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New Onset Hypoglycemia in Non-diabetic Adult Patients: Where Do We Go from Here?

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Lam, Fred and Bokhari, Ali, "New Onset Hypoglycemia in Non-diabetic Adult Patients: Where Do We Go from Here?" (2020). *Appalachian Student Research Forum*. 55.
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INTRODUCTION

Hypoglycemia is defined as a blood glucose <70 mg/dL in a diabetic patient or a blood glucose <50 mg/dL in a non-diabetic patient. It is a commonly encountered situation in the inpatient population. However, it is uncommon in individuals not being treated for diabetes mellitus. Hypoglycemic symptoms include autonomic symptoms (tremors, palpitations, anxiety, sweating, paresthesias) and neuroglycopenic symptoms (dizziness, weakness, drowsiness, confusion). Consequences of uncorrected hypoglycemia can lead to seizures, arrhythmias, or other complications that may ultimately result in death. The reasons for hypoglycemia in a non-diabetic patient can vary from medication use to uncommonly encountered disease states. Due to the adverse risks associated with hypoglycemic episodes, it is important to pursue the proper work-up in a timely manner, initiate measures to prevent further hypoglycemic episodes, and ensure proper treatment aimed at the cause of the problem.

OBJECTIVE

To highlight possible causes of hypoglycemia and the appropriate work-up for normally euglycemic patients.

FIGURE 1: LABORATORY WORK-UP INTERPRETATION CHART

Probable Cause of Hypoglycemia from Lab Work-up ¹								
Glucose (mg/dL)	Insulin (µU/mL)	C-peptide (nmol/L)	Proinsulin (pmol/L)	Beta-Hydroxybutyrate (mmol/L)	Increase in glucose post glucagon (mg/dL)	Oral Hypoglycemic screen	Antibody to insulin	Explanation
<55	>>3	<0.2	<5	≤2.7	>25	-	-	Exogenous Insulin
<55	≥3	≥0.2	≥5	≤2.7	>25	-	-	Insulinoma
<55	≥3	≥0.2	≥5	≤2.7	>25	+	-	Oral Hypoglycemic agent
<55	>>3	>>0.2	>>5	≤2.7	>25	-	+	Insulin Autoimmune
<55	<3	<0.2	<5	≤2.7	>25	-	-	IGF
<55	<3	<0.2	<5	>2.7	<25	-	-	Neither Insulin of IGF mediated

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CASE DESCRIPTION

A 36-year-old woman with lupus related end stage renal disease on hemodialysis via Ash-catheter presented to the emergency department (ED) due to peritonitis secondary to a peritoneal dialysis (PD) catheter that was no longer in use. Patient was bacteremic; antibiotics were started, and her PD and Ash-catheter were removed. Repeat blood cultures were negative for over 48 hours and patient was kept fasting at midnight (NPO) for a new Ash-catheter. The day of surgery, the patient had multiple low blood sugar readings as low as 15mg/dL. She was asymptomatic until her blood sugar was <45. Symptoms were limited to drowsiness and shortness of breath. She was given 4 boluses of D50, glucagon IV, and transitioned from a D5 drip to a D15 drip that finally stabilized her blood sugar while NPO. In her chart a blood sugar of 30 was documented 2 months prior for an admission with autoimmune hemolysis. She denied any recollection or symptoms. She also denied a history of diabetes or low blood sugars. She proceeded to surgery that day and went into cardiac arrest on the operating table after being sedated by anesthesia. She was resuscitated after 1 round of CPR & a new Ash-catheter was placed. During her hypoglycemic episodes, labs to investigate for causes of hypoglycemia were drawn (glucose, insulin, C-peptide, proinsulin, beta-hydroxybutyrate, insulin antibodies, and sulfonylurea/meglitinide screen). These labs returned with an inappropriately normal insulin level, high C-peptide, normal proinsulin (if diabetic), normal BHB, and borderline positive for antibodies. The sulfonylurea/meglitinide screen was still pending. The patient's hypoglycemia spontaneously resolved after being allowed to resume her normal diet and she did not require further IV dextrose. She was discharged in stable condition to a rehabilitation center with appropriate words of caution given.

DISCUSSION

Episodes of low blood sugar seen in non-diabetic patients can stem from an array of causes: exogenous insulin administration, an insulin secreting tumor (insulinoma), insulin antibodies, insufficient cortisol or glucagon levels, an increase in insulin like growth factor (IGF) [due to increased growth hormone (GH) release], improper sulfonylurea/meglitinide use or other medications, etc. Initial work-up involves gathering further history & taking into consideration the possibility of other hormone deficiencies (cortisol). If the cause is still inapparent, further lab work-up should be done. During a hypoglycemic episode, measurements of glucose, insulin, IGF, C-peptide, proinsulin, & beta-hydroxybutyrate should be drawn along with a sulfonylurea/meglitinide screen. If concern for an autoimmune pathology is present, a test for insulin autoantibodies & anti-insulin receptor antibodies can also be drawn. Furthermore, if labs cannot be drawn appropriately, a 72-hour fast can be conducted where these labs can be taken at specific intervals in a controlled setting. Additionally, a Glucagon Tolerance Test can be administered to further determine if the hypoglycemia is due to an insulin-mediated etiology (insulinoma). Ultimately, the results of these labs should help elucidate the cause of hypoglycemia (as shown in Figure 1) & guide treatment in the prevention of future episodes.