

Case Report

Diabetic ketoacidosis precipitated by atypical coronavirus disease in a newly diagnosed diabetic girl

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المخلص

الالتهابات الفيروسية لها تأثير على الفيزيولوجيا المرضية لداء السكري من النوع الأول. هناك القليل من البيانات حول تأثير مرض كوفيد-19 على داء السكري من النوع الأول لدى الأطفال وأيضاً على الحمض الكيتوني السكري. يمثل هذا العمل الحالة الوحيدة التي تم الإبلاغ عنها لطفل مشخص حديثاً بداء السكري من النوع الأول مع الحمض الكيتوني السكري ووجد بالمصادفة أنه مصاب بفيروس كورونا المستجد دون وجود أي أعراض في الجهاز التنفسي. نحن نُبلغ عن فتاة تبلغ من العمر 7 سنوات قدمت تاريخاً من العطاش، والتبول، وفقدان الوزن. وأكدت التحاليل تشخيص داء السكري من النوع الأول مع الحمض الكيتوني السكري. وفقاً لبروتوكول مكافحة العدوى، خضعت لفحص فيروس كورونا المستجد المخبري، مما أسفر عن نتيجة إيجابية. خلال إقامتها في المستشفى، لم تظهر عليها أي حمى أو أعراض تنفسية. تم علاج الحمض الكيتوني دون أي مضاعفات. نستنتج أن فيروس كورونا المستجد قد يؤدي إلى ظهور داء السكري من النوع الأول لدى الأطفال وقد يعجل حدوث الحمض الكيتوني في مرضى السكري حتى مع غياب أعراض الجهاز التنفسي.

الكلمات المفتاحية: فيروس كورونا؛ الحمض الكيتوني السكري؛ داء السكري؛ الأطفال؛ فيروس كورونا المستجد.

Abstract

Viral infections have a well-known influence on the pathophysiology of type 1 diabetes mellitus (T1DM). There is scant data about the impact of COVID-19 T1DM and diabetic ketoacidosis (DKA) on paediatric patients. This case presents a newly diagnosed paediatric patient with T1DM and DKA who was found to have

SARS-CoV-2 without any respiratory symptoms. A 7-year-old girl presented with a history of polydipsia, polyuria, and weight loss. This presentation was complicated by a 2-day history of fatigue and vomiting. Investigations into the patient's condition confirmed T1DM with DKA. Following the infection control protocol, she underwent screening for SARS-CoV-2, which yielded a positive result. During her hospital stay, she did not develop fever or respiratory symptoms. The ketoacidosis was treated without any complications. We conclude that SARS-CoV-2 may trigger the onset of T1DM and may precipitate the occurrence of DKA in paediatric diabetic patients, even in the absence of respiratory symptoms.

Keywords: Coronavirus; Diabetic ketoacidosis; Diabetes mellitus; Paediatric; SARS Virus

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Introduction

Since the coronavirus disease (COVID-19) outbreak began in China in late 2019, more than 320,000 confirmed cases and about 4,000 COVID-19-related deaths have been recorded in KSA (as of September 6, 2020).¹ Although the scientific literature concerning COVID-19 is evolving day by day, there is scant data on the effects of COVID-19 on the pathophysiology of type 1 diabetes mellitus (T1DM), especially in the paediatric population.

T1DM leads to a demolition of the pancreatic β -cells via an autoimmune process and is characterised by the presence

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of circulating autoantibodies to pancreatic islet cell antigens. However, the exact aetiology behind such autoimmunity to islet cell antigens is not entirely understood. Genetic factors may have a strong impact, but the immoderate global rise in the incidence of type 1 diabetes over the last few decades is mostly attributable to environmental factors that are yet to be determined.² An example of such factors is viral infection. A relationship between viral infections and diabetic ketoacidosis (DKA) in patients with T1DM has been proposed in numerous studies.^{3,4}

After reviewing the available literature, this case report appears to be the first reported case of newly diagnosed diabetes mellitus with COVID-19 in the paediatric population without any respiratory involvement. Here, we have described a case of COVID-19 in which the patient presented with DKA as the first presentation of T1DM during the COVID-19 outbreak in KSA.

