Newly Diagnosed Type 1 Diabetes Presenting with Diabetic Ketoacidosis After SARS-CoV-2 Vaccine

ABSTRACT

The COVID-19 pandemic has deeply affected the whole world in the last 3 years due to the mortality and morbidity it causes. Billions of doses of vaccines have been administered to overcome the pandemic. The increased incidence of various autoimmune diseases during the pandemic has given rise to the thought that COVID-19 infection or vaccine may be the triggering factor. Recently, new-onset autoimmune phenomena after COVID-19 vaccination have been reported for some autoimmune diseases like Guillain–Barré syndrome and other neurological autoimmune diseases, IgA nephropathy, rheumatoid arthritis and systemic lupus erythematosus, immune thrombotic thrombocytopenia, autoimmune liver diseases, and autoimmune thyroid diseases. Here, we present a case of newly diagnosed type 1 diabetes that developed 1 month after the SARS-CoV-2 vaccine.

Keywords: Autoimmunity, COVID-19, diabetes, vaccine

Introduction

More than 600 million people have been infected with the SARS-CoV-2 virus during the COVID-19 pandemic. Various vaccines have been introduced to prevent the disease during the pandemic. The increased incidence of various autoimmune diseases in the pandemic has raised the idea that COVID-19 infection or vaccines might have contributed to the development of autoimmune diseases. There is increasing number of evidence in this regard.[1-5] It has been discovered that the pancreas, pituitary gland, thyroid gland, adrenals, and gonads are affected by the virus. It has been asserted that these endocrine glands express angio tensin-converting enzyme 2 (ACE2) receptor, which facilitates SARS-CoV-2 binding and thus induces cell damage.[6] There is also emerging data about the increased frequency of autoimmune diabetes. It has been revealed that some receptor similarities are present between pancreatic beta cells and SARS-CoV-2 virus besides ACE2 receptor interaction. Therefore, it has been concluded that various pancreatic diseases may develop after COVID-19 infection and SARS-CoV-2 vaccine.[7,8] The number of post-vaccine type 1 diabetes cases in the literature is low.[9-11] Here, we present an unusual case of newly diagnosed type 1 diabetes with atypical presentation that developed 1 month after the SARS-CoV-2 vaccine in an elder patient. Written informed consent was obtained from the patient.

Case Presentation

A 69-year-old woman presented with complaints of weakness, increased frequency of urination, and dry mouth. She told her complaints had become more evident in the last 48 hours, and her speech was lisped. She had no known history of any chronic disease other than asthma. She was taking desloratadine 5 mg twice a day. The family history was unremarkable except for a known maternal history of type 2 diabetes mellitus. She did not have a recent or past COVID-19 infection. She had 3 doses of Pfizer BioNTech® (BNT162b2) vaccine against COVID-19 and the last one was administered 1 month ago.

At physical examination, there were no remarkable signs other than extremely dry mucosa and severely decreased skin turgor. Her height was 156 cm, weight was 51 kg, and she denied weight loss. Capillary blood glucose measurement was 520 mg/dL. Her pH was 7.09, HCO3 was 10.3 mmol/L, and base excess was -17.5 mmol/L in blood gas analysis and there were 3 positive ketone bodies in her urine. Her plasma blood glucose was 464 mg/dL.

The patient was diagnosed with diabetic ketoacidosis. Intravenous fluid besides insulin therapy was started immediately. Blood glucose and pH-HCO3-base excess returned to

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Table 1. Comparison of the Laboratory Analyses of Our Case with 4 Cases of B (Aydoğan et al[9])

Parameter	Our Case	Case-1	Case-2	Case-3	Case-4
Age (years)	69	56	48	27	36
Plasma glucose (mg/dL)	464	440	352	320	526
Hemoglobin A1c (%)	13.2	8.2	10.1	12.5	12.6
C-peptide (ng/mL)	0.190 ng/ml	1.5	0.97	0.87	0.38
Glutamic acid decarboxylase antibody (IU/mL)	1453	>2000	94	725	234
Time from vaccination to symptom onset (weeks)	4	2	8	3	3

normal and ketone bodies in the urine became negative. In the laboratory analysis; hemoglobin A1c (HbA1c) level was 13.2%, islet cell antibody (ICA) was positive at 1:320 titer, glutamic acid decarboxylase antibody (anti-GAD) was 1453 IU/mL (reference range<10), and C-peptide level was 0.190 ng/mL. In light of these findings, the patient was diagnosed with type 1 diabetes.

Discussion

The COVID-19 pandemic has caused millions of deaths worldwide. It was initially thought that COVID-19 is a disease affecting only the respiratory system, but it has been understood that the disease is a syndrome that can affect many systems as well as endocrine organs.[6] The most effective way to prevent the disease is vaccination. Billions of doses of COVID-19 vaccine have been administered around the world.

There are emerging data that the COVID-19 vaccines,-especially the mRNA vaccine, may create a hyperimmune state. Recently, an increasing number of new-onset autoimmune phenomena (e.g., neurological autoimmune diseases, IgA nephropathy, rheumatoid arthritis and systemic lupus erythematosus, immune thrombotic thrombocytopenia, autoimmune liver diseases) after COVID-19 vaccination have been reported.[1-6] In addition, it has been reported that various endocrinopathies may develop after COVID-19 infection and vaccination. Due to receptor similarity of the pancreas and the SARS-CoV-2 virus, especially ACE2 receptor, new-onset insulin-dependent diabetes cases have been reported.[6,7,10]

Vojdani et al[11] have observed similarities and cross-reactive interactions between SARS-CoV-2 proteins and host's self-antigens and considered these interactions as a possible link between autoimmunity and COVID-19 infection and/or vaccination against SARS-CoV-2. They showed that monoclonal anti-SARS-CoV-2 spike proteins and some nucleoprotein antibodies interact with some human proteins, especially glutamic acid decarboxylase 65 (GAD65) which is related to type 1 diabetes.

The risk of diabetes in patients infected with COVID-19 has been searched in a large cohort of patients and controls. The control group consisting of 84 million people was compared with 181280 COVID-19 patients. The incidence of diabetes and the rate of usage of antihyperglycemic drugs were higher in the infected group.[12] Additionally,

a large number of diabetic ketoacidosis case series triggered by COVID-19 infection have been reported to date by different centers.[13]

In our case, the SARS-CoV-2 vaccine was administered 1 month before the diagnosis of diabetes. There were no signs of COVID-19 infection and SARS-CoV-2 rapid antigen test was negative. The patient was 69 years old and developed diabetic ketoacidosis only 1 month after vaccination without previous diagnosis of diabetes and took a diagnosis of type 1 diabetes mellitus. We have considered that autoimmune diabetes mellitus might have been triggered by vaccination in our patient.

Type 1 diabetes mostly manifests in children and young adolescents, although rarely, there are few cases diagnosed in adults and even in advanced ages like in our patient. Considering the natural course of type 1 diabetes, our case was quite unusual. She was too old for diagnosis of type 1 diabetes. She was also older than the other type 1 diabetes cases in the literature that were thought to have developed after SARS-CoV-2 vaccine. In addition, while the HbA1c level of our case was higher than the other cases, the C-peptide level was much lower than in the other cases. The comparison of our case with another study's cases is given in Table 1.[9]

Conclusion

Vaccine is the most powerful weapon we have against the SARS-CoV-2 virus pandemic. It was the first time using mRNA technology to produce a vaccine against COVID-19. Pfizer-BioNTech® (BNT162b2) mRNA vaccine was allowed for emergency use authorization by the Food and Drug Administration in December 2020. Therefore, the long-term effects of the mRNA vaccine are not clear and well-known yet. Reports of autoimmune diseases developing after SARS-CoV-2 mRNA vaccination are consistently increasing in the literature. This increase may be related to either vaccination or infection.

Type 1 diabetes is an autoimmune disease. It is believed that genetic and environmental factors both affect the development of autoimmunity. Because of the structural similarity between SARS-CoV-2 virus antigens and various host proteins, SARS-CoV-2 antibodies can cross-react with human proteins and cells. When this reaction occurs in the pancreas, especially in the islet cells, it is hypothesized that it can lead to the development of type 1 diabetes. Therefore, vaccination history should be questioned while investigating environmental factors in autoimmune diseases, especially in those with atypical presentations. In people with genetic predisposition, COVID-19 infection and/or vaccine may be the triggering factor for any autoimmune disease even if at an advanced age like our case. To make clearer judgments, larger case series are needed.

Informed Consent: Written informed consent was obtained from the patient.

Peer-review: Externally peer-reviewed.

MAIN POINTS

- Diagnosis of type 1 diabetes at an advanced age is extremely rare.
- Some autoimmune processes may develop after COVID-19 infection or vaccination.
- Vaccination history should be questioned, especially for atypically presenting autoimmune diseases.

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