American Journal of Medical Case Reports, 2021, Vol. 9, No. 8, 394-396
Available online at http://pubs.sciepub.com/ajmcr/9/8/3
Published by Science and Education Publishing
DOI:10.12691/ajmcr-9-8-3

Immune Thrombocytopenic Pupura after COVID-19 Vaccine, a Case Report

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Received March 08, 2021; Revised April 15, 2021; Accepted April 24, 2021

Abstract Immune Thrombocytopenic Purpura (ITP) is an autoimmune disorder caused by different entities, one of them being the administration of certain vaccines, most commonly MMR vaccines that have been linked with the development of this disease. We report a 26-year-old female presented to the hospital with a petechial rash and mucosal bleeding after three weeks of administration of the COVID-19 vaccine. Thrombocytopenia workup was done, ITP was diagnosed. The ITP in this case was refractory to initial treatment of IVIG and steroid. Rituximab was initiated and she had an excellent response to it.

Keywords: *ITP, bleeding, COVID vaccine, rituximab*

Cite This Article: Hafsa Parpia, Eman EL-Sawalhy, Maher Khadra, Raisa Mayers, Samyuktha Madishetty, and Faisal Musa, "Immune Thrombocytopenic Pupura after COVID-19 Vaccine, a Case Report." *American Journal of Medical Case Reports*, vol. 9, no. 8 (2021): 394-396. doi: 10.12691/ajmcr-9-8-3.

1. Introduction

Immune thrombocytopenia is an acquired autoimmune disease. Its physiopathology is explained by the development of autoantibodies against the platelet antigens. ITP is usually asymptomatic but symptoms can range between petechiae and purpura to life-threatening bleeds. Different studies have shown an association between ITP and some vaccines such as MMR and influenza [3,4]. In the setting of the COVID-19 pandemic, COVID-19 vaccines were developed emergently. By December 2020 several vaccines showed safety and efficacy in clinical trials [1,2] and during the same period, the Food and Drug Administration (FDA) issued an emergency use authorization for these vaccines. Until this date, there's not enough data to link the associations between these new vaccines and the side effects related to their administration.

2. Case Presentation

A 26-year-old healthy woman presented to the hospital with worsening cutaneous and mucosal bleeding. One day before admission she experienced widespread petechiae on her lower extremities (Figure 1), abdomen, and gums associated with blisters around her mouth. She denied any history of similar symptoms, hematochezia, melena, hemoptysis, heavy menses, autoimmune disease, infection, or history of adverse reaction to vaccination. Three to four weeks before her admission, she completed the second dose of the COVID-19 vaccine (Moderna, mRNA vaccine). She reported experiencing fever, chills, and intermittent headache after receiving the second dose, however, all her symptoms resolved after a day except for her headache that lasted for several days and she was talking Motrin for relief. Vital signs and the remainder of her exam were normal. Initial workup revealed severe thrombocytopenia with a platelet count of 3 Thousand/uL with normal hemoglobin level and white blood cell count. Results of chemistry profile and routine blood coagulation tests were normal except for the low level of fibrinogen of 197 mg/dl. A computed tomography scan (CT) of the head was negative for intracranial bleed. She reported that her last blood count was done at her primary care's office a few months ago and she was never alerted of any abnormal platelet count.

