

Euglycemic diabetic ketoacidosis due to small bowel perforation: a case report

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Abstract

Diabetic Ketoacidosis (DKA) is a potentially life-threatening condition that complicates diabetes mellitus. Euglycemic DKA (eDKA) is emerging as a variant in both type 1 and type 2 diabetes mellitus. The rise in its presentation is being caused by newer medicines using SGLT-2 inhibitors, with a complex underlying pathophysiology. Here we report a case of a 70-year-old woman present-

ing to the emergency department complaining of shortness of breath and abdominal pain. She suffers from type 2 diabetes mellitus and is on oral therapy, including the SGLT-2 inhibitor empagliflozin. Further testing revealed a high-anion-gap metabolic acidosis without elevation of lactate levels and a glucose level of 160 mg/dL. CT imaging of the abdomen showed a small bowel perforation. The case required aggressive medical therapy before surgical repair in the operating room. EDKA is a medical emergency that can be challenging to identify due to its atypical presentation compared to the traditional DKA (which is hyperglycemic). These characteristics can delay effective and timely treatment.

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Case Report

A 70-year-old woman presented to the emergency department complaining of abdominal pain for the past seven days and acute-onset shortness of breath. She suffered from hypertension and type 2 diabetes mellitus on empagliflozin/metformin therapy (with reported good compliance); she was not on insulin therapy. Her Body Mass Index (BMI) was 33. She claimed that she was awaiting elective surgery to repair an incisional hernia. She denied any allergy. On evaluation, she was awake and oriented, tachypneic (28 breaths/min) with an almost periodic breathing pattern, and a peripheral oxygen saturation above 95%. On auscultation, the lung sounds were clear without any abnormal findings. She was well perfused with no signs of congestion; the blood pressure was 120/80 mmHg and the heart rate was 110 bpm. The EKG showed sinus tachycardia without any other concerning signs. She was fully alert and oriented, with a GCS of 15. The pupils were equal in diameter and both reactive to light. Her cranial nerve examination was completely normal. She had no speech or coordination deficits. The patient had no sensory or motor deficits in the limbs, but she complained of generalized weakness. She had no rigidity on the neck examination. The abdomen was tender in the lower quadrants, where the known incisional hernia was palpable and firm. She also complained of having a closed bowel for seven days, associated with nausea and persisting vomiting, resulting in lower caloric intake before presentation. The chest X-ray showed no signs of pulmonary pathology, and the abdomen X-ray (acquired in the supine position) showed signs of dilated small bowel without free air. The arterial blood gas showed a pO₂ of 124 mmHg (room air) associated with a severe high anion gap metabolic acidosis (pH 7.2, pCO₂ 11 mmHg, HCO₃ 4.5 mmol/L, BE -22, anion gap 22, Lactate 1 mmol/L, glucose 160 mg/dL, Sodium 132 mmol/L, Potassium 2 mmol/L, Chloride 105 mmol/L). The anion gap was calculated by the point-of-care blood gas analyzer by subtracting the sum of bicarbonate and chloride from the sodium level (without accounting for the potassium level). Laboratory exams revealed a mild leukocytosis (neutrophil 84%, lymphocytes 7.4%, neutrophil-to-lymphocyte ratio 11), normal kidney function (Creatinine 1.1, BUN 20 mg/dL) and normal hepatic function

(ALT 15 U/L, total bilirubin 0.4 mg/dL, INR 1.09). There was severe hypokalemia (1.9 mmol/L) and a mild elevation of the C-reactive protein (7.45 mg/dL, nv <0.5 mg/dL). Later, the patient received 100 mEq of intravenous sodium bicarbonate 8.4% twice and 40 mEq of potassium chloride in normal saline.

The patient was transferred to the observation unit of the emergency department and was then re-evaluated by another physician (the main author of this paper). The overall clinical picture was unchanged, as did the blood gas analysis. A point-of-care ketone fingerstick finally revealed ketonemia above the detection limit (>10 mmol/L) leading to the Diagnosis of Euglycemic Diabetic Ketoacidosis (eDKA). The patient received rapid volume expansion with 1000 ml of Lactated Ringer solution. Shortly after, rapid human insulin infusion was initiated at a dose of 0.1 UI/kg/hour. Alongside insulin therapy, intravenous potassium replacement was prescribed: the patient received 60 mEq of potassium chloride diluted in 500 mL of 10% dextrose and infused via a central venous catheter that was placed by the treating physician.

