CLINICAL VIGNETTE

Evaluation of Hypoglycemia in the Elderly Patient

Anita Srinivasa, MD

Introduction

Hypoglycemia is common in older patients with diabetes, however, in older, non-diabetic patients it is less well recognized and underreported by both patients and medical professionals.[1] Hypoglycemia in this age group is associated with significant morbidities and cognitive dysfunction. Because neurological symptoms like dizziness or visual disturbance are common, rather than autonomic symptoms, it is often misdiagnosed.[1] Patients may present with behavioral changes, further confusing the clinical picture as dementia. Hypoglycemia is defined by an arbitrary plasma glucose of less than 3.9mmol/l and is broadly categorized as reactive or non-reactive hypoglycemia.[2] Some common causes of hypoglycemia in older patients include: liver and kidney disease, alcohol consumption, hormone deficiencies or insulin overproduction from rare tumors in the pancreas.[3] The case highlights the importance of recognizing hypoglycemia, and identifying the etiology of hypoglycemia.

Case

An 88-year-old female presented to the Emergency Department after syncope at home. This was her second episode in the past month , and she was admitted for further evaluation. Her PMHx included hyperlipidemia, depression, insomnia and migraine headaches. Home medication included daily Rosuvastatin 10 mg, Sertraline 50 mg and Trazadone 50 mg.3) Trazodone 50mg.

She was in no distress and admission vitals included: BP 120/70 without orthostatic changes, regular pulse at 88/min. ECG was normal and labs included: normal CBC and Comprehensive Metabolic Panel remarkable for glucose of 47, with normal electrolytes and other chemistries. The low glucose was non-fasting and unexplained.

The patient reported increasing daily sertraline from 25 mg to 50 mg one week prior to admission. Because of reports of hypoglycemia associated with serotonin reuptake inhibitors, she was advised to reduce the dose of sertraline. She returned for follow-up after discontinuing sertraline, with repeat glucose of 47.

The fasting glucose to insulin ratio was 0.4, which was not consistent with insulinoma, however her proinsulin and c peptide levels were elevated, and fasting 72-hour test was advised. The patient was apprehensive to schedule the test and alternate evaluation was scheduled. CT abdomen demonstrated a 1.2 cm cyst in the body of the pancreas. Repeat labs included: fasting glucose 44; Insulin 28(ULN 25); C PEPTIDE5,5(ULN 4.3); PROINSULIN 48.9(ULN<8). These results were consistent with insulinoma, and she underwent endoscopic ultrasound and biopsy, which confirmed the diagnosis of insulinoma.

Discussion

Insulinomas are rare tumors of the beta cells of the pancreas that produce excessive insulin.[3] Insulin's function is to maintain balanced blood glucose levels. When excessive insulin is produced blood sugars may drop to dangerously low levels. While, only 10% of insulinomas are malignant, all may cause fasting hypoglycemia.

The cause of insulinoma is still unknown. Risk factors include female gender, age 40-60 years, and a few genetic diseases associated with increased risk for insulinomas. These include: Multiple Endocrine Neoplasia, Type 1, Von Hipple-Lindau Syndrome, Neurofibromatosis Type 1 and Tuberous Sclerosis.

The most common symptom is fasting hypoglycemia, which can present insidiously and mimic various psychiatric or neurological disorders. CNS symptoms include headache, confusion, visual disturbance, motor weakness, loss of consciousness, and even seizures. Autonomic symptoms of sympathetic stimulation like weakness, tremulousness, sweating are often present.[4]

Diagnosis is established with low glucose levels, elevated insulin levels with normal C peptide and proinsulin levels, followed by endoscopic ultrasound and biopsy. Plasma glucose should be measured while fasting[5]. Thresholds include glucose < 55 if symptoms are present, or < 40 without symptoms. Insulin level should be measured with a simultaneous sample. Elevated levels above > 6 mcu/ml or 42 pmol/l suggests an insulin mediated cause as does a serum insulin to plasma glucose ratio > 0.3.

Insulin is secreted as proinsulin, which consists of an alpha and a beta chain connected by a C peptide. Exogenous pharmaceutical insulin only contains the beta chain, so surreptitious insulin administration can be detected by measuring the C peptide and proinsulin levels.[5] With insulinoma, the C peptide

is $\geq$ 0.2nmol/L and proinsulin is $\geq$ 5. Normal or low levels are found in patients administering insulin.

Because many patients minimal to no symptoms at the time of evaluation, the diagnosis of insulinoma often requires hospitalization for a 48 – 72 hour fasting test. Hypoglycemia is defined by meeting the Whipple Triad: 1) symptoms occurring during the fast; 2) symptoms occur in the presence of hypoglycemia; and 3) ingestion of carbohydrates relieves the symptoms.[5] If Whipple Triad is not observed, the C Peptide Suppression test can be done. Endoscopic ultrasound has greater than 90 % sensitivity in localizing the tumor.

Surgical resection has a cure rate of 90%. Small superficial lesions can be surgically enucleated, though larger lesions may require a distal subtotal pancreatectomy.[5] Hypoglycemia can be treated with either Diazoxide or Octreotide. Patients using octreotide need supplemental pancreatic enzymes, as octreotide suppresses secretion. Chemotherapy with Streptozotocin and 5 flurouracil are effective, with greater than 60% cure.[5]

REFERENCES

1. **Virally ML, Guillausseau PJ**. Hypoglycemia in adults. *Diabetes Metab*. 1999 Dec;25(6):477-90. Review. PubMed PMID: 10633872.
2. Mayo Clinic: Hypoglycemia. Available from: https://www.mayoclinic.org/diseases-conditions/hypoglycemia/symptoms-causes/syc-20373685.
3. Healthline: Can you have hypoglycemia without having diabetes: Available from: https://www.healthline.com/health/hypoglycemia-without-diabetes.
4. Johns Hopkins Medicine Health: Insulinoma. Available from:https://www.hopkinsmedicine.org/health/conditions-and-diseases/insulinoma.
5. **Nguyen M**. Insulinoma. Available from: https://www.merckmanuals.com/professional/gastrointestinal-disorders/tumors-of-the-gastrointestinal-tract/insulinoma.