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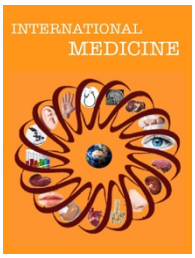

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Case Report

Rapid and severe worsening of diabetes in a heart transplant recipient after Johnson & Johnson's Janssen COVID-19 vaccine administration

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Abstract

The COVID-19 vaccines are usually safe, effective, and well-tolerated by the general population. After the COVID-19 vaccines are widely used, rare and potentially severe vaccine complications become more manifest. Here reported is a case of rapid and severe worsening of diabetes after the Johnson & Johnson's Janssen COVID-19 vaccine (J&J COVID vaccine) administration. A 55-year-old male heart transplant recipient with metformin (500 mg twice daily)-controlled mild diabetes started to have flu-like symptoms a few days after receiving the J&J COVID vaccine. His fasting glucose levels had ranged between 130-150 mg/dL (normal 65-99) before he received the J&J COVID vaccine. The fasting glucose rose to ~200 mg/dL one day after the vaccine administration and gradually rose to ~400 mg/dL over the next few weeks. He presented to the endocrine clinic urgently. Point-of-care fasting glucose was 382 mg/dL and A1c 13.0 (which was 6.7 six months before). Bicarbonate and anion gap were normal, insulin and C-peptide in the low normal range, and β cell autoantibodies negative. Multi-dosing insulin treatment was immediately started and the doses titrated up to insulin glargine 30 units daily and insulin lispro 10 units before each meal. He improved clinically with well-controlled glycemia. The rapid and severe worsening of his diabetes after the vaccination suggests that the J&J COVID vaccine could severely deteriorate diabetes control in some patient populations.

Keywords: COVID vaccine; diabetes; heart transplant; hyperglycemia

1. Introduction

The COVID-19 vaccines are usually safe, effective, and well-tolerated by the general population. After the COVID-19 vaccines are widely used, rare and potentially severe vaccine complications become more manifest. The thrombotic events associated with the use of the Oxford-AstraZeneca COVID-19 vaccine and the Johnson & Johnson's Janssen COVID-19 vaccine (J&J COVID vaccine) have received much publicity [1,2]. Other complications such as new-onset Graves' disease have been reported in two patients and hyperosmolar hyperglycemic state in one patient following the Pfizer-BioNTech COVID-19 vaccine administration [3,4]. Here reported is a case of rapid and severe worsening of diabetes in a heart transplant recipient after the J&J COVID vaccine administration.

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2. Case Report

A 55-year-old male patient visited the endocrine clinic urgently for severe hyperglycemia. Four weeks before presentation, the patient had received the J&J COVID vaccine. A few days later, he developed flu-like symptoms; he felt warm without fever, weak, sleepy, and anorexic and he had to sleep most of the day. These symptoms lasted for a few days then abated. Most of the same symptoms recurred a few days later; in addition, he developed insomnia even though he was tired, polyuria, and thirst, and lost 9 lbs. His fasting glucose readings had ranged between 130-150 mg/dL (normal 65-99) before he received the J&J COVID vaccine. The fasting glucose rose to 200 mg/dL one day after the vaccine administration and gradually rose to 400 over the next few weeks. On the morning of the presentation, a routine blood test showed fasting glucose of 422 mg/dL. He was asked to go to the endocrine clinic immediately for advice.

The patient had developed ventricular tachycardia at age 35 and congestive heart failure at age 42. He was found to have normal coronary arteries during the heart transplant evaluation. He received an orthotopic heart transplant at age 49, six years before the current presentation. Histology of the native heart showed nonischemic cardiomyopathy. His immunosuppression regimen initially consisted of prednisone, mycophenolate, and tacrolimus but prednisone was tapered off several months later. The transplanted heart functioned well. The patient had had normal hemoglobin A1c (5.2, normal <5.7) three years before the heart transplant. Two months before heart transplant, A1C was 6.6. Although he required insulin treatment right after the heart transplant, his glycemia promptly normalized and he was discharged home without any diabetes medications. One year after the heart transplant, while on mycophenolate 250 mg twice daily and tacrolimus 3.5 mg every morning and 3 mg every afternoon, his A1c was 6.1. One and half years after the heart transplant, while on the same immunosuppression regimen, his A1c rose to 8.4. He did not recall significant changes in his diet and exercise before the A1c rise. Metformin 250 mg daily was started but his postprandial glucose still ranged between 200-300 mg/dL. Metformin dose was raised to 500 mg twice daily; 3 months later, A1c decreased to 6.5. He continued metformin 500 mg twice daily until the current presentation and his A1c varied between 5.9-7.6, depending on diet and exercise compliance. In the 16 months before the current presentation, his A1c was tested three times and was 6.7 each time, and his fasting glucose ranged between 113-145 mg/dL. The last A1c test and last fasting glucose test were done six months and four months, respectively, before the current presentation. He had no known diabetic complications. He also had myofibrillar myopathy due to c.571 G>C mutation in the MYOT gene. A few siblings of the patient had diabetes. His medications at the current presentation included aspirin 81 mg daily, gabapentin 300 mg twice daily, mexiletine 150 mg twice daily, rosuvastatin 5 mg tablet three times weekly, magnesium oxide 400 mg twice daily, metformin 500 mg twice daily, mycophenolate 250 mg twice daily, and tacrolimus 3 mg twice daily.

Table 1. Laboratory test results

	Reference range	4 months before presentation	At presentation
Sodium	135 - 146 mmol/L	139	134
Potassium	3.6 - 5.3 mmol/L	4.6	5.3
Chloride	96 - 106 mmol/L	102	95
Bicarbonate	20 - 30 mmol/L	24	27
Anion gap	8 - 19 mmol/L	13	12
Urea nitrogen	7 - 22 mg/dL	17	29
Creatinine	0.60 - 1.30 mg/dL	0.89	0.97
Calcium	8.6 - 10.4 mg/dL	9.3	9.5
Magnesium	1.4 - 1.9 mEq/L	1.6	1.6
Glucose	65 - 99 mg/dL	145	422
Hemoglobin A1c	<5.7	6.7 (6 months before presentation)	13.0
Amylase	31 - 124 U/L		56
Lipase	9 - 63 U/L		49
Insulin	3 - 25 uU/mL		6
C-Peptide	1.1 - 4.3 ng/mL		2.3
Glutamic acid decarboxylase-65 autoantibody	0.0 - 5.0 IU/mL		<5.0
ICA-512 autoantibody	0.0 - 7.4 U/mL		<5.4
Insulin antibody	0.0 - 0.4 U/mL		<0.4

At the endocrine clinic, he appeared anxious and thin but was in no acute distress. He denied abdominal pain. His temperature was 36.5 °C (97.7 °F), blood pressure 114/80 mmHg, heart rate 104 beats/minute, weight 53.6 kg, and body mass index (BMI) 19.67 kg/m². He had moist mucosa. Auscultation revealed tachycardia and clear lungs. He had no lower extremity edema. Point-of-care glucose was 382 mg/dL and A1c 13.0. The same blood specimen which showed glucose of 422 mg/dL also showed mild hyponatremia and hypochloremia but normal creatinine, bicarbonate, and anion gap [Table 1]. Additional tests were added to the existing blood specimen collected earlier that day. Amylase and lipase levels were normal; insulin and C-peptide levels were in the low normal range, which showed β cell function deficiency in the face of severe hyperglycemia. β cell autoantibodies including those against glutamic acid decarboxylase-65, ICA-512, and insulin were tested but the results were not immediately available. The patient was deemed stable enough to be managed as an outpatient. Insulin glargine 10 units daily and insulin lispro 5 units before each meal were started and metformin was held. In two days, Insulin glargine dose was raised to 15 units daily and insulin lispro to 7 units. A week later, he was seen at the endocrine clinic again. He felt much better and regained 1-2 lbs. β cell autoantibodies were all negative. Fasting glucose levels were 137-150 mg/dL and daytime glucose 273 to 330 mg/dL. Insulin glargine dose was raised to 18 units daily and insulin lispro to 10 units. On the last follow-up 16 days after the urgent endocrine clinic visit, his glycemia was well controlled with insulin glargine 30 units daily and insulin lispro 10 units before each meal. He felt that he had been back to his baseline health before receiving the J&J COVID vaccine.

3. Discussion

As COVID-19 could have devastating consequences in patients with diabetes or organ transplant recipients, those patients should receive the COVID-19 vaccine as priority populations [5,6]. The patient described here with diabetes and heart transplant appropriately received a COVID-19 vaccine, the J&J COVID vaccine. The rapid and severe worsening of his diabetes after the vaccination suggests that the J&J COVID vaccine could severely deteriorate diabetes control in some patient populations.

Adverse reactions to vaccines are caused by multiple mechanisms such as reversion of virulence of attenuated live organisms and immune-mediated reactions to the active components or adjuvants of the vaccines [7]. The rapid and severe worsening of diabetes in this patient is characterized by β cell dysfunction as his insulin and C-peptide levels were inappropriately low normal in the face of severe hyperglycemia. The J&J COVID vaccine uses non-replicating adenovirus expressing the SARS-CoV-2 coronavirus spike protein. Although replicating adenovirus may cause β cell injuries [8], non-replicating adenovirus should not induce significant such injuries. Reversion of the non-replicating adenovirus to a replicating form is extremely unlikely. It is possible that the J&J COVID vaccine induces an autoimmune or allergic response in the recipients [3,7,9], but there is no evidence of immune-mediated β cell destruction as all three β cell autoantibodies were negative, neither is there evidence of general pancreatic inflammation as amylase and lipase levels were normal. It is likely that the β cell dysfunction is not caused by decreased β cell mass but is caused by an acute deficit in properly secreting insulin during severe hyperglycemia [10]. This patient had fluctuations in glycemic control before and after heart transplant; he already had a brief period of mild type 2 diabetes shortly before heart transplant but his A1c went to pre-diabetic level 1 year after heart transplant but rose to 8.4, a mere six months later without clear explanation. The glycemic fluctuation may indicate intrinsic volatility in his β cell function similar to that in ketosis-prone diabetes where β cells insufficiently respond to hyperglycemia after a threshold glucose level [11]. The acute increase in his glucose levels is likely caused by insulin resistance associated with vaccine-induced inflammation [12], which exceeds the threshold glucose level. Although organ transplant recipients have a relatively lower seroconversion rate after COVID-19 vaccination [13], the vaccine-induced inflammation can be nonetheless strong, as shown in this patient.

In summary, a patient with a history of metformin-controlled diabetes and heart transplant developed rapid and severe hyperglycemia after receiving the J&J COVID vaccine and he had to be treated with multi-dosing insulins. Based on existing evidence, this adverse reaction to the J&J COVID vaccine was likely due to his intrinsic β cell dysfunction and triggered by vaccine-induced inflammation.

Conflict of interest

The author declares that he has no competing interests.

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