Diabetes Mellitus and Glucose Metabolism

DIABETES CASE REPORTS

Endoscopic Ethanol Ablation as Definitive Therapy for Suspected Insulinoma

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Introduction: Hypoglycemia is defined as plasma glucose <70mg/dL, with autonomic and/or neuroglycopenic symptoms often occurring at levels less than 55mg/dL. Diagnostic workup of hypoglycemia unrelated to use of hypoglycemic agents is crucial as it is linked to increased mortality. After ruling out common culprits such as drugs (insulin, sulfonylureas), ethanol and malnutrition, further testing should be pursued for patients who meet the Whipple's Triad: symptoms of hypoglycemia, documented low plasma glucose and relief of symptoms upon raising plasma glucose. We present the case of an 85-year old male with a suspected insulinoma who underwent endoscopic alcohol ablation as definitive therapy.
Case: An 85-year-old male with a history of metastatic prostate cancer was found to have recurrent episodes of asymptomatic hypoglycemia with fasting plasma glucose levels as low as 50-60s during an unrelated inpatient admission. He had no history of diabetes mellitus or insulin use. On further investigation, he was noted to have recurrent falls, though these symptoms could not be temporally linked to documented hypoglycemia as the patient was not monitoring blood sugars at home. Further workup revealed fasting plasma glucose of 58mg/dL and negative sulfonylurea screen. Plasma C-peptide and fasting plasma insulin levels during an episode of hypoglycemia were elevated at 6.42ng/mL and 38uIU/mL respectively. IGF-II and insulin autoantibody testing was negative. Abdominal imaging revealed a 1.3cm hypervascular pancreatic head lesion consistent with a neuroendocrine tumor, concerning for an insulinoma in view of his lab findings. Surgical removal of this lesion was not within the patient's goals of care. Attempts at medical management included escalating doses of prednisone and subcutaneous octreotide; however, he continued to have hypoglycemic episodes despite therapy. His cardiac history precluded the use of other medical therapies. After careful evaluation, he underwent ultrasound-guided ethanol ablation of his neuroendocrine tumor as potential definitive therapy, with successful resolution of hypoglycemic episodes noted during his post-procedural hospital stay.
Discussion: Traditionally, insulinomas are primarily managed surgically. Poor surgical candidates can benefit from medical management including diazoxide, somatostatin analogs and verapamil among others. Ultrasound-guided ethanol ablation is a newer modality aimed achieving cure in selected patients, thus avoiding need for surgery. Our case highlights the challenges in management of insulinomas, especially in complicated patients like ours who are not surgical candidates and who may be resistant to medical therapy. Though there are not many studies on the long-term efficacy and outcomes with ethanol ablation of insulinomas, it appears to be a promising option and certainly deserves further study.

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Euglycemic Diabetic Ketoacidosis Post Bariatric Surgery in Type II DM in the Setting of SGLT2-Inhibitor Use

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Introduction: **C**urrent AACE recommendations is to stop the SGLT-2 inhibitor at least 24 hours prior to elective surgery, planned invasive procedures, or anticipated severe stressful physical activity. However, case reports suggest that the pharmacologic effects of SGLT2 inhibitors persist beyond 5 half-lives of elimination (2–3 days), with glucosuria and ketonemia lasting as long as 9 to 10 days after discontinuation.
Case: A 51 year old female with a past medical history of hypertension, morbid obesity, DM type II, admitted to the hospital electively for bariatric surgery. Post-op day 1, she became tachypneic and lethargic. However, alert, oriented and responding appropriately. Lab work showed blood glucose levels <200 mg/dl (70–200 mg/dl), pH 7.21 (7.35–7.45), anion gap of 36 (4–14 mol/L), bicarbonate of 3 (23–34 mmol/L), pCO2 of 6 (35–45) and Potassium of 2.6 (3.5–5.2 mmol). UA showed glucose >500 mg/dl (0 mg/dl) and ketones 80 mg/dl (0 mg/dl). She was transferred to SICU. After reviewing her home medications, she was on Canagliflozin which was stopped 2 days prior to surgery and Glargine/Lixisenatide which was stopped 2 weeks prior to surgery as recommended by her endocrinologist. Patient was then diagnosed with euglycemic DKA. She was started on an insulin drip following potassium replacement and IV fluids. Over the course of few days, she started to feel better. Her PH, bicarb, anion gap and potassium all trended toward normal limits. She was transitioned off insulin drip to basal-bolus insulin regimen and then she was discharged on post-operative day 7 with the instruction to not take any SGLT2 inhibitors.
Discussion: **S**GLT-2 inhibitors is known to cause euglycemic DKA and ketosis. Our case brings to attention that discontinuation of SGLT2 inhibitor treatment 48 hours prior to surgery may not be adequate specially giving the half-life of the medication. The optimal timing of discontinuation remains unknown. Further studies are needed to evaluate if longer withholding period may be necessary (1).
1.Yehuda Handelsman, Robert R. Henry, Zachary T. Bloomgarden, Sam Dagogo-Jack, Ralph A. DeFronzo, Daniel Einhorn, Ele Ferrannini, Vivian A. Fonseca, Alan J. Garber, George Grunberger, Derek LeRoith, Guillermo E. Umpierrez, and Matthew R. Weir (*2016*) AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS AND AMERICAN COLLEGE OF ENDOCRINOLOGY POSITION STATEMENT ON THE ASSOCIATION OF SGLT-2 INHIBITORS AND DIABETIC KETOACIDOSIS. Endocrine Practice: June 2016, Vol. 22, No. 6, pp. 753–762.

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DIABETES CASE REPORTS

Euglycemic Diabetic Ketoacidosis Secondary to SGLT2-inhibitor Use in Combination With a Ketogenic Diet

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Sodium-glucose cotransporter 2 (SGLT-2) inhibitors are cardiorenal protective agents increasingly used in patients with diabetes. Cases of euglycemic diabetic ketoacidosis (euDKA) have been reported particularly among patients with type 1 diabetes. Our case is an example that highlights the role SGLT-2 inhibitors play in the development of euDKA in a patient with type 2 diabetes with confounding factors of strict adherence to a ketogenic diet and ankle fracture.

A 72-year-old female with a history of type 2 diabetes presented to the emergency department (ED) with right ankle pain and obvious deformity after a mechanical fall. Radiography of the right lower extremity confirmed distal fracture of the tibia and fibula. After reduction of her fracture in the ED, she was admitted in anticipation of an open reduction internal fixation. Her diabetes was controlled on empagliflozin monotherapy and adhering to a ketogenic diet. She monitored her blood ketones daily at home and reported values in the 3–4 mmol/L range. On admission, her basic metabolic panel (BMP) revealed a blood glucose of 148 mg/dL, bicarbonate of 20 mEq/L, anion gap of 18 mEq/L, Cr of 1.3 mg/dl, and eGFR of 40 mL/min. Her beta-hydroxybutyrate (BHB) was 5.09 mmol/L. The initial assessment was presumed starvation ketosis.

On hospital day three, she complained of continued nausea, polydipsia, and abdominal pain. Chart review revealed nocturia with approximately 3–4 voids per night. Repeat BMP showed a blood glucose of 152 mg/dL, bicarbonate of 16 mEq/L, anion gap still at 18 mEq/L, Cr 1.4 mg/dl, and eGFR of 37 mL/min. Since admission, all of her blood glucose levels ranged between 118–178 mg/dL. She denied dyspnea but exhibited Kussmaul respirations on physical exam. Repeat labs revealed a BHB of 8.92 mmol/L, and arterial blood gas (ABG) showed pH 7.2, pCO2 23, pO2 100, bicarbonate 8.6 mEq/L, consistent with high-anion gap metabolic acidosis, confirming the diagnosis of euDKA. Her empagliflozin had been held since admission, but she had not received any insulin up to this point due to euglycemia. She was immediately started on a weight-based dose of 12 units of insulin glargine with subsequent improvement of her BHB and anion gap.

This patient's use of an SGLT2-inhibitor in combination with her being on a ketogenic diet, contributed to a nonregulated state of ketone production leading to euDKA in the perioperative period. As SGLT2-inhibitors become more readily available, it is important to educate physicians and patients about the risk of euDKA during fasting, ketogenic diets, and the perioperative period.

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DIABETES CASE REPORTS

Euglycemic Diabetic Ketoacidosis With SGLT-2 Inhibitor

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Introduction: The SGLT-2 inhibitors (SGLT-2i) are a newer anti-diabetic drugs. Their use has tremendously increased due to their favorable profile but they are also the focus of attention because of their side effect of euglycemic diabetic ketoacidosis (euDKA), which is challenging to diagnose because of its rarity and normal or mildly elevated blood glucose levels. SGLT2i decrease blood glucose independently of insulin secretion, by reversibly inhibiting SGLT2 protein which is responsible for reabsorbing glucose from the proximal renal tubule. Beside glycemic control with reduced glycated hemoglobin, they also decrease all-cause mortality, cardiovascular mortality, and hospitalization for heart failure. The major side effect is genitourinary infections, euDKA and volume depletion. EuDKA is characterized by blood glucose <200mg/dl, anion gap metabolic acidosis and positive serum ketones. It can, therefore, present without hyperglycemia and the symptoms of dehydration, making it challenging to identify. DKA is rarely seen in DM-2 and the normal glucose levels can cause misinterpretation of the patient's condition, causing a delay in treatment. The beta-hydroxybutyrate and arterial pH should be checked in suspected SGLT2i associated euDKA. The mainstay of treatment of euDKA is immediately stopping SGLT2i and traditional DKA treatment protocol. Patient should be educated regarding adequate hydration and adequate calorie intake while using SGLT2i and physician should avoid using SGLT2i in patients with poor oral intake, alcohol dependence or pregnancy. **Case Presentation:** A 52-year-old male with uncontrolled type 2 diabetes, on Metformin and Sitagliptin, presented to clinic. Canagliflozin (SGLT-2i) was added to his oral hypoglycemic regimen. Six days later he presented with blurred vision, lightheadedness, nausea, vomiting, and abdominal pain. On examination, he had tachycardia and tachypnea. Labs were significant for glucose levels of 131mg/dL, bicarbonate 12meq/l, anion gap 20, creatinine 0.7mg/dl, normal lactic acid. Serum ketones were positive with elevated beta-hydroxybutyrate of 5.9mmol/l. Blood gas analysis showed a pH of 7.14. The patient was admitted to ICU and managed according to the guidelines for DKA. The symptoms resolved within 24 hours, with a reduction of anion gap to 12. Canagliflozin was discontinued indefinitely and the patient was discharged with the diagnosis of SGLT2i-induced euDKA. **Conclusion:** SGLT2i-induced euDKA can present without the classical laboratory findings of DKA. The patients, with a history of SGLT2i use and, signs and symptoms of DKA, even in the absence of hyperglycemia, should be suspected of euDKA. The complete lab work with blood gas analysis, blood and urine ketones including beta-hydroxybutyrate level must be done to ensure that the