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CASE REPORT

Petechial Rash and Thrombocytopenia after the Booster Dose of Covid-19 Vaccine: A Case Report and Literature Review

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Abstract

Since December 2020, the Pfizer-BioNTech BNT16B2b2 mRNA vaccine has been widely used to prevent COVID-19 infection. Vaccination is now widely regarded as the most effective way to reduce the pandemic's morbidity and death. Except for mild and infrequent adverse effects, almost all vaccinations are considered safe. One of the documented adverse effects of the COVID-19 immunizations is vaccine-induced immune thrombocytopenic purpura. We discuss the case of a 25-year-old gentleman who received an uneventful first and second vaccination doses but experienced widespread petechial rash, oral bleeding, and thrombocytopenia within three days of receiving the booster dose. Based on the existing literature and the absence of any other triggering factors, immune thrombocytopenia caused by the booster dose of Pfizer-BioNTech BNT16B2b2 mRNA vaccine was diagnosed. In this article, we present the patient's case and review the existing literature on vaccine-induced immune thrombocytopenia.

Keywords

COVID-19, SARS-CoV-2, Rash, Bleeding, Thrombocytopenia, Vaccine

Introduction

Coronavirus disease (COVID-19), which is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has caused significant damage and challenges globally [1]. For billions of people throughout the world, COVID-19 has been a nightmare, incurring devastating economic, physical, and psychological losses [2,3]. This necessitated the immediate availability of COVID-19 vaccines. Since December 2020, the Pfizer-BioNTech BNT16B2b2 mRNA vaccine has been widely used to prevent COVID-19 infection [4]. The Pfizer-BioNTech BNT16B2b2 mRNA vaccination is advised to be given in two doses, three weeks apart. A booster (third) dose is now suggested for moderate to severely immunocompromised persons four weeks following the second dose of vaccine. People taking chemotherapy, organ transplant recipients, untreated HIV infection, post stem transplant, and active treatment with glucocorticoids are included in this group, according to the Centers for Disease Control and Prevention (CDC) [5]. Everyone else should receive the booster dose six months after the second dose [6]. In the vaccine's clinical trials, side effects occurred within seven days following vaccination, however, the degree of these side effects was mainly mild to moderate [6]. After the second dose of the vaccination, chills, low-grade fever, malaise, headache, and myalgia were more prevalent. Only a few patients experienced serious adverse effects that need aggressive care or even hospitalization [7]. As a result of the administration of SARS-CoV-2 vaccinations, a few incidences of immune thrombocytopenic purpura (ITP)

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have been documented. This is a case report of a 25-year-old male patient who had a widespread petechial rash, oral bleeding, and thrombocytopenia three days after receiving the booster COVID-19 vaccination dose.

Case Presentation

A 25-year-old healthy Asian male presented to the hospital after three days of receiving the Pfizer-BioNTech BNT16B2b2 mRNA vaccine. He received the second and first doses of COVID-19 vaccine respectively 6 months and 7 months before receiving the booster dose. His first and second SARS-CoV-2 vaccination doses were uneventful, but he developed painless, non-pruritic, petechiae and oral hemorrhage on day three after the booster dose of vaccine, prompting his presentation. He denied having any respiratory or gastrointestinal problems, as well as a history of other illness. He didn't have any personal history or family history of autoimmune illness or bleeding disorders. He had never been diagnosed with thrombocytopenia or any other platelet disorders in the past. His prior blood tests did not show any abnormalities. Three months prior to receiving the booster dose of COVID-19 vaccination, the patient had a platelet count of 220,000/mm^3 of blood. His medication history is unremarkable. He denied having any past exposure/history of COVID-19, history of recent infections, medications. He denied receiving any other immunizations prior to his presentation. His vitals and the rest of his examination were all normal. His vital signs were as follows when he arrived: 37.8 °C body temperature; 88 beats/min pulse rate; 21 breaths/min respiration rate; 132/76 mmHg blood pressure; and 98 percent oxygen saturation on room air. Physical examination revealed extensive pinpoint petechial rashinvolving trunk, both upper and lower extremities. A systemic evaluation was otherwise found negative since the patient denied any discomfort, soreness, fever, pruritus, or lymphadenopathy. The evaluation found no evidence of hepatosplenomegaly.With a platelet count of 13,000/mm^3 of blood, laboratory testing indicated normal hemoglobin, white blood cell count, and thrombocytopenia.

Fibrinogen, prothrombin time, activated partial thromboplastin time, blood urea nitrogen, creatinine, electrolytes, bilirubin, alkaline phosphatase, lactate dehydrogenase, total protein, albumin, globulin, and haptoglobin were all normal or negative in the emergency department on day three after immunization. The levels of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were somewhat increased (ALT- 48, AST- 85), but they returned to normal in two days. He also had negative Hepatitis B, Hepatitis C antibody, human immunodeficiency virus, influenza, cytomegalovirus, and Epstein-Barr Virus serology results. SARS-CoV-2 antigen was not found in a nasopharyngeal swab. Table 1 summarizes his laboratory test findings.

There were no factors that could cause the thrombocytopenia and he was admitted with the chief diagnosis of immune thrombocytopenia. Based on the existing literature and the absence of any other triggering factors, immune thrombocytopenia caused by the booster dose of Pfizer-BioNTech BNT16B2b2 mRNA vaccine was diagnosed. The symptoms and signs appeared shortly after immunization and could not be explained by any other cause, suggesting the diagnosis of vaccine-induced immune thrombocytopenia. There were no other clinical manifestations or laboratory evidence to explain other potential differential diagnoses including drug-induced thrombocytopenia, thrombotic thrombocytopenic purpura, hemolytic uremic syndrome, or disseminated intravascular coagulation. The patient was hospitalized and given dexamethasone 40 mg/day orally, as well as a unit of platelet transfusion. Platelet counts rose to 28,000/mm^3 after the transfusion. Dexamethasone was continued for five days, and platelet counts were observed. His platelet counts improved gradually over the course of hospitalization.

Petechiae and oral hemorrhage subsided on day nine after immunization, and the patient was released with a platelet count of 121,000/mm^3 of blood. The patient was sent home with instructions for outpatient follow-up. The patient's platelet count normalized to 158,000/mm^3 of blood at follow-up on day twelve, and he tested positive for plasma IIb/IIIa and Ia/IIa platelet autoantibodies and negative for anti-PF4 autoantibodies.

Discussion

We describe a case of thrombocytopenia, oral bleeding, and a petechial rash that may be caused by COVID-19 immunization. The patient might have developed these symptoms after receiving the COVID-19 vaccine. Given the quick emergence of symptoms, absence of prior comparable episodes, brief latency time following immunization, and exclusion of other possible etiologies, the thrombocytopenia was thought to be due to COVID-19 immunization. The elimination of other probable etiologies was used to make the diagnosis of ITP. Other causes of thrombocytopenia, such as autoimmune disorders and infections, were ruled out in this patient. Based on her typical presentation [8] and excellent response to ITP-directed therapy [9], a bone marrow examination was unnecessary. The absence of hemolysis and thromboembolism ruled out thrombotic thrombocytopenic purpura and vaccine-induced thrombotic thrombocytopenia. We hope to examine the existing research on mRNA vaccine-induced rash, bleeding, and the pathophysiology of thrombocytopenia in relation to COVID-19 vaccinations in this study.

On December 11, 2020, the FDA granted an Emergency Use Authorization (EUA) for the Pfizer-BioNTech COVID-19 Vaccine as a two-dose series delivered 21 days

Table 1: The patient's laboratory range at the time of admission.

Laboratory Parameter	Admission Value	Reference Range
Hemoglobin	12 g/dl	12-18 g/dl
WBC	6200/mm^3	5000-11,000/mm^3
Platelet count	13,000/mm^3	150,000-400,000/mm^3
INR	1.1	0.8-1.2
Prothrombin time	12.5 seconds	10-14 seconds
Activated partial thromboplastin time	31.9 seconds	25-36 seconds
Total bilirubin	0.9 mg/dl	0.1-1.0 mg/dL
Total protein	7.6 g/dl	6.0-7.8 g/dL
Albumin	3.9 g/dl	3.5-5.5 g/dL
Globulin	3.1 g/dl	2.3-3.5 g/dL
Alkaline phosphatase	88 U/L	25-100 U/L
Lactate dehydrogenase	165 U/L	45-200 U/L
Aspartate aminotransferase	85 U/L	12-38 U/L
Alanine aminotransferase	48 U/L	10-40 U/L
Serum creatinine	1.1 mg/dl	0.6-1.2 mg/dL
Blood urea nitrogen	15 mg/dl	7-18 mg/dl

apart [4]. Prior to the EUA for this vaccine being issued, FDA and CDC intended to monitor their safety through passive and active surveillance, including increased surveillance for adverse events of specific concern such thrombocytopenia [10]. Furthermore, the EUA for vaccinations required reporting of major adverse events (regardless of attribution to vaccination) to the Vaccine Adverse Event Reporting System (VAERS), a nationwide spontaneous reporting (passive surveillance) system for vaccine safety monitoring [4]. Immune thrombocytopenia is an autoimmune condition in which the body's immune system targets the platelets in circulation and the generation of platelets. It can be both primary and secondary in nature. Idiopathic immune thrombocytopenia is the most prevalent cause, although secondary causes include infection, immunodeficiency, autoimmune disorders, and immunization, all of which result in platelet destruction and thrombocytopenia, which can lead to mucocutaneous and severe hemorrhage [11]. FDA received complaints of immune thrombocytopenia in close vicinity after COVID-19 immunization to VAERS shortly after authorization. Platelet counts of fewer than 100×10^9/mm^3, immune-mediated platelet destruction, and decreased megakaryocytopoiesis are all symptoms of ITP [12]. Thrombocytopenia was observed seldom in clinical trials using mRNA COVID-19 vaccines, and there were no imbalances between the vaccinated and placebo groups [13,14].

Vaccine-related immune thrombocytopenia has been associated with various vaccinations such as hepatitis A, hepatitis B virus, mumps-measles-rubella, human papillomavirus, diphtheria-tetanus-acellular pertussis, varicella-zoster, pneumococcus, polio and even influenza vaccines in both children and adults [15,16]. Following the COVID-19 vaccine, many cases of ITP have been documented. However, immune thrombocytopenia caused by the Pfizer Bio-NTech Covid-19 vaccination has not been extensively documented. The United States VAERS documented 28 occurrences of thrombocytopenia (not all of which were ITP) after immunization with mRNA (Pfizer-BioNTech and Moderna) COVID-19 vaccines [14]. The onset of ITP can occur within hours, 2-3 days or 2 weeks following vaccination [17].

Covid-19 may be linked to secondary ITP, which may be ascribed to a variety of causes such as immunological dysregulation, molecular mimicry, cryptic antigen expression on platelets, and so on [18]. Furthermore, thrombocytopenia may worsen in people who already have chronic ITP after receiving the COVID-19 vaccination. [19].

The pathogenesis of vaccine-induced ITP is a difficult phenomenon to understand. Ovalbumin, gelatin, and specific milk proteins used in the development of routinely used vaccinations have been blamed for severe thrombocytopenia following vaccine delivery [20]. These components, however, are missing from both the mRNA (Pfizer-BioNTech and Moderna) COVID-19 vaccines [20]. COVID-19 mRNA-based vaccines are novel vaccines that vary from inactivated or live-attenuated vaccinations. These vaccines comprise RNA encapsulated within a lipid nanoparticle (LNP) that encodes the spike protein [14]. The negative effects associated with COVID-19 vaccinations may be linked to LNPs. The vaccine's mRNA component is unlikely to cause an allergic reaction on its own, but the presence of modified RNA trace impurities in the Pfizer-BioNTech COVID-19 vaccine might explain the thrombocytopenia [21]. There is a chance that these erroneous proteins will set off an immune reaction that will result in thrombocytopenia [21].

In our case, the patient responded to dexamethasone and maintained a stable platelet count afterward. There is very little evidence to support that IVIG plus high dosage steroids should be used as the first line of therapy. The regularly used rituximab from the initial therapy is not advised in most situations because it might impede the response to immunization [22].

Conclusions

The research on the COVID-19 vaccine's side effect profile is quite scarce. In our situation, we believe the petechial rash was caused by the Pfizer-BioNTech BNT16B2b2 mRNA vaccination. It emphasizes the need of evaluating autoimmune illness in the differential diagnosis following immunization. With the extensive distribution and administration of the SARS-CoV-2 vaccine, we may expect to learn more about the side effect profile of mRNA and other vaccines against COVID-19, as well as the mechanisms and pathophysiology of these side effects. COVID-19 shots are said to have few side effects, and if the advantages of the vaccine outweigh the dangers, this article should not change the advice to get the vaccine. Nonetheless, we want to make practitioners aware of this probable link between immune thrombocytopenia and SARS-CoV-2 immunization.

Conflict of Interest

The authors declare that they do not have any conflict of interest.

Ethics Approval and Consent to Participate

Ethical approval was not required for this case report.

Consent for Publication

Written informed consent has been taken from the patient for this study.

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