World Journal of Biology Pharmacy and Health Sciences
eISSN: 2582-5542
Cross Ref DOI: 10.30574/wjbphs
Journal homepage: https://wjbphs.com/

(CASE REPORT)

Dapagliflozin-associated euglycemic diabetic ketoacidosis in 66-year-old with type 2 Diabetes: A clinical case report

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World Journal of Biology Pharmacy and Health Sciences, 2024, 19(03), 194–197

Publication history: Received on 03 June 2024; revised on 04 September 2024; accepted on 06 September 2024

Article DOI: https://doi.org/10.30574/wjbphs.2024.19.3.0602

Abstract

Euglycemic diabetic ketoacidosis (EDKA) is a rare but serious complication of type 2 diabetes, often associated with the use of SGLT2 inhibitors. This case report describes an episode of EDKA in a 66-year-old male with a long history of type 2 diabetes and multiple comorbidities, who developed this complication following the introduction of dapagliflozin. Although his blood glucose levels remained within normal limits, laboratory tests revealed elevated ketonemia and severe metabolic acidosis. The patient was successfully treated with intravenous hydration and insulin therapy, leading to a rapid improvement in his clinical condition. This case underscores the importance of clinical vigilance and patient education for those treated with SGLT2 inhibitors to prevent and effectively manage this potentially life-threatening complication.

Keywords: Euglycemic diabetic ketoacidosis; Dapagliflozin; SGLT2 inhibitors; Type 2 diabetes; Insulin therapy

1. Introduction

Diabetic ketoacidosis (DKA) is an acute and potentially life-threatening complication of diabetes, most commonly associated with severe hyperglycemia, typically observed in patients with type 1 diabetes, but also in those with type 2 diabetes under conditions of significant metabolic stress (1). Traditionally, DKA is characterized by elevated blood glucose levels, metabolic acidosis, and increased ketonemia, resulting from an absolute or relative insulin deficiency. However, the recent introduction of sodium-glucose cotransporter 2 (SGLT2) inhibitors in the management of type 2 diabetes has led to the emergence of an atypical form of ketoacidosis, known as euglycemic diabetic ketoacidosis (EDKA) (2).

SGLT2 inhibitors, such as dapagliflozin, have revolutionized the management of type 2 diabetes by improving glycemic control and reducing cardiovascular and renal risks (3). These drugs act by blocking glucose reabsorption in the renal tubules, thereby increasing urinary glucose excretion and lowering blood glucose levels independently of insulin action (4). However, this mechanism can also induce a reduction in endogenous insulin levels and an increase in glucagon production, promoting ketogenesis even in the absence of hyperglycemia (5). This scenario presents a major diagnostic challenge as the lack of typical hyperglycemia may delay the recognition of ketoacidosis, thereby increasing the risk of morbidity and mortality (6).

EDKA is a rare but serious complication that requires heightened clinical vigilance and thorough patient education. Clinicians must be aware of this entity to diagnose and treat it promptly, especially in patients with multiple comorbidities who are treated with SGLT2 inhibitors. This case report illustrates an episode of EDKA in a 66-year-old patient treated with dapagliflozin, highlighting the clinical challenges and effective management strategies.

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2. Case Report

A 66-year-old male with type 2 diabetes diagnosed in 1998 was under regular follow-up for multiple microvascular and macrovascular complications. The patient had stable diabetic retinopathy, macroalbuminuria managed with an angiotensin receptor blocker, stage 3b chronic kidney disease, and a diabetic foot ulcer associated with Charcot neuroarthropathy, which had been evolving since 2020. His medical history was also notable for recurrent cellulitis and osteomyelitis, treated with prolonged antibiotic therapy.

