Insulinoma Presenting with Neuropsychiatric Symptoms

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Abstract
An insulinoma is a rare pancreatic endocrine tumor which is typically a hypervascular, solitary small tumour. 90% of tumors are benign and less than 2 cm in size. Some insulinomas are associated with MEN-1 syndrome. Some cases of insulinoma may present with neuropsychiatric symptoms and may be wrongly diagnosed as psychosis. We report a case of insulinoma in a 55 years old female who presented with episodes of abnormal behavior and altered sensorium. On detailed investigations she was diagnosed as a case of hyperinsulinemic hypoglycemia due to insulinoma (in her case MRI abdomen was normal) DOTANOC PET CT confirmed the insulinoma in body/tail of pancreas.

Introduction
Pancreatic endocrine tumors are rare lesion, with a reported incidence of four cases per 1 million patient-yr.1 Insulinomas are the most common pancreatic endocrine tumors. The majority of patients diagnosed with an insulinoma are between 30 and 60 years of age, with women accounting for around 60% cases.2,3 Insulinomas causes predominantly fasting hypoglycaemia due to excessive secretion of insulin. Patient may present with neuropsychiatric symptoms and may be wrongly diagnosed and treated as a neuropsychiatric illness. We report a case of patient of insulinoma who was misdiagnosed as psychotic disorder and treated with antipsychotic drugs for several months.

Case Report
A 55-year-old female presented in emergency department with complaints of altered behavior and decreased sensorium on and off since two years. In emergency department on investigation blood glucose was found to be 36 mg/dl. After glucose infusion (100 ml of 25%) Dextrose she regained consciousness. She was admitted in ward for evaluation. She gave history of altered behavior on and off since two years for which she was taking antipsychotic treatment from a private practitioner. These episodes were associated with tremors, anxiety, palpitations and diaphoresis. Symptoms mainly occurred in prolonged fasting state. These symptoms improved after eating some sweets. However, these episodes gradually increased in frequency. She noticed weight gain of 7-8 kg since her illness. There were no history of chest pain, dyspnea, involuntary movements of body, frothing from mouth, tongue bite, urinary incontinence, renal calculus, galactorhea, jaundice, facial puffiness. There were no history suggestive of insulin or oral hypoglycemc drug intake. Pulse rate of 114/min and blood pressure of 134/86 mm of Hg was noted. Patient was kept fasting in ward and blood glucose was monitored hourly. Patient developed symptoms of sympathetic overactivity and blood glucose was found to be 32 mg/dl. At the same time blood sample was taken and sent for laboratory evaluation. She was given intravenous dextrose and patient improved symptomatically within 5 minutes. Laboratory evaluation showed low plasma glucose of <40 mg/dl, insulin of 14.00 µU/ml (for insulinoma it should be greater than 3 µU/ml at the time of hypoglycemia), C-peptide of 3.88 ng/ml (for insulinoma it should be greater than 0.6 ng/ml at the time of hypoglycemia). Her insulin antibody was normal at 4.32 units/ml (normal range<=12 units/ml). Plasma thyroid-stimulating hormone and insulin-like growth factor-1 and insulin like growth factor BP3 levels were all within normal ranges. Serum cortisol was 12.89 mcg/dl (normal range, 4-22 mcg/dl). USG abdomen revealed no abnormality. CT brain was normal. MRI abdomen showed no evidence of pancreatic abnormality. In strong suspicion of insulinoma DOTANOC whole body PET-CT study was done in which abdomen and pelvis area showed focal increased tracer uptake in the region of body/tail of pancreas, measuring 1.2 x 1.1 cm without any associated CT changes (Figure 1). These scan evidence of somatostatin expressing pathology in the body/tail of pancreas consistent with insulinoma. With all these investigations, hypoglycemia due to insulinoma was established as the cause of neuropsychiatric illness.

She underwent segmental resection of the tumor (Figure 2) which was confirmed to be an insulinoma an histopathology examination (Figure 3). She is now asymptomatic.

Discussion
Hypoglycemia is a common medical emergency. Hypoglycemia is defined by Whipple’s criteria consisting of central nervous system symptoms of neuroglycopenia, a simultaneous low blood glucose level and improvement of these symptoms by intake of glucose. Drugs are the most common causes of hypoglycemia mainly insulin and insulin secretagogues. Other causes of hypoglycemia includes alcohol, severe liver and kidney disease, starvation. Hypoglycemia due to hyperinsulinism is found in patients with insulinoma, insulin hyperplasia and insulin autoimmune hypoglycemia. Signs and symptoms

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of hypoglycaemia are diaphoresis, warmth, hunger, weakness, tingling sensations, paraesthesia, difficulty in thinking, confusion, shaking, tiredness, drowsiness palpitations, tachycardia, faintness, dizziness, nervousness, anxiety, difficulty in speaking, blurred vision, seizure, stupor or coma. Misdiagnosis of insulinoma is common. There are some case reports of insulinoma who presented with behavioral abnormalities and psychiatric manifestations. Insulinoma is diagnosed with insulin concentrations of at least 3 µU/ml (18 pmol/l), c-peptide concentrations of at least 0.6 ng/ml (0.2 nmol/l) when the fasting glucose concentrations are below 55 mg/dl without detectable oral hypoglycemic agents levels and no circulating insulin antibodies. After clinical and biochemical investigations non invasive procedures to localize the tumour should be used. Conventional imaging studies such as ultrasonography, CT, and MRI fail to detect the majority of insulinomas due to small size of tumours. Portal vein sampling and intra-arterial stimulation of insulin secretion with calcium is a useful technique to detect almost all insulinomas but they are invasive and complicated techniques. Intraoperative ultrasonography (IOUS) alone identifies approximately 95% of tumours. In our case, 68Ga-DOTANOC PET/CT correctly detected an insulinoma with high expression of SSTR2, which was missed by MRI abdomen. Combined functional imaging using different PET radiopharmaceuticals could be a useful diagnostic strategy to detect insulinomas.

Surgical removal through enucleation or segmental resection is the treatment of choice. The target is to remove the tumor while preserving as much as normal pancreas. Surgery may be curative in 75% to 98% of patients.

Medical treatment with diazoxide, octreotide or verapamil can be used in patients who are not good candidates for surgery, with metastatic disease or who refuses surgery.

Conclusion

Neuropsychiatric presentation can often mislead the diagnosis in insulinomas. We should be aware of such red-herrings.

References