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CASE REPORT

Infectious Disease

Immune thrombocytopenia in 2 healthy young women after the Pfizer-BioNTech BNT16B2b2 messenger RNA coronavirus disease 2019 vaccination

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Abstract

Immune thrombocytopenic purpura (ITP) is a rare complication associated with vaccines targeting various diseases, including influenza, measles-mumps-rubella, hepatitis B, and diphtheria-tetanus-pertussis. We report 2 cases of ITP in healthy 20-year-old and 21-year-old women presenting to Emory University in Atlanta, GA, 2 days after the second dose and 11 days after the first dose (respectively) of the Pfizer-BioNTech messenger RNA severe acute respiratory syndrome coronavirus 2 vaccine. Both patients recovered quickly. With more than a billion doses of coronavirus disease 2019 vaccines safely administered worldwide as of May 2021, discussions with patients should put into perspective the low risks of vaccination against the enormous societal benefit of the coronavirus disease 2019 vaccine.

KEYWORDS
coronavirus disease 2019 vaccine, ITP, thrombocytopenia

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1 | INTRODUCTION

Serious adverse events such as vaccine-induced immune thrombocytopenic purpura (ITP; previously observed in other vaccines) are a concern with worldwide coronavirus disease 2019 vaccinations.[1–10] Although its pathogenesis is unclear, ITP is characterized by a decrease in platelet count secondary to impaired production of and destruction of platelets.[5] Typical clinical presentations include petechiae, bruising, and mucosal bleeding and occasionally severe thrombotic complications.[1,6] Although this syndrome is rare given the millions of safely administered doses, vigilance and awareness by frontline providers in considering this diagnosis is important during postvaccination clinical evaluation. We present 2 cases of acute ITP after the Pfizer-BioNTech coronavirus disease 2019 vaccine. The first is a 20-year-old woman presenting 2 days after her second dose of the vaccine (no significant adverse reaction to the first dose) with fevers, tachycardia, and no evidence of bleeding. The second is a 21-year-old woman presenting 11 days after the first dose of the vaccine with 2 days of a petechial rash located on the extremities and trunk and in her mouth as well as abnormal bruising on extremities.

2 | NARRATIVE

2.1 | Case 1

A 20-year-old woman with depression received her second dose of the Pfizer-BioNTech coronavirus disease 2019 vaccine 2 days before presentation. Within a few hours, she experienced mild fatigue and muscle pain. The next morning, she developed headache, fever, and chills, which were treated with acetaminophen. Symptoms continued to worsen on day 2, with fever reaching 40.1°C. Upon arrival to the emergency department (ED), her blood pressure was 104/59 mmHg, heart rate was 167 bpm, temperature was 39.5°C, respiratory rate was 25 bpm, and oxygen saturation was 99% on room air. She appeared anxious, flushed, and diaphoretic. Physical examination was otherwise normal. Electrocardiogram (ECG) showed sinus tachycardia at 167 bpm. She received 2 L of lactated ringer's solution, broad-spectrum antibiotics, and acetaminophen given the concern of sepsis. Within 1 hour, her heart rate improved to 116 bpm, temperature reduced to 37.4°C, and blood pressure was 97/54. D-dimer was 1744 ng/mL. Polymerase chain reaction test was negative for severe acute respiratory syndrome coronavirus 2 and influenza. Computed tomography angiography chest excluded pulmonary embolism. White blood cell count was 3800/μL, hemoglobin was 13.3 g/dL, and platelet count was 12,000/μL. International normalized ratio was 1.14. A peripheral blood smear excluded pseudothrombocytopenia and showed no schistocytes. Hematology was consulted, recommending intravenous immunoglobulin (IVIG), but not steroids as sepsis remained in the differential.

Given the high suspicion for ITP, she received 1 g/kg IVIG for 2 days. As ITP is a diagnosis of exclusion, other etiologies for thrombocytopenia were investigated. Lactate dehydrogenase, bilirubin, and haptoglobin levels were normal, lowering suspicion for microangiopathic hemolytic anemia and thrombotic thrombocytopenic purpura. Elevated fibrinogen and normal international normalized ratio excluded disseminated intravascular coagulation (DIC). Human immunodeficiency virus, hepatitis B, and hepatitis C tests were negative. D-dimer peaked at 2158 ng/mL. After 1 dose of IVIG, platelets improved to 320,000/μL. Given clinical stability and low suspicion for bacterial infection, broad-spectrum antibiotics were discontinued. On hospital day 2, the patient's clinical condition continued to improve, and she received a second dose of IVIG. Although still leukopenic, her platelet count remained stable, and she was discharged. At 3-week follow-up, CBC had normalized.

