

## COVID-19 감염 후 발생한 전격성 1형당뇨병 1예

서동우<sup>1</sup>, 이차곤<sup>2</sup>, 이홍규<sup>3</sup>, 김진택<sup>1</sup>

을지대학교 의과대학 노원을지대학교병원 <sup>1</sup>내분비내과, <sup>2</sup>소아청소년과, <sup>3</sup>서울대학교 의과대학 서울대학교병원 내분비내과

### A Case of Fulminant Type 1 Diabetes Mellitus after Recovery from COVID-19 Infection

Dong Woo Suh<sup>1</sup>, Cha Gon Lee<sup>2</sup>, Hong Kyu Lee<sup>3</sup>, Jin Taek Kim<sup>1</sup>

<sup>1</sup>Department of Internal Medicine,

<sup>2</sup>Department of Pediatrics, Nowon Eulji University Hospital, Eulji University College of Medicine,

<sup>3</sup>Department of Internal Medicine, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea

#### Abstract

With the ongoing spread of coronavirus disease 2019 (COVID-19) infection, various complications have been reported. Here, we report a case of fulminant type 1 diabetes mellitus (T1DM) that developed abruptly after recovery from COVID-19 infection. A 41-year-old man with no relevant medical history visited the emergency room for polydipsia and polyuria 1 week in duration. The patient had just completed self-isolation at home after he tested positive for COVID-19 two weeks prior. Blood tests showed severe hyperglycemia of 721 mg/dL of glucose, elevated lipase (409 IU/L; normal range, 12~53 IU/L), elevated ketone bodies and metabolic acidosis (pH 7.18, bicarbonate 9.3 mEq/L). Glycated hemoglobin (HbA1C) was 6.0% and C-peptide 0.0 ng/mL. Meal-stimulated C-peptide level during hospitalization was also 0.0 ng/mL. GAD (glutamic acid decarboxylase) antibody was elevated (3.3 U/mL; normal, 0.0~0.9 U/mL) and insulin autoantibody was negative. Computed tomography showed no evidence of pancreatitis. Those findings fulfilled the diagnostic criteria of fulminant T1DM. Genetic

Corresponding author: Jin Taek Kim

Division of Endocrinology and Metabolism, Department of Internal Medicine, Nowon Eulji University Hospital, 68 Hangeulbiseok-ro, Nowon-gu, Seoul 01830, Korea, E-mail: bessy@hanmail.net

Received: Aug. 22, 2022; Accepted: Oct. 4, 2022

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/4.0/>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

Copyright © 2022 Korean Diabetes Association

testing revealed that the patient was positive for HLA-DRB1\*04, HLA-DRB1\*12, HLA-DQB1\*03, and HLA-DQB1\*04. To the best of our knowledge, this is the first case of fulminant T1DM reported to occur immediately after COVID-19 infection.

**Keywords:** Type 1 diabetes; COVID-19

## INTRODUCTION

With the ongoing spread of COVID-19 infection, various complications have been reported. Here, we report fulminant type 1 diabetes mellitus (T1DM), which abruptly developed after recovery from COVID-19 infection. The Institutional Review Board (IRB) in Nowon Eulji University Hospital approved our study protocol (IRB No. 18-11-35). Informed consent was obtained from the subject included in the current study.

## CASE REPORT

A 41-year-old man with no medical history visited the emergency room for polydipsia and polyuria from 1 week ago. The patient was released from quarantine after receiving self-isolation treatment at home after he was tested positive for COVID-19 two weeks ago. For COVID-19, he had only mild myalgia and no fever. The 3 P's symptoms of diabetes developed suddenly and shortly after the symptoms of infection improved. At time of the first visit, his blood pressure was 126/72 mm Hg, heart rate was 104 beats per minute, and body temperature was 36.8°C. Physical examination revealed dehydrated tongue, decreased skin turgor and no abdominal tenderness. Height was 174 cm, bodyweight was 70 kg, and body mass index

was 23.1 kg/m<sup>2</sup>. The blood tests showed severe hyperglycemia of 721 mg/dL of glucose, elevated lipase (409 IU/L; normal range, 12~53 IU/L), elevated C-reactive protein (2.69 mg/dL; normal range, 0~0.3 mg/dL), elevated ketone body with metabolic acidosis (pH 7.18, bicarbonate 9.3 mEq/L). Computed tomography showed no evidence of pancreatitis. And his lipid profile showed no evidence of hypertriglyceridemia (total cholesterol, 234 mg/dL; LDL [low density lipoprotein] cholesterol, 153 mg/dL; triglyceride, 172 mg/dL; and HDL [high density lipoprotein] cholesterol, 62 mg/dL). He was admitted to the intensive care unit with a diagnosis of diabetic ketoacidosis. After intravenous hydration and administration of intravenous insulin, his acidosis improved and glucose level stabilized. He was then transferred to the general ward and started regular diet and subcutaneous multiple insulin injections.