Case history

A 7-year-old previously medically free school-aged girl presented with a 2-week history of increased thirst, urination, and subjective weight loss, followed by a 2-day history of fatigue and vomiting. There was no history of fever or respiratory symptoms. The only significant family history was that the father was diabetic.

Upon her presentation, her Glasgow Coma Scale (GCS) score was 14/15, and her vital signs showed that her heart rate was 124 beats per minute, her respiratory rate was 21 breaths per minute, her blood pressure was 112/75 mmHg, she had an oxygen saturation of 98% in room air, and her temperature was 37.3 °C. She was haemodynamically stable, apart from mild tachycardia and mild dehydration in the form of dry mucus membranes. The chest was clear on auscultation with no Kussmaul's breathing and no supplemental oxygen required. Her weight was in the 25th percentile for her age, and she did not have any evidence of insulin resistance. Her initial laboratory investigations confirmed the clinical diagnosis of T1DM with DKA (Table 1). As per our general hospital policy concerning paediatric patients presenting with DKA, admission to the Intensive Care Unit (ICU) is warranted, regardless of the severity of the patient's presentation, in order to facilitate proper management and close observation. In addition,

based on the concurrent hospital's strict infection control guidelines during the COVID-19 pandemic, all patients who require admission to the hospital must be tested for COVID-19. Therefore, our patient was screened for COVID-19 using the severe acute respiratory syndrome coronavirus-2-polymerase chain reaction (SARS-CoV-2 PCR) test, which yielded a positive result. The laboratory PCR methodology used was a rapid real-time RT-PCR automated in vitro diagnostic test for qualitative detection of nucleic acid from SARS-CoV-2 using Xpert Xpress SARS-CoV-2. The specimen was collected from the patient via nasopharyngeal swabbing. This test is FDA-approved and has been validated and considered acceptable for patient testing. The manufacturers of Xpert Xpress SARS-CoV-2 test performed strict clinical and analytical evaluation processes. These evaluations showed a 97.8% (95% CI: 88.4%–99.6%) positive percent agreement (PPA) and a 95.6% (95% CI: 85.2%–98.8%) negative percent agreement (NPA). Additionally, its analytical sensitivity (limit of detection) was claimed to be 0.0200 PFU/mL with 95%–100% hit rates. The test's analytical specificity (exclusivity) confirmed its ability to only detect human and bat SARS-coronavirus with no unintended cross reactivity with other organisms.⁵

Serological testing was not undertaken due to its unavailability at our centre at the time. The patient was started on the DKA management protocol for the correction of her metabolic derangements. The management consisted of intravenous (IV) fluid resuscitation, initially in the form of a 0.9% normal saline solution and an insulin infusion (0.1 U/kg/hr); the patient was then started on IV fluid maintenance plus deficit. The types of IV fluids were decided based on her hourly glucose level during the DKA period. Potassium chloride and phosphate were added to her maintenance fluid regimen as part of the attempt to correct her metabolic derangements. Eventually, DKA resolved within 21 h. Her 24-hour heart rate, urine output, and intravenous fluid rate trends are shown in Figure 1. Other parameters that were monitored during her ICU stay included her GCS, blood pressure, oxygen saturation, respiratory rate, and temperature; these were all within the normal ranges.

Afterwards, the patient was successfully transitioned to subcutaneous insulin therapy. During her stay, she did not exhibit any respiratory symptoms, and she required no extra breathing support. She stayed in the ward for more than

Table 1: Patient's significant laboratory values.