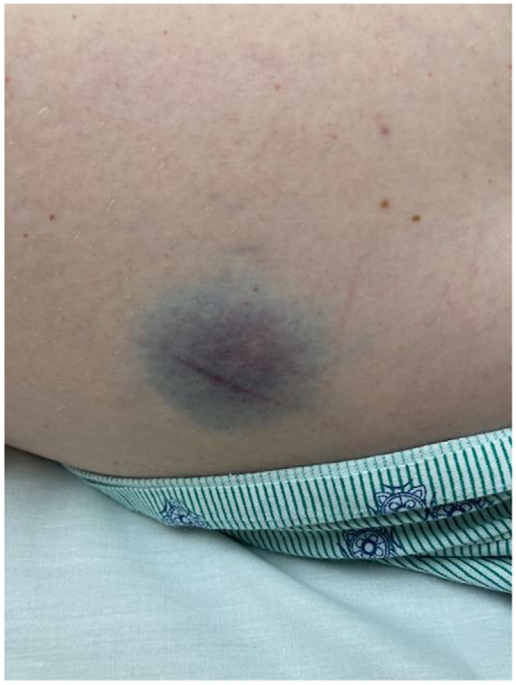

FIGURE 1. Purpura over left greater trochanter

2.2 | Case 2

A 21-year-old woman with attention deficit hyperactivity disorder and depression presented to the ED 11 days after a first dose of the Pfizer-BioNTech coronavirus disease 2019 vaccine with a painless, nonpruritic, generalized petechial rash that began 2 days before arrival, initially on her arm and progressing to her trunk and legs. She denied fever, upper respiratory infectious symptoms, sore throat, or headache. On presentation, her temperature was 36.3°C, blood pressure was 111/69 mmHg, pulse was 88 bpm, respiratory rate was 18 bpm, and saturation rate was 98% on room air. Examination revealed diffuse petechial rash on her trunk and extremities (Figure 1), a 6-cm ecchymosis over the greater trochanter of her left lower extremity (Figure 2) and 2,1-cm areas of ecchymosis on her right forearm. All lesions were nontender. There was minimal sole and palmar involvement. Oral examination revealed ecchymosis of the tongue, angles

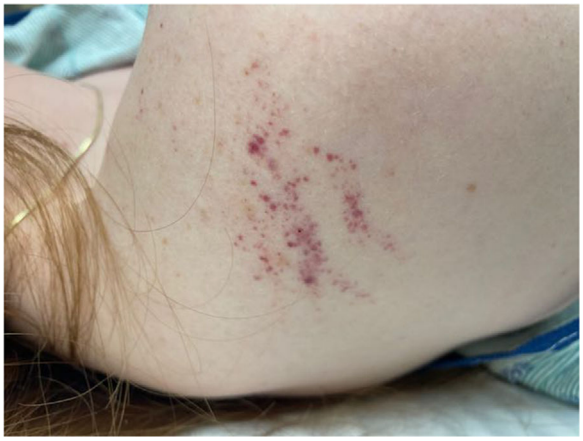

FIGURE 2. Petechial rash over right shoulder

of the mouth, and buccal mucosa. The rest of her physical examination was unremarkable. Platelet count was 5000/μL, white blood cell count was 8100/μL, hemoglobin was 15.2 g/dL, and international normalized ratio was 1.09. Human immunodeficiency virus, hepatitis C antibody, and severe acute respiratory syndrome coronavirus 2 polymerase chain reaction were negative. Epstein-Barr Virus (EBV) nuclear antigen-antibody and viral capsid antigen Immunoglobulin G (IgG) and Immunoglobulin M (IgM) were positive, but EBV DNA polymerase chain reaction was undetected. DIC was excluded with normal D-dimer and fibrinogen levels. Microangiopathic hemolytic anemia was excluded with no schistocytes on smear and normal lactate dehydrogenase, bilirubin, and haptoglobin levels.

Hematology recommended transfusion of 1 unit of platelets that did not improve the platelet count. The patient received dexamethasone 40 mg intravenously daily for 4 days with improvement in platelet counts to 86,000/μL by day 4. At the 3-week follow-up, platelets normalized. Her mouth sores resolved, and no further petechial rash was noted. Laboratory results eventually revealed direct IgM-mediated antibodies to platelets, suggesting an immune-mediated process.

