Clinical Analysis of a Case of EDKA Presenting with Acute Abdomen

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Abstract: This study aims to explore the diagnostic and therapeutic methods for a patient with Euglycemic Diabetic Ketoacidosis (EDKA) presenting primarily with acute abdomen. On December 12, 2021, our hospital admitted a patient who experienced abdominal pain and vomiting after drinking alcohol. Upon admission, the patient underwent laboratory tests including blood glucose, complete blood count, renal function, liver function, cardiac enzyme profile, urinalysis, and electrolytes, as well as gastroscopy. Based on the results of blood gas analysis and urine ketone bodies, combined with a history of type 2 diabetes mellitus, alcohol consumption, and recent oral administration of dapagliflozin, the patient was diagnosed with EDKA. The treatment involved large volumes of fluid replacement and administration of insulin with glucose to clear ketones. The patient's urine ketone levels gradually returned to normal, abdominal pain symptoms were relieved, and the patient was discharged in good condition. The incidence of EDKA is relatively low, making it prone to misdiagnosis or missed diagnosis in clinical practice, which can delay treatment. Therefore, it is essential for physicians to be vigilant, integrate the results of various examinations, past medical history, and other factors for early and accurate diagnosis to formulate targeted treatment plans and improve patient prognosis.

***Keywords*:** Diabetic Ketoacidosis; acute abdomen; diagnosis; treatment

1. Introduction

Diabetic Ketoacidosis (DKA) is a common acute complication in diabetic patients characterized by rapid onset, severe illness, and rapid progression, and improper emergency management can be life-threatening[1]. Euglycemic Diabetic Ketoacidosis (EDKA) is a special type of DKA with normal blood glucose levels, making it relatively rare in clinical cases but an increasingly discussed topic in emergency medicine literature. Because EDKA presents with normal blood glucose levels, it often mistakenly rules out the possibility of DKA, making it more misleading than DKA. If clinicians are not sufficiently aware, the diagnostic difficulty and misdiagnosis rate are higher[2][3]. This article reports and analyzes the diagnosis and treatment process of a successfully diagnosed case of EDKA presenting with acute abdomen, aiming to enhance emergency physicians' awareness of this disease.

2. Materials and Methods

2.1 Case Data

The patient is a 37-year-old male with a history of type 2 diabetes mellitus without complications, recently managed with oral acarbose, metformin, and an SGLT-2 inhibitor (dapagliflozin) for blood glucose control. There is no family or genetic history of illness. The patient presented to the emergency department of a local hospital on December 12, 2021, with complaints of abdominal pain and vomiting for 10 hours following alcohol consumption.On December 11, 2021, at 23:20, the patient began experiencing persistent abdominal pain after drinking alcohol. The pain was intermittent, primarily located under the xiphoid process, and accompanied by nausea and five episodes of vomiting. The vomit consisted of gastric contents without coffee-ground material. The patient had three bowel movements, which were formed and without melena. There was no fever, cough, palpitations, chest tightness, chest pain, blurred vision, or syncope. Urination was normal. On December 12, 2021, at 09:20, the patient's family brought him to the local hospital. Upon admission, the patient had severe abdominal pain, was unable to walk, and experienced increased pain with breathing. Despite administration of pain relief medication, the pain persisted, and the patient was transferred to our hospital for further treatment.

Physical Examination: Temperature (T): 36.7°C, Pulse (P): 67 beats/min, Respiratory Rate (R): 16 breaths/min,Blood Pressure (BP): 137/83 mmHg (1 mmHg = 0.133 kPa), Oxygen Saturation (SPO2): 98%. The patient was conscious, coherent, and displayed a pained expression. He answered questions appropriately. Pupils were equal in size and round, with sensitive light reflexes. There was no jaundice in the sclera. The skin was moist, and the complexion was slightly pale. Breath sounds

in both lungs were clear with no rales. Cardiac auscultation revealed no valve murmurs. The abdomen was soft, with significant tenderness under the xiphoid process but no rebound tenderness. Murphy's sign (-). The liver and spleen were not palpable. Neurological examination (-).

2.2 Auxiliary Examinations

2.2.1 Laboratory Examinations

On December 12, 2021, the following laboratory results were obtained:

Fingerstick Blood Glucose (GLU): 8.7 mmol/L.Complete Blood Count:White Blood Cells (WBC): 12.15 × 10^9/L (↑),Red Blood Cells (RBC): 4.8 × 10^{12}/L,Neutrophil Percentage (NEUT): 85.4% (↑),Lymphocyte Percentage (LYM): 12.6%,C-Reactive Protein (CRP): 10 mg/L.,Liver Function:Alanine Aminotransferase (ALT): 32.9 U/L,Aspartate Aminotransferase (AST): 20.1 U/L,Total Bilirubin (Tbil): 9.7 μmol/L

Direct Bilirubin (DBIL): 3.14 μmol/L.Renal Function:Blood Urea Nitrogen (BUN): 5.4 mmol/L,Creatinine (Cr): 84.4 μmol/L.Electrolytes:Potassium (K+): 3.8 mmol/L,Sodium (Na+): 143 mmol/L,Chloride (Cl-): 106 mmol/L,Uric Acid (UA): 543.50 μmol/L (↑),Blood Amylase (AMY): 106.9 U/L.Cardiac Enzymes:Creatine Kinase (CK): 73 U/L,Creatine Kinase-MB (CKMB): 2.6 U/L,Troponin T (TNT): 18.09 pg/mL (normal range: 3-14 pg/mL),D-Dimer: 0.1 μg/mL.Urinalysis:Urine Glucose: 3+,Urine Ketones: 3+,Urine Protein: 1+

On December 12, 2021, the patient underwent arterial blood gas analysis while receiving 2 L/min of oxygen via nasal cannula:Arterial pH: 7.571 (↑),Arterial Partial Pressure of CO_2 (PCO_2): 22.5 mmHg,Arterial Partial Pressure of O_2 (PO_2): 140 mmHg,Blood Glucose (GLU): 8.30 mmol/L,Lactic Acid (cLac): 1.8 mmol/L.After the relief of abdominal pain, a repeat arterial blood gas analysis showed:Arterial pH: 7.2,Arterial Partial Pressure of CO_2 (PCO_2): 42.1 mmHg,Arterial Partial Pressure of O_2 (PO_2): 120 mmHg,Blood Glucose (GLU): 5.7 mmol/L,Lactic Acid (cLac): 1.7 mmol/L

2.2.2 Imaging Examinations

Electrocardiogram (ECG): Sinus arrhythmia (64 bpm), with no dynamic changes observed on re-examination.Cardiac Ultrasound: Abnormal echo observed within the aortic lumen, suggesting aortic dissection (DeBakey type II), with a recommendation for further examination.Complete Aortic CTA and Enhanced CT of the Entire Abdomen: No abnormalities detected.Gastroscopy: Chronic non-atrophic gastritis; no other abnormalities observed.

2.3 Diagnosis and Treatment Process

Upon admission, the patient experienced severe and unbearable abdominal pain, requiring morphine for pain relief. Considering the patient's medical history and physical examination findings, the initial attending physician suspected DKA induced by alcohol consumption. However, initial blood glucose measurements were normal, and preliminary blood gas analysis showed no acidosis, which initially excluded DKA. Further investigations were necessary to rule out acute abdomen and other causes.While awaiting results, the non-contrast CT scan of the entire abdomen and blood amylase results showed no abnormalities, effectively ruling out possibilities of gastrointestinal perforation and pancreatitis. Elevated troponin T (TNT) prompted another ECG, which showed no dynamic changes. A consultation with a cardiologist recommended bedside cardiac ultrasound, which revealed abnormal echoes in the aortic lumen, suggesting aortic dissection (DeBakey type II). Due to the lack of capability to treat aortic dissection at our hospital, the patient was transferred to a higher-level hospital for further examination and treatment.At the referral hospital, complete aortic CTA and enhanced CT of the entire abdomen were performed immediately, both of which showed no abnormalities, effectively ruling out serious cardiac and vascular conditions. The patient experienced slight relief in abdominal pain after using morphine and other analgesics. A repeat blood gas analysis showed a decreased pH indicating acidosis, and urine ketones remained positive. Hospitalization was advised, but the patient refused and signed out against medical advice.

On December 13, 2022, the patient was re-admitted with severe abdominal pain. A gastroscopy was performed, which showed no significant abnormalities, and chronic gastritis could not explain the current severe abdominal pain. The attending physician, after thorough consideration of the patient's condition and consultations with related departments, noted that although the patient's blood glucose remained within normal range, blood gas analysis and urine ketone results indicated ketoacidosis. Considering the patient's history of type 2 diabetes, alcohol consumption, and recent oral administration of dapagliflozin, an initial diagnosis of EDKA was made. Treatment involved discontinuing dapagliflozin, administering large volumes of fluids, and insulin combined with glucose to clear ketones. The patient's urine ketone levels gradually normalized, and abdominal pain gradually subsided. The patient improved and was discharged. Follow-up after discharge showed no recurrence of abdominal pain.

