

COVID-19 Vaccine Related Hyperosmolar Hyperglycemic State and Normalized Glycemia within 2 Months

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Abstract

To protect from COVID-19 pandemic, several vaccines were developed infection with expected immunity against a SARS-CoV-2 infection. Short time side effects are reported. New onset diabetes was reported after SARS-CoV-2 infection. Here we report a case of new onset diabetes presenting with hyperosmolar hyperglycemic state, whose symptoms followed right after the second dose of Pfizer-BioNTech COVID-19 Vaccine. He is a 56-year old, obese Afro-American Veteran with no family history of diabetes and with HbA1C of 5.6 forty-five days prior to the hospitalization. He noted polyuria and excessive thirst following the second dose Pfizer-BioNTech COVID-19 vaccine. Hospitalized with hyperosmolar state and HbA1C of more than 14, he was treated initially with insulin drip and changed to basal, bolus regimen. In addition, he had new onset of oral thrush, requiring antifungal therapy. He needed higher doses of insulin during hospitalization and at discharge. He rapidly recovered and could be tapered off insulin in 4 months and recovered to normal glycemic state. We conclude that this is the second state to present with hyperosmolar state, and first case with rapid recovery of glycemic state.

Keywords

Diabetes, Pfizer-BioNTech COVID-19 Vaccine CAD, Hyperosmolar Hyperglycemic State, Anemia

1. Introduction

First descriptions of the hyperosmolar hyperglycemic state (HHS) was said to be in 1880s by von Frerichs and Dreschfeld. Current diagnostic criteria include a plasma glucose level of more than 600 mg/dL and increased effective plasma

osmolality > 320 mOsm/kg in the absence of ketoacidosis. The incidence of HHS is estimated to be <1% of hospital admissions of patients with diabetes. The reported mortality is between 10% and 20%, which is about 10 times higher than the mortality rate in patients with diabetic ketoacidosis (DKA). To protect the public from COVID-19 pandemic several vaccines were developed and continue. These vaccines can protect those recipients from a SARS-CoV-2 infection with expected immunity against a SARS-CoV-2 infection. Short term side effects were reported but long side effects are not clear. Here we report a 56-year-old male with no family history of diabetes, with HbA1C of 5.6, 45 days prior to presentation with hyperosmolar state and HbA1C of more than 14 with symptoms of polyuria and nocturia following second dose of Pfizer-BioNTech COVID-19 vaccine.

2. Case Report

A 56-year-old obese Afro-American male with a past medical history of hypertension, primary hyperparathyroidism, goiter and primary hypothyroidism on levothyroxine, obesity and hyperlipidemia was hospitalized to medical intensive care unit with hyperosmolar hyperglycemic state with blood sugar more than 900 and acute renal insufficiency with creatinine of 2.7. His symptoms of polyuria and increased thirst following second dose of Pfizer-BioNTech COVID-19 vaccine. Thirst was so severe, drank three gallons of juice and water, couple of days prior to hospitalization. He felt confused and spilled gasoline on his clothes and became unsteady on the day of hospitalization. In addition, he had throat pain and mild cough, decreased visual acuity (blurring). Personal history significant for former smoker of 37 pack years. Quit smoking and alcohol use two years prior to hospitalization. Never heavy alcohol user. No family history of diabetes. His at home meds included antihypertensives, atorvastatin and levothyroxine 125 mcg a day. Baseline labs and at discharge bmp are shown in **Table 1**. Physical exam revealed obese male with BMI of 33.5, cooperative and not in distress, appeared to be appropriate for stated age, well-built and nourished male. Had thyromegaly and oral thrush. No other abnormalities on physical exam.

He was hospitalized and appropriately treated in MICU with large doses of intravenous fluids, intra venous insulin drip of moderate doses and other supportive care. Later the insulin doses were transitioned to basal bolus insulins. Relevant diabetes related labs with changes over time are shown in **Table 1**. Blurring and visual acuity improved as sugars improved. Creatinine and eGFR normalized after IV fluids and treatment with insulin. Oral thrush was treated with oral nystatin suspension.

Follow up: Post discharge he received gradual tapering doses of insulin and later insulin was discontinued and recovered to normal glycemic state off anti diabetic meds. His HbA1C came down to 4.9 by 40 days after discharge. Rapid changes in blood counts at hospitalization also improved rapidly after discharge without any intervention as shown in **Table 2**. His glycemic state remains normal five months after discharge

Table 1. With Basal metabolic parameters at admission and at follow up.

