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ACR ISSN 2637-3793 ARCHIVES OF CASE REPORTS

Case Presentation

Euglycemic Diabetic Ketoacidosis Induced by Sodium-glucose Cotransporter-2 Inhibitor in the Setting of Chronic Kidney Disease with Dehydration Induced by Nausea and Vomiting: A Case Report

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Abstract

Background: Euglycemic diabetic ketoacidosis (EDKA) is a recognized but uncommon adverse effect of sodium–glucose cotransporter-2 (SGLT2) inhibitors. It presents with metabolic acidosis and significant ketosis, yet with normal or near-normal blood glucose levels, making its diagnosis frequently delayed. SGLT2 inhibitors are increasingly used for their cardiovascular and renal benefits in patients with type 2 diabetes mellitus; however, clinicians should remain alert to this potential complication, especially when additional risk factors such as dehydration, fasting, or renal impairment coexist.

Case presentation: We report the case of a 54-year-old male with long-standing type 2 diabetes mellitus, hypertension, and chronic kidney disease who developed euglycemic diabetic ketoacidosis following two days of nausea, vomiting, and poor oral intake. The patient had been on empagliflozin and pioglitazone therapy. On admission, he appeared dehydrated and mildly tachycardic. Laboratory findings revealed metabolic acidosis (pH 7.10, bicarbonate 15 mmol/L, with an elevated anion gap), positive serum ketones, and a normal blood glucose level of 9 mmol/L. After exclusion of other causes, the diagnosis of EDKA secondary to SGLT2 inhibitor use was established. Empagliflozin was discontinued, and the patient was treated with dextrose-containing intravenous fluids, continuous insulin infusion, and electrolyte replacement. His metabolic derangements resolved within 48 hours, and he was discharged in stable condition with appropriate counseling and outpatient follow-up.

Conclusion: This case highlights the importance of considering EDKA in diabetic patients presenting with unexplained metabolic acidosis, even when glucose levels are not elevated. Recognition of SGLT2 inhibitor–induced EDKA is vital, particularly in the presence of precipitating factors such as dehydration and chronic kidney disease. Early identification and prompt management are crucial for preventing morbidity and mortality.

More Information

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Submitted: October 22, 2025
Accepted: October 30, 2025
Published: November 03, 2025

Citation: Mahmoud EH, Ismail OA. Euglycemic Diabetic Ketoacidosis Induced by Sodium-glucose Cotransporter-2 Inhibitor in the Setting of Chronic Kidney Disease with Dehydration Induced by Nausea and Vomiting: A Case Report. Arch Case Rep. 2025; 9(11): 339-341. Available from: https://dx.doi.org/10.29328/journal.acr.1001170

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Keywords: Euglycemic Diabetic Ketoacidosis (EDKA); Sodium-Glucose Cotransporter-2 (SGLT2) inhibitors; Empagliflozin; Metabolic acidosis; Dehydration and ketogenesis; Insulin infusion therapy; Glucagon and lipolysis mechanism; Adverse drug reaction in diabetes management

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Introduction

Sodium–glucose cotransporter-2 inhibitors (SGLT2i) have emerged as a pivotal therapeutic class in the management of type 2 diabetes mellitus due to their proven cardiovascular and renal protective effects [1,2]. Despite these advantages, they have been associated with rare but serious adverse events such as euglycemic diabetic ketoacidosis (EDKA) [3-5]. EDKA differs from typical diabetic ketoacidosis (DKA) by the absence of significant hyperglycemia, posing a diagnostic challenge that may delay appropriate therapy [6,7].

Since their introduction, several case reports and reviews have described EDKA episodes precipitated by conditions such as fasting, infection, dehydration, surgery, or renal impairment [8-10]. The pathophysiology involves an imbalance between insulin and glucagon secretion, enhanced lipolysis, and increased ketone production in the setting

of reduced renal glucose reabsorption [4,7,10] . Here, we describe a patient with chronic kidney disease who developed EDKA after gastrointestinal illness while on empagliflozin therapy, underscoring the need for clinician awareness and patient education regarding sick-day management [2].

Case presentation

A 54-year-old male presented to the emergency department with a two-day history of nausea, repeated vomiting, and generalized weakness following consumption of restaurant food. He reported an inability to tolerate oral intake and decreased urine output. His medical history included type 2 diabetes mellitus, hypertension, benign prostatic hyperplasia, and stage 3 chronic kidney disease. His medications were empagliflozin 10 mg daily, pioglitazone 30 mg daily, amlodipine 5 mg daily, and tamsulosin 0.4 mg daily. He denied recent infection, fever, chest pain, or alcohol intake. There was no history of insulin use.

Upon presentation, the patient appeared dehydrated but alert. His vital signs showed blood pressure 110/70 mmHg, heart rate 98 beats per minute, respiratory rate 20 breaths per minute, and oxygen saturation 98% on room air. Capillary blood glucose was 9 mmol/L. Systemic examination was unremarkable except for mild epigastric tenderness.

Key laboratory findings are summarized below (Table 1):

Arterial blood gas confirmed metabolic acidosis with an elevated anion gap. Urine dipstick was positive for ketones. Serum lactate was within normal limits, and infection screening was negative. Based on clinical and biochemical findings, a diagnosis of euglycemic diabetic ketoacidosis secondary to SGLT2 inhibitor use was established.

The patient was admitted to the intensive care unit (ICU). Empagliflozin was discontinued. He received intravenous dextrose-saline fluids and a continuous insulin infusion, titrated according to capillary glucose and ketone monitoring. Potassium supplementation was administered as required. Over the following 48 hours, his metabolic parameters normalized. Once ketones cleared and bicarbonate improved to 22 mmol/L, insulin infusion was discontinued and subcutaneous basal-bolus insulin therapy initiated. He tolerated oral intake and was transferred to the medical ward before discharge on day four.

Table 1: Key laboratory findings on hospital admission.

Parameter	Result	Reference Range
pH	7.10	7.35 - 7.45
Bicarbonate (HCO_3^-)	15 mmol/L	22 - 28
Anion Gap	Elevated	—
Serum Ketones	4+	Negative
Blood Glucose	9 mmol/L	4 - 10
BUN	13 mmol/L	2.5 - 7.1
Creatinine	154 µmol/L	62 - 115
WBC	9×10^9/L	4 - 11

At outpatient follow-up, the patient remained stable with no recurrence of ketoacidosis. His renal function improved (serum creatinine 138 µmol/L). He was maintained on insulin therapy, and education on the avoidance of SGLT2 inhibitors during illness or reduced oral intake was reinforced.

Discussion

Euglycemic diabetic ketoacidosis represents a diagnostic challenge due to the absence of marked hyperglycemia [6,7]. In classical DKA, plasma glucose levels exceed 13.9 mmol/L (250 mg/dL), whereas in EDKA, glucose is typically below this threshold. SGLT2 inhibitors, by promoting urinary glucose excretion, can mask hyperglycemia while sustaining the metabolic milieu conducive to ketogenesis [4,10].

The mechanism involves several interrelated pathways: (1) reduced insulin secretion due to lower plasma glucose levels; (2) increased glucagon secretion promoting lipolysis and ketogenesis; (3) decreased renal clearance of ketone bodies; and (4) volume depletion from osmotic diuresis, which concentrates ketone levels. Patients with chronic kidney disease are particularly vulnerable due to impaired renal handling of acids and delayed clearance of ketone bodies [1,10]. Dehydration, as seen in this case from vomiting and poor oral intake, further amplifies these effects.

Several case reports have documented similar presentations of EDKA associated with SGLT2 inhibitors. Alkatheeri, et al. [8] described a fasting-related episode in a patient on dapagliflozin, while Peters, et al. [5] and Hamblin, et al. [9] reported cases triggered by acute illness or perioperative fasting. Collectively, these reports emphasize that SGLT2 inhibitor–induced EDKA can occur even in the absence of precipitating infections and may be the first presentation of metabolic decompensation in otherwise stable diabetic patients.

In our patient, both chronic kidney disease and dehydration acted synergistically to precipitate EDKA. The diagnosis was established after exclusion of sepsis, lactic acidosis, and toxic ingestion. The cornerstone of management remains discontinuation of the offending agent, adequate fluid resuscitation with dextrose-containing solutions, and continuous insulin infusion to suppress ketogenesis [7]. Close monitoring of electrolytes, particularly potassium, is critical. Recovery typically occurs within 48 to 72 hours if treated promptly.

This case underscores the need for clinician awareness and patient education regarding the risk of EDKA [8]. Patients should be advised to withhold SGLT2 inhibitors during any illness causing reduced oral intake, vomiting, or dehydration. Furthermore, clinicians should maintain a high index of suspicion when encountering unexplained metabolic acidosis in diabetic patients—even when blood glucose appears normal.

Conclusion

Euglycemic diabetic ketoacidosis is a serious but reversible adverse effect of SGLT2 inhibitors. This case illustrates the importance of recognizing subtle presentations of DKA and understanding the unique biochemical profile associated with SGLT2 inhibition. Prompt identification and management can prevent significant morbidity. Clinicians must educate patients on the potential risks and the importance of temporary drug discontinuation during acute illness.

Ethical approval and consent

Written informed consent was obtained from the patient for publication of this case report and accompanying data. Institutional ethical approval was granted by the Medical Research Committee at Care Medical Al-Rawabi Hospital, Riyadh, Saudi Arabia.

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