2.4 Discussion

Euglycemic Diabetic Ketoacidosis (EDKA) in patients with type 1 (T1DM) or type 2 (T2DM) diabetes mellitus is characterized by normal blood glucose levels (typically less than 250 mg/dL), anion gap metabolic acidosis, ketonemia or ketonuria, and is a clinical syndrome [4]. Its clinical presentation is similar to DKA, but specific symptoms can vary, including nausea, vomiting, shortness of breath, general discomfort, drowsiness, loss of appetite, or abdominal pain. Severe cases may lead to hypovolemic shock, lethargy, respiratory failure, coma, and death. Therefore, timely detection and treatment of EDKA are crucial, as delayed management can lead to serious consequences[5]. In clinical practice, DKA is often relatively straightforward to diagnose. However, EDKA presents a diagnostic challenge due to various causes and normal blood glucose levels. This can lead to delays in diagnosis, as seen in this case where the patient presented with symptoms resembling acute abdomen, necessitating extensive tests and examinations before EDKA could be confirmed. Abdominal pain is a common and diverse symptom in emergency medicine, ranging from minor ailments to life-threatening conditions. Comprehensive differential diagnosis is essential, posing significant challenges for emergency physicians [6]. In this case, the patient had a history of type 2 diabetes mellitus and presented with symptoms of abdominal pain and vomiting upon admission. The initial treating physician considered the possibility of DKA and conducted comprehensive blood glucose and arterial blood gas analyses. However, the patient's blood glucose levels were within normal range. Intense respiratory compensation due to severe abdominal pain led to respiratory alkalosis, maintaining a normal pH on arterial blood gas analysis, thereby masking metabolic acidosis. This misled the physician into relaxing vigilance for DKA, significantly disrupting clinical diagnostic reasoning and increasing diagnostic complexity.

The potential pathophysiological mechanisms of EDKA include absolute or relative insulin deficiency, leading to glucagon production and the release of free fatty acids, which subsequently cause ketone body formation and acidosis. EDKA can also occur due to reduced glucose production and availability during starvation states (often associated with certain stressors) or increased glycosuria related to excess counterregulatory hormones[7][8]. Therefore, any condition leading to reduced glucose availability or production, decreased insulin secretion, and increased counterregulatory hormone secretion can potentially cause EDKA. These conditions mainly include starvation, pregnancy, chronic alcohol consumption, liver disease, infection, sepsis, and the use of SGLT2 inhibitors[9][10]. With the widespread clinical use of the new antidiabetic drugs SGLT-2 inhibitors, there have been numerous reports of SGLT-2 inhibitor-related EDKA in recent years, making SGLT-2 inhibitors a notable cause of EDKA and garnering significant attention. In this case, the patient had type 2 diabetes and had been taking an SGLT-2 inhibitor (dapagliflozin) to control blood glucose levels, along with a history of alcohol consumption and fasting, leading to the onset of EDKA under multiple triggers[11]. EDKA is a diagnosis of exclusion and can be challenging to diagnose. As in this case, there were multiple potential causes for the acute abdomen, requiring step-by-step exclusion before the final diagnosis could be made, presenting a significant challenge to clinicians. However, once diagnosed, the treatment is relatively straightforward and similar to DKA treatment. The main treatment methods include rapid correction of dehydration through intravenous fluids and the administration of insulin with glucose infusion, with regular checks of urine ketones and arterial blood gas analysis, and removal of the trigger (e.g., discontinuing SGLT-2 inhibitors) until the anion gap, bicarbonate levels, and ketones normalize[12][13].Early diagnosis and aggressive management with fluids and insulin can easily reverse EDKA, reducing morbidity and mortality. In this case, the patient's abdominal pain did not alleviate until the diagnosis of EDKA was confirmed, after which standardized treatment led to complete relief of abdominal pain symptoms.

3. Conclusion

DKA is often readily diagnosed by emergency department physicians, but EDKA is relatively rare in clinical practice. Clinicians should be able to recognize and treat EDKA, and understand that excluding DKA based solely on normal blood glucose levels is insufficient. For patients who may have DKA but present with normal blood glucose levels, EDKA should be considered, especially in those with potential risk factors such as treatment with SGLT2 inhibitors or recent history of starvation or vomiting. Proactively ruling out other causes and shortening the time to diagnose EDKA can lead to earlier detection and treatment, thereby reducing morbidity and mortality.

