

SARS-CoV-2 and community-acquired pneumonia leading to euglycemic diabetic ketoacidosis in two patients with type-1 diabetes mellitus who were not using SGLT2 inhibitors

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Abstract

Diabetic patients are at high risk for mortality after contracting several infections. Additionally, diabetes has been mentioned as an independent factor for progression to severe disease in seasonal influenza and in-hospital deaths due to coronavirus 2019 (COVID-19). Diabetic ketoacidosis is a well-known complication of type-1 diabetes and is characterized by hyperglycemia, metabolic acidosis, and high ketone levels. Euglycemic diabetic ketoacidosis (EDK) is a rare variant of diabetic ketoacidosis in which the blood glucose levels remain within normal limits, but ketoacidosis develops. Although EDK has often been associated with the use of sodium-glucose transport-2 (SGLT-2) inhibitors, it can be induced by several factors, including infectious diseases. EDK may present during the course of an infection, and it also can be a manifestation indicating infection. In this report, two cases of EDK due to pneumonia caused by two different pathogens are presented. Moreover, it is important to emphasize that EDK can occur in type-1 diabetic patients who are not using SGLT-2 inhibitors. Additionally, EDK can be a manifestation of infection and a possible marker of progression to severe disease in patients with type 1 diabetes.

Keywords: Acidosis, COVID-19, Diabetic ketoacidosis, Euglycemia, Ketosis, Pneumonia

Introduction

Impaired immunity due to chronic hyperglycemia leading to dysfunctional lymphocyte and macrophage functions causes diabetic patients to become more susceptible to bacterial and viral infections [1, 2]. Previous studies indicate that diabetic patients are at high risk for mortality in influenza A (H1N1), severe acute respiratory syndrome coronavirus and Middle Easter respiratory syndrome infections (SARS-CoV, and MERS-CoV, respectively) [3, 4]. Furthermore, diabetes was found to be an independent risk factor for progression to severe disease in seasonal influenza [5]. Also, it was shown that types-1 and -2 diabetes are associated with in-hospital deaths due to COVID-19 [6].

Diabetic ketoacidosis is a well-known complication of type-1 diabetes, which is characterized by hyperglycemia, metabolic acidosis, and high ketone levels [7]. Euglycemic diabetic ketoacidosis (EDK) is a rare variant of diabetic ketoacidosis in which the blood glucose levels remain within normal limits. Although EDK has often been associated with the use of sodium-glucose transport-2 (SGLT-2) inhibitors, it can be induced by several factors, including those related to infections. EDK may also occur over the course of infections; furthermore, it may be a manifestation of infections, including COVID-19 [8].

In this report, two cases of EDK due to pneumonia caused by two different pathogens are presented. Thus, it must be emphasized that EDK can be seen in type-1 diabetic patients who are not using SGLT-2 inhibitors. Additionally, EDK can be a manifestation of infection and maybe a marker of progression to severe disease in patients with type 1 diabetes.

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Informed Consent

The authors stated that the written consent was obtained from next-of-kin and the patient presented with images in the study.

Conflict of Interest

No conflict of interest was declared by the authors.

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Case presentation

Case 1

The first case involved a 24-year-old female patient with type-1 diabetes who was admitted to the emergency department for vomiting and confusion. Based on blood gas analysis, blood pH was 6.80 (normal range: 7.35 - 7.45), bicarbonate 7 mmol/L, oxygen saturation 94%, and carbon dioxide pressure was 10 mmHg. The urinary analysis was positive for 3+ ketonuria. Her blood glucose was 198 mg/dL, and her glycosylated hemoglobin (HbA1c) level was 15. Her parents stated that her oral intake has decreased for the past few days, but she has continued to inject insulin at the same dosage. The patient deteriorated shortly and was intubated and then transferred to the intensive care unit. The leucocyte level was 21×10^9 /L, the C-reactive protein level was 23 mg/dL, and the patient was diagnosed with community-acquired pneumonia. Although her blood pH normalized within days, the infection led to a fatal septic shock three weeks later.

Case 2

The second case was a 37-year-old male with type-1 diabetes who was admitted to the hospital with the symptoms of confusion and vomiting. Blood gas analysis revealed metabolic acidosis with pH 6.90 and bicarbonate 9 mmol/L. Ketonuria (3+) appeared in the urine analysis, and the blood glucose level was 187 mg/dL. Three days before, the patient's polymerase chain reaction (PCR) analysis was positive for SARS-CoV-2. The chest computed tomography (CT) scan showed bilateral infiltrations indicative of COVID-19 pneumonia after which the patient then was transferred to the intensive care unit (ICU). During the follow-up in the ICU, mechanical ventilation was not needed. After medical treatment of ketoacidosis, the patient was discharged from the ICU to the ward.