A PoCUS (Point of Care Ultrasound) was performed by the authors and showed a normal diameter abdominal aorta with no signs of dissection and no free fluid in the abdominal recesses. There was no hydronephrosis bilaterally and no signs of cholecystitis. Bowel-focused ultrasound was challenging due to copious subcutaneous fat tissue but showed dilated bowels (30 to 40 mm diameter) with nearly absent movement inside the hernia but without fluid around the bowel loops. For further diagnostic evaluation of the abdominal findings, the patient underwent a contrast CT scan, with raised concerns for bowel obstruction. She was diagnosed with a small bowel perforation due to obstruction of the known incisional hernia, which likely triggered the DKA. The consultant surgeon was alerted and the patient was then admitted to the ICU for perioperative management.

Discussion

Diabetic ketoacidosis (DKA) is a life-threatening complication of diabetes mellitus. Risk factors for DKA include newly diagnosed diabetes mellitus, omission of chronic insulin therapy, infec-

tions, acute myocardial infarction, cocaine use, thyrotoxicosis, and many more, as any critical illness can induce DKA. This condition is characterized by an insulin deficit (absolute or relative associated with insulin resistance) leading to hyperglycemia, osmotic diuresis (resulting in extracellular volume losses), elevated levels of blood ketones (also mediated by glucagon effect), and electrolyte imbalances (with hypokalemia and hyperkalemia being the most concerning). Unfortunately, there are no definite criteria for diagnosing DKA. Typically, the pH is below 7.30, sodium bicarbonate is less than 15 mmol/L, and anion gap (AG) is above 12 mmol/L, associated with positive urine or serum ketones (> 3 mmol/L).¹ Euglycemic DKA (eDKA) was first described in 1973 by Munro *et al.*² The available literature reports that 2.6 to 7% of DKA admissions are euglycemic. Furthermore, SGLT-2 inhibitors (such as empagliflozin, canagliflozin, and dapagliflozin) increase the risk of eDKA by a factor of 7.³ The mechanism by which SGLT-2 inhibitors cause eDKA is complex: they enhance glucose excretion by the kidney and promote reabsorption of ketone bodies. These drugs also appear to inhibit beta-cells and stimulate alpha-cells, ultimately increasing lipolysis and ketone body production, and causing an overall imbalance between glucagon and insulin levels.⁴ In the context of eDKA, the hyperglycemia is moderate (below 300 mg/dL). The management of these variants of DKA differs slightly from the classic DKA approach. Reversal of concomitant shock and hypoperfusion is paramount, as well as aggressive correction of electrolyte imbalances (*i.e.*, hypokalemia). Many protocols have been published, but they all agree on holding the insulin infusion until a potassium level of at least 3.5 mEq/L is reached. Potassium levels between 3.5 and 5.5 mEq/L require intravenous supplementation with 10 mEq per liter of infused crystalloid. Potassium infusion is held above 5.5 mEq/L. In the context of eDKA, the intravenous insulin infusion must be paired with dextrose infusion to prevent hypoglycemia. Sodium bicarbonate in DKA is generally unnecessary, although it can be considered in the presence of profound acidosis (pH <7.0), hemodynamic instability, or life-threatening hyperkalemia.³ In our case, the patient did well overnight and by continuing the above-mentioned treatment, the anion gap was reduced, the potassium returned to baseline values, and the pH began to rise (Table 1).

Table 1. Changes in arterial blood gas parameters.

