Euglycemic Diabetic Ketoacidosis Associated with Empagliflozin Use in the Course of the SARS-Cov-2 Pandemic

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ABSTRACT

Sodium glucose cotransporter 2 (SGLT2) inhibitors are among the new generation oral anti-diabetic drugs that have started to be used in the treatment of type 2 diabetes mellitus. Although these drugs are highly beneficial, life-threatening side effects such as euglycemic diabetic ketoacidosis (eDKA) are reported with their use. In eDKA, metabolic acidosis and anion gap appear in blood gases and serum glucose in less than 200 mg/dl. This can delay diagnosis and treatment. In our case, a 42-year female presented to the Emergency Room with nausea and vomiting. It was observed that the patient had been using empagliflozin for a year. Her blood gas analyses and laboratory tests showed metabolic acidosis and ketosis. The patient was initially suspected to be a case of coronavirus disease-2019 (COVID-19) complicating the course of diabetes, finally it was diagnosed as a case of eDKA due to empagliflozin use. We noticed that during the current pandemic, some other diagnoses can be missed or their diagnosis can be delayed.

Key Words: *Euglycemic diabetic ketoacidosis, Empagliflozin, COVID-19, Diabetes mellitus.*

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INTRODUCTION

Turkish Endocrinology and Metabolism Society has defined diabetic ketoacidosis (DKA) with the following diagnostic criteria: plasma glucose >300 mg/dl, ketonemia ≥3 mmol/l, urine ketone ≥2 +, blood pH ≤7.30, serum sodium bicarbonate <15 mEq/l.[1] Unlike the classic DKA, serum glucose level is less than 200 mg/dl in euglycemic DKA (eDKA).The possible etiology of eDKA includes reduced calorie intake, heavy alcohol consumption, chronic liver disease and glycogen storage disorders. Recently, the use of sodium glucose cotransporter 2 (SGLT2) inhibitors has been shown as another possible cause of eDKA.[2]

SGLT-2 inhibitors are among the new group of oral antidiabetic drugs. These drugs function by reducing the renal absorption of glucose. While these have positive effects such as weight loss and low incidence of cardiovascular events; many side effects have also been reported, including genitourinary infections, acute kidney injury, eDKA, lower limb amputations, and bone fractures.[3]

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CASE REPORT

A 42-year woman with a 10-year history of type 2 diabetes mellitus (DM), for which metformin (1000 mg/day) and empagliflozin (10 mg/day) were prescribed, presented with nausea,vomiting and dyspnea. Vital signs at presentation were: temperature 36.1°C, pulse rate 110 beats/ min, respiratory rate 18 breaths/min, and blood pressure 127/65 mm Hg. Laboratory tests showed blood glucose as 196 mg/dl, blood pH 7.08, serum bicarbonate 8.9 mmol/L, anion gap 20 mEq/L, and urine ketones 2+. Serum electrolytes, serum lactate and creatinine were within normal limits. Firstly, the patient was evaluated for coronavirus disease-2019 (COVID-19) infection because of the prevalent severe acute respiratory syndrome coronavirus 2 *(SARS-CoV-2)* pandemic. As a result of the final evaluation, the diagnosis of COVID-19 was ruled out. Meanwhile, the patient's acidosis increased. Then, we thought of eDKA due to empagliflozin use. She was taken to the intensive care unit for treatment. As a first intervention, intravenous isotonic fluid replacement and insulin infusion were started. To the treatment, 5% dextrose infusion was also added. Sodium bicarbonate was given for acidosis. Oral anti-diabetic medications were discontinued. Following this treatment, her acidosis resolved after 12 hours. Approximately 30 hours later, urine ketones became negative. She was discharged with insulin glargine and insulin aspart.

DISCUSSION

SGLT-2 inhibitors are among the new generation oral anti-diabetic drugs. These are an advantageous group of drugs for weight loss, and a decrease in blood pressure and cardiovascular events. However, serious life-threatening side effects are

also observed with their use. Possible side effects should be evaluated before starting the SGLT-2 inhibitors.[4] Our patient also had a history of DKA in the past.

There are not many cases of eDKA associated with empagliflozin use in the literature. In one study, eDKA was shown in a patient who started a low-carb diet while taking empagliflozin.[5] In another case, eDKA was shown in a patient who underwent surgery 48 hours after the empagliflozin was discontinued.[6] In both cases, acidosis was not as severe as in our patient.

Risk assessment should be performed in patients before choosing SGLT-2 inhibitors. These drugs should not be started for patients at risk for side effects such as eDKA. The later complication can occur with milder degrees of hyperglycemia. A blood glucose level is usually less than 200 mg/dl. This can delay diagnosis and treatment.

In addition, the point we want to emphasise in this case report is that the diagnosis and treatment of diseases other than COVID-19 infection can be delayed in the current pandemic. Our patient was initially evaluated for COVID-19; in the end, we considered the patient for eDKA due to empagliflozin use. We emphasise that other diseases and diagnoses should not be overlooked during COVID-19 pandemic, especially in Emergency Room, as delay in accurate diagnosis and treatment can result in serious consequences.

PATIENT'S CONSENT:
Written informed consent was obtained from the patient to publish the data concerning this case.

CONFLICT OF INTEREST:
The authors declare that they have no conflict of interest.

AUTHORS' CONTRiBUTiON
OO, GY: Have collected data, searched the literature, written the case report and reviewed the final version of the manuscript.

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