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A Case of Immune Thrombocytopenia After BNT162b2 mRNA COVID-19 Vaccination

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Conflict of interest: None declared

Patient: Female, 39-year-old
Final Diagnosis: Immune thrombocytopenic purpura
Symptoms: Purpuric skin lesions • thrombocytopenia
Medication: —
Clinical Procedure: None
Specialty: Hematology • Immunology

Objective: Unusual clinical course

Background: Immune thrombocytopenic purpura (ITP) is an immune response that destroys platelets and increases the risk of bleeding, which can range from bruising to intracranial hemorrhage. ITP is a known complication of coronavirus disease 2019 (COVID-19). In the first studies of the BNT162b2 messenger RNA (mRNA) COVID-19 vaccine, there were no reports of ITP and the incidence of serious adverse events (AEs) was low overall. Here, we present a case of ITP as a complication of the BNT162b2 mRNA COVID-19 vaccine.

Case Report: Three days after receiving a second dose of the BNT162b2 mRNA COVID-19 vaccine, a 39-year-old woman presented with a petechial rash on her trunk, legs, and arms, and fatigue and muscle aches. At the time of her hospital admission, her platelet count was 1000/μL. A peripheral smear showed profound thrombocytopenia. During the course of the patient's hospitalization, she was treated with 2 units of platelets, 2 infusions of i.v. immunoglobulin, and i.v. methylprednisolone. Her platelet count increased to 92 000/μL on the day of discharge and she was prescribed a tapered dose of oral prednisone. One day later, her rash had resolved and her platelet count was 243 000/μL. The patient recovered completely with no complications.

Conclusions: ITP should be considered a severe AE of the BNT162b2 mRNA COVID-19 vaccine. Knowing the early signs and symptoms of ITP will become increasingly important as more of the population receives this vaccine. Quick diagnosis and management are essential to avoid life-threatening bleeding.

Keywords: COVID-19 Vaccine • Purpura • Thrombotic Thrombocytopenic Purpura, Acquired

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/931478

983 3 — 5

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Background

ITP is an immune response targeting platelets and can result in critically low platelet counts that increase the risk of bleeding. This bleeding can range from mild bruising to life-threatening cases of intracranial hemorrhage. No cases of ITP were reported in the first studies of the BNT162b2 messenger RNA (mRNA) COVID-19 vaccine, and overall, the incidence of serious adverse events (AEs) was low [1]. One publicized case of ITP after exposure to the BNT162b2 mRNA COVID-19 vaccine was reported in the media in January 2021 and is still under investigation [2]. ITP is a known complication of COVID-19 [3]. It also is a complication of other vaccines, particularly for influenza and for measles, mumps, and rubella (MMR) in children [4,5]. The risk of ITP after vaccination is extremely low, and estimated at 1 in 25 000 after MMR vaccination [5]. Most cases of vaccine-induced ITP are self-limiting and resolve with standard treatment.

The BNT162b2 mRNA COVID-19 vaccine was approved for emergency use by the US Food and Drug Administration on December 11, 2020 after results of the phase 3 trial were published [6]. The vaccine is administered in 2 doses, 21 days apart and the study included more than 40 000 participants. AEs were monitored through 14 weeks after the second dose. Patients reported systemic AEs such as fatigue and fever. However, there were no reported cases of ITP in this landmark study. The case we present, of severe ITP after exposure to the BNT162b2 mRNA COVID-19 vaccine, is an important addition to the safety profile of this novel vaccine.

Case Report

A 39-year-old woman received the second dose of the BNT162b2 mRNA COVID-19 vaccine at a community hospital in Michigan; 3 days later, she presented to the same institution with a petechial rash. Approximately 12 h after her vaccination, she had experienced fatigue and muscle aches. She did not have fever, cough, runny nose, a change in taste or smell, or any other associated symptoms. Her medical history included polycystic ovary syndrome, for which she took norgestimate-ethinyl estradiol. She had no pertinent family or travel history and no history of use of tobacco or alcohol or of substance abuse. The patient had a complete blood count (CBC) and differential 5 months before, during a routine health examination, which was entirely within normal limits. At that time, she also was tested for COVID-19 antibodies; the results were negative. The patient did not have any illnesses or known COVID-19 exposures before the incident reported here.

On presentation, the patient had a heart rate of 109 bpm, blood pressure of 127/80 mm Hg, respiratory rate of 18 breaths/min, and a temperature of 36.6°C. Physical examination revealed petechiae on her legs, abdomen, chest, and arms which extended to the base of her neck. A CBC revealed a platelet count of 1000/μL (Table 1). She had an elevated erythrocyte sedimentation rate of 75 mm/h and normal coagulation studies (Table 2). A peripheral smear showed profound, isolated thrombocytopenia

Table 1. Complete blood count and differential.

Variable	Results	Reference range
White blood cells (thousands/μL)	3.7	4.5-10.5
Red blood cells (millions/μL)	4.79	3.9-5.0
Hemoglobin (g/dL)	14.9	12.0-15.5
Hematocrit (%)	45	35-45
MCV (fL)	94.8	80.0-100.0
MCH (pg)	31.1	27-34
MCHC (g/dL)	32.8	31.0-35.0
RDW (%)	12.4	12.0-16.0
Platelets (thousands/μL)	1	150-400
Neutrophils%	40.8	46-78
Lymphocytes%	38.8	20-45
Monocytes%	16.4	5.0-13.0
Eosinophils%	2.4	0.0-7.0
Basophils%	1.1	0.0-2.0
Immature granulocytes%	0.5	0.0-1.0

MCH – mean cell hemoglobin; MCHC – mean cell hemoglobin concentration; MCV – mean cell volume; RDW – red cell distribution width.

