Recurrent Seizures Due to Pancreatic Insulinoma

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Abstract
We present the case of a 70 year old man who was admitted with history of generalized tonic clonic seizures on and off since 6 years in spite of being on regular therapy with anticonvulsants. Patient was found to have hypoglycemia and was evaluated for same. He was diagnosed to have endogenous hyperinsulinemia due to pancreatic insulinoma. Patient underwent enucleation of tumor and was relieved of his symptoms.

Introduction
Recurrent seizures can often arise due to underlying metabolic disturbance. Herein, we report a case of insulinoma presenting with recurrent seizures due to hypoglycemic spells.

Case Report
A 70 year old man presented with generalized tonic clonic seizures since 6 years. He had history of dizziness and sweating prior to the convulsion which would occur mainly in mornings and before meals. On enquiry, patient reported relief from symptoms after meals. He has been started on Phenytoin (100 mg thrice daily) tds by a private physician. He had stopped phenytoin on his own and continued to have seizures. Patient had no history of diabetes mellitus, no significant medical or surgical illness in past and no family history of similar illness and denied addiction. On examination patient was well built (BMI-29.9) higher mental functions were normal, pulse was 80/min, BP was 130/80 mm of Hg. Systemic examination was within normal limits. His complete blood count, liver profile, creatinine and electrolytes were normal. However, his random blood sugar was 28 mg/dl. CT-brain and EEG was normal. In view of patient’s blood sugar level of 28 mg/dl, we decided to find cause of hypoglycemia. His serum insulin level was 6.83 μIU/L and C-peptide level was 2.1 ng/ml during the seizure episode. The HbA1c was found to be <4 gm%. In the hospital, he needed regular infusion of dextrose for hypoglycemia prevention. CT abdomen triple phase contrast demonstrated a 1.7 cm enhancing mass at head-neck junction of pancreas (Figure 1). Contrast-enhanced USG abdomen was performed to augment the CT findings and it showed an ill-defined 9 mm × 7 mm hypoechoic nodule at head-neck junction of pancreas. In lieu of these findings, patient was diagnosed to have pancreatic insulinoma with hypoglycemic seizures. Further work-up for multiple endocrine neoplasia was negative. Serum AFP and PSA level were also normal. Patient underwent enucleation of the pancreatic nodule. An intra pancreatic mass measuring 2.5 cm × 2 cm (Figure 2) was removed and patient became asymptomatic and seizure free after that Tables 1 and 2 show pre and post-operative blood sugars. Histopathology report showed a well circumscribed mass composed of cell arranged in nets and sheets. Cells contained round nuclei and eosinophilic cytoplasm without any nuclear atypia or mitotic activity. Focal presence of papillae were seen. Mass was surrounded by fibrous condensation. Above Findings suggestive of well differentiated neuroendocrine tumor (Figure 3).

Discussion
Insulinomas are the most common cause of hypoglycemia related to endogenous hyperinsulinemia in adults.¹ It is a rare neuroendocrine pancreatic tumor. The estimated incidence is one case per 2,50,000 patient-years.² Median age at presentation is 5th decade in sporadic cases and 3rd decade in multiple endocrine neoplasia syndrome. It is typically sporadic, solitary and less than 2 cm in diameter. Ninety percent or more of all insulinomas are benign. Fewer than 5% of insulinomas are larger than 3 cm. Larger tumors are more likely to be malignant.

Hypoglycemia is clinically evident by Whipple’s triad (symptoms consistent with hypoglycemia, a low plasma glucose concentration, and relief of those symptoms when the plasma glucose concentration is raised). Our patient had typical triad. Symptoms of hypoglycemia can be divided into two categories, neuroglycopenic and neurogenic (autonomic) symptoms.³,⁴ Neuroglycopenic symptoms are the direct result of CNS neuronal glucose deprivation. They include behavioral changes, confusion, fatigue or weakness, visual changes, seizure, loss of consciousness, and, if hypoglycemia is severe and prolonged, death. Neurogenic symptoms are the

Table 1. Pre-operative Blood Sugar Levels

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<th>Time (h)</th>
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Table 2. Post-operative Blood Sugar Levels

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Blood Sugar (mg/dl)</th>
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<tbody>
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<td>90</td>
</tr>
<tr>
<td>1</td>
<td>60</td>
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<td>2</td>
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Fig. 1: CT abdomen showing a 1.7 cm enhancing mass at head-neck junction of pancreas (arrow)

Fig. 2: Excised intra-pancreatic mass measuring 2.5 cm × 2 cm

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result of the perception of physiologic changes caused by the sympathoadrenal discharge triggered by hypoglycemia. They include adrenergic symptoms such as palpitations, tremor, and anxiety and cholinergic symptoms such as sweating, hunger, and paresthesias. Our patient presented with both type of symptoms like recurrent seizures and sweating. Hypoglycemia is mostly seen after exercise and prolonged fasting. Our patient was overweight; this feature is present in approximately 25% of total cases of insulinoma and reason for the same is hyperalimentation due to hypoglycemic symptoms.

The criteria used at the Mayo clinic to diagnose endogenous hyperinsulinemic hypoglycemia is (1) fasting plasma glucose concentration less than 2.5 mmol/L (45 mg/dL) (2) immunochemiluminometric plasma insulin concentrations greater than 18 pmol/L (3 μU/mL) (3) C-peptide concentrations greater than 200 pmol/L (0.60 ng/mL), and (4) proinsulin greater than 5 pmol/L. Our patient satisfied three out of four criteria. Computed tomography can detect approximately 70% to 80% of insulinomas and magnetic resonance imaging can detect about 85%. Transabdominal ultrasound identifies many insulinomas and endoscopic ultrasound has a sensitivity of about 75%. Intraoperative palpation and ultrasound are the gold standards for localizing an insulinoma with a reported success rate of 96–100%.

Somatostatin receptor scintigraphy detects about 50% of patients only. Invasive procedures like selective pancreatic arterial calcium injection with the endpoint of sharp increase in hepatic venous insulin levels, recognizes insulinoma with high sensitivity but this invasive procedure is seldom necessary.

Surgery is the recommended therapy in insulinomas as the tumors are often solitary and related to benign adenomas. For small and benign characteristic adenomas enucleation is enough and distal pancreatectomy may be suitable for the lesions which are located on the corpus and on the tail of the pancreas. Distal pancreatectomy is suggested for the lesions which cannot be diagnosed by palpation and Intra operative USG. Total pancreatectomy is suggested for the malignant, multiple and large tumors. Recurrence after surgery are noted in with more cumulative 20 year frequency of 21% in patients with MEN compared to 7% in patient without. Medical treatment alone is advised when there is contraindication for surgery and in uncontrolled preoperative hypoglycemia. Streptozocin, Diazoxide, Verapamil, Phenytoin or somatostatin may be used for the medical management.

**Conclusion**

A high index of suspicion for a rare cause like insulinoma is warranted for patients presenting with intractable seizure, which is amenable to complete cure. The CT abdomen triple phase augmented along with contrast enhanced USG Abdomen has good sensitivity and specificity for detection of Insulinomas.

**Acknowledgements**

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**References**