In the blood test confirmed later, glycated hemoglobin (HbA1C) was 6.0% and C-peptide of 0.0 ng/L. Meal-stimulated C-peptide level followed up during his admission period was also 0.0 ng/mL. His glutamic acid decarboxylase (GAD) antibody was elevated (3.3 U/mL; normal range, 0.0~0.9 U/mL) and insulin autoantibody was negative. Those findings fulfilled for the diagnostic criteria of fulminant T1DM. Genetic typing test showed positive for HLA-DRB1\*04, HLA-DRB1\*12, HLA-DQB1\*03, HLA-DQB1\*04. After being discharged from the hospital, he is currently

under follow-up at the outpatient for 2 months. He is checking his blood glucose with continuous glucose monitoring system and using 50 units of insulin per day as a multiple daily injection without honeymoon period.

## DISCUSSION

Fulminant T1DM is one of the subtypes of T1DM, which shows sudden hyperglycemia, absolute insulin deficiency, and near normal HbA1C at the time of first presentation, and negative beta cell autoimmunity at diagnosis is common. In this case, the patient had no history and family history of diabetes, came to the hospital for the first time as diabetic ketoacidosis. HbA1C was 6.0%, which was close to normal. Elevated lipase level suggests that it was accompanied by the destruction of the pancreas without radiologic evidence. He was not an alcohol drinker. He showed complete loss of beta cell function with meal-stimulated C-peptide of 0.0 ng/mL. His GAD antibody was positive, and several fulminant T1DM showed positive for GAD antibody and T-cell autoimmunity was shown to be involved in the pathogenesis in fulminant T1DM in previous studies [1,2].

Previous observational study showed HLA-DRB1\*04:05-HLA-DQB1\*04:01 haplotype was significantly associated with increased risk of fulminant T1DM in Korean population [3]. His genetic typing showed positive for HLA-DRB1\*04, HLA-DRB1\*12, HLA-DQB1\*03, HLA-DQB1\*04. It can be assumed that susceptible genotype and combined autoimmunity evoked irreversible beta cell destruction and fulminant T1DM, although further investigations are required to find more evidence.

In vitro study showed pancreas islet beta cells can be infected by COVID-19 virus. It is known that this can lead to islet cell dysfunction and may trigger beta cell autoimmunity [4,5]. Indeed, several previous studies reported that COVID-19 increased new-onset T1DM in European pediatric populations [6,7]. In this case, it is meaningful in that fulminant T1DM with a clear temporal precedence after COVID-19 infection. Fulminant T1DM is rarely reported outside of Asia. There are one case report from China that Fulminant T1DM developed soon after COVID-19 vaccination [8]. To our knowledge, this is the first case of fulminant T1DM that occurred after COVID-19 infection, here we report this case.

## CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

## REFERENCES

1. Wang Z, Zheng Y, Tu Y, Dai Z, Lin J, Zhou Z. Immunological aspects of fulminant type 1 diabetes in Chinese. *J Immunol Res* 2016;2016:1858202.
2. Chujo D, Kawabe A, Matsushita M, Takahashi N, Tsutsumi C, Haseda F, et al. Distinct phenotypes of islet antigen-specific CD<sup>4+</sup> T cells among the 3 subtypes of type 1 diabetes. *J Clin Endocrinol Metab* 2020;105:dga447.
3. Kwak SH, Kim YJ, Chae J, Lee CH, Han B, Kim JI, et al. Association of HLA genotype and fulminant type 1 diabetes in Koreans. *Genomics Inform* 2015;13:126-31.
4. Müller JA, Groß R, Conzelmann C, Krüger J, Merle U, Steinhart J, et al. SARS-CoV-2 infects and replicates in cells of the human endocrine and exocrine pancreas. *Nat*

- Metab 2021;3:149-65.
5. Wu CT, Lidsky PV, Xiao Y, Lee IT, Cheng R, Nakayama T, et al. SARS-CoV-2 infects human pancreatic  $\beta$  cells and elicits  $\beta$  cell impairment. *Cell Metab* 2021;33:1565-76.e5.
6. Unsworth R, Wallace S, Oliver NS, Yeung S, Kshirsagar A, Naidu H, et al. New-onset type 1 diabetes in children during COVID-19: multicenter regional findings in the U.K. *Diabetes Care* 2020;43:e170-1.
7. Vlad A, Serban V, Timar R, Sima A, Botea V, Albai O, et al. Increased incidence of type 1 diabetes during the COVID-19 pandemic in Romanian children. *Medicina (Kaunas)* 2021;57:973.
8. Tang X, He B, Liu Z, Zhou Z, Li X. Fulminant type 1 diabetes after COVID-19 vaccination. *Diabetes Metab* 2022;48:101324.