Euglycemic Diabetic Ketoacidosis in COVID-19 Patient Caused by Empagliflozin: A Case Report from Intensive Care Unit

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Received: April 13, 2021; Accepted: May 08, 2021; Published: May 15, 2021

Case Presentation

A 67-year-old male with a history of diabetes type 2 for 7 years presented to our emergency department in Melk general hospital in Austria with 5 days of fever, dyspnea, and sore throat. The patient’s diabetes medications before hospital admission were metformin and empagliflozin. Other medications were atorvastatin, aspirin, and bisoprolol. The patient had also had a stroke and hypertension.

Due to the Covid-19 outbreak, we conducted PCR assays for Covid-19 detection, and the result was positive. His vital signs on admission were: blood pressure, 140/85 mmHg; temperature, 38.0°C; respiratory rate, 26/min; pulse, 90/min; and oxygen saturation, 96% (breathing room air). The patient’s initial blood test results were: HbA1c, 7.0% (53mmol/l); creatinine, 0.77mg/dl (0.70-1.20); CRP, 139.9mg/l (0.0-5.0); sodium, 138mmol/l (136-145); potassium, 4.2mmol/l (3.5-5.1) mild lymphopenia; and initial procalcitonin, 0.2ng/ml (0.0-0.5).

Twenty-four hours later, the patient’s condition deteriorated, and he was admitted to the intensive care unit with the diagnosis of severe viral pneumonia, which was also confirmed by chest x-ray. In intensive care, the patient’s blood glucose was 180mg/dl, with serum pH of 7.25, pCO2 of 33mmHg (base excess -12mmol/l), serum bicarbonate of 13mmol/l, increased anion gap of 27mmol/l, and creatinine of 0.95mg/dl (0.70-1.20). Initially, it was not clear why the patient had metabolic acidosis. Metformin associated lactic acidosis was considered, but the patient had normal lactate of 1.0mmol/L and normal creatinine, and so this diagnosis was ruled out. After reviewing the medications of the patient, a diagnosis of euglycemic DKA was confirmed with blood ketones of 4.4mmol/l (<0.6 using the ketone meter).

The patient was started on Intravenous (IV) insulin with an infusion rate of 2-3 unit/h and dextrose 5% to keep the blood glucose at ~150mg/dl, in addition to a conservative IV fluid regime as per Covid-19 local guidelines. It is essential to mention that we did not use our DKA insulin infusion protocol (which needs hourly assessment) to minimize the medical staffs’ exposure to the virus. Twenty-four hours later, the pH improved (7.38), with 22mmol/l bicarbonate, and 0.7mmol/l blood ketones. Unfortunately, the patient developed a secondary bacterial infection as a complication of Covid-19 and was intubated and ventilated, and an ampicillin/sulbactam IV antibiotic was started, as per local Covid-19 guidelines. The patient was extubated after 9 days, and recovered well.

Discussion

Sodium-Glucose Cotransporter 2 (SGLT2) inhibitors have many advantages, such as lowering blood glucose, blood pressure, and improved cardiovascular outcomes [1], but they also have many disadvantages, such as increased risk of urinary tract infection, genital fungal infections, and DKA [2]. DKA can be induced by SGLT inhibitors through a reduction in the carbohydrate availability, with a decrease in insulin dose, increased lipolysis, increased delivery of the free fatty acid to the liver, increased production of ketone bodies, and high glucagon level in the blood [3].

In March 2020, the World Health Organization declared Covid-19 as a pandemic that has infected over 100 million of patients worldwide, and unfortunately, nearly three millions of patients have died from this viral infection [4]. The virus that causes Covid-19, SARS-CoV-2, infects patients’ cells through binding to the Angiotensin-Converting Enzyme 2 (ACE2) receptor, which is found in epithelial cells (mainly in the lung but also in the intestine, blood vessels, and kidney) [5]. Studies have suggested that the expression of ACE2 is significantly increased in patients with both types of diabetes and treated with ACE inhibitors and angiotensin II type 1 receptor blockers (ARBs) [5,6], but this hypothesis needs to be confirmed.

Many studies conducted in China - where the Covid-19 outbreak started - show that about 13-16% of patients admitted to the hospital...
with Covid-19 had diabetes [7,8]. In another study from the intensive care unit of the Wuhan Jin Yin-tan hospital, about 20% of the non-survivors had diabetes [9].

It is well known that hyperglycemia increases susceptibility to various infections [10,11] and that hyperglycemia leads to immune dysfunction through decrease lymphocyte response, decrease neutrophil dysfunction, dysfunction of the humoral immunity, and reduction of inflammatory cytokines secretion [10,11]. It is well documented that diabetes is associated with various respiratory infections similar to the Covid-19 infection, such as influenza and swine flu and SARS-CoV-1 [10-12].

A recent review showed that the Covid-19 virus could damage the pancreatic β cells and leading to DKA due to insulin deficiency, and many diabetic patients infected with Covid-19 may need higher insulin doses than usual [13].

The importance of this case is to emphasize the need for reasonable blood glucose control in such an outbreak and to consider severe, and life-threatening adverse effects, such as SGLT2 inhibitor-induced DKA, even in difficult cases, such as COVID-19 infection, which might explain the acidosis in such patients.

References