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Euglycemic diabetic ketoacidosis after bariatric surgery: a case report

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Abstract

The use of sodium-glucose cotransporter 2 inhibitors (iSGLT-2) is widely used in patients with type 2 Diabetes Mellitus (DM2), having proven a clear benefit in glycemic control and cardiovascular risk. A rare complication associated with thwm is euglycemic diabetic ketoacidosis (euCAD), characterized by metabolic acidosis with elevated anion GAP, ketosis, and blood glucose <250 mg/dl. We present a case of euCAD in a patient with DM2 and obesity treated with empagliflozin after laparoscopic bariatric surgery, in the context of surgical stress and a very low calories and carbohydrates diet. It presented as general malaise and abdominal pain, with metabolic acidosis and blood glucose of 195 mg/dl on the third day since discharge, requiring ICU admission. After excluding an early surgical complication, the acidosis was attributed to the use of SGLT2i and resolved after establishing intravenous insulin therapy and fluid therapy, with normalization of blood gases and remission of symptoms. Despite being a recognized entity, its diagnosis and management continues to be a challenge for professionals.

Keywords:

- Euglycemic diabetic ketoacidosis
- Bariatric surgery
- Type 2 diabetes mellitus
- iSGLT-2

Introduction

Euglycemic diabetic ketoacidosis (euCAD)is a potential metabolic complication in patients with type 2 Diabetes Mellitus (DM2) treated with sodium-glucose cotransporter 2 (iSGLT-2) inhibitors (1). The mechanism of action of these drugs consists in the blockage of glucose reabsorption at the proximal tubule of the nephron, increasing urinary glucose loss. Some situations, such as fasting or very low carbohydrate diets, can trigger this rare complication, which is characterized by metabolic acidosis with a high anion gap, ketosis and blood glucose generally <250 mg/dl. Given the potential severity of the condition, recognising this complication is essential to reach an early diagnosis and prevent potential risk situations.

Material and method

A 42-year-old female patient with a history of hypertension, hepatic steatosis, grade 2 obesity (body mass index (BMI) 38,4, 102,4 kg), mixed dyslipidemia and DM2 diagnosed more than 10 years ago without micro or macrovascular complications, with active follow-up by Endocrinology. She had a 8,4% glycated hemoglobin (HbA1c) prior to admission (previous HbA1c between 7,0-8,0%), treated with empagliflozin/metformin 5/1000mg every 12 hours and pioglitazone 30mg. Treatment with oral semaglutide was prescribed, being rejected by the patient by her own choice. Given the poor control, the introduction of insulin therapy was considered, being rejected by the patient.

She underwent laparoscopic gastric bypass in July 2023, and the postoperative period in the hospital was uneventful, with correct oral tolerance and blood glucose during admission

between 103-220 mg/dl managed exclusively with a corrective regimen of fast-acting insulin. The patient was discharged on the third postoperative day without incident, with treatment upon discharge consisting of empagliflozin/metformin 5/1000 mg every 12 hours, in addition to vitamin supplements, calcium carbonate/cholecalciferol and oral iron, and Pioglitazone was suspended. Liquid diet during the first 2-3 days after discharge was prescribed, consisting of infusions, broths, milk and juices conditioned by tolerance.

Results

The patient went to the Emergency Department three days after discharge with symptoms of progressive general malaise that had started since discharge, non-radiated lumbar pain and abdominal pain, without pathological stools or vomiting, without signs of bleeding, with no fever. Venous blood gas analysis upon arrival at the Emergency Department revealed metabolic acidosis with pH 7,0, pCO2 23mmHg, pO2 30mmHg, bicarbonate 8,2mmol/L, base excess -25,4mmol/L, lactate 1,1 mmol/L, GAP anion 21,4 mmol/L and glucose 195 mg/d, 16,500 leukocytes (77,3% neutrophils and 14,8% lymphocytes), with positive urine ketone bodies and intense glycosuria.

A thoraco-abdomino-pelvic CT was performed, ruling out post-surgical complications, and replacement with 1M bicarbonate was started without improvement in the metabolic condition. Finally, admission to the ICU was decided with worsening acidosis (pH 6,9, pCO2 28mmHg, HCO3 5,7 mmol/L, glucose 160 mg/dl) and the need for invasive mechanical ventilation. In the ICU, treatment with up to 1000 mEq of 1M bicarbonate was needed. She subsequently presented dyselectrolytaemia with hypernatremia, hypokalemia and hypophosphatemia, requiring a conventional dialysis session.

