A rare case of insulinoma presenting as cardiac arrest

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Abstract:
Insulinomas are rare neuroendocrine tumours of pancreas arising from the Islets of Langerhans cells with an incidence estimated at 1 to 4 new cases per million persons per year. Patients with insulinomas usually develop neuroglycopenic symptoms presenting as recurrent headache, lethargy, diplopia, and blurred vision, particularly with exercise or fasting. We report a case of a young female patient presenting with unwitnessed cardiac arrest later diagnosed as Insulinoma.

Keywords:
Cardiac arrest, coma, insulinoma

Insulinoma is a rare neuroendocrine tumor which is usually benign and solitary. The reported incidence varies from 1 to 4 per million persons per year. Insulinoma may present as a sporadic event in patients without an inherited syndrome or it can be part of multiple endocrine neoplasia type 1.

Hypoglycemic episodes caused by inappropriately elevated insulin levels characterized by neuroglycopenic symptoms are characteristic here. Neuroglycopenic and associated catecholaminergic symptoms vary in spectrum and severity. A delay in diagnosis is common due to the attribution of symptoms to psychiatric or neurologic diseases. Here, we describe a rare case of sporadic insulinoma presenting initially in a hypoglycemic coma and consequent hypoxic cardiac arrest.

Case Report
A 23-year old hospital staff nurse presented to the emergency with abdominal pain and vomiting for 3 days. Past history and family history were noncontributory. Clinical examination did not reveal anything specific. She was successfully managed symptomatically with a provisional diagnosis of acute gastroenteritis with antibiotics and intravenous fluids.

A day before her scheduled discharge from the hospital, she was discovered in cardiac arrest by the internal medicine trainee resident. Immediate cardiopulmonary resuscitation was initiated with a return of spontaneous circulation within 5 min. The patient was intubated and mechanical ventilation was initiated. Bedside blood glucose was <20 mg/dl and was treated with intravenous 25% dextrose. A provisional diagnosis of hypoglycemia of unknown duration and consequent hypoxic cardiac arrest was made. On attaining euglycemia, the patient was transferred to the intensive care unit (ICU) for postcardiac arrest care and mechanical ventilation. The neurological status on ICU admission was decorticated rigidity, sluggishly reacting pupils, bilateral mute plantar reflexes, and a Glasgow Coma Scale (GCS) of E2V1M3. Hemodynamic stability required dopamine infusion of 5–10 µg/kg/min.

Invasive vital parameter monitoring was initiated in the ICU along with hourly recording of blood sugars. Various differential diagnoses of secondary adrenal...
insufficiency, intracranial space-occupying lesion, sudden cardiac arrest due to intrinsic cardiac pathology, myocarditis, possible intoxication, seizure disorder, and other causes of hypoglycemia were considered. Hematology investigations, abdominal ultrasound, and plain computed tomography (CT) of the head were within the normal limits. The serum cortisol level was 854.9 U/mL (laboratory normal range: 171–536 U/mL), ruling out the possibility of adrenal insufficiency. Electrocardiography and echocardiography were also normal, excluding the possibility of sudden cardiac arrest syndromes and myocarditis. Chances of intoxication were ruled out from the history and absence of specific toxidromes. Electroencephalography showed diffuse beta activity with no epileptogenic focus.

During further stay in the ICU, multiple episodes of hypoglycemia were recorded and corrected by dextrose infusions. The diagnoses of autoimmune pancreatitis with insulin surges and insulin-secreting tumor were considered. Abdominal ultrasonography detected no abnormality. The serum lipase and amylase were within the acceptable range.

Further management was directed toward the possibility of insulin-secreting pancreatic tumor and a nesidioblastosis. A 128-slice biphasic contrast-enhanced CT of the abdomen detected an ill-defined hypodense lesion of 8 mm × 8 mm in the head of the pancreas [Figure 1]. The diagnosis of insulinoma was confirmed biochemically by a serum insulin level of 59.66 U/mL (laboratory normal range: 25 U/mL) and C-peptide of 6.5 U/mL (laboratory normal range: 4 U/mL).

Due to hypoxia sustained during the initial cardiac arrest, the patient’s GCS deteriorated to E1V1M1 over the next 7 days. A 3-tesla magnetic resonance imaging (MRI) of the brain showed diffuse T2/fluid-attenuated inversion recovery hyperintensity with diffusion restriction involving bilateral cerebral hemisphere, predominantly in the parieto-occipital region, suggestive of hypoxic insult associated with metabolic disorder [Figure 2].

In view of the anticipated prolonged mechanical ventilation, elective tracheostomy was done. Acinetobacter-related ventilator-associated pneumonia was diagnosed on the 10th day of mechanical ventilation and was treated with parenteral colistin and teicoplanin. Caspofungin was also administered on an empirical basis. Over the next 4 days, the patient developed septic shock requiring multiple ionotropes and diabetes insipidus requiring vasopressin. On the 14th day of the ICU stay, the patient’s GCS deteriorated to E1V1M1 (no eye opening and no motor response to a painful stimulus with endotracheal intubation for mechanical ventilation and) and she sustained a nonrevivable cardiac arrest on the 20th day.

**Discussion**

The importance of this case lies in the fact that insulinomas are rare tumors, and hypoxic cardiac arrest in this condition is reported more rarely.

“Whipple’s triad” stated as hypoglycemia and neuroglycopenic symptoms corrected by carbohydrate administration is a hallmark to the diagnosis of insulinoma. Exercise precipitates the symptoms but can also occur postprandially. Features of insulinoma and frequency of clinical symptoms vary widely with different neuroglycopenic (visual disturbances, altered mental status, abnormal behavior, amnesia, coma, seizures, or weakness) and adrenergic (sweating palpitations, tremors, or hyperphagia/obesity) mode of presentation. The diagnostic criteria for insulinoma include:
- Documentation of blood glucose level <50 mg/dl with hypoglycemic symptoms
• Relief of symptoms after eating
• Increased plasma insulin level (≥ 6 μU/ml)
• Increased C-peptide level (≥ 0.2 nmol/l)
• Increased proinsulin level (≥ 5 pmol/l)
• Absence of plasma sulfonylurea.

Various imaging modalities localize the lesion with different sensitivities and specificities. As virtually all sporadic insulinomas are small and intrapancreatic, localization fails 10%–27% of the time. The success rate of transabdominal ultrasound for localization varies widely across institutions from 9% to 66%. Multiphase helical CT localizes 50%–80%, MRI: 40%–70%, and stereotactic radiosurgery: 17% of all insulinomas. All of these imaging studies in concert can localize around 80% of the tumors. Transhepatic portal venous sampling,[6] intra-arterial calcium stimulation,[7,8] and endoscopic ultrasound[9] are more specific in localization of the tumor.

Apart from insulinoma, other differential diagnosis to be considered in cases of hyperinsulinemic hypoglycemia are transient hyperinsulinism, noninsulinoma pancreatogenic hypoglycemia syndrome or nesidioblastosis, congenital disorders of glycosylation, inherited fructose intolerance, exercise-induced hypoglycemia, glycogen storage diseases, defects of fatty acid oxidation, gluconeogenesis disorders, organic aciduria, biotin-responsive multiple carboxylase deficiency, respiratory chain defects, pancreatic β-cell K$_{ATP}$ channelopathies, mutations in the mitochondrial uncoupling protein 2 gene, and the Munchausen syndrome.[10]

Sporadic insulinomas are mostly amenable to cure by surgical resection. Medical management includes dietary modification and pharmacologic agents such as diazoxide, octreotide, lanreotide, propranolol, phenytoin, and verapamil.

A high index of suspicion toward insulinomas and noninsulinomatous hyperinsulinemic hypoglycemia syndromes in all young adults presenting with suggestive symptoms can provide early diagnosis amenable to cure in this potentially lethal condition.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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