Case Report

Hypoglycemic encephalopathy caused by insulinoma: A case report

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ABSTRACT

Hypoglycemic encephalopathy is a critical condition associated with a poor prognosis. Tumor-induced hypoglycemia is a rare clinical condition of hypoglycemia that occurs when a pancreatic islet beta-cell tumor insulinoma produces excessive insulin. We present the case of a non-diabetic 62-year-old woman with a 15-year history of recurrent fasting hypoglycemia, whose symptoms of weakness and giddiness would develop in the early mornings, prompting her to request sweetened tea and glucose cookies, after which her symptoms would improve. Investigations showed raised levels of insulin, C-peptide, pro-insulin, as well as a decreased value of beta-hydroxybutyrate and a negative screen for urine sulfonylureas. Computed tomography abdomen revealed a focal lesion in the body of the pancreas suggestive of insulinoma. Based on these investigations, a diagnosis of endogenous hyperinsulinism was made. This case emphasizes the importance of thorough history taking, attention, and observation in making a new diagnosis that has the potential to alter a patient's health care and alleviate clinical outcomes, where the patient ignored the symptoms for nearly 15 years, leading to the development of hypoglycemic encephalopathy.

Key words: Fasting hypoglycemia, Hypoglycemic encephalopathy, Insulinoma

Severe hypoglycemia is a common metabolic event in the emergency room. It has the potential to produce irreversible changes in awareness, cognitive decline, and death [1]. Coma/stupor with blood glucose levels <50 mg/dl on admission, the persistence of coma/stupor for more than 24 h after normalization of blood glucose levels, and exclusion of any other cause of coma/stupor are all signs of hypoglycemic encephalopathy [2]. Hypoglycemia is generally associated with endogenous hyperinsulinism due to insulinoma, nesidioblastosis, and insulin autoimmune hypoglycemia in otherwise healthy non-diabetic people. Other times, the cause of hypoglycemia in these people can be unintentional, covert, or malevolent [3]. We present a case of undetected atypical insulinoma presenting as hypoglycemia encephalopathy.

CASE REPORT

A 62-year-old woman reported with a history of altered sensorium and irregular movements of all four limbs for 12–15 days. History by relatives revealed that she had experienced frequent episodes of early morning weakness, inability to get up, and drowsiness for the past 15 years. Her relatives would give her sweet tea and glucose cookies, following which she would feel better, get up, and go to work. During these occasions, no reports were made, but she was investigated in between these episodes but no abnormalities were discovered.

At the time of admission, her capillary blood sugar level on the glucometer was 40 mg/dl and her venous blood glucose level was 38 mg/dl. She had hyperhidrosis, tachycardia, and her blood pressure was 110/70 mmHg in the right arm supine position with a mercury sphygmomanometer. She was irritable, disoriented, not obeying oral commands, and moving all four limbs spontaneously. The rest of the systemic examination did not reveal any positive findings. The patient was diagnosed to have hypoglycemic encephalopathy with generalized tonic–clonic convulsions and started on treatment immediately.

Her routine blood parameters were within the normal range for liver and renal function tests. The serum glutamic-oxaloacetic transaminase was 39.2 U/L (0–40 U/L) and serum glutamic-pyruvic transaminase was 32.1 U/L (0–40 U/L). The serum creatinine was 0.77 mg/dL (0.5–1.50 mg/dL). Her venous blood glucose on admission was 38 mg/dL. She had glycated hemoglobin of 3.94% (4–5.7%). Her serum 8.00 am cortisol was 14.7 mcg/dl (6–23 mcg/dl). Her beta-hydroxybutyrate levels were low, whereas, her serum insulin, pro-insulin, and C-peptide levels were high. Antibodies to insulin were found to be negative in her blood (Table 1).

Contrast-enhanced computed tomography (CT) brain showed generalized prominence of the bilateral ventricular system, basal

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Table 1: Endogenous hyperinsulinism

Parameter	Observed value	Endogenous hyperinsulinism
Insulin (μU/mL)	120	≥3
Pro-insulin (pmol/L)	10.1	≥5
C-peptide (ng/mL)	12.84	≥0.2
Beta-hydroxybutyrate (mmol/L)	0.9	≤2.7
Urine screen for oral antidiabetic agents	Negative	Negative
Insulin antibody	Negative	Negative

cisterns, and cortical sulci suggestive of generalized cerebral atrophy and chronic small vessel ischemic changes. The CT scan of the abdomen showed a well-defined lobulated hypodense lesion of size 1.5 × 2.4 × 1.4 (AP × TRA × CC) focal lesion in the body of the pancreas. It shows diffuse contrast enhancement predominantly arterial phase and shows a small focus of central calcification within (Fig. 1). In view of the history of hypoglycemic episodes, this most likely represents an insulinoma.