Investigation	Result	Reference range	Comment
Venous glucose (mg/dL)	555	80–140	Diabetic range hyperglycaemia
Arterial blood gas			
pH (mmHg)	7.10	7.35–7.45	Metabolic acidosis
Bicarbonate (mmol/L)	10	22–26	Metabolic acidosis
pCO ₂ (mmHg)	26.8	35–45	Respiratory alkalosis
Sodium (mmol/L)	134	136–146	Corrected sodium for hyperglycaemia: 145 (hypernatremic dehydration)
Chloride (mmol/L)	103	98–107	Normal
Anion gap	23	8–16	High-anion gap metabolic acidosis secondary to DKA
Creatinine (mg/dL)	0.96	0.5–0.9	Normal for age
Glycated haemoglobin (%)	10.3	4–6	High
C peptide (ng/ml)	0.29	0.8–5.2	Low
Insulin level (µU/mL)	<1.6	6–27	Low

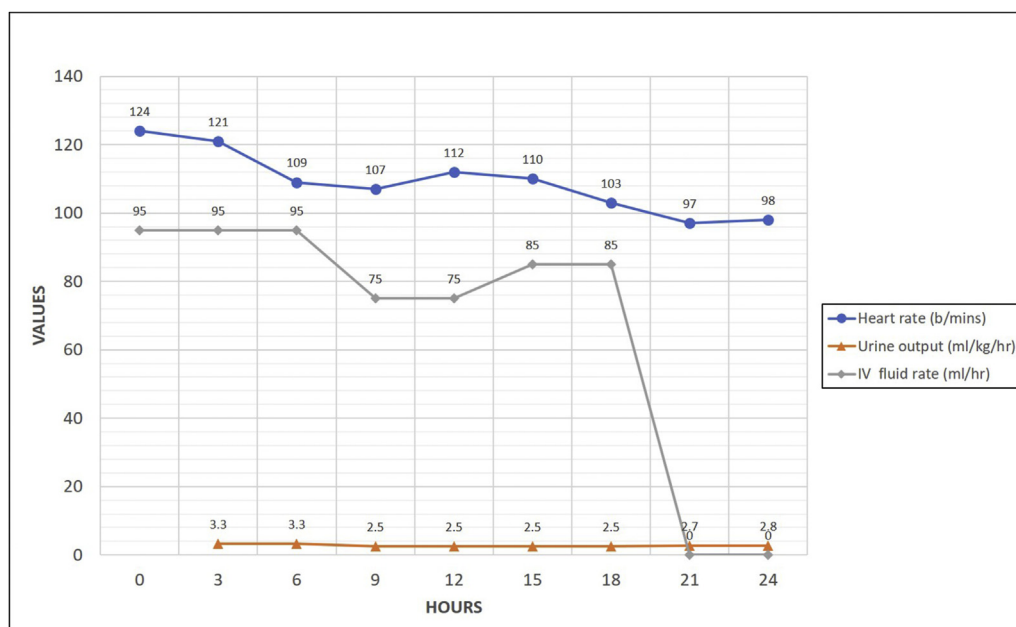


Figure 1: Patient's heart rate, urine output, and intravenous fluid rate trends for the first 24 h of admission. Explanation: The figure demonstrates the trends of three clinical parameters, namely heart rate, urine output, and the rate of intravenous fluid received by the patient during the first 24 h of admission at 3-hour intervals. The relatively low urine output for this diabetic patient may second the suggested interaction between the renin-angiotensin system (RAS) and the coronavirus.^{9,10} In addition, this may have prevented the occurrence of a severe degree of dehydration due to the water retention effect caused by the increased synthesis of aldosterone, which is reflected by her relatively stable heart rate.

three days, only for the purpose of education regarding diabetes and nutrition.

