Messenger ribonucleic acid vaccine-associated immune thrombocytopenia: A rare complication of vaccine

Mehmet Sami Islamoglu1*, Mehmet Dokur2, Betul Borku Uysal1, Mehmet Gunduz3

1Departments of Internal Medicine, 2Emergency Medicine and 3Hematology, Biruni University Medical Faculty, Istanbul, Turkey

*Corresponding author

Abstract:
Coronavirus disease-2019 continues to have a serious impact in countries with the effect of new variant viruses emerging with mutations. While the effectiveness and protection of the vaccine have been determined all over the world, some vaccine-related side effects can be detected in the form of cases. In our case, the patient was admitted to the emergency department of our hospital with complaints of weakness and progressive rash on his legs. Diffuse petechiae purpura on the legs of the patient was observed and complete blood count revealed thrombocytopenia. Peripheral blood smear supported the blood count test results with thrombocytopenia, secondary causes of thrombocytopenia were excluded, and the patient was diagnosed with vaccine-induced immune thrombocytopenia.

Keywords: COVID 19, COVID 19 Vaccines, Coronavirus disease-2019 vaccine, immune thrombocytopenia, purpura, severe acute respiratory coronavirus-2, SARS-CoV-2 Infection

Introduction
Coronavirus disease-2019 (COVID-19) continues to have severe mortality and morbidity rates all around the world, and vaccination is assumed to be the most important step toward protecting society from this disease.[1] On December 11, 2020, the Food and Drug Administration (FDA) approved emergency use authorization for a COVID-19 vaccine delivered in two doses with an interval of 21 days.[2] This vaccine, produced by Pfizer-BioNTech, is based on messenger ribonucleic acid (mRNA) that encodes the severe acute respiratory coronavirus-2 (SARS-CoV-2) spike glycoprotein.

The Vaccine Adverse Event Reporting System has received reports of immune thrombocytopenia (ITP) in people administered the mRNA vaccine.[3] ITP is characterized by immunity-related destruction of thrombocytes, disruption of thrombocyte production, and proneness to bleeding. In ITP, the thrombocyte count is below 100 × 10^9/L. ITP affects 2–4 out of every 100,000 adults.[4] Primary ITP diagnosis is possible after the elimination of secondary causes and nonautoimmunity-related symptoms.[5] Cases of ITP related to the measles-mumps-rubella vaccine, mumps, and rubella have been reported in the past.[6] Although SARS-CoV-2 infection-related ITP cases have been reported, mRNA-related ITP cases were seldom reported.[7,8] In this case report, we evaluated an ITP case admitted to the hospital with petechial...
purpura after being dosed with the Pfizer-BioNTech mRNA vaccine.

**Case Report**

A 59-year-old male patient received his first dose of the mRNA vaccine on May 19, 2021. Fifteen days later, the patient displayed symptoms of fatigue, weakness, and a rash on his legs and was admitted to the emergency department. Physical examination revealed petechiae and purpuric lesions on pretibial regions [Figure 1].

In addition to the fact that the patient does not have a chronic disease and drug use, there is no bleeding disorder or coagulation disorder in his anamnesis or family history. The patient’s thrombocyte count was low in another biochemistry laboratory. A sample of the patient’s blood was sent for testing and the following results were obtained, leukocyte count = 9,900 K/µL, lymphocyte count = 2,700 K/µL, hemoglobin = 11.2 g/dl, prothrombin time = 9.8 s, International normalized ratio = 1, C-reactive protein = 40 mg/L, and thrombocyte count = 5000 K/µL. A SARS-CoV-2 polymerase chain reaction test and influenza test were both negative. The D-dimer count was 2600 ng/ml. The Hepatitis B surface antigen, Hepatitis C, Human immune deficiency virus, Cytomegalovirus, Toxoplasma, Epstein Barr virus, Herpes simplex virus, Brucella, Rubella, and Venereal Diseases Research Laboratory serological results were all negative. There were no bleeding spots. Peripheral blood smear showed a low thrombocyte count (below 10,000 K/µL), and no atypical cells were observed.

A thorax tomography scan did not show COVID-19 pneumonia, and an abdominal tomography scan did not show splenomegaly or any other pathologies. Contrasted abdominal and thorax tomography scans did not show arterial or venous thrombosis. Secondary symptoms were eliminated and ITP was diagnosed. After being dosed with dexamethasone as the initial treatment, the patient was transferred to the hematology department for the continuation of treatment and monitoring. For publication of this case report, written informed consent was obtained from the patient.

**Discussion**

The patient presented to the emergency department of our hospital with fatigue, weakness, and an incremental rash in his legs. A blