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.

Diabetes & Metabolism 48 (2022) 101338

Available online at
ScienceDirect
www.sciencedirect.com

Elsevier Masson France
EM|consulte
www.em-consulte.com

Letters to the editor

Could the development of COVID-19 vaccine-induced type 1 diabetes be explained by a simple mechanism?

To the Editor,

We read with great interest the article “Fulminant type 1 diabetes (T1DM) after Covid-19 vaccination” by Tang et al. in this journal [1]. The authors examined islet autoantibodies, HLA alleles, and the capacity for insulin secretion specifically after the treatment of a 50-year-old patient who developed diabetic ketoacidosis following Covid-19 vaccination. The work and efforts of the authors in reporting this valuable case are highly appreciated. Almost simultaneously, cases of acute-onset T1DM in Japanese women induced by Covid-19 vaccination were reported [2, 3], including the case we presented. In these cases, both patients were administered mRNA vaccines, and the patients’ islet autoantibodies were positive, which was different from the type of vaccine and characteristics of T1DM reported in this journal. However, very interestingly, in agreement with this journal’s report, both patients had one of the disease-susceptible HLA haplotypes, i.e., *DRB1*04:05-DQB1*04:01* [2] and *DRB1*09:01-DQB1*03:03* [3], so we totally agree with the authors’ opinion that vaccination of genetically susceptible recipients should be cautious concerning future development of T1DM. Although the authors made little mention about the mechanisms of the development of vaccine-induced T1DM, we would focus on the difference in the time from vaccination to the appearance of hyperglycemic symptoms between this case and the previous reports of Covid-19 vaccine-induced acute-onset T1DM. That is, in the present report [1], hyperglycemic symptoms occurred within just one week after the first vaccination, whereas these symptoms in new-onset of T1DM with positive for autoantibodies occurred four to seven weeks after the first or second vaccination [2–4], indicating a clear difference. Although we cannot exclude the possibility that this discrepancy was attributable to the different types of vaccines, i.e., inactivated vaccine [1] versus mRNA vaccine [2–4], such a wide variation in the duration of disease onset suggests that there might be no single mechanism of beta-cell destructions and the development of hyperglycemia associated with Covid-19 vaccination [2]. In the former case, negative autoantibodies and the earlier onset suggested that direct damage to beta cells by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike proteins or proinflammatory cytokines induced by Covid-19 vaccination might be the primary etiology. Indeed, some researchers suggested that direct infection with SARS-CoV-2 triggers apoptosis and transdifferentiation of beta cells [5]. On the other hand, the latter might require a certain period for the process of cross-immunity [2]. Since the major histocompatibility complex class II molecules of these patients are made from disease-susceptibility genes, vaccination of patients having these genes could easily trigger autoimmunity if the presented viral antigen proteins are similar to beta-cell antigens. We expect that the pathogenesis of new-onset T1DM following Covid-19 vaccination will be clarified by accumulating detailed information on the time from vaccination to the onset, the presence of islet autoantibodies, and genetic background, and investigating their relationships.

Declaration of Competing Interest

The authors declare no conflicts of interest.

Funding

No funds were provided for this report.

References

[1] Tang X, He B, Liu Z, Zhou Z, Li X. Fulminant type 1 diabetes after Covid-19 vaccination. Diabetes Metab 2022:101324. doi: 10.1016/j.diabet.2022.101324.
[2] Sasaki H, Itoh A, Watanabe Y, Nakajima Y, Saisho Y, Irie J, et al. Newly developed type 1 diabetes after coronavirus disease 2019 vaccination: A case report. J Diabetes Investig 2022. doi: 10.1111/jdi.13757.
[3] Yano M, Morioka T, Natsuki Y, Sasaki K, Kakutani Y, Ochi A, et al. A Case of new-onset type 1 diabetes after Covid-19 mRNA vaccination. Intern Med 2022. doi: 10.2169/internalmedicine.9004-21.
[4] Patrizio A, Ferrari SM, Antonelli A, Fallahi P. A case of Graves' disease and type 1 diabetes mellitus following SARS-CoV-2 vaccination. J Autoimmun 2021; 125:102738. doi: 10.1016/j.jaut.2021.102738.
[5] Shirakawa J. Pancreatic β-cell fate in subjects with Covid-19. J Diabetes Investig 2021;12:2126–8. doi: 10.1111/jdi.13671.

Hironobu Sasaki[a,b]
Arata Itoh[a*]
Hiroshi Itoh[a]
[a] *Division of Nephrology, Endocrinology and Metabolism, Department of Internal Medicine, Keio University School of Medicine, 35 Shinanomachi, Shinjuku-ku, Tokyo, 160-8582, Japan*
[b] *Center for Preventive Medicine, Keio University School of Medicine, 35 Shinanomachi, Shinjuku-ku, Tokyo, 160-8582, Japan*

*Corresponding author at: 35 Shinanomachi, Shinjuku-ku, Tokyo, 160-8582, Japan.
E-mail address: arata.itoh@keio.jp (A. Itoh).

Received 15 February 2022
Accepted 26 February 2022

Available online 9 March 2022

https://doi.org/10.1016/j.diabet.2022.101338