Discussion

T1DM is an autoimmune-induced illness characterised by progressive autoantibody-mediated devastation of the pancreatic β -cells, leading to an insulin deficiency. Over the last three decades, T1DM incidence has been increasing due to the involvement of multiple different factors, such as genetic, environmental, and lifestyle factors.⁶ These factors play an integral role in promoting the initiation of an autoimmune reaction against β -cells, resulting in islet cell destruction and insulin degradation, and eventually an increase in serum glucose levels. In our patient, the evidence supporting the diagnosis of T1DM was clear due to the presence of a very low insulin serum level ($<1.6 \mu\text{U/mL}$) and high serum glucose levels ($>500 \text{ mg/dL}$) (Table 1). Viruses have been universally linked to T1DM pathophysiology as one of the causative environmental factors. Examples of triggering viruses are enterovirus, rotavirus, cytomegalovirus, mumps, rubella, and retroviruses.^{7,8}

Autoimmune destruction of pancreatic β -cells could be initiated by viral illnesses through several processes. The devastation of β -cells might be directly caused by either the virus amplification process and/or viral antigen diffusion from circulation.⁹ In a recently published report, SARS-CoV-2 has been recognised as one of the viruses associated with DKA in adults; the suggested mechanism linking the pathophysiology of DKA and SARS-CoV-2 is the

interaction between the coronavirus and the renin-angiotensin-aldosterone system (RAAS).¹⁰ One of the key enzymes in RAAS is the angiotensin-converting enzyme 2 (ACE2), which helps in converting angiotensin II to angiotensin. The lungs and the pancreas are the two organs with the highest expression of ACE2. ACE2 expression is down-regulated after the introduction of SARS-CoV-2 into the lungs and the pancreatic β -cells.¹¹ As a result of this intrusion, two parallel processes may aggravate the pathophysiology of DKA. Firstly, SARS-CoV-2's direct invasion of the islet cells might lead to β -cell injury. Secondly, the accumulation of unopposed angiotensin II due to the decline of ACE2 after viral incursion may prevent insulin secretion.¹²

Our patient was found to be infected with SARS-CoV-2, an incidental finding that might have been missed in the absence of strict infection control measures and policies directed towards screening critically ill patients in our hospital for SARS-CoV-2. In the absence of respiratory symptoms or a positive history of contact with a confirmed COVID-19 case, our case report highlights the possibility of discovering similar future cases due to both the increasing global incidence and prevalence of T1DM in general and the worsening COVID-19 pandemic in particular. Future studies are needed to investigate the exact pathophysiology.

During the current coronavirus pandemic, the number of patients visiting paediatric emergency departments has declined dramatically. Although medical emergencies unrelated to COVID-19 continue to occur, parents are delaying seeking medical help out of fear of going to hospitals. Such a delay might lead to the worsening of the clinical condition in

the majority of paediatric cases presenting to emergency departments. Screening patients who require ICU admission for SARS-CoV-2 during this pandemic should be kept in mind to ensure the consistent implementation of proper infection control strategies and the safe allocation of resources.

Conclusion

In conclusion, this case report suggests that SARS-CoV-2 may trigger the onset of newly diagnosed T1DM and may precipitate the occurrence of DKA in paediatric diabetic patients even without respiratory involvement. With the ongoing increase in the number of COVID-19 cases worldwide, we might expect a surge of patients with newly diagnosed T1DM. Additionally, COVID-19 screening is highly recommended for critically ill patients presenting with DKA, even without clear respiratory involvement. Further studies can help determine the exact pathophysiology of the relationship.

Recommendations

We recommend screening all diabetic patients presenting with DKA for SARS-CoV-2 regardless of the severity of the clinical presentation, even in the absence of any respiratory symptomatology. This case report highlights the possibility that COVID-19 may trigger the onset of newly diagnosed T1DM and/or precipitate the occurrence of DKA without the existence of the typical COVID-19 phenomena.

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Conflict of interest

The authors have no conflict of interest to declare.

Ethical approval

The Institutional Review Board (IRB) at Imam Abdulrahman Bin Faisal University excludes case reports/series from the acquisition of ethical approval, so formal ethical approval for this work was not sought. However, the patient's parent signed a participation consent form as per our institutional policies for paediatric case reporting. In addition, both authors declare that the principles outlined in the Declaration of Helsinki were followed.

Authors contributions

WHB conceived the report, conducted the literature review, and collected and organised data. NAG drafted the

initial and final versions of this work. All authors have carefully reviewed and approved the final draft of this manuscript and are responsible for its content and similarity index.

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