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Case Report

Euglycemic Diabetic Keto Acidosis Presentation in Association with SGLT-2 Inhibitor- Dapagliflozin

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Abstract

Euglycemic diabetic keto acidosis is a rare form of DKA seen in patients who are taking SGLT-2 inhibitor medication for the treatment of diabetes mellitus. It is a life-threatening condition and should be diagnosed early. The absence of hyperglycemia poses challenges to the treating emergency physicians in diagnosing this entity at an early stage. Here we report a case of euglycemic DKA in a patient with type 1 diabetes mellitus who was on SGLT-2 inhibitor.

Keywords: *Sodium Glucose Co-Transporter-2 Inhibitor (SGLT-2); Euglycemic Diabetic Keto Acidosis; Diabetes Mellitus*

Introduction

Sodium glucose co-transporter-2 inhibitor (SGLT-2) is a recent popular oral hypoglycemic agent. It acts on the SGLT-2 receptors in the proximal convoluted tubules in the kidney. The inhibition of these receptors prevent the reabsorption of glucose from the tubules, thereby initiating glycosuria and improving glycemic control [1]. It is usually used in the treatment of type 2 DM but may occasionally be used in type 1 DM as well. DKA is defined as the presence of triad of hyperglycemia, ketosis and acidosis. Euglycemic DKA lacks the hyperglycemic component. Decreased oral intake, alcohol intake, surgery or perioperative preparations, insulin reduction or cessation, infections, hepatic or renal impairments, acute coronary events and pancreatitis are some of the risk factors associated with the development of euglycemic DKA [2].

Case Presentation

A 42 years old male patient with a background history of type 1 DM presented to the emergency department with a 2 day history of vomiting and poor oral intake. He has been experiencing extreme tiredness as well. He did not complain of any abdominal pain, fever, diarrhoea, chest pain or cough. He has been diagnosed with T1DM for more than 20 years and has had a previous episode of DKA 7 years ago. His medications include humulin, lantus, dapagliflozin and metformin.

On presentation to the emergency department, his vitals revealed a heart rate of 110 beats/min, blood pressure of 137/82 mm of Hg, saturations of 97% on room air and temperature of 37 degrees celsius. He was conscious, oriented to time, place and person and was self-

ventilating on room air. Clinical examination was unremarkable. His initial blood gas showed a pH of 7.17, bicarbonate of 11.7, lactate of 1.3 mmol/L, potassium of 4.8 meq/L, sodium of 137 meq/L, glucose of 10.5 mmol/L, anion gap of 29 and base excess of -16.8. His blood ketones were 6.8 mmol/L. He was immediately transferred to a monitored bed. A diagnosis of euglycemic DKA was made and treatment was initiated.

We followed the Joint British Diabetes Society guideline for DKA management. He was started simultaneously on insulin infusion and IV fluids. His insulin infusion was started at 0.1 units/kg/hour. Initially 1000 mls of 0.9% sodium chloride was given over 60 minutes which was then followed by 1000 mls of 0.9% sodium chloride with 40 milliequivalents (meq) of potassium. He was also started on 10% dextrose at 125 mls/hour to prevent any hypoglycaemic episodes.

His ketones and blood glucose levels were checked hourly and his potassium was checked every 2 hours. His urine output was monitored as well. He was admitted to the acute medical unit. His blood tests showed a white cell count of 9.9, creatinine of 103 micromol/L and urea of 4.5 mmol/L. His chest Xray did not show any collapse or consolidation. His ECG revealed sinus tachycardia. The targets for treatment were reduction of the blood ketone concentration by 0.5 mmol/L/hour, increase the venous bicarbonate by 3.0 mmol/L/hour, reduce capillary blood glucose by 3.0 mmol/L/hour and maintain potassium between 4.0 and 5.5 mmol/L.

Venous blood gas on admission

pH	7.17
pO_2 (kPa)	4.2
pCO_2 (kPa)	1.8
Bicarbonate (mmol/L)	11.7
Blood Glucose (mmol/L)	10.5
Anion Gap	29
Base excess	-16.8
Lactate (mmol/L)	1.3

Laboratory parameters on admission

WBC (x 10^9/L)	9.9
Haemoglobin (g/L)	166
Platelets (x 10^9/L)	471
Sodium (meq/L)	142
Potassium (meq/L)	4.9
Urea (mmol/L)	4.5
Creatinine (micromole/L)	103
eGFR (ml/min/1.73m^2)	62

Venous blood gas after 24 hours of treatment

pH	7.35
pO_2 (kPa)	6.2
pCO_2 (kPa)	4.5
Bicarbonate (mmol/L)	18.8
Blood Glucose(mmol/L)	12.1
Anion Gap	11
Base excess	-6.8
Lactate(mmol/L)	0.7

Over the course of his admission, his ketones started to fall, acidosis improved and his blood glucose levels were stable. His dapagliflozin was stopped and his fixed rate insulin infusion was converted to subcutaneous regime. His blood cultures did not grow any organisms. He improved significantly and was eating and drinking as normal. He was discharged after 72 hours of admission. He was advised not to restart his dapagliflozin.

Discussion

Diabetic ketoacidosis (DKA) is traditionally defined as a triad of hyperglycaemia (> 11 mmol/L), anion gap acidosis, and increased plasma ketones. Euglycemic DKA is a rare entity where there is DKA without the hyperglycaemia factor. It is mostly seen in patients with type 1 DM, but also can occur in type 2 DM people. The exact mechanism of euglycemic DKA is unknown, but is thought to be attributed towards partial treatment of diabetes, carbohydrate food restriction, alcohol intake and inhibition of gluconeogenesis. It is most commonly associated with sodium-glucose cotransporter 2 (SGLT-2) inhibitor medications [3].

The SGLT-2 inhibitor dapagliflozin has been indicated for the treatment of type 2 diabetes since 2012 and is also indicated in adults for the treatment of symptomatic chronic heart failure with reduced ejection fraction and for the treatment of chronic kidney disease. Dapagliflozin (Forxiga) was authorised in 2019 in the United Kingdom as an adjunct to insulin in patients with type 1 diabetes with a body-mass index (BMI) of 27 kg per m^2 or higher, when insulin alone does not provide adequate glycaemic control despite optimal insulin therapy [7]. These act on the SGLT-2 receptors in the proximal convoluted tubules in the kidney. The inhibition of these receptors prevent the reabsorption of glucose from the tubules, thereby initiating glycosuria and improving glycemic control. The decreased glucose levels and low insulin activity increases the lipolysis and free fatty acid oxidation and this increases the ketone production leading to ketosis and acidosis. Also, the increased glucagon in the body decreases the activity of acetyl Co-A carboxylase and this in turn increases carnitine palmitoyltransferase-1 causing increased beta oxidation of free fatty acids and increased ketone production. This leads to the development of DKA [1,4]. The evidence that SGLT-2 inhibitors causes euglycemic DKA is not robust but few case reports and case series have been published [2,5].

Clinical features are similar that to that of DKA. It includes vomiting, abdominal pain, dehydration, fever, confusion, generalized weakness and loss of consciousness. There are no specific designed treatment protocols for euglycemic DKA. The usual DKA treatment protocol is followed with the aim to restore hydration, switch off ketosis, close the anion gap and maintain euglycemia. This is achieved through IV fluids, fixed rate insulin infusion and IV dextrose to prevent any hypoglycaemic episodes. The dose of fixed rate insulin recommended by the Joint British Diabetes Society in DKA is to start at 0.1 units/kg/hour along with 10% dextrose at 125 mls/hour. Where the blood glucose continues to fall despite 10% glucose, consider reducing the dose of insulin to 0.05 units/kg/hour as this reduces the instances of hypoglycemia and hypokalaemia [6].

Conclusion

We report a case of euglycemic DKA in a type 1 DM patient associated with SGLT-2 inhibitor medication use. Early recognition of this entity by emergency physicians is very important and should not rely on the blood glucose levels to make a diagnosis of DKA. We believe this case description gives a valuable insight and awareness among clinicians in diagnosing and developing a treatment strategy for euglycemic DKA.

Authors' Contribution

All authors contributed equally.

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