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Case Report

Refractory Hypoglycemia in Non-Diabetic Patient: A Case Report

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Abstract: Refractory hypoglycemia in non-diabetic patients is a rare condition characterized by low blood glucose levels (< 70 mg/dL) that do not respond to the conventional treatment. It can be caused by serious underlying issues such as liver failure, adrenal insufficiency, insulin-secreting tumors, or sepsis. This form of hypoglycemia requires rapid interventions to avoid severe neurological complications. Management involves addressing the underlying cause and providing supportive measures such as glucose infusion or pharmacological agents like glucocorticoids or diazoxide. A multidisciplinary approach and early identification are key to improving the prognosis of affected patients.

Keywords: Refractory Hypoglycemia, Insulin, C-Peptide, Insulinoma.

INTRODUCTION

Refractory hypoglycemia in non-diabetic patients is a rare and challenging clinical condition, characterized by persistently low blood glucose levels (< 70 mg/dL) that do not respond to conventional therapeutic interventions [1]. Unlike hypoglycemia in diabetic patients, which is usually related to improper insulin management of hypoglycemic medications, refractory hypoglycemia in non-diabetic individuals can be secondary to various underlying causes, such as insulin-secreting tumors (insulinomas), liver failure, adrenal insufficiency, or sepsis [2]. Diagnosing and treating this condition requires a multidisciplinary approach that includes identifying the specific etiology, continuous glucose monitoring, and the administration of specific treatments such as glucagon or intravenous dextrose solutions [3]. Recent literature emphasizes the need for personalized management based on the underlying cause and highlights the clinical challenge these cases pose in terms of diagnosis and treatment.

CASE PRESENTATION

A 67-year-old female with a history of primary hypothyroidism under treatment, severe chronic gastropathy, and depression. presented sudden blurred vision onset, distal muscle weakness, fine hand tremors, excessive hunger, and thirst, improving after food intake.

The condition began in February 2024 with a sudden decrease in visual acuity, along with fatigue, lack of energy, and peripheral muscle weakness. Later, the patient developed fine tremors and irritability, which improved temporarily after eating. Two hours later, the symptoms returned, prompting her to seek medical attention, where a capillary blood glucose level of 38 mg/dL was documented. Symptoms resolved after glucose was administered, and the patient was

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discharged with outpatient monitoring of capillary blood glucose. For one week, glucose levels were recorded between 35 and 50 mg/dL, improving after food intake.

She went to the emergency department, where a serum glucose level of 59 mg/dL was confirmed, and parenteral dextrose solutions were initiated, though hypoglycemia persisted. The patient was admitted to internal medicine, where steroid treatment was started. A fasting test was performed, during which the patient presented with symptoms of sweating, distal tremor, headache, and insomnia, with a capillary glucose level of 49 mg/dL. Laboratory tests showed a central glucose level of 51 mg/dL, insulin of 8.1, and C-peptide of 2.79 ng/dL (reference range: 0.5 - 2 ng/dL), findings consistent with endogenous hyperinsulinism.

The evaluation was completed with an abdominal CT scan, which reported simple liver cysts in segment 8, simple cysts in the right kidney, and no evident pancreatic abnormalities on this imaging study.

Due to the patient's clinical course and the positive fasting test, an endoscopic ultrasound was performed, revealing a 10 x 9 mm hypoechoic cystic lesion in the distal body of the pancreas, round, vascularized, and soft to pressure. A biopsy was taken. Based on these findings, a somatostatin receptor scintigraphy was conducted, which showed an abnormal study with evidence of somatostatin receptor overexpression in a nodular lesion in the body of the pancreas, consistent with a probable insulinoma.

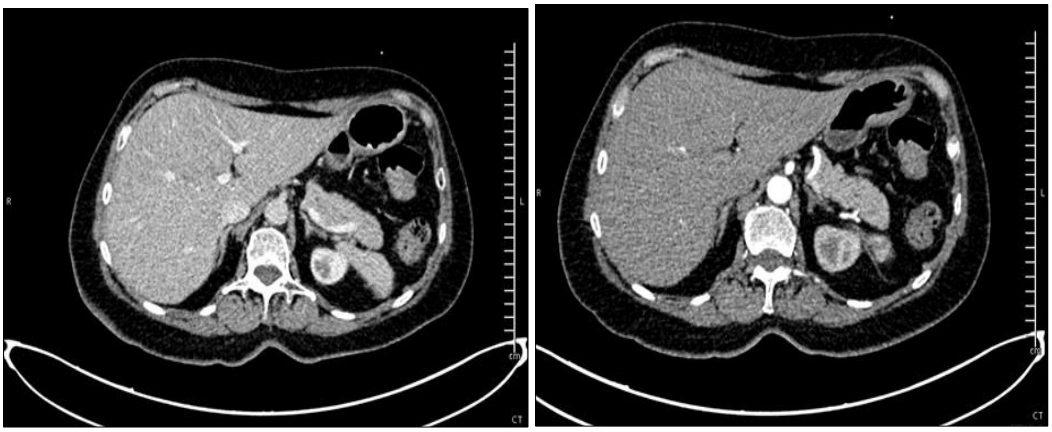

Figure 1: Abdominal CT scan portal and arterial phase, with no evident pancreatic abnormalities

