CASE REPORT

Euglycaemic ketoacidosis: a potential new hazard to plastic surgery day case and inpatient procedures

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SUMMARY

A woman aged 44 underwent elective standard abdominoplasty and bilateral mastopexy (superiorly based pedicle with vertical scar) following weight loss of 8.5 stone (53.9 kg) over a 5-year period. She had type 2 diabetes and her antidiabetic medications included metformin, liraglutide and empagliflozin. Towards the end of the first postoperative day, she reported gradual onset of nausea, vomiting and abdominal pain. Her condition continued to deteriorate overnight, becoming tachycardic and tachypnoeic. Urgent investigations showed severe diabetic ketoacidosis with euglycaemia. She was managed with fluid resuscitation, insulin infusion and intravenous sodium bicarbonate in the high dependency unit. She made a complete clinical and biochemical recovery and was discharged on day 9 postoperatively. This case illustrates a diagnostic challenge of a serious life-threatening complication of diabetes in the postoperative period associated with a novel class of antidiabetic medications, sodium-glucose cotransporter 2 inhibitors.

weight loss of 8.5 stone (53.9 kg) over a 5-year period. Relevant medical history included type 2 diabetes mellitus for 15 years. Antidiabetic medications included metformin (12 years), liraglutide (6 years) and empagliflozin (7 months). These were omitted on the morning of surgery and resumed the following day. Her endocrinology review 1 month preoperatively reported no serious issues. Her glycated haemoglobin level (Hb A1C) was 77 mmol/mol.

The procedure went well without complications. Intraoperative monitoring of her glucose levels was satisfactory. She received a total of 2 L of intravenous crystalloid perioperative.

Her blood glucose levels remained stable in the early postoperative period and she was allowed to have food and fluids per oral.

Towards the end of the first postoperative day, she reported gradual onset of nausea, vomiting and abdominal pain. Her condition continued to deteriorate overnight, becoming tachycardic and tachypnoeic.

BACKGROUND

Sodium-glucose cotransporter 2 inhibitors (SGLT2i) are recommended by the National Clinical Institute for Health and Care Excellence (NICE) as monotherapy and/or combination therapy in the treatment of diabetes mellitus.^{1 2} This orally administered medication lowers serum glucose by blocking the reabsorption of glucose in the kidneys, thereby promoting glycosuria. Euglycaemic diabetic ketoacidosis (EuDKA) is an emerging morbidity associated with their usage.^{3 4}

Inappropriate perioperative and postoperative management of antidiabetic medications combined with surgical stress and periods of reduced oral intake can cause a metabolic acidosis. However, normoglycaemia is unique to this drug class, unlike the classical picture of hyperglycaemic ketoacidosis. This combined with non-specific symptomatology can mask the diagnosis.

An elective case within our regional plastic surgery unit required admission to a high dependency unit for intensive medical supportive therapy, following the development of EuDKA late in the first postoperative day.

CASE PRESENTATION

A 44-year-old female underwent elective standard abdominoplasty and bilateral mastopexy (superiorly based pedicle with vertical scar) following

INVESTIGATIONS

Urgent investigations following senior medical review on day 2 revealed severe metabolic ketoacidosis with high anion gap and euglycaemia (pH 6.8, bicarbonate 1 mmol/L, pO₂ 20 kPa, pCO₂ 1.2 kPa, base excess -30 mmol/L, anion gap 25.6 mEq/L, glucose 9 mmol/L (arterial blood gas analysis)). Urine cultures showed no significant growth and methicillin-resistant *Staphylococcus aureus* (MRSA) screen was negative. Other causes of high anion gap metabolic acidosis were excluded including lactic acidosis, uraemia and infection. Remaining investigations were unremarkable (see table 1).

DIFFERENTIAL DIAGNOSIS

The differential diagnosis included other causes of metabolic acidosis (eg, renal failure, lactic acidosis).

Treatment

The treatment included supportive management, intravenous fluids and intravenous infusion of insulin for 48 hours. She also received 50 mL of 8.4% sodium bicarbonate. After resolution of acidosis, the patient was started on subcutaneous insulin and her oral antidiabetic medications restarted. However, the patient did not continue on empagliflozin due to fear of similar illness.

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Table 1 Investigations in the perioperative period

Investigations	Preoperative results	Day 1 postoperative (before EuDKA)	Day 2 postoperative	Day 3 postoperative
Sodium (serum) (mmol/L)	140	138	143	138
Potassium (serum) (mmol/L)	4.1	4.2	5.1	3.8
Chloride (serum) (mmol/L)	101	104	103	113
Urea (serum) (mmol/L)	6.7	4	8.5	5.2
Creatinine (serum) (mmol/L)	48	51	70	52
eGFR (mL/min/1.73 m ²)	>60	>60	>60	>60
Osmolarity (serum) (mOsm/kg)	–	–	327	–
Hb (g/L)	152	121	126	102
WCC 10 ⁹ /L	7.6	9.9	23.3	11.8
pH (arterial blood gas)	–	–	6.8	7.37
Bicarbonate (arterial blood gas)	–	–	1	15.2
Lactate (arterial blood gas)(mmol/L)	–	–	1	1
Glucose (mmol/L)	7.3*	6.3*	9†	11.1†

*Capillary blood sample.

†Arterial blood sample.

eGFR, estimated glomerular filtration rate; EuDKA, euglycaemic diabetic ketoacidosis; HB, haemoglobin; WCC, white cell count.