3 | DISCUSSION

ITP is an autoimmune disorder characterized by mucocutaneous bleeding and thrombocytopenia with platelet levels <150,000/μL. The estimated incidence of ITP is 2 to 5 in 100,000 persons per year, with 50% of cases occurring in pediatric patients.[11,12] There is a 2:1 female to male predominance. Pathogenesis is secondary to autoantibodies targeting multiple platelet glycoproteins, leading to macrophage-mediated destruction and the inhibition of platelet production.[11] In adults, onset is typically chronic and insidious rather than acute. Petechiae and ecchymosis develop at platelet levels between 10,000 and 30,000/μL, and mucosal bleeding and hemorrhage are associated with levels <10,000/μL.[11] In this article, we described 2 cases of ITP in healthy young women presenting 2 to 11 days post-dose of the Pfizer-BioNTech messenger RNA severe acute respiratory syndrome coronavirus 2 vaccine with platelet counts of <20,000/μL treated successfully with IVIG and steroids, respectively. The 2 patients did not present any evidence of thrombocytopenia and thrombosis simultaneously, as has been reported with the Janssen, Johnson & Johnson, and AstraZeneca vaccines. This report also adds to the few reported cases of thrombocytopenia related to the Pfizer vaccine.

Vaccines are safe with very low adverse event rates of 1 to 7 in 1 million. Vaccinations are a rare but known cause of ITP after vaccination against influenza, measles-mumps-rubella, hepatitis B, and diphtheria-tetanus-pertussis.[2,5,8–10,13] Related to the coronavirus disease 2019 vaccine, as of January 2021, 36 cases of ITP were reported to the Vaccine Adverse Event Reporting System (VAERS) registry, and the *British Medical Journal* reported 150 cases of thrombocytopenia, the majority of which are attributed to non-Pfizer vaccines.[5]

Instances of symptom onset associated with thrombocytopenia are reported anywhere from 1 to 23 days post-vaccination with the AstraZeneca, Moderna, and Pfizer vaccines. Reported presentations include petechiae and purpura of the skin and oral mucosa, gingival bleeding, thrombocytopenia, absence of hemolysis, negative peripheral smears, elevated D-dimer levels, negative coronavirus disease 2019 antibody testing, elevated platelet autoantibodies, and negative workups for other drivers of thrombocytopenia. Treatment with steroids as monotherapy or in conjunction with IVIG is followed by the rapid improvement of platelet levels.[1–6]

Outpatient observation is recommended for asymptomatic platelet levels >30,000/μL. Admission is suggested for minor bleeding or platelet levels <20,000/μL.[14,15] Corticosteroids are conditionally recommended as a first-line therapy for platelet levels <30,000/μL, either as prednisone 1 mg/kg for 2 to 3 weeks or up to 3 rounds of 4-day courses of dexamethasone 40 mg intravenously. Treatment involving corticosteroids ± IVIG is initiated based on clinical suspicion while the remainder of the workup is completed. Platelet level is closely monitored for response with a goal of >20 to 30,000/μL, the point at which bleeding is usually reversed.[15]

There are no high-quality data or consensus-based guidelines to support recommendations about the administration of the coronavirus disease 2019 vaccine in the post-convalescent ITP patient. The risk of recurrent ITP with subsequent doses of the coronavirus disease 2019 vaccine is unknown, and revaccination discussions should follow a shared decision-making model. Questions may arise about whether future vaccination is safe, whether an appropriate immune response against coronavirus disease 2019 was achieved in patients treated with steroids for vaccine-related ITP, and if resuming vaccination, the second dose should be given or if the series should simply be restarted. Patient 2 was vaccinated <14 days before the initiation of high-dose dexamethasone treatment. She was advised that full vaccination benefits were most likely not achieved and told to continue following Centers for Disease Control and Prevention guidelines regarding safe practices (wearing a mask, physical distancing, hand hygiene). She did not belong to a high-risk population, so she may choose to delay her subsequent dose. If she gets vaccinated, she has been counseled to have

regular laboratory monitoring of platelet counts and be vigilant about signs of platelet disorder.

It is incumbent on healthcare professionals in emergency, ambulatory, and inpatient settings to consider vaccine-related adverse effects on patients who are seen for these complications as well as reporting them to the US Department of Health and Human Services managed VAERS registry (https://vaers.hhs.gov/esub/index.jsp). It is also important for physicians to appropriately put into perspective for healthcare professionals, patients, and the public the very low rate of rare, treatable vaccine complications against the enormous societal benefit in the reduction of incidence and severity of coronavirus disease 2019 during this devastating pandemic.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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