Table 2. Hematology and coagulation studies.

Variable	Results	Reference range
Reticulocytes (thousand/μL)	103	44-106
Haptoglobin (mg/dL)	144	30-200
Fibrinogen (mg/dL)	229	204-408
Erythrocyte sedimentation rate (mm/h)	75	0.0-20.0
PT (s)	11.6	10.3-13.5
INR	1.0	
PTT (s)	28.1	26.6-38.2

INR – international normalized ratio; PT – prothrombin time; PTT – partial thromboplastin time.

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Table 3. Chemistry studies.

Variable	Results	Reference range
Random glucose (mg/dL)	142	80-200
Sodium (mEq/L)	138	136-145
Potassium (mEq/L)	4.7	3.5-5.1
Chloride (mEq/L)	103	98-107
Carbon dioxide (mEq/L)	22.5	22.0-29.0
BUN (mg/dL)	8.00	6.0-20.0
Creatinine (mg/dL)	0.6	0.5-0.9
Calcium (mg/dL)	9.4	8.6-10.2
Bilirubin-total (mg/dL)	0.26	0.00-1.20
Alkaline phosphatase (U/L)	70.0	35.0-104.0
Aspartate aminotransferase (U/L)	20.0	0.0-31.0
Alanine aminotransferase (U/L)	12.0	0.0-32.0
B_{12} (pg/mL)	319	211-946
TSH (mIU/L)	1.70	0.27-4.20
Lactate dehydrogenase (U/L)	194.00	135.0-214.0
Hepatitis A virus antibody, IgM	Negative	
Hepatitis B virus core antibody, IgM	Negative	
Hepatitis B virus surface antigen	Negative	
Hepatitis C virus antibody	Negative	
Antinuclear antibody	Negative	
HIV-1,2 screen	Negative	
HIV-1 P24 antigen	Negative	
HIV-1 antibody	Negative	
HIV-2 antibody	Negative	
C-reactive protein (mg/dL)	0.37	0.00-4.99
Heliobacter pylori breath test	Negative	

BUN – blood urea nitrogen; TSH – thyroid-stimulating hormone.

that was consistent with immune thrombocytopenia (ITP) with no schistocytes, blasts, microspherocytes, or agglutination. An ultrasound of the spleen was normal. The patient was not tested for COVID-19. Tests for viral hepatitis, HIV, and *Helicobacter pylori* were negative. An antinuclear antibody test also was negative. The results of investigatory tests are summarized in **Table 3**.

On the day of her admission, the patient received a transfusion of 1 unit of platelets and 1000 mg of i.v. methylprednisolone. Approximately 6 h after initial treatment, her platelet count improved to 16 000/µL. The following day, her platelets decreased to 4000/µL. She was treated with a second platelet transfusion and started on i.v. immunoglobulin (IVIG). On her second and third hospital days, she received 70 mg of IVIG. After discussion among the vaccination clinic, primary care team, and hematologist, the team determined that the most likely cause of the patient's ITP was vaccination. The event was then reported through the Vaccine Adverse Event Reporting System. After 3 days of hospitalization and approximately 6 days after vaccination, the patient was discharged with no major bleeding events. Her platelet count on discharge was 92 000/µL.

When the patient followed up with her primary care physician the day after discharge, her platelets had further increased to 243 000/µL. Her recovery was uncomplicated. She tested negative for antiplatelet antibodies (APAs) after her discharge and treatment.

Discussion

This case highlights a potential consequence of the BNT162b2 mRNA COVID-19 vaccine that has implications for monitoring after vaccination. Considerations for other causes of ITP were viral hepatitis, HIV, and *H. pylori*. Tests for these conditions were negative. The isolated thrombocytopenia on peripheral smear and normal reticulocytes, lactate dehydrogenase, and bilirubin (**Table 3**) ruled out Evans syndrome. The patient was up to date on age-appropriate cancer screening. She had not received any other vaccinations or new medications, nor had she experienced any illness in the preceding months that may have caused the ITP. Her only medication was norgestimate-ethinyl estradiol. Given the geography and her lack of travel, she was not tested for tropical illnesses that can cause thrombocytopenia. The main limitation is that the diagnosis of ITP is one of exclusion. The patient was not tested for COVID-19, which can cause ITP. Another limitation is the delay in testing of APAs after her recovery. Causally linking the vaccine and ITP with certainty poses challenges.

Conclusions

Because of the lack of medications or conditions that could have caused ITP in our patient, we feel that this outcome was most likely due to the BNT162b2 mRNA COVID-19 vaccine. The established relationship between ITP and COVID-19 and ITP and other immunizations further supports this hypothesis. We feel that this case provides insight into a potential new AE for which monitoring should be performed after vaccination. Further investigations are required to determine the risk and frequency of this association.

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Conflict of interest

None.

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