Location	ICU	ICU	ICU	ICU	ICU	ICU	ICU	ICU	ICU	ICU	ICU	OR	ICU	ICU	ICU	ED	ED	ED
Date and time	Day 5	Day 4	Day 4	Day 4	Day 3	Day 3	Day 3	Day 3	Day 2	Day 2	Day 2	Day 2	Day 2	Day 2	Day 2	Day 1	Day 1	Day 1
	5.36	22.14	15.43	9.11	21.28	14.01	09.54	03.55	23.50	15.45	12.14	11.11	09.02	04.48	02.47	23.08	16.43	15.27
pH	7.53	7.54	7.54	7.53	7.45	7.42	7.36	7.34	7.29	7.18	7.05		7.2	7.27	7.19	7.26	7.32	7.21
pCO ₂ (mmHg)	44	41	40	34.3	29	24	25	25	28	34	35		19	18	13	14	16	12
pO ₂ (mmHg)	85	82	80	77	103	103	97	103	106	106	93		110	106	117	122	109	124
P/F	304	293	286	308	412	343	323	343	353	265	233		524	505	557	581	519	590
FiO ₂ (%)	28	28	28	25	25	30	30	30	30	40	40		21	21	21	21	21	21
HCO ₃ (mmol/L)	37	35	35	29	20	17	14	13	13	12	9		7	8	5	6	8	5
Sodium (mmol/L)	146	148	150	153	149	147	146	143	144	147	135		144	141	140	136	135	132
Potassium (mmol/L)	2.9	3.3	3	3.1	2.7	2.7	2.8	2.7	2.7	3	3.1		3.1	2.9	2.6	2	2	2
Chloride (mmol/L)	108	110	115	118	122	122	122	121	120	123	121		118	117	115	106	106	105
Ionized calcium (mmol/L)	1.15	1.17	1.18	1.21	1.16	1.23	1.22	1.17	1.18	1.2	1.25		1.27	1.19	1.12	1.18	1.19	1.27
Anion Gap (mmol/L)	1	3	0	6	7	8	10	9	11	12	5		19	16	20	24	21	22
Serum osmolarity (mosm/L)	300	305	311	317	310	308	N/A	286	300	302	282		297	289	289	279	279	272
Glucose (mg/dL)	145	163	187	200	208	236	267	225	226	165	210		160	112	178	148	154	161
Lactate (mmol/L)	1.4	2	2.1	1.3	1.1	1	1	1.2	1.2	0.8	0.6		0.7	0.6	0.8	1.4	1.5	1

Unfortunately, a quantitative trend of ketone clearance is not available, since finger-stick β -hydroxybutyrate (β -OHB) test results were charted only in the emergency department; although a urine dipstick was probably performed during the first evaluation in the ED, it was not reported in the charts and we could not find it when we reviewed the case. The patient underwent an urgent surgical operation the following morning. The surgeons were able to identify the source of perforation and performed a terminal-terminal resection of the bowel. From there, the patient had a positive intrahospital course and was first transferred to the surgical ward, and then to the medicine ward for optimization of her diabetes treatment. She was discharged home 14 days later without complications. Usually, metabolic acidosis and ketosis are not the primary goals of care for DKA patients. This case was different because the profound metabolic derangement precluded safe induction of general anesthesia, which was required to treat the underlying cause of the overall clinical picture and sustain the DKA itself. The patient was also profoundly hypokalemic, so insulin was delayed until safe levels of serum potassium were obtained. Typically, metabolic acidosis due to DKA presents with hyperkalemia due to insulin deficiency,⁵ however, this patient was hypokalemic likely due to renal excretion of potassium promoted by SGLT-2 inhibitor therapy. The patient stayed too little time in the emergency department, but the intensive care unit team reported polyuria, which likely was caused by the osmotic effect of glucose.⁶

Glucose was not highly elevated because of multiple factors: the patient continued to comply with her prescription and SGLT-2 inhibitors can promote ketoacidosis with normal to slightly elevated glucose levels, as described above. She was also eating very little in the days before the presentation (due to nausea, vomiting, and abdominal pain) which probably contributed to the euglycemia observed. The patient was on empagliflozin for more than six months before this presentation, so it is unlikely that empagliflozin alone triggered the EDKA. The obstruction and subsequent perforation of a bowel loop likely acted as the triggering event of the DKA; while her anti-diabetes therapy and poor food intake favored near-normal glucose levels.

She was not even brought to the operating room in perfect metabolic balance because, after fourteen hours of medical management, the metabolic acidosis was still ongoing. However, she required definitive treatment of her bowel perforation. She was not induced into general anesthesia but kept awake with a loco-regional block.

Conclusions

Euglycemic DKA is a challenging diagnosis to make during an emergency evaluation because its presentation pattern is different from classic hyperglycemic DKA: it lacks hyperglycemia by definition. Emergency physicians often rely on pre-existing mental maps and cognitive shortcuts (which can generate biases), and eDKA differs from the classic high anion gap metabolic acidosis with hyperglycemia. This diagnosis requires an extra cognitive step, which can be challenging to make if simultaneously caring for other life-threatening conditions (*i.e.*, severe hyperkalemia, shock, severe respiratory failure). This specific patient tricked an experienced emergency doctor. For this reason, it is important to be aware that eDKA exists and to know who is the most at risk of developing it. With the spread of SGLT-2 inhibitors, this relatively rare condition is expected to increase in overall number of cases annually. Delay in recognition and, consequently, in treatment can be life-threatening. These patients require the same expedited therapy as those with hyperglycemic DKA.

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