New-Onset Fulminant Type 1 Diabetes After SARS-CoV-2 Infection

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Fulminant type 1 diabetes (FT1D) is a subtype of type 1 diabetes that is characterized by the hyperacute and completely irreversible destruction of islet cells. Laboratory examinations have shown insulin depletion with negative islet-associated autoantibodies and mildly elevated hemoglobin A_{1c}. This disease is more common in East Asian individuals than in members of other ethnicities. Four cases of new-onset FT1D after coronavirus disease 2019 (COVID-19) vaccination have been reported, two in Japan (1,2) and two in China (3,4), and this has increased the focus on the relationship between COVID-19 and FT1D. Here, we report the case of a 46-year-old patient who was diagnosed with FT1D, which started with diabetic ketoacidosis 12 days after severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.

The patient had no history of diabetes or obesity. She received the third dose of the BNT162b2 mRNA COVID-19 vaccine on 10 March 2022 without experiencing any discomfort after vaccination. She developed flu-like symptoms 12 days before admission, and her SARS-CoV-2 PCR result was positive. Her flu-like symptoms were relieved 2 days later without any medicine. Three days before admission, the patient felt thirsty and drank approximately 6 L of water per day. She also ate twice as much as she did previously and felt continuous epigastric pain with nausea. Therefore, she came to our hospital, where she was transferred to the emergency room because of hyperglycemia (serum glucose 34.37 mmol/L) and ketoacidosis (urine ketone 2+, pH 7.086). On examination, the patient had a slim build (BMI 22.31 kg/m^2) and signs of acute illness. She was admitted after being diagnosed with diabetic ketoacidosis. After admission, the patient received approximately 2,100 mL of fluid supplement and a continuous intravenous infusion of insulin of approximately 43.6 units per day. Her metabolic status improved with the improvement in blood glucose levels. On the third day, her ketonuria had normalized, and fluid supplementation was stopped. On the seventh day, the patient was started on a basal-bolus subcutaneous insulin regimen (15 units insulin glargine once daily and 9 units [breakfast], 6 units [lunch], and 6 units [dinner] insulin aspart daily with meals). Antiviral therapy was not given, as the patient had a normal temperature without coughing and expectoration and little exudation on chest computed tomography. The patient was discharged with subcutaneous insulin therapy 10 days after admission. Data from examinations after admission are shown in detail in Table 1. On the basis of these findings, we diagnosed the patient with FT1D. The results of pancreatic magnetic resonance imaging were normal. Given that further tests showed no evidence of recent viral infections that could have triggered FT1D, we highly suspect that SARS-CoV-2 infection induced FT1D in this patient.

To our knowledge, this is the first report of new-onset FT1D caused by SARS-CoV-2 infection. Several cases of newly diagnosed diabetes with ketosis or ketoacidosis onset and associated with SARS-CoV-2 infection have been reported since the outbreak of COVID-19 in 2019. In contrast to previously reported cases, our case is the only one that is consistent with the diagnosis of FT1D. The specific etiology and pathogenesis of FT1D remain unclear. A nationwide survey revealed that approximately 70% of FT1D patients experience preceding flu-like or digestive symptoms, suggesting the involvement of viral infection in the development of the disease (5). Given that our patient had no symptoms or evidence of other viral infections for half a year before she was infected with SARS-CoV-2, we hypothesize that SARS-CoV-2 infection triggered the onset of FT1D. Whether and how SARS-CoV-2 infection triggers the damaging of pancreatic β-cells remain unclear. The interaction between SARS-CoV-2 and the renin-angiotensin-aldosterone system (RAAS) may provide a mechanism that explains the pathophysiology. Angiotensin-converting enzyme 2 (ACE2) is the main receptor for the internalization of SARS-CoV-2. The virus may directly damage β-cells after entry. The downregulation of ACE2 after SARS-CoV-2 enters pancreatic cells also can lead to an increase in angiotensin II, which may block insulin secretion. In addition, SARS-CoV-2 may infect β-cells directly, inducing β-cell apoptosis and transdifferentiation. Further, cytokine storms in COVID-19 constitute a highly inflammatory pathological state, and this may contribute to the dramatic destruction

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Table 1—Laboratory findings on admission

Parameter	Results	Reference range
Arterial blood gas analysis		
pH	7.086	7.350–7.450
pCO_2, mmHg	11.5	35.0–45.0
pO_2, mmHg	134	80.0–110.0
HCO_3^-, mmol/L	7.6	22.0–27.0
Base excess, mmol/L	−27.9	−3.0 to 3.0
Lactic acid, mmol/L	1.6	0.5–1.6
Hematology		
White blood cells, 10^9/L	14.2	3.5–9.5
Red blood cell, 10^{12}/L	5.45	3.80–5.10
Platelet, 10^9/L	343	125.0–350.0
Biochemistry		
Plasma glucose, mmol/L	34.37	3.90–6.10
Blood urea nitrogen, mmol/L	7.32	3.20–7.14
Creatinine, μmol/L	149	44.0–132.6
Sodium, mmol/L	128.3	137–147
Potassium, mmol/L	4.83	3.50–5.30
Chlorine, mmol/L	102.0	99.0–110.0
Hemoglobin A_{1c}, %	6.7	4.0–6.2
Fasting C-peptide, ng/mL	0.19	1.10–4.40
Postprandial C-peptide, ng/mL	0.25	1.10–4.40
Lipase, units/L	32	13–60
Amylase, units/L	29.1	20.0–125.0
Free T4, ng/mL	1.21	0.70–1.48
Thyroid stimulating hormone, μIU/mL	2.999	0.350–4.940
Immunological tests		
Anti-GAD antibody, IU/mL	1.36 (negative)	<10.00
Anti-IA-2A antibody, IU/mL	<0.70 (negative)	<10.00
Anti-insulin antibody, cutoff index	0.07 (negative)	<1.00
Anti-islet cell antibody, cutoff index	0.05 (negative)	<1.00
Antithyroglobulin antibody, IU/mL	0.40	<4.11
Antithyroid peroxidase antibody, IU/mL	0.31	<5.61
Urinalysis		
Ketones	Positive (2+)	Negative
Infection		
Epstein-Barr virus IgM antibody	Negative	Negative
Coxsackievirus IgM antibody	Negative	Negative
Cytomegalovirus DNA PCR	Negative	Negative
Adenovirus	Negative	Negative
Bordetella pertussis PCR	Negative	Negative
Mycoplasma pneumoniae PCR	Negative	Negative
Chlamydia pneumoniae PCR	Negative	Negative
Influenza A virus PCR	Negative	Negative
Influenza B virus PCR	Negative	Negative
Respiratory syncytial virus PCR	Negative	Negative
SARS-CoV-2 PCR	Positive	Negative

of pancreatic cells. More studies are needed to better understand the characteristics of FT1D associated with SARS-CoV-2 infection and the mechanism through which SARS-CoV-2 leads to pancreatic cell destruction or hypofunction and whether this effect is transient or permanent.

This unique case lends further support to the role of SARS-CoV-2 infection in the onset of FT1D. Finally, this case draws attention to the need for vigilance for FT1D in patients who present with diabetic ketoacidosis during COVID-19 infection or infection with other viruses.

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and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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