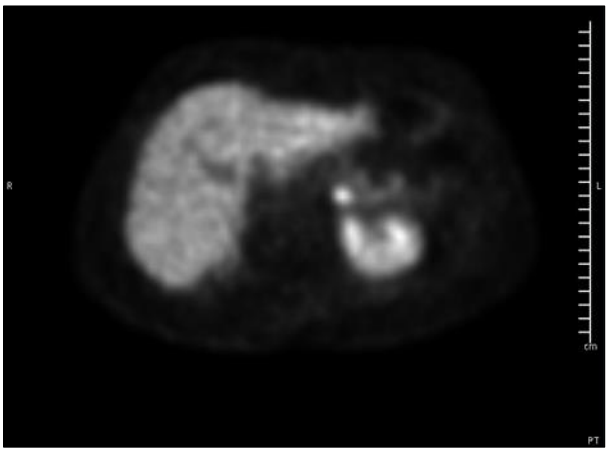

Figure 2: Somatostatin receptor scintigraphy, evidence of somatostatin receptor overexpression in a nodular lesion in the body of the pancreas 10x9mm

DISCUSSION

Hypoglycemia is an uncommon clinical problem in individuals without diabetes mellitus. Fulfillment of Whipple's triad (symptoms consistent with hypoglycemia, a low plasma glucose concentration measured by laboratory assay when symptoms are present, and resolution of hypoglycemic symptoms after plasma glucose levels are raised) supports the presence of pathologic hypoglycemia [1]. We present this case to emphasize that a sequential approach to decision-making is necessary to make a timely diagnosis, provide appropriate treatment, and prevent complications associated with severe hypoglycemia, especially when they are refractory to first-line treatment [4].

Once Whipple's triad is confirmed, and in the context of a healthy patient without comorbidities (such as alcoholism, hepatic or renal failure, sepsis, hypocortisolism, etc.) or chronic use of drugs associated with hypoglycemia, a detailed clinical and biochemical evaluation becomes key. Adrenal insufficiency should always be considered first, as acute cortisol deficiency can be life-threatening if untreated. However, the patient did not present any suggestive findings (weight loss, weakness, hyponatremia, or fatigue) [3].

The next step was to obtain additional laboratory measurements during a spontaneous or provoked episode of hypoglycemia in a monitored environment. The 72-hour fasting test is the diagnostic gold standard to confirm this condition (the test was stopped because the patient presented symptoms of hypoglycemia and glucose < 55 mg/dl) [1]. The finding of hypoglycemia, together with inappropriately high levels of insulin and C-peptide > 0.2nmol/L (> 0.6 ng/mL) during prolonged fasting, confirmed endogenous hyperinsulinism [5].

Because insulinoma is the most common cause of organic hypoglycemia in non-diabetic individuals, complementary studies were performed (endoscopic ultrasound and somatostatin analogue scintigraphy). These showed a hypoechoic cystic lesion in the distal body of the pancreas and overexpression of somatostatin receptors, thus confirming the diagnosis of insulinoma [6].

Insulinoma is a rare, usually benign pancreatic tumor derived from beta cells, characterized by excessive and uncontrolled insulin secretion, leading to recurrent episodes of hypoglycemia [5]. Clinically, patients present with recurrent neuroglycopenic symptoms such as confusion, weakness, seizures, or loss of consciousness, along with autonomic symptoms such as sweating, palpitations, and hunger [1]. Patients with insulinoma may also report weight gain due to the need for frequent eating to prevent or treat hypoglycemic episodes [6].

The main treatment is surgical resection of the tumor, which is curative in most cases [6]. In patients who are not surgical candidates, pharmacological management includes the use of diazoxide, which inhibits insulin release, and somatostatin analogues [5]. The prognosis is generally favorable, with a low recurrence rate in benign cases [6].

CONCLUSIONS

Addressing refractory hypoglycemia in non-diabetic patients is crucial due to the serious neurological and systemic complications that can arise if it is not treated promptly. Identifying the underlying cause, such as endocrine disorders or liver disease, is essential for implementing appropriate treatment. A multidisciplinary approach, with timely and personalized interventions, significantly improves patient prognosis. Additionally, the use of supportive strategies, such as glucose infusion or specific medications, helps prevent the recurrence of hypoglycemia and reduces the risk of permanent damage.

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