

A Case of Insulinoma with Neuropsychiatric Symptoms and Cerebral Infarction

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Abstract

Insulinoma is one of the most common neuro-endocrine tumors of the pancreas. Some cases with insulinoma present with neuropsychiatric symptoms and are often misdiagnosed as psychosis so patients may remain symptomatic from one week to as long as several decades before diagnosis. We present a case who presented in our hospital with episodic abnormal behavior and seizures 7 years ago. Further investigations proved her to be a case of insulinoma. Nucleation of the tumor was done following which the patient was relieved of symptoms for 3 years after which the symptoms relapsed and admitted with coma and stroke. Her biochemical profile revealed fasting blood glucose of 25 mg/dl. Unfortunately, insulinoma may be so small and diffuse throughout the pancreas that they are not apparent to the surgeon and it is important to realize that blood glucose levels often start to fall within a few months even following successful surgery.

INTRODUCTION

Hypoglycemia is low blood sugar that could cause by pancreatic tumors called insulinomas or islet cell tumors. The incidence is 1–4 per million (1). While these tumors are usually benign, they produce large amounts of insulin, which lowers blood glucose levels. This is the opposite of the diabetes mellitus in which low insulin levels lead to hyperglycemia. Insulinomas present with the neuroglycopenic and sympathoadrenal symptoms induced by hypoglycemia (2). Recurrent confusional states are typical of insulinoma. Other symptoms include visual changes, unusual behavior, palpitations, diaphoresis, and tremulousness (3).

Some cases with insulinoma present with neuropsychiatric symptoms and are often misdiagnosed as psychosis (4). In one study, as many as 20% of patients had been misdiagnosed with a psychiatric, seizure, or other neurological disorder before the true diagnosis of insulinoma was made (5). Insulinomas are frequently a recurring problem. Fasting hypoglycemia in the insulinoma patients is usually due to suppression of glucose production and acceleration of glucose utilization, as is widely thought (6).

Insulinoma diagnostic tests are: during a monitored 72 hours fasting: low blood glucose, high serum insulin level and high C-peptide level. A serum insulin concentration of $\geq 6 \mu\text{U/ml}$ in the presence of glucose concentration of $< 45 \text{ mg/dl}$

indicates inappropriate secretion of insulin, consistent with insulinoma. CT scan or MRI of the abdomen to look for a pancreatic tumors and Octreotide scan to look for pancreatic tumors (when CT or MRI scan is unrevealing) are another tests. Also when CT and MRI are not successful, pancreatic arteriography or pancreatic venous sampling with calcium stimulation for insulin could be recommended. According to Besim, endoscopic pancreatic ultrasonography has promising results and may replace invasive angiographic studies in the future (7).

Treatment recommendations for insulinomas may vary, but insulinomas initially are best treated by surgical exploration and removal if possible. This allows definite diagnosis, and it provides the veterinarian with an opportunity to remove any obvious pancreatic masses. Insulinomas may occur singly or as groups of small tumors. Unfortunately, these tumors may be so small and diffuse throughout the pancreas that they are not apparent to the surgeon.

Here we report our practice with a case of insulinoma who presented with neuropsychological disorders and stroke.

CASE REPORT

In November 2004, a 42-year-old woman presented to our hospital emergency center with loss of consciousness. Her admission laboratory values were significant for a glucose level of 25 mg/dl. After glucose infusion (50 ml of 50%) the

level of consciousness became better and she was only lethargic. The patient was subsequently admitted to the hospital for further work up.

Six years ago she admitted in our hospital because of recurrent seizure like attacks in the form of convulsive (tonic-clonic seizures) and also non-convulsive confusional states. Because of some other psychiatric symptoms like depressive complaints and also some psychotic behaviors the attacks was diagnosed as pseudoseizure and she admitted in psychiatry department with initial diagnosis of manic-depressive disorder. The episodes were occurring typically in the morning, just after waking. Over the 8–10 months before presentation, the patient noted that the episodes were increasing in frequency as well as occurring throughout the day. The biochemical examinations in fasting frequently showed hypoglycemia. During 72 hours fasting test, the serum glucose level was 20 mg/dl after 12 hours fasting and the serum insulin level was 10.5 μ u/ml, then CT study of pancreas was done and showed tumor in pancreas tissue (fig 1). All findings were compatible with diagnosis of insulinoma. Surgery was done in 1998 and symptoms significantly reduced for 3 years.

Figure 1

Figure 1: Dynamic enhanced CT scan shows a round well defined enhanced lesion in pancreas



In recent years the hypoglycemic attacks occurred frequently in the form of recurrent loss of consciousness that were responding to glucose infusions. On examination she was found to be a cachectic woman in mild distress. Her vital signs were significant only for mild tachycardia. Her physical examination showed a 3/5 murmur in cardiac auscultation. Neurological examination in this stage showed severe right hemiplegia and global aphasia. Brain CT scan showed a hypodense area with moderate edema due to arterial infarction in the territory of left middle cerebral

artery (fig 1).

