Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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New-onset Type 1 Diabetes Mellitus with Diabetic Ketoacidosis and Pancreatitis in a Patient with COVID-19 ☆

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ABSTRACT

Coronavirus Disease 2019 (COVID-19) had struck the world with health and economic catastrophes and recently with unusual autoimmune presentations, including new-onset Type 1 Diabetes.

Herein we present a 17-year-old male patient who presented to the outptient clinic with fever, palpitation, and cough of four-week duration; he was referred to the emergency room and was found to have DKA. CT of the chest showed ground-glass opacities suggestive of COVID-19 pneumonia, and abdominal cuts showed dilated intrahepatic biliary radicles with pancreatic loculations suggestive of pancreatitis. The patient was admitted to the ICU, started on intravenous fluids and insulin infusion then COVID-19 PCR returned positive. We hypothesize that SARS-CoV-2 has a vital role in eliciting an autoimmune response triggering type 1 diabetes, and further studies are needed to confirm this hypothesis. SARS-CoV-2 may cause pancreatitis, and the first presentation could be high blood sugar or DKA.

Background

Coronavirus Disease 2019 (COVID-19) and the causative agent Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) had struck the world with health and economic catastrophes, and recently with unusual autoimmune presentations including new-onset Type 1 Diabetes Mellitus (T1DM). Herein, we report a case of a 17-year-old male who presented with Diabetic ketoacidosis (DKA) in the setting of COVID-19 with associated positive autoantibodies, laboratory, and radiological findings of pancreatitis.

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Table 1
(Inpatient investigations).

Investigation	Result	Reference range
pH	6.8	7.38–7.44
Glucose (mg/dL)	566	65–110
Urinary ketones	Positive	Negative
Glycated haemoglobin(%)	14.7	5.7–6.4%
Amylase U/L	285	<100
Lipase U/L	273	<60
Anti GAD	Positive	Negative
Anti Islet Cell antibodies	Positive	Negative
SARS-CoV-2 IgG	Negative	Negative
SARS-CoV-2 IgM	Negative	Negative
Hemoglobin(gm/dl)	13.3	13.2–17
Platelets (per mm^3)	107,000	150,000–350,000
White Cell Count (per mm^3)	8220	3800–11,000
Absolute Lymphocyte count (per mm^3)	990	1100–4000
D-dimer (ng/ml)	2300	<400
C-Reactive Protein (mg/liter)	144	<6
Ferritin (ng/mL)	470	30–233
Lactate Dehydrogenase (U/liter)	366	120–246

Case report

A 17-year-old male patient with a past medical history of hypothyroidism on levothyroxine 50 mcg/day and bipolar disorder on no treatment, no history of smoking, drinking alcohol, or substance abuse presented to an outpatient clinic with fever, palpitation, and cough of four-week duration. Then he was referred to the emergency room and was found to have DKA, being hemodynamically stable but febrile at 38 °C. He was screened as per Cairo university protocol with a CT of the chest, which showed ground-glass opacities suggestive of COVID-19 pneumonia, and abdominal cuts showed dilated intrahepatic biliary radicles with pancreatic loculations suggestive of pancreatitis; pancreatic enzymes were elevated. The patient was admitted to the Intensive Care Unit (ICU), started on normal saline infusion (1L in 30 min, then 1L in one hour, then 1L in two hours, then 1L in 4 h) and insulin infusion with electrolyte replacement, further workup was sent (Table 1), and a nasopharyngeal swab for SARS-CoV-2 RT-PCR returned positive. He was started on COVID-19 treatment as per the national protocol, including azithromycin and hydroxychloroquine, and continued to improve and switched to subcutaneous insulin. After 12 days, he was transferred to an isolation hospital.

Discussion

This case represents a recently discovered T1DM in a patient with COVID-19 disease. He was diagnosed with COVID-19 with a positive RT-PCR from a nasopharyngeal swab, although serology was negative either because it was early in the disease or the sensitivity of the testing kits was low. Regarding pancreatitis, it was diagnosed based on Atlanta criteria given radiological findings in CT and elevated both amylase and lipase more than three times the upper limit of normal. He was managed with intravenous fluids and insulin infusion as per Cairo university protocol, and his pancreatitis was managed conservatively. His pancreatic autoantibodies were positive suggestive of an autoimmune process, and this finding makes this case unique given the diagnosis of T1DM with evidence of autoimmune pancreatitis in association with COVID-19.

The emerging data showed that the novel Coronavirus seems to be more than a respiratory virus. Various studies suggested the direct effect of the novel Coronavirus on different organs [1–4]. We assume that COVID-19 disease has a vital role in eliciting an autoimmune response triggering T1DM.

Type 1 diabetes has been recognized as an autoimmune genetic disorder caused by the destruction of pancreatic β-cells by autoreactive CD4+ and CD8+ T-cells that recognize endogenous pancreatic antigens [5]. Nevertheless, Various studies highlighted the pivotal role of nongenetic and environmental factors in the developing and progression of T1DM [6,7]. Some of the literature linked certain viruses as promoters for autoimmunity. Enteroviruses such as Coxsackievirus B have been identified as the prime viral candidates for causing T1DM in humans [8,9]. Moreover, with the growing knowledge, the accusation list has been expanded to include other viruses such as Rotavirus [10,11], Mumps virus [12], and Cytomegalovirus [13].

Diabetes is a crucial factor in determining the course and outcome of the disease, as in SARS-CoV or H1N1 viral infection [14,15]. Recent data support that diabetes may have a significant role in increasing the severity of COVID-19 patients. Diabetic patients without other comorbidities have a mortality rate of about 16% [16].

On the other hand, the data about the different mechanisms of actions of the novel Coronavirus suggests that this interaction may be bi-directional [17]. The wide expression of Angiotensin-Converting Enzyme 2 (ACE2) receptors in the pancreatic endocrine cells [18] highlighted the possibility of direct invasion of pancreatic cells by the novel Coronavirus as the ACE2 receptors are considered the access door for the novel Coronavirus to enter human cells [19]. This may lead to the destruc-

tion of pancreatic cells and predisposition to diabetes in nondiabetic subjects. Moreover, various studies found a significant link between COVID-19 disease and the overexpression of Interleukin-6 (IL-6), which is a pleiotropic cytokine. It has a role in acute-phase inflammatory responses of diabetic patients [20].

Various studies highlighted the significant role of IL-6 in eliciting immune response [21]. Tocilizumab is a monoclonal antibody against the IL-6 receptor. It is approved to manage some autoimmune diseases such as Graves orbitopathy, severe Rheumatoid Arthritis (RA), and Giant Cell Arteritis [22]. Moreover, an increase in IL-6 receptor surface expression in pancreatic β-cells was linked to the mechanism of development and progression of T1DM [23].

A systematic review that included 15 studies showed that the prevalence of T1DM in patients with COVID-19 ranged from 0.15 to 28.98%, and there was an increased incidence of DKA [24].

Current literature reported cases of newly diagnosed T1DM with DKA either at COVID-19 onset or during recovery, and some hospitals started to report more cases of DKA than usual with increased severity [25].

The aforementioned data suggest the significant bi-directional relationship between COVID-19 disease and T1DM. We lack knowledge about the role of COVID-19 in eliciting an immune response and the development of autoimmune disorders. More studies are needed to expand our knowledge about the different mechanisms of the novel Coronavirus's actions, which help us withstand against our new enemy.

Conclusion

We hypothesize that SARS-CoV-2 has a vital role in eliciting an autoimmune response triggering T1DM, and further studies are needed to confirm this hypothesis. SARS-CoV-2 may cause pancreatitis, and the first presentation could be DKA.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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