Finally, given the finding of positive ketonuria, metabolic acidosis and elevated GAP anion, in addition to the history of taking Empagliflozin and fasting after surgery, the diagnosis of euCAD secondary to iSGLT-2 triggered by fasting and post-surgical stress was reached. Finally, treatment with intravenous insulin therapy and 5% dextrose solution was started to maintain blood glucose in range, until analytical parameters normalized and finally recovered from ketoacidosis. After resolution of the condition and normalization of analytical parameters, the patient was discharged with Glargine U100insulin, 18 IU and adjustment regimen indications between 100-150 mg/dl.

Discussion

iSGLT-2 are a group of drugs that have been widely used in recent years for the treatment of DM2 initially, with increasingly indications, including heart failure and chronic kidney disease, with recognized cardiovascular benefits. (2). These drugs act both by improving the glycemic profile (reduction of HbA1c, decrease in glucotoxicity, insulin resistance) and by promoting weight loss and blood pressure control.

Its mechanism of action involves an inhibition of glucose reabsorption in the renal proximal tubule through the inhibition of the sodium-glucose transporter 2, causing a loss of glucose and sodium through the urine and a consequent decrease in plasma glucose levels (3). On the one hand, this decrease in plasma glucose reduces insulin requirements, increasing the lipolysis ratio at the level of adipose tissue. There is also an increase in glucagon secretion, resulting in an increase in hepatic ketogenesis. Furthermore, the increase in urinary sodium concentration in the renal tubule increases the electrical gradient, causing the reabsorption of ketone bodies (with a negative charge) at that level. This situation of relative insulinopenia and decreased renal clearance of ketone bodies seems to be the trigger for euCAD, defined as a situation of metabolic acidosis with elevated GAP anion, ketosis and glucose <250 mg/dl (4, 5).

Situations have been described in the literature that could favor the appearance of euCAD. One of them are those situations that lead to a very reduced intake of carbohydrates. Diets known as ketogenic or very low carbohydrate diets, with a carbohydrate content of less than 10% (different from low carbohydrate diets, which have between 30% and 45% carbohydrate content), have been popularized in recent years, and they even appear in clinical practice guidelines (6). Cases have also been described, especially in geriatric patients with swallowing disorders and other comorbidities that can precipitate situations of prolonged fasting or a significant decrease in intake, such as dysphagia, nausea or vomiting (7). In these patients, the appearance of euCAD has been associated with an increase in the average hospital stay. Another factor to take into consideration is the surgical stress, with cases documented in the post-surgical period in

patients under this treatment (8).

In the clinical case we present, two potential precipitating causes of ketoacidosis coincided in our patient: surgical and immediate postoperative stress combined with the prescribed very low in carbohydrates and calories diet. Given that type DM2 is closely related to overweight and obesity, it is not uncommon for patients candidates to bariatric surgery to be treated with iSGLT-2. Special caution must be taken when prescribing this type of drugs and ensuring an adequate intake of carbohydrates is key to prevent the appearance of this complication, especially during the perisurgical period.

Other drugs should be prioritized in similar situations to the one described, delaying the reintroduction of this pharmacological group until progress has been made in the postoperative period and higher caloric and carbohydrate intake is ensured.

The appearance of euCAD could be prevented by considering those situations that can precipitate its appearance, such as severe acute illness, surgery, situations of fasting or dehydration, acute myocardial infarction, serious infections, or excessive exercise (9; 10). Due to the half-life of these drugs, they should be suspended at least three days before surgery, in addition to evaluating the patient's situation in the postoperative period to avoid cases similar to the one described in our patient.

The diagnosis of this complication associated with the use of i-SGLT2 can be a challenge for professionals, as they have relatively normal blood glucose levels, which can mean a delay in reaching the correct diagnosis (11). It is essential to suspect euCAD in patients being treated with these drugs, given that correct and early management of ketoacidosis is related to lower mortality and complications derived from the condition.

Likewise, it is imperative to educate patients who are treated with iSGLT-2 about the potential risk situations in which their use should be interrupted and about the signs and symptoms that could help identify possible ketoacidosis.

Conclusions

euCAD secondary to i-SGLT2 use is a rare but potentially serious complication that is triggered by different situations, including prolonged fasting and very low in carbohydrates diets, in addition to surgical stress. In patients with type 2 DM in whom bariatric surgery is performed, special caution should be taken when using this type of drugs.

Considering the risk situations in which the use of iSGLT2 is not recommended and knowing this entity reach an early diagnose and treatment is essential to improve the prognosis of these patients.

Conflict of interest

None of the authors has any conflicts of interest that could bias the information transmitted here.

Disclosure Statement

None of the authors present any financial or personal relationship that could inappropriately bias the work

Responsibility of the authors

I guarantee that the submitted manuscript has not been previously published in any other publication.

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