Date	Na	K	Cl	CO ₂	Glu	BUN	Cre	eGFR
5/3/21	118	6.1	82	13	997	38	2.7	30
5/4/21	139	3.1	103	30	136	18	1.3	>60
6/18/21	139	4.4	109	19	158	19	1.1	>60

Na: Sodium; K: Potassium; Cl: Chloride; Glu: Glucose; BUN: Blood urea nitrogen; Cre: Creatinine; eGFR: estimated glomerular filtration rate.

Table 2. Change in blood counts over time.

Date	WBC	HGB	HCT	MCV	Platelets
5/3/21	16.4	13.3	41.7	95.9	196
5/5/21	11.7	9.9	30.6	92.3	141
5/14/21	14.7	5.6	17.5	100.9	335
7/15/21	11.7	12.5	337.4	92.4	243

WBC: white cell count; HGB: Hemoglobin; HCT: Hematocrit; MCV: Mean Corpuscular Volume.

Interesting features:

- 1) Development of hyperosmolarity starting after the second dose of the vaccine in a patient with no family history of diabetes and HbA1C of 5.6, forty-five days prior to presentation with HbA1C of >14 and hyperosmolarity state.
- 2) Rapid rise and rapid recovery of glycemic state.
- 3) Rapid drop in blood counts and rapid recovery.

3. Discussion

Diabetes is high risk factor for severe complications including severe diabetic ketoacidosis, hyperosmolar state including high risk for death [1] [2] [3] [4] [5]. Severe metabolic complications of preexisting diabetes, including diabetic ketoacidosis and hyperosmolarity for which exceptionally high doses of insulin are warranted, have been observed in patients with COVID-19. There are several studies reporting new onset diabetes and COVID-19 [6]-[14]. Since angiotensin-converting enzyme 2 (ACE2) receptors are expressed (immunostaining) in several organs and but not in hepatocytes [15], it is considered possible that SARS-CoV-2 may lead to alterations in glucose metabolism and lead to complicating preexisting diabetes and or new onset diabetes [14]. In a study of SARS 1 pneumonia compared hyperglycemia (38.0% vs. 9.8%; $p = 0.0001$), suggesting that SARS caused lesions to that of non-SARS pneumonia, mortality was higher in patients within the pancreatic islets [16]. In pancreas, immunostaining for ACE2 protein was strong in the pancreatic islets but very weak in the exocrine tissues [16]. The above studies support the potential high risk in preexisting diabetes and new onset diabetes in COVID-19. Based on the immunostaining for ACE2 protein to be strong in the pancreatic islets but very weak in the exocrine

tissues, Coate *et al.* postulated that the interaction of diabetes and SARS-CoV-2 is mediated by systemic inflammation and/or metabolic changes in other organs such as the liver, muscle, or adipose tissue [16]. Yang *et al.* reported that the localization of ACE2 expression in the endocrine part of the pancreas suggests that SARS coronavirus enters islets using ACE2 as its receptor and damages islets causing acute diabetes [17].

Serious Vaccine-related adverse events among BNT162b2 recipients from the trial include shoulder injury related to vaccine administration, right axillary lymphadenopathy, paroxysmal ventricular arrhythmia, and right leg paresthesia as reported from the safety and efficacy of the BNT162b2 mRNA COVID-19 vaccine study [18]. Hyperglycemia secondary to vaccine might have been relatively later and may explain the hyperosmolar state in our experience is a delayed side effect. We cannot explain the exact mechanism for severe and acute onset of diabetes leading to hyperosmolar state except that his c-peptide levels are low suggestive of pancreatic damage. There was one case report of hyperosmolar state [19], and one patient with pancreatitis after the vaccine [20].

In addition to glycemic changes, he had changes in hemoglobin and hematocrit, with recovery in 3 months. The possible explanation is the effect of vaccine on bone marrow with complete recovery.

4. Conclusion

Our patient presented with a hyperosmolar state and his symptoms started right after the second dose after receiving the BNT162b2 vaccine and had no other risk factors for the condition. Hence it is considered that the acute hyperglycemic state is the effect of the BNT162b2 vaccine. In addition, he recovered his pancreatic function to a prediabetic state within less than 2 months. This publication is for the clinicians to be aware of possible side effects of the vaccine as consideration and need for close follow-up care to avoid hypoglycemia as they recover. In addition to glycemic changes, he had changes in hemoglobin and hematocrit, with recovery in 3 months, probable effect on bone marrow.

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Conflicts of Interest

None of the authors have conflict of interest.

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