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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Letters to the editor

Fulminant type 1 diabetes after COVID-19 vaccination

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To the editor,—The ongoing pandemic of coronavirus 2019 disease (COVID-19) has led to an unprecedented acceleration of anti-COVID-19 vaccine development. Here we report the first case of fulminant type 1 diabetes mellitus (FT1DM) with complete and irreversible islet destruction after vaccination with a COVID-19 inactivated vaccine (CoronaVac®).

A 50-year-old male (body mass index 18•1 kg/m^2) presented to a local hospital due to abrupt onset of polydipsia and polyuria for one day. Six days ago, he received the first dose of a COVID-19 vaccine and developed a fever over 38.5 °C for five days after vaccination. At presentation, physical examination was normal and laboratory findings showed hyperglycemia, ketosis, metabolic acidosis, and a near normal hemoglobin A1c (HbA1c). He was diagnosed with diabetes and diabetic ketoacidosis (DKA) and was treated with fluid resuscitation and intravenous insulin infusion. DKA was resolved promptly and he was placed on a subcutaneous insulin regimen for glycemic control. He was in good health previously and not on any medication. His 75-year-old mother has type 2 diabetes mellitus. There is no family history of type 1 diabetes.

Two weeks after initial presentation, his serum ketone bodies became negative. Further laboratory tests showed slightly elevated pancreatic enzymes, elevated HbA1c, normal lipids, slightly increased glycated serum protein, undetectable/low serum C-peptide level, and negative islet autoantibodies including glutamic acid decarboxylase (GADA), insulinoma-associated antigen-2 antibody (IA-2A) and zinc-transporter 8 antibody (ZnT8A). He had a negative-enhanced pancreas segmentation on the abdominal computed tomography scan with no signs of pancreatic edema. Flow cytometry showed the frequency of CD8$^+$ central memory cells (CD57$^-$CD45RA$^-$) was high in this patient (Fig. 1). And the frequency of PD-1$^+$CD4$^+$and PD-1$^+$CD8$^+$ cells was high. The susceptibility human leukocyte antigen (HLA) alleles for FT1DM (DQB1*02:03/03:03 and DRB1*09:01/09:01) was positive. A diagnosis of FT1DM was made [1]. Four weeks after disease onset, he still had an almost complete loss of islet function as evidenced by low levels of C-peptide during a mixed meal test (fasting C-peptide 32.0 pmol/l and 2 h postprandial C-peptide 29.1 pmol/l).

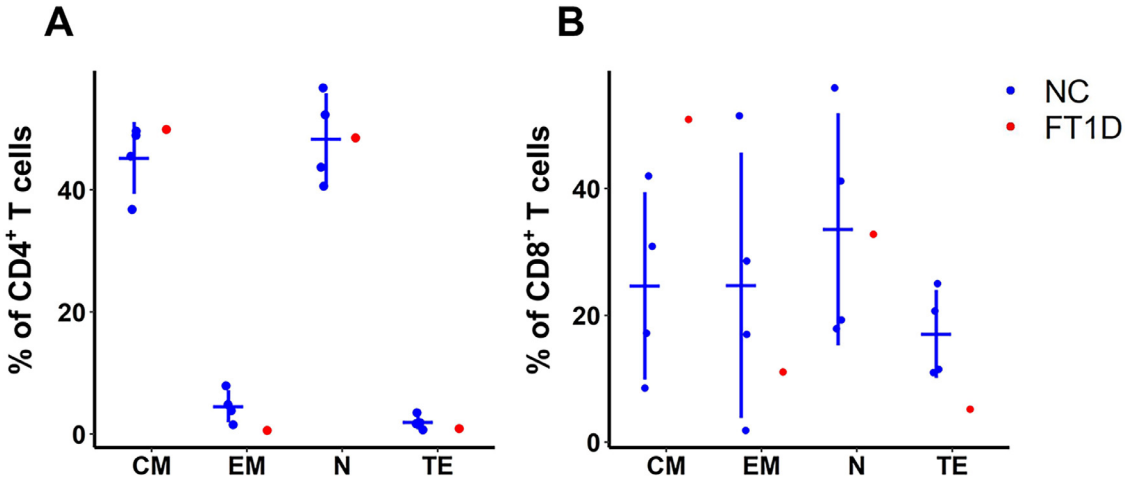

Fig. 1. Comparison of T lymphocyte subsets among groups. The percentage of central memory (CM) cells, effector memory (EM) cells, naïve (N) cells and terminal effector (TE) cells in CD4$^+$ T cells (Panel A) or CD8$^+$ T cells (Panel B) was compared between normal control (NC) group (n = 4) and the fulminant type 1 diabetes mellitus (FT1DM) patient. Graphs represent mean/group and error bars=standard deviation.

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The described patient, who was healthy and totally asymptomatic prior to vaccination, developed mild fever and then abruptly polydipsia and polyuria shortly after CoronaVac® vaccination. The chronological order of events clearly associated the onset of FT1D in this patient to vaccine administration.

While the precise mechanisms underlying FT1DM pathogenesis remain unclear, our results suggest that genetic susceptibility and autoimmunity might have been involved in the development of FT1DM in this patient, indicating that vaccination might evoke autoimmunity in individuals with susceptible genetic background and cause irreversible islet beta cell destruction and FT1DM.

Cases with FT1DM due to immune-related factors such as drugs [2] and virus infection [3] have been reported. A recent study also showed that T-cell autoimmunity may be involved in FT1DM [4]. However, no islet-associated autoantibodies were detected in this patient. It is likely that this patient did not have sufficient time to develop islet-associated antibodies given the sudden onset of the disease. Interestingly, a case of FT1DM after influenza vaccination was reported several years ago [5]. Whether these two cases share a similar underlying mechanism is unknown and deserves further research.

Overall, this case reminds clinicians to be vigilant for the possibility of FT1DM associated with COVID-19 vaccination, particularly in patients with genetic susceptibility.

Declaration of Competing Interest

The authors declare no conflicts of interest.

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References

[1] Imagawa A, Hanafusa T, Awata T, Ikegami H, Uchigata Y, Osawa H, et al. Report of the committee of the Japan diabetes society on the research of fulminant and acute-onset type 1 diabetes mellitus: new diagnostic criteria of fulminant type 1 diabetes mellitus. J Diabetes Investig 2012;3:536–9.
[2] Okamoto M, Okamoto M, Gotoh K, Masaki T, Ozedi Y, Ando H, et al. Fulminant type 1 diabetes mellitus with anti-programmed cell death-1 therapy. J Diabetes Investig 2016;7:915–8.
[3] Hollstein T, Schulte DM, Schulz J, Glück A, ziegler AG, Bonifacio E, et al. Autoantibody-negative insulin-dependent diabetes mellitus after SARS-CoV-2 infection: a case report. Nat Metab 2020;2:1021–4.
[4] Chujo D, Kawabe A, Matsushita M, Takahashi N, Tsutsumi C, Haseda F, et al. Distinct phenotypes of islet antigen-specific CD^{4+} T cells among the 3 subtypes of type 1 diabetes. J Clin Endocrinol Metab 2020;105:dgaa447.
[5] Yasuda H, Nagata M, Moriyama H, Kobayashi H, Akisaki T, Ueda H, et al. Development of fulminant type 1 diabetes with thrombocytopenia after influenza vaccination: a case report. Diabet Med 2012;29:88–9.

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