Figure 2

Figure 2: Head CT scan of patient in recent admission.



The patient had frequent attacks of loss of consciousness and seizure during hypoglycemic periods. According to patient's clinical state (severe cerebral infarction) and clear history of documented hypoglycemic attacks, we didn't perform 72 hour fasting test in this admission. In echocardiography there was left ventricular systolic dysfunction with an ejection fraction of about 25-30%. There was no evidence of vegetation on valve leaflets or gross valvular disorder. The ECG showed some ischemic changes and left bundle branch block. Other test results were as following: Antinuclear Antibody: negative; antiphospholipid and anticardiolipin: normal range; protein C and protein S: normal levels, and erythrocyte sedimentation rate: normal range. Patient discharged in 29 November 2004 with diazoxide and phenytoin prescription but unfortunately the patient died in home because of poor care and aspiration pneumonia.

DISCUSSION

Misdiagnosis of insulinoma is common and to make a diagnosis of insulinoma, the physician must consider it. There are numerous reports of cases of insulinoma who presented with behavioral abnormalities and psychiatric manifestations (8). Nakamura et al. reported a case of insulinoma masquerading as hysteria. She was a 28-yr-old

woman presented with substupor, mutism, mannerism, restlessness, and incoherence (4). Saleemah reported a case with a 10-year history of episodic confusion and somnolence (9). Also in our case there was a significant time between the first symptoms and definite diagnosis. There are Lessons to be learned and Insulinoma should be suspected in all patients who present with symptoms of neurological (recurrent seizures, especially when multiple and without response to anticonvulsive drugs) and psychiatric symptoms with a fluctuating course and psychotic attacks.

It is important to realize that blood glucose levels often start to fall within a few months even following successful surgery. This may be due to multiple small tumors in pancreas. Expertly performed intraoperative ultrasonography assists in tumor localization and in delineating important related anatomy and has become virtually routine in the some center's surgical practice (10). Insulinomas are typically benign, single, and small, and are generally firmer than surrounding normal pancreas. Extensive surgical exposure may be required to identify and safely remove the tumor. Enucleation is preferred by some author, but distal pancreatectomy for tumors in the body or tail is an excellent method as well. Tumors in the head of the pancreas are usually enucleated, and pancreatoduodenectomy is rarely performed.

Management of patients with biochemical evidence of insulinoma and negative preoperative imaging studies (occult) tumors is controversial, varying from primarily medical management to aggressive, blind nearly total pancreatectomy to extirpate the tumor. Some authors used portal venous sampling to localization of the insulinomas. Intraoperative ultrasound (IOUS) is the single best method to identify occult tumors because it correctly identifies most insulinomas that are pancreatic head tumors that are not palpable. The results support the strategy of preoperative PVS and operation with IOUS to localize and remove insulinoma in patients with occult tumors. Morbid blind pancreatic resections are no longer indicated and long-term medical management of hypoglycemia should be reserved for the occasional patient who fails preoperative PVS and operation guided by IOUS (11). Recently Reynolds has recommended the combination of calcium infusion localization and a minimally invasive surgical procedure as an efficient management approach in the diagnosis and treatment of insulinoma (12).

There are some reports of Insulinomas accompanied other

medical conditions. Peripheral neuropathy (13), renal failure (14), pregnancy (15), diabetes mellitus (16) and tuberous sclerosis (17) had reported with insulinoma. In our case there were some medical conditions as heart failure, stroke and a history of obstructive uropathy. Control of blood sugar levels can be achieved by frequent small meals which are high in protein and complex carbohydrates, but low in simple sugars. For patients who are not good surgical candidates, who refuse surgery, or whose insulinoma was missed during surgery, as well as for patients with metastatic disease, medical therapy should be attempted. The goal of medical therapy is to prevent symptomatic hypoglycemia. Medications that have been used for this purpose include diazoxide, verapamil, phenytoin, and octreotide. Diazoxide diminishes insulin secretion and is the most effective drug for controlling hypoglycemia. Octreotide, the somatostatin analog, is also a common treatment for patients with unresectable tumors (9).

There are some reports of sudden focal neurological abnormalities in the course of insulinoma. Two different mechanisms have been suggested as the causes of hypoglycemia-related stroke like episodes. First, the brain uses glucose predominantly for oxidative metabolism. Different brain regions have different metabolic demands. The need for glucose is highest in the cerebral cortex and basal ganglia. The cerebellum and the subcortical white matter have less demand for this substrate. Focal deficits may be a result of asymmetric distribution of glucose transporters. Also, Gold and Marshall suggest that coagulation defects may be the cause of stroke like episodes (18). Although in our case the heart was a certain cause of emboli to brain.

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