References

[1] Muneer M, Akbar I. Acute Metabolic Emergencies in Diabetes: DKA, HHS and EDKA. Adv Exp Med Biol. 2021;1307:85-114. doi: 10.1007/5584_2020_545. PMID: 32488607.

[2] Thompson BD, Kitchen A. Euglycemic Diabetic Ketoacidosis in Type 1 Diabetes on Insulin Pump, with Acute Ap-

pendicitis: A Case Report. Clin Pract Cases Emerg Med. 2021 Aug;5(3):136-138. doi: 10.5811/cpcem.2021.1.48905. PMID: 34437030; PMCID: PMC8373175.
[3] Muppidi V, Meegada S, Challa T, Siddamreddy S, Samal S. Euglycemic Diabetic Ketoacidosis in a Young Pregnant Woman Precipitated by Urinary Tract Infection. Cureus. 2020 Mar 19;12(3):e7331. doi: 10.7759/cureus.7331. PMID: 32313772; PMCID: PMC7164719.
[4] McCabe DE, Strollo BP, Fuhrman GM. Euglycemic Diabetic Ketoacidosis in the Surgical Patient. Am Surg. 2020 Dec 14:3134820956352. doi: 10.1177/0003134820956352. Epub ahead of print. PMID: 33316172.
[5] Plewa MC, Bryant M, King-Thiele R. Euglycemic Diabetic Ketoacidosis. 2021 Nov 7. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan–. PMID: 32119457.
[6] Michael M, Kleophas A, Keitel V, Flügen G, Bernhard M. Vom Leitsymptom zur Diagnose: abdominelle Beschwerden [Acute Abdominal Pain in the Emergency Department]. Anasthesiol Intensivmed Notfallmed Schmerzther. 2021 Jun;56(6):448-458. German. doi: 10.1055/a-1191-1374. Epub 2021 Jun 29. PMID: 34187077.
[7] Long B, Willis GC, Lentz S, Koyfman A, Gottlieb M. Evaluation and Management of the Critically Ill Adult With Diabetic Ketoacidosis. J Emerg Med. 2020 Sep;59(3):371-383. doi: 10.1016/j.jemermed.2020.06.059. Epub 2020 Aug 4. PMID: 32763063.
[8] Karakaya Z, Topal FE, Topal F, Payza U, Akyol PY. Euglisemic diabetic ketoacidotic coma caused by dapagliflozin. Am J Emerg Med. 2018 Nov;36(11):2136.e1-2136.e2. doi: 10.1016/j.ajem.2018.08.054. Epub 2018 Aug 21. PMID: 30150107.
[9] Muppidi V, Meegada S, Challa T, Siddamreddy S, Samal S. Euglycemic Diabetic Ketoacidosis in a Young Pregnant Woman Precipitated by Urinary Tract Infection. Cureus. 2020 Mar 19;12(3):e7331. doi: 10.7759/cureus.7331. PMID: 32313772; PMCID: PMC7164719.
[10] Steinmetz-Wood S, Gilbert M, Menson K. A Case of Diabetic Ketoacidosis in a Patient on an SGLT2 Inhibitor and a Ketogenic Diet: A Critical Trio Not to Be Missed. Case Rep Endocrinol. 2020 Aug 13;2020:8832833. doi: 10.1155/2020/8832833. PMID: 32855828; PMCID: PMC7443033.
[11] Yu X, Zhang S, Zhang L. Newer Perspectives of Mechanisms for Euglycemic Diabetic Ketoacidosis. Int J Endocrinol. 2018 Oct 2;2018:7074868. doi: 10.1155/2018/7074868. PMID: 30369948; PMCID: PMC6189664.
[12] Long B, Lentz S, Koyfman A, Gottlieb M. Euglycemic diabetic ketoacidosis: Etiologies, evaluation, and management. Am J Emerg Med. 2021 Jun;44:157-160. doi: 10.1016/j.ajem.2021.02.015. Epub 2021 Feb 16. PMID: 33626481.
[13] Rawla P, Vellipuram AR, Bandaru SS, Pradeep Raj J. Euglycemic diabetic ketoacidosis: a diagnostic and therapeutic dilemma. Endocrinol Diabetes Metab Case Rep. 2017 Sep 4;2017:17-0081. doi: 10.1530/EDM-17-0081. PMID: 28924481; PMCID: PMC5592704.