Continuous blood glucose monitoring, intravenous glucose utilizing 25% and 5% dextrose, injection octreotide 6 h, anti-epileptics, and wide-spectrum antibiotics were used to stabilize the patient in the medical intensive care unit. Corn starch meals (30–50 g) were also given to her through a Ryles tube. The patient declined surgery and was prescribed T. diazoxide 150 mgs (25 mg 2 tablet TDS) as well as dietary changes.

DISCUSSION

Hypoglycemic encephalopathy is a condition with a wide range of clinical outcomes, ranging from totally reversible neurologic impairments to irreversible coma [4,5]. Hypoglycemic symptoms caused by the tumor's excessive and uncontrolled insulin secretion are most common in the fasting state (73%); however, they can also be present solely in the postprandial state (6%), or both fasting and postprandial phases (3%) [6].

Insulinoma symptoms might appear anywhere from a week to several decades before a diagnosis is made. In a large series of 59 patients, the median age was 24 months and the range was 1 month–30 years [7]. Our patient had symptoms of hypoglycemia for about 15 years, which were either neglected or not thoroughly investigated, resulting in hypoglycemic encephalopathy. The hypoglycemia attacks are episodically attributed to the tumor's intermittent insulin secretion [8]. Diaphoresis, tremor, and palpitations are common autonomic signs of an insulinoma, whereas, confusion, behavioral abnormalities, visual problems, seizure, and coma are neuroglycopenic signs [9]. Our patient presented with neuroglycopenic signs.

The classic diagnosis of insulinoma is based on meeting Whipple's triad criteria, which remain the cornerstone of the screening process; hypoglycemia (plasma glucose <50 mg/dl); neuroglycopenic symptoms; and fast symptom alleviation after glucose administration [10]. The gold standard for biochemical diagnosis in individuals with symptoms of neuroglycopenia

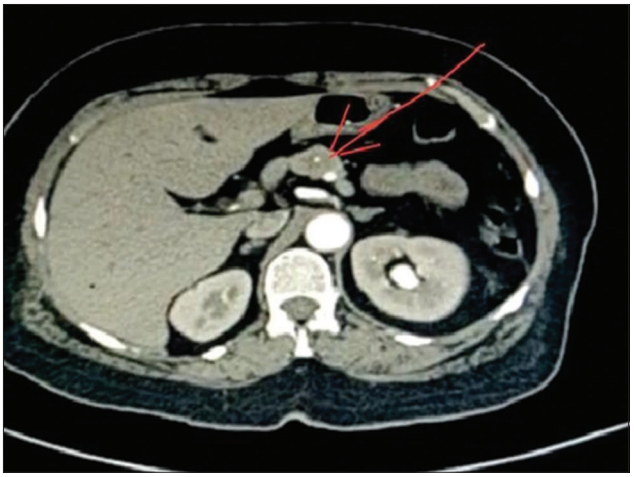

Figure 1: Insulinoma: Arterial phase and shows a small focus of central calcification

or verified low blood glucose levels is 72 h measurements of plasma glucose, insulin, C-peptide, and pro-insulin. Up to 99% of insulinomas can be detected using this extended fasting test [11]. Despite the fact that we were unable to perform the gold standard fast test in our patient, the results of the blood investigations revealed low blood glucose, elevated insulin, C-peptide, and pro-insulin levels, as well as a negative screen for beta-hydroxybutyrate and sulfonylureas all of which were suggestive of an insulinoma. Anti-insulin antibodies were negative. It's vital to note that the majority of tumors are intrapancreatic, 90% are solitary, 90% are <2 cm in diameter, and tumors are evenly distributed throughout the pancreas' head, body, and tail [12]. The quality of CT has improved in recent years, with a recent study reporting that a multidetector CT was able to visualize 94.4% of insulinomas [13].

Insulinomas are typically hypervascular, and as a result, show greater enhancement during the capillary and arterial phases of contrast bolus than normal pancreatic parenchyma [14]. The index patient had a well-defined lobulated hypodense lesion in the body of the pancreas, showing diffuse contrast enhancement predominantly in the arterial phase and showed a small focus of central calcification within. Intravenous glucose, octreotide injections, and continuous glucose monitoring were used to treat the patient.

CONCLUSION

Insulinomas are the most frequent pancreatic neuroendocrine tumors, and they produce hypoglycemia due to endogenous hyperinsulinism. Insulinomas are benign tumors that are often tiny, well encapsulated, and solitary. In this case, the diagnosis was delayed, and the patient developed hypoglycemia encephalopathy; therefore, a high level of suspicion and early diagnosis will protect the patient from potentially fatal consequences.

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