In January 2023, dapagliflozin, an SGLT2 inhibitor, was added to his antidiabetic regimen to improve glycemic control and reduce proteinuria. However, in 2024, the patient presented to the emergency department with severe fatigue, profuse sweating, and dizziness. On examination, he was afebrile, but clinical signs suggested moderate dehydration. Laboratory investigations revealed elevated ketonemia at 3.9 mmol/L (normal range: <0.6 mmol/L), decreased pH at 7.21 (normal range: 7.32-7.43), normal blood glucose at 86 mg/dL (normal range: 60-100 mg/dL), and reduced bicarbonate levels at 12.8 mmol/L (normal range: 22-31 mmol/L). These findings confirmed the diagnosis of euglycemic diabetic ketoacidosis.

The patient was immediately managed with intravenous isotonic saline to correct dehydration and acidosis. Continuous intravenous insulin infusion was initiated to reduce ketonemia and restore acid-base balance. Within 48 hours, there was significant improvement in laboratory parameters, with normalization of pH and reduction of ketonemia to normal levels. The patient was closely monitored and subsequently transferred to the internal medicine ward for further recovery.

Table 1 Evolution of blood test results

	Day 1: Admission	**Day 4 : Discharge**	**Reference marge**
pH (venous blood gas)	7,21	7,36	7.32-7.43
HCO3 (venous blood gas)	12,8	20,9	22.0-26.0 mmol/L
Glucose (serum)	86	158	60-100 mg/dL
Ketonemia	3,9	0,2	<0,6 mmol/L
Chloride	101	106	100-110 mmol/L
PCO2	27	27	22-29 mmol/L
Anion gap	11	15	0-20 mmol/L
Potassium	5	4,6	3.5-5.1 mmol/L
Sodium	128	137	136-145 mmol/L

3. Discussion

Euglycemic diabetic ketoacidosis is an emerging and underdiagnosed complication in patients treated with SGLT2 inhibitors. While these drugs are widely beneficial for glycemic control and reducing cardiovascular risks, they carry an increased risk of ketoacidosis due to their unique mechanism of action (7). By inhibiting renal glucose reabsorption, SGLT2 inhibitors induce increased glucose excretion, which can maintain normal blood glucose levels even in the presence of excessive ketogenesis (8). This phenomenon may be exacerbated by a reduction in insulin levels, a key regulator of ketone body production, and an increase in glucagon secretion, thereby promoting metabolic acidosis (9). The case presented highlights the diagnostic challenges associated with EDKA. The absence of hyperglycemia, a hallmark of classic DKA, complicates diagnosis, particularly in patients presenting with nonspecific symptoms such as fatigue and dizziness (10). Delayed diagnosis can lead to severe complications if metabolic acidosis is not promptly corrected. Therefore, it is crucial that clinicians remain alert to this possibility in patients treated with SGLT2 inhibitors, particularly those with additional risk factors such as infections, dehydration, or prolonged fasting (11).

In terms of management, this case demonstrates the effectiveness of intravenous hydration and insulin therapy in rapidly correcting acidosis and preventing further complications. The importance of early intervention cannot be overstated, as it minimizes the risk of decompensation and reduces hospitalization time (12). Furthermore, patient education is crucial in preventing future episodes. Patients on SGLT2 inhibitors must be informed about the early signs

of ketoacidosis and the need for prompt medical consultation if suspicious symptoms arise (13). Finally, this case underscores the necessity for continuous monitoring of patients on SGLT2 inhibitors, particularly during the initiation of therapy or in the presence of risk factors. Clinicians should consider temporary discontinuation of the SGLT2 inhibitor in high-risk situations, such as severe infections or planned surgical interventions (14). Regular monitoring of metabolic parameters, including ketonemia and bicarbonate levels, is also recommended to detect early abnormalities (15).

4. Conclusion

Euglycemic diabetic ketoacidosis, although rare, represents a serious complication of SGLT2 inhibitor use. Early recognition and prompt management are critical to prevent severe outcomes. Patient education and clinical vigilance are essential to prevent and effectively manage this condition.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare no conflict of interest related to this publication.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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