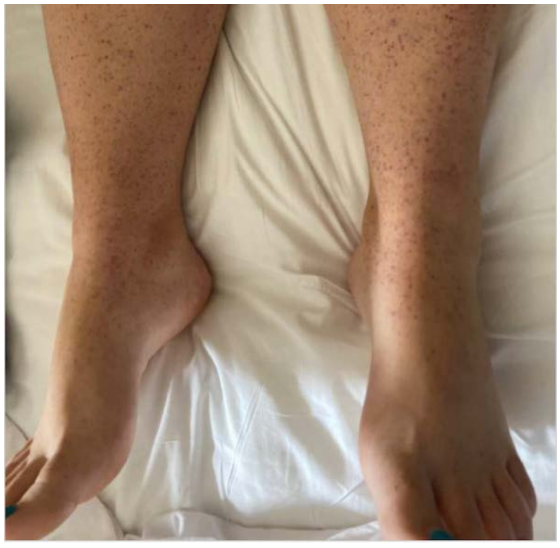

Figure 1. showing widespread petechiae on the lower extremities

Given her history of COVID-19 vaccine and thrombocytopenia, ITP was strongly suspected. The patient was started on steroids (Solumedrol 80 mg /daily), IVIG (1g/kg for 2 days), and a platelet transfusion. Subsequent workup for thrombocytopenia including HIV, hepatitis B, hepatitis C antibody, liver function test, kidney function, ADAMT 13 were normal, however, Vitamin B12 and Folic acid were low. A nasopharyngeal swab also returned negative for SARS-CoV-2 antigen, peripheral smear showed marked thrombocytopenia without microangiopathic RBC changes (Figure 2). As a part of the workup, the patient had an ultrasound abdomen that did not show splenomegaly. On day 2 of admission, Platelet count did show a slight improvement to 6 Thousand/uL, Solumedrol increased to 60 mg every 6 hours and the patient was started on vitamin B12 and folic acid supplementation. On Day 3 of admission, Platelets count improved to 21 Thousand/uL but unfortunately, it started trending down the next day to 4 Thousand/uL. Given her poor response to steroids and IVIG, a bone marrow biopsy was done and other secondary causes of ITP were ruled out (Figure 3 & Figure 4). The patient was started on Nplate (romiplostim, 1mg/kg weekly) as an alternative treatment for ITP, solumedrol dose was decreased to 40 mg every 8 hours and she was scheduled for platelet transfusion every 12 hours to keep platelets counts >10 Thousand/uL, however, the patient's platelet continued trending down. Due to the lack of response to platelet transfusion HLA antibody screen was ordered, which came back negative. On day 10 of the admission, the decision to start the patient on B cell-selective ablation with anti CD20 antibody was made by hematology specialists due to failure of previous treatment and possible hyperactive immune system to COVID-19 vaccine. NPlate was discontinued and the patient was started on Rituximab plus platelet transfusion every 12 hours to keep platelet counts >10 Thousand/uL. On day 11 of admission, the Platelet count improved to 57 Thousand/uL. She was discharged with a platelet count of 62 Thousand/uL and was prescribed 3 more doses of weekly rituximab as an outpatient. The case was reported to the CDC through the vaccine adverse event reporting system (VAERS).

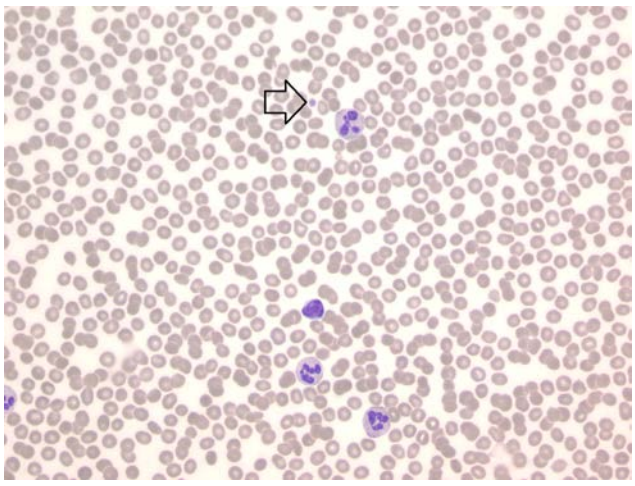

Figure 2. Peripheral blood smear, showing thrombocytopenia without microangiopathic RBC changes. Arrow points a single platelet in the field

