CASE REPORT

A Case Report of Insulinoma Treated for Refractory Seizures

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ABSTRACT

Insulinoma is a functional endocrine tumor of the pancreas that secretes insulin. Insulinoma comprises 25% of the pancreatic endocrine tumors. Patients may have heterogeneous presentation of symptoms varying from mild autonomic symptoms to severe hypoglycemic episodes. Sometimes, insulinoma may present with neuropsychiatric symptoms which can be mistaken for seizure disorder or dissociative disorder. Careful evaluation of the patient with such symptoms is advised to avoid delay in diagnosis of Insulinoma. Here, we are reporting a case who presented with episodic confusional state of 7 years' duration that was misdiagnosed as refractory seizures. On further evaluation and monitoring, he was diagnosed with insulinoma, the details of which are elaborated in this case report.

KEY WORDS: Dissociative disorder, insulinoma, pancreatic tumors, refractory seizures.

Introduction

Pancreatic endocrine tumors are classified, according to the symptomatology, as secreting and non-secreting tumors. The non-secreting tumors (silent, in hormonal terms) represent about 50% of the total; they are followed by insulinomas - 25% and gastrinomas - 15%.[1,2] Insulinoma is a functional neuroendocrine tumor of the pancreas that secretes insulin. The incidence is 1–4/million.[3] It presents with a variety of symptoms, which includes adrenergic symptoms such as palpitations, tremor, anxiety, warmth, and dry mouth and cholinergic symptoms comprising of hunger, sweating, and paraesthesia's.[4] In a retrospective study of 59 patients with histologically confirmed islet cell adenomas, it was found that 39% of these patients were originally diagnosed with a seizure disorder.[5] A patient diagnosed to have seizure disorder has been described in a very few cases of persistent hypoglycemia later on diagnosed as insulinoma two of them reported by Akanji *et al*. in 1992 followed by Bazil and Pack in 2001.[6,7] The median age of diagnosis of insulinoma is 47 years. Many of the patients present with neuropsychiatric manifestations and are misdiagnosed as either dissociative disorder or seizure disorder. The present case is reported for its rarity and the diagnostic dilemma with which it presented.

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Case Report

Mr. K, a 47-year-old school teacher, from a middle socioeconomic status Hindu family of rural background reported to the hospital with a history suggestive of episodic confusional state of 7 years' duration. The patient was referred to the Department of Psychiatry due to the uncharacteristic nature of the symptoms and duration of the illness to rule out dissociative disorder. On detailed evaluation, the patient and his wife gave a history suggestive of difficulty in getting up in the morning associated with confusion and unresponsiveness during the episode. The patient informed that he is able to hear everyone around him but is not able to give a response. These episodes were also associated with excessive sweating and were present on most occasions in the early morning hours. The patient was on treatment with tablet phenytoin 200 mg 0-0-1, and from the treatment records, it was found that he was on treatment for refractory seizures from the past 7 years and had been tried on many antiepileptics with minimal response. There was no history of any other medical comorbidities and no family history of any psychiatric illness. The

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patient had been admitted to multiple hospitals for similar complaints, and investigations such as electroencephalogram (EEG), computed tomography (CT) scan of the brain, and magnetic resonance imaging (MRI) of the brain had not picked up any abnormality.

The patient was admitted for further evaluation. Complete blood picture, liver function tests, and random blood sugar level were done and found to be normal. On evaluation of psychosocial factors, stressors at the work place due to recent change of position and added responsibilities at work were reported by the patient and a tentative diagnosis of dissociative disorder was made keeping in mind the uncharacteristic presentation, temporal relation with a stressor, and lack of evidence of a physical disorder that might explain the symptoms.

On the day 2 of admission, the nursing staff was instructed to monitor capillary blood glucose (CBG) level during the episode in the morning hours. On day 1, CBG level was found to be 18 mg/dl, following which an intravenous fluid Domain Name Server (DNS) was administered with significant improvement of the symptoms. The same was repeated on the next day with CBG level of 22 mg/dl and improvement of symptoms following DNS administration.

The patient was referred to endocrinologist for further evaluation. Fasting serum insulin and C-peptide levels were advised and found to be 57.22 mIU/L (n < 25 mIU/L) and 6.11 ng/ml (n - 0.8–3.1 ng/ml), respectively. CT scan abdomen was done which showed 1.7*1.3 cm intensely enhancing isodense pancreatic mass in the body and tail junction suggestive of islet cell tumor in the pancreas. The patient was advised surgical intervention for the removal of the tumor and distal pancreatectomy and splenectomy were performed, following which the biopsy done revealed a well-differentiated neuroendocrine tumor (Grade-1) with vascular invasion.

Following the surgery, the symptoms of episodic confusional state stopped, and fasting serum insulin and C-peptide levels were 11.02 mIU/L and 1.77 ng/ml, respectively. The patient has been maintaining well on further follow-ups.

Discussion

Insulinoma is the most common neuroendocrine tumor of the pancreas. Insulinoma is characterized clinically by the Whipple's triad:

1. Low blood glucose level (40–50 mg/dl);
2. Symptoms of hypoglycemia (confusion, anxiety, stupor, convulsions, and coma); and
3. Dramatic reversal of central nervous system abnormalities by glucose administration.

Symptoms may be present from 1 week to as long as several decades before the diagnosis (1 month to 30 years, median 24 months, as found in a large series of 59 reports).[5] Hypoglycemic symptoms start as the blood glucose falls to approximately 50–55 mg/dL (2.8–3.1 mmol/L), which include slurred speech, blurred vision, confusion, drowsiness, and difficulty in concentrating.[8] These symptoms are confusing and can be easily misdiagnosed as seizures. However, in this patient, seizure disorder appeared unlikely due to (1) clinical observation during the episodes when admitted, (2) duration of the episodes, (3) no EEG abnormalities, (4) persistence of episodes even with antiepileptics for a long duration, and (5) trial of various anti-epileptics. Other conditions such as panic attacks and postural hypotension can also mimic this condition and should be kept in mind for detailed evaluation. However, these conditions were ruled out in this patient.

The diagnosis of insulinoma is usually done by the estimation of fasting plasma insulin and C-peptide levels and insulin:glucose ratio. Imaging techniques such as CT, MRI, and ultrasonography lack sensitivity but are useful. Imaging procedures such as selective pancreatic arteriography with calcium stimulation can help in localization of tumor.[9] Surgery is the most effective treatment for insulinoma.[10] Medical therapy is limited to diazoxide, calcium channel blockers, dilantin, and somatostatin.[11]

Conclusion

Insulinoma should be kept in mind when dealing with refractory seizures and also the patients who come with a history of episodic confusional state. Once the patient is diagnosed with refractory seizure disorder, the patient receives aggressive pharmacotherapy, although some of these patients do not have epilepsy. The presentation with neuropsychiatric manifestations further adds to the confusion. Insulinoma should be thought of in patients presenting with the above-mentioned complaints. Misdiagnosis and delayed diagnosis of insulinoma are common, which leads to increased patient morbidity. This case highlights the need of careful evaluation of patients presenting with refractory seizure disorder or dissociative states not

responding to antiepileptic treatment and evaluate for insulinoma whenever the need arises.

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