Discussion

Diabetic ketoacidosis can be the diagnostic symptom of diabetes mellitus or the hallmark of an underlying condition, such as an infection in a patient with type-1 diabetes. On the other hand, in EDK cases, patients usually present with ketonemia and metabolic acidosis, but marked hyperglycemia is absent [7]. In these cases, diagnosis is often delayed leading to a more perilous condition due to its unique presentation.

Cocaine use, pancreatitis, pregnancy, and Ramadan fasting had previously been suspected as contributing to EDK etiology [9–12]. Recently, data concerning SGLT-2 inhibitors suggest EDK occurs in both type-1 and type-2 diabetes patients with the concomitant use of these drugs. Additionally, after the beginning of the outbreak, several cases of COVID-19-associated EDK in both types of diabetes in the setting of SGLT-2 inhibitor use were presented [13, 14]. Furthermore, it has been suggested that EDK may be one of the endocrinological manifestations of COVID-19 [8, 15]. However, the feature common to all of these COVID-19-induced EDK cases was the use of SGLT-2 inhibitors during the infection. In contrast to the previous cases, none of the patients presented in this report were using any blood glucose-lowering medication other than insulin, and EDK was caused by pneumonia in both patients.

Conclusion

In conclusion, bacterial and viral pneumonia, including COVID-19 infection, may cause EDK in type-1 diabetes mellitus patients who are not using SGLT-2 inhibitors.

References

- Dooley KE, Chaisson RE. Tuberculosis and diabetes mellitus: convergence of two epidemics. *Lancet Infect Dis.* 2009;9:737–46.
- Odegaard JI, Chawla A. Connecting type 1 and type 2 diabetes through innate immunity. *Cold Spring Harb Perspect Med.* 2012;2:a007724.
- Schoen K, Horvat N, Guerreiro NFC, de Castro I, de Giassi KS. Spectrum of clinical and radiographic findings in patients with diagnosis of H1N1 and correlation with clinical severity. *BMC Infect Dis.* 2019;19:964.
- Song Z, Xu Y, Bao L, Zhang L, Yu P, Qu Y, et al. From SARS to MERS, thrusting coronaviruses into the spotlight. *Viruses.* 2019;11:59.
- Hong KW, Cheong HJ, Choi WS, Lee J, Wie SH, Baek JH, et al. Clinical courses and outcomes of hospitalized adult patients with seasonal influenza in Korea, 2011–2012: hospital-based Influenza Morbidity & Mortality (HIMM) surveillance. *J Infect Chemother.* 2014;20:9–14.
- Barron E, Bakhai C, Kar P, Weaver A, Bradley D, Ismail H, et al. Associations of type 1 and type 2 diabetes with COVID-19-related mortality in England: a whole-population study. *Lancet Diabetes Endocrinol.* 2020;8:813–22.
- Schumann C, Faust M. Diabetic ketoacidosis and hyperosmolar hyperglycemic state. *Dtsch Med Wochenschr.* 2018;143:384–91.
- Dass B, Beck A, Holmes C, Morton G. Euglycemic DKA (euDKA) as a presentation of COVID-19. *Clin Case Rep.* 2020;9:395–8.
- Abu-Abad Abdin A, Hamza M, Khan MS, Ahmed A. Euglycemic diabetic ketoacidosis in a patient with cocaine intoxication. *Case Rep Crit Care.* 2016;2016:4275651.
- Prater J, Chaiban JT. Euglycemic diabetic ketoacidosis with acute pancreatitis in a patient not known to have diabetes. *AAACE Clin Case Rep.* 2015;1:88–91.
- Franke B, Carr D, Hatem MH. A case of euglycaemic diabetic ketoacidosis in pregnancy. *Diabet Med.* 2001;18:858–9.
- Baş VN, Uytun S, Torun YA. Diabetic euglycemic ketoacidosis in newly diagnosed type 1 diabetes mellitus during Ramadan fasting. *J Pediatr Endocrinol Metab.* 2015;28:333–5.
- Vitale RJ, Valtis YK, McDonnell ME, Palermo NE, Fisher ND. Euglycemic diabetic ketoacidosis with COVID-19 infection in patients with type 2 diabetes taking SGLT2 inhibitors. *AAACE Clin Case Rep.* 2021;7:10–3.
- Oriot P, Hermans MP. Euglycemic diabetic ketoacidosis in a patient with type 1 diabetes and SARS-CoV-2 pneumonia: case report and review of the literature. *Acta Clin Belg.* 2022;77:113–7.
- Tsai PH, Lai WY, Lin YY, Luo YH, Lin YT, Chen HK, et al. Clinical manifestation and disease progression in COVID-19 infection. *J Chin Med Assoc.* 2021;84:3–8.

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