m²).

The physical examination using devices was anodine. The general laboratory tests showed blood sugar levels of 3.2 mmol/L (4.1–6.9) and haemoglobin (HbA)1c of 5.6%. A fasting test was performed and it was positive at 3 h with blood sugar levels of 2.4 mmol/L (4.1–6.9); insulinemia: 1.033 pmol/L (21–174); C peptide: 4.10 nmol/L (0.26–1.44); and cortisol 419 nmol/L (155–678). The determination of urine sulfonylurea was negative. IAA determination was done.

A treatment with fractionated diet and 200 g of iv glucose was established, with recurrence of hypoglycaemia and occasional postprandial hyperglycaemia episodes.

Complementary examinations were required to rule out insulinoma as the most frequent cause of endogenous hyperinsulism. Given her history, 3 bolus of 50 mg/day of prednisone i.v. were administered prior to the computed tomography with contrast, which was normal. The echoendoscopy described a 3 mm nodule in the pancreatic head, whose citological analysis (fine-needle aspiration [FNA]) was consistent with normal pancreas. Table 1 shows the results of the selective angiography with calcium stimulation. Finally, a diagnostic laparotomy was performed. Manual examination and intraoperative ultrasound scan of the pancreas were normal; thus, only an extended biopsy was performed. After the intervention, the blood sugar levels were normalised and gave place to the progressive withdrawal of i.v. glucose contribution.

The received results of the IAAs (RIA) were 85.8% (normal: <8.20%). In a new targeted history, ALA intake (200 mg/day) as nutritional supplement (to prevent hair loss) during 15 days was discovered. The histological result showed hyperplasia of the pancreatic islets affecting approximately 10% of them and with insulin predominant expression. At the moment of discharge, the patient did not show new episodes of hypoglycaemia and insulinoma was normalised. After one year, the IAA levels have decreased without reaching normalisation. Corticosteroids as preparation for the radiological techniques were the only immunomodulator treatment administered.

The IAS, first described by Hirata in 1970, is a rare cause of hypoglycaemia, except in Japan where it constitutes the third cause. The cases described in Caucasian population are scarce. It affects patients aged between 40 and 80 years old, with no difference in gender. It is associated to autoimmune diseases (related to HLA-DRB1*0406 and HLA-DRB1*0403) such as systemic lupus erythematous (SLE), among others, and to the use of drugs with sulfhydryl groups (e.g., methimazole). The histopathology is barely known; the hypothesis is that the activity reducing the sulfhydryl group causes the rupture of the insulin disulphide bridges, exposing it to the cells that carry the antigen. Hypoglycaemia is the consequence of the dissociation of insulin and the IAAs, which occurs asynchronously with blood sugar levels. Insulinemia is higher than expected for an insulinoma, generally over 1000 pmol/L. Little data has been reported about the histology of these cases, and they are about cells hyperplasia. In 80% of the cases, the symptoms are resolved in weeks. The treatment includes a diet fractionated in carbohydrates as first line, discontinuation of any medication associated to IAS and glucocorticoids (prednisone 30–60 mg/day). Plasmapheresis and other treatments have demonstrated different results.

The ALA is an antioxidant with sulfhydryl groups. In 2004, it was approved as nutritional supplement and it is widely used nowadays. Seventeen cases of IAS related to the ALA have been described in Japan, and recently 7 cases were reported in the Caucasian population. IAS was our definitive diagnosis considering the presence of hypoglycaemia with occasional episodes of postprandial hyperglycaemia, very high levels of insulinemia and positive IAAs, selective arteriography with increased levels.

Table 1

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