Diabetic ketoacidosis in a patient with type 2 diabetes precipitated by infection, steroids and SGLT2 inhibitor

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Abstract
Diabetic ketoacidosis (DKA) is a serious, life-threatening hyperglycaemic emergency commonly associated as a complication of type 1 diabetes (T1DM). The pathophysiology associated with type 2 diabetes (T2DM) makes it less likely to develop DKA, though it still could be precipitated by certain coexisting factors such as infection, medication non-compliance, vascular events such as myocardial infarction and stroke, medications such as steroids, thiazides or sodium glucose co-transporter 2 (SGLT2) inhibitors, and pancreatic neoplasm. DKA associated with the use of SGLT2 inhibitors, although not common, is a well-recognised complication. Glucocorticoid use is not a commonly described association for DKA in T2DM. The diabetogenic propensity of steroids is due to a combination of increased insulin resistance as well as β-cell dysfunction. We report a case of T2DM who presented to our hospital with DKA following exacerbation of his hyperglycaemia by concomitant sepsis, steroid usage and use of SGLT2 inhibitor. Copyright © 2019 John Wiley & Sons.

Key words
diabetic ketoacidosis; steroids; infection; type 2 diabetes

Introduction
Diabetic ketoacidosis (DKA) is usually associated with type 1 diabetes (T1DM) wherein an autoimmune process leads to β-cell destruction resulting in absolute insulin deficiency. Traditional teaching is that the insulin levels in type 2 diabetes (T2DM) are sufficient to prevent lipolysis and DKA. However, in recent years there is increasing recognition of DKA presentations in T2DM patients. More often they have other associated factors like severe infection, medication non-compliance, acute cardiovascular presentation such as stroke or myocardial infarction, use of drugs such as steroids, thiazide diuretics, SGLT2 inhibitors, antipsychotics, pancreatic neoplasm (adenocarcinoma) etc.1–3

Steroids, especially glucocorticoids, are widely used in a variety of clinical conditions for their anti-inflammatory and immunosuppressive properties. Despite their widespread use, they are known to have several side effects, including adverse effects on the carbohydrate metabolism. Corticosteroids increase gluconeogenesis, antagonise the metabolic action of insulin, enhance the effects of counter-regulatory hormones such as glucagon and epinephrine, and reduce the peripheral glucose uptake and induction of insulin resistance via the nuclear peroxisome proliferator-activated receptor (PPAR) α.4

Steroids can worsen hyperglycaemia in those already diagnosed with diabetes and there are also case reports of DKA induced by steroids.5,6 SGLT2 inhibitors are widely used for the management of T2DM due to the effects of blood glucose reduction, weight loss and favourable cardiovascular outcomes. Although not common, the risk of euglycaemic DKA associated with the use of SGLT2 inhibitors is well described in studies and reports.7,8

We report a patient with suboptimally controlled T2DM who developed DKA possibly exacerbated by sepsis, steroids and the concomitant use of SGLT2 inhibitor.

Case report
A 43-year-old Caucasian male with a background history of eczema and T2DM of 13 years, was admitted to the emergency department. He had a BMI of 32kg/m² and family history of T2DM on his mother’s side. Anti-GAD and anti-IA2 antibodies were negative. His diabetes was managed on alogliptin 25mg, pioglitazone 15mg and dapagliflozin 10mg with an HbA1c of 71mmol/mol. He was previously on metformin 1g b.d. but
it was stopped five weeks ago and changed to dapagliflozin by his primary care physician for unclear reasons. Four weeks prior to admission, his primary care physician also started him on prednisolone 20mg along with topical steroid cream for control of severe leg eczema.

On admission, he felt generally unwell with fever and symptoms of polyuria and polydipsia. On examination, he appeared dehydrated and had bilateral lower limb cellulitis. System examinations were normal. Observations showed a pulse rate of 105 beats per minute, blood pressure of 157/75mmHg, temperature of 38.4°C and SpO2 of 98% on air. Blood investigations revealed a pH of 7.12, HCO3 of 5.6mmol/L, blood glucose of 15mmol/L and capillary blood ketone of 5.0mmol/L. Renal and liver function tests were normal. Inflammatory markers were elevated with a CRP of 503mg/L, white cell count of 26.4 and neutrophils of 24.8. An HbA1c was found to be 110mmol/ mol. His ECG, chest X-ray, Doppler ultrasound scan of the leg and CT of abdomen/pelvis were normal with no obvious pancreatic mass lesion seen. Blood cultures did not grow any organisms. A diagnosis of DKA and sepsis secondary to bilateral leg cellulitis was initially reported as limited ketosis-prone type 2 diabetes (KPD). This is now termed as insulin resistance with recent initiation of dapagliflozin which could be one of the precipitating factors for the development of DKA. It was noted that, compared to the degree of acidosis, our patient’s blood glucose was modestly elevated (15mmol/L).

In summary, we presented a patient with a long-standing suboptimally controlled diabetes who developed DKA due to combination of sepsis, use of SGLT2 inhibitor and steroids. We should bear in mind the possibility of DKA in those who are recently started on SGLT2 inhibitors as blood glucose levels in those patients may not be very high. In addition, caution is advised on starting glucocorticoid treatment in T2DM patients since it may worsen insulin resistance and β-cell dysfunction precipitating DKA.

**Declaration of interests**

There are no conflicts of interest declared.

**References**

References are available online at www.practicaldiabetes.com.
Case report

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References