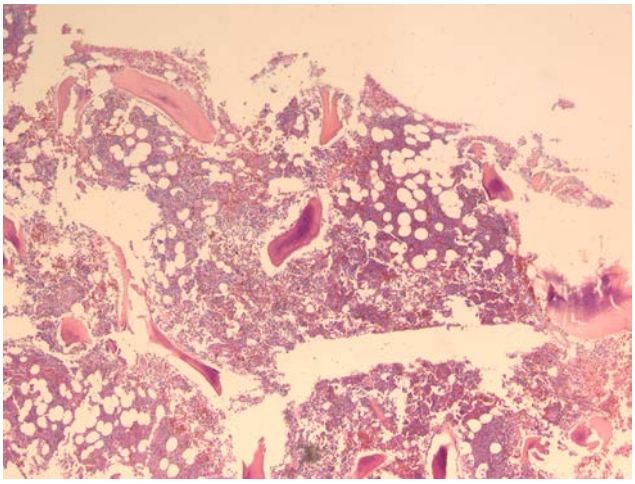

Figure 3. Low power view of bone marrow core showing normal cellularity

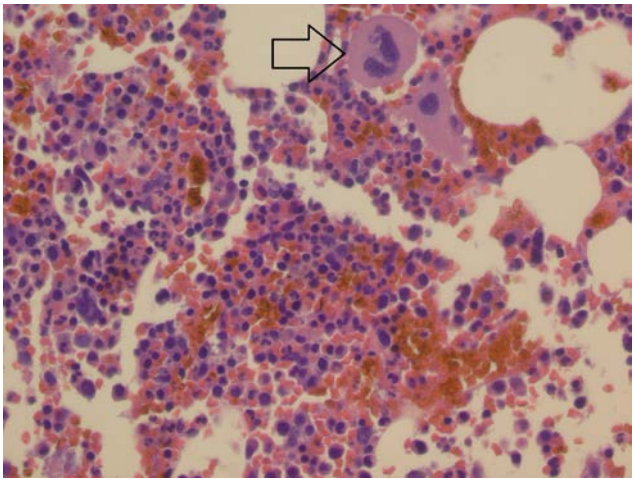

Figure 4. High power view of bone marrow showing normal maturing trilineage hematopoiesis. Arrow points normally appearing megakaryocyte

3. Discussion

In December 2020, the US Food and Drug Administration (FDA) issued emergency use authorizations for two mRNA-based vaccines: Pfizer-BioNTech and Moderna COVID-19 vaccines [7]. With the emergency authorization of the vaccines, many doubts about the safety of the vaccinations came along. In our case above, we describe a case of ITP in a 26-year-old lady after three weeks of receiving the second dose of the mRNA Moderna vaccine.

Exploring more into the literature of ITP after Moderna/Pfizer vaccinations, the incidence has been noted in at least 36 people in the United States as reported recently in The New York Times [5]. With more than 80 million people vaccinated thus far, this is a very rare side effect. Although the cases noted so far have not resulted in any fatal outcomes, one case of severe acute ITP, complicated by a fatal intracranial hemorrhage, was diagnosed three days following vaccination with the Pfizer COVID vaccine [8]. The best available knowledge from all phases of the vaccine clinical trials and individuals vaccinated to date suggests that the link was most likely unrelated but more studies are warranted as this is a new vaccine of its kind [8].

Although the pathophysiology of the thrombocytopenia is uncertain, the likely mechanism can be linked to prior vaccine-related ITP cases with Measles vaccination-related ITP cases being the most common. It is presumed to be through virally-induced molecular mimicry, that is, development of autoantibodies that cross-react with naturally present antigenic targets on platelets as COVID-19 viral infection has been noted to cause ITP itself [6].

Secondly, we looked into epidemiological data that can increase predisposition to ITP risk, remarkably, there are no epidemiological trends noted that linked the vaccine and ITP development. furthermore, we explored the incidence of thrombocytopenia in patients with a personal history of ITP, no such increased incidence was found in the to-date reported cases. It may be appropriate to obtain baseline and post-vaccination platelet counts in certain ITP patients, particularly in those with ongoing thrombocytopenia or a history of unstable platelet counts [8].

Finally, looking into treatment options for these patients, they should follow the guidelines for ITP treatment induced by other causes. Having a hematologist expert opinion on individual cases can help guide treatment approaches. Our patient above did not respond to initial treatment options including IVIG and steroids which could be interestingly patient-based as other reported COVID vaccine-related ITP cases have responded to the first-line treatment options. Thus, treatment should be geared toward patient response based on platelet count trends and bleeding risks, and incidents.

4. Conclusion

In conclusion, ITP onset or worsening has been reported with some frequency following viral infections and anecdotally following other vaccines. Although the link is biologically plausible, the causal relationship between the vaccine and thrombocytopenia needs more evidence. As such, based on current knowledge, the risks associated with COVID-19 disease appear to outweigh the risks associated with SARS-CoV-2 vaccination in ITP patients.

Conflict of Interest

None of the authors have any conflicts of interest to declare.

Disclosure of Funding

None of the authors have any source of funding to declare.

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