OUTCOME AND FOLLOW-UP

The patient was transferred to the high dependency unit for emergency supportive medical therapy, fluid resuscitation and insulin infusion. The metabolic acidosis resolved after 30 hours of treatment. However, intravenous insulin infusion continued for 48 hours. She made a complete clinical and biochemical recovery and was discharged on day 9 postoperatively.

DISCUSSION

The obesity epidemic has inundated the elective plastic surgery case mix, with post-massive weight loss patients, who inevitably are diabetic. Increasing numbers of these cases along with other procedures, in a population with high level of comorbidities, are becoming a common practice. There is a trend to perform more day case and short stay procedures, and the selection of these cases requires careful assessment of their medical complexity, operative intervention and social circumstances.⁵ Delayed complications like EuDKA can pose a significant risk.

The mechanism of EuDKA is not fully elucidated. The first description was in a series by Munro *et al* in 1973. In their series, 211 episodes of metabolic decompensation were reported in patients with type 1 diabetes, 37 episodes (in 17 patients) had EuDKA. The authors reported successful management without mortality. However, they were not able to explain the aetiology of the phenomenon.⁶ Both Ireland *et al* and Yabe *et al* hypothesised that the aetiology of EuDKA was due to a lower renal threshold for glucose and a loss of large amounts of glucose in the urine in the presence of an increased rate of gluconeogenesis and free fatty acid release.^{7,8}

The state of hydration and fasting contributes to the levels of glucose in case of acidosis. Burge *et al* showed that glucose levels in patients with type 1 diabetes in case of insulin withdrawal decrease when fasting and increase in state of dehydration.⁹

In case of SGLT2i, the increased levels of glucose in urine lead to lower insulin levels and increased levels of counter regulatory hormones. This leads to glycogenolysis, gluconeogenesis and lipolysis in an attempt to compensate for lower glucose levels. The liver storage of glycogen will eventually deplete. Higher levels of fatty acids and ketones are produced. These changes

contribute to ketosis and acidosis.⁷ Beta cell dysfunction may further contribute to lower insulin levels; this is especially true for the population from east Asia.^{10,11}

The original criteria to define EuDKA described blood glucose less than 16.7 mmol/L and plasma bicarbonate of 10 or less.⁶ Jenkins *et al* described refined criteria for ‘true’ EuDKA of blood glucose <10 mmol/L, with an incidence of 0.8%–1.1%, in their review of 722 cases of diabetic ketoacidosis.¹² A third definition describes EuDKA as DKA without hyperglycaemia with glucose levels less than 13.9 mmol/L.³

SGLT2i are novel antidiabetic medications, approved for management of type 2 diabetes. They act by blocking glucose resorption in the kidney thus increasing glucose elimination via urine. They are administered orally as a single daily dose. They are not recommended for patients with poor kidney function.² SGLT2i approved by FDA and NICE include: canagliflozin, dapagliflozin, empagliflozin as a single medication or combined with other classes of antidiabetic medications. The terminal half-life of these medications is (10.6–13.1), 12.9, 13.1 hours, respectively.

Their unique action in controlling glucose levels, combined with weight-reducing properties and oral mode of administration, makes them more appealing for use in overweight population.¹³ Hence, increasing number of patients coming for aesthetic procedures related to obesity are expected to be on this novel class of medications. However, there are increasing reports describing the association of EuDKA and usage of SGLT2i.^{3,4,14}

The non-specific symptoms of nausea and vomiting associated with normal glucose levels make it easy to miss the correct diagnosis, unless there is a high index of suspicion. More investigations in the form of arterial blood gas analysis and ketone levels must be requested. The complexity of surgical patients and postoperative complications makes it inherently more difficult to identify the problem. In one case report, a patient treated with SGLT inhibitor, underwent a negative exploratory laparotomy following a colorectal procedure as he presented with severe acidosis in the postoperative period.³

There have been similar cases reported in the literature in which patients with type 2 diabetes treated with SGLT2i,

presented with euglycaemic ketoacidosis. One case reported EuDKA 5 days following discharge from hospital after having an elective procedure.¹⁵ Another case reported the start of symptoms 10 hours following bilateral cervical foraminotomy.³ However, the majority of cases reported in the literature were triggered by factors other than surgery.

The learning point from this case report is that a high index of suspicion is warranted for patients with diabetes, treated with SGLT2i. We recommend stopping the drug, 1–2 days in the preoperative period and switching to other alternatives to avoid such complication. It may also be prudent to stop SGLT2i in all hospitalised patients for the same reason. The non-specific symptoms of nausea and vomiting should be thoroughly investigated. Further analysis of arterial blood gas and ketone bodies must be requested.

We also emphasise the importance of appropriate counselling in the perioperative period about the risk of such complication as a potential life-threatening hazard and the need to change or stop the medication perioperatively, especially in aesthetic procedures where risk to life should be minimised. More cases and information are needed about the scale of such complication postoperatively to be able to make a judgement about its use in the perioperative period.

Learning points

- ▶ A high index of suspicion is warranted for patients with diabetes, treated with sodium-glucose co-transporter 2 inhibitors (SGLT2i) to reach the correct diagnosis.
- ▶ The non-specific symptoms of nausea and vomiting postoperatively should be thoroughly investigated in patients with diabetes treated with SGLT2i.
- ▶ Further analysis of arterial blood gas and ketone bodies must be requested.
- ▶ Appropriate counselling in the perioperative period about the risk of such complication as a potential life-threatening hazard, especially in aesthetic procedures where risk to life should be minimised.

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