Acute pancreatitis and diabetic ketoacidosis associated with compounded semaglutide

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Abstract

This case describes a patient without a history of diabetes who, after three months of compounded semaglutide use, presented with acute pancreatitis complicated by diabetic ketoacidosis (DKA). The patient presented to the ED with nausea, vomiting and mild abdominal pain. She was found to be in high anion gap metabolic acidosis, hyperglycemic and with elevated lipase. The patient was treated for DKA, with resolution of her symptoms. She was ultimately discharged without insulin and advised to stop her semaglutide.

Keywords: Glucagon-Like Peptide 1, pancreatitis, Diabetic Ketoacidosis, hyperglycemia

Introduction

Ketoacidosis is a state of metabolic acidosis caused by the accumulation of ketone bodies, which are produced from fat breakdown. This process typically occurs when insulin levels are insufficient or the body shifts to using fat as its primary energy source.[1,2] In rare cases, ketoacidosis can develop even when blood glucose levels are normal, a condition known as euglycemic ketoacidosis.

Semaglutide, a glucagon-like peptide-1 receptor agonist, is a medication that has demonstrated effects in controlling blood sugar in diabetic patients,[3] weight loss management in obese and overweight patients,[4,5] and in non-diabetic patients as well.[6] Acute pancreatitis is one of the GI complications that can lead to life-threatening complications and can cause the sudden onset of diabetic ketoacidosis.[7,8]

Semaglutide is considered to be safe to use, but rare complications, including acute pancreatitis, can occur.[9,11] Hypotheses regarding GLP-1RA-induced pancreatitis include overstimulation of pancreatic cells, hyperplasia, ductal obstruction, and vascular injury.[11]

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Patient Information

A 37-year-old female with a BMI of 18 and a past medical history of anxiety presented to the emergency department due to intractable nausea and vomiting for two days. She reported no epigastric pain, fever, or diarrhea.

Earlier in the week, she visited Telehealth and was prescribed Zofran for symptom relief, but she did not get better. Additionally, she has been using compounded semaglutide for a few months to aid in weight control, and she has lost 30 pounds since starting semaglutide. She had titrated up to 50 mg of semaglutide but noticed some side effects and titrated the dose back down to 40. History was positive for social alcohol use, marijuana, and nicotine vaping. She presented close to a holiday and endorsed some increased drinking in the past few days.

Her vital signs on admission were 36.3°C, 130/93, 20 respiratory rate, and a heart rate of 134. On physical examination, she was breathing normally and had no fruity odor. Her abdomen was soft, not tender, and with no guarding. Her skin did not show ecchymosis

or purpura. Lab results revealed a high blood sugar level of 466 but a normal HbA1c of 4.5%, high anion gap metabolic acidosis of pH 7.2, and an anion gap of 31. Her acetone blood level was moderate, and her urine ketone level was more than 150 mg/dL. She had a significantly elevated lipase level of 896 (Normal reference 13–60) and an amylase level of 235 (Normal reference 13–53). Blood toxins, including alcohol, acetaminophen, and salicylate, were negative. Her triglyceride level was 161 mg/dL.

Diagnostic Assessment

CT abdomen pelvis was positive for wall thickening of the gallbladder with possible pericholecystic fluid,inflammation at head of pancreas, fat stranding. Follow-up ultrasound was positive for hepatic steatosis with pulsatile flow in the portal vein and possible portal hypertension. No acute cholecystitis was noted on abdominal ultrasound. Hepatitis profile and HIV profile were normal. In terms of autoimmune labs, results were negative for Islet Cell antibody and <5 of Glutamic Acid Decarboxylase-65 Auto Ab (GAD-65 Ab).

Therapeutic Intervention

After being admitted to the medical intensive care unit, she received intravenous potassium, an insulin drip, and intravenous maintenance fluids as per our institution's DKA guidelines. She was NPO during this time. She was also placed on the Clinical Institute Withdrawal Assessment for Alcohol protocol and given as-needed Reglan for nausea. CIWA scores were never elevated and no intervention was warranted. Electrolytes were replaced as needed. Her high anion gap normalized, and she transitioned to subcutaneous insulin and oral diet. However, her blood glucose was always within normal range on point of care testing; subsequently, she never received subcutaneous insulin. She was discharged without insulin and advised to stop semaglutide (Table 1).

Follow-up and Outcomes

The patient was lost to follow-up as she lived out of town. Attempts to reach her by phone were unsuccessful.

Table 1. Timeline of Hospital Course

	Findings	Treatment
Day 1	Blood glucose: 466 mg/dL Anion gap: 31 Bicarbonate: 9 mEq/L Ph: 7.2 Lipase: 896 U/L Actone: present	4 L Lactated ringers Insulin drip Electrolytes replaced
Day 2	HA1c : 4.5% C peptide: 6.04 ng/mL Glucose: 94 mg/dL CT abdomen: inflammation at head of pancreas, fat stranding	10 units long acting insulin, with low dose sliding scale insulin Later in day long acting insulin was held by endocrinology consult
Day 3	Blood glucose POC: remained ~100 without need for insulin Negative for Islet Cell antibody and Glutamic Acid Decarboxylase-65 Auto Ab	Discharged without insulin

Discussion

Diabetic ketoacidosis (DKA) is defined by hyperglycemia, metabolic acidosis, and ketonemia. Euglycemic DKA presents with glucose ≤250 mg/dL.[2] Our patient had hyperglycemic DKA (>250 mg/dL) with no history of diabetes and normal HbA1c, highlighting medication-related adverse events.

Semaglutide, a GLP-1RA, increases insulin secretion, suppresses glucagon, delays gastric emptying, and promotes weight loss.[3–5] While generally safe, GLP-1RAs have been linked to acute pancreatitis.[6–8] Mechanisms include ductal hyperplasia, acinar hypertrophy, and vascular injury.[11] Starvation states from nausea may worsen ketosis, and pancreatitis-associated inflammation can trigger transient insulin deficiency.

This case is notable for semaglutide-induced pancreatitis and DKA in a non-diabetic, underweight patient. Compounded semaglutide formulations may

carry added risk. Recent binge alcohol use may have contributed, though alcohol alone would not explain DKA development.

Of note, this patient presented with a BMI of 18 on semaglutide for weight loss. The SUSTAIN trials did include patients who had a BMI below 25, and these patients lost weight at a proportional rate to their BMI.[5] However, more work is needed to determine the safety profile of using semaglutide in a very low BMI population. When semaglutide is used off-label for weight loss in normal BMI populations, extra caution is warranted. Furthermore, the patient was utilizing compounded semaglutide, which has been shown to have variable concentrations of active ingredients.

Summary

Semaglutide, prescribed off-label for weight loss in an underweight patient, precipitated pancreatitis and DKA. The case expands the known risk profile of GLP-1RAs, underlining the importance of vigilance when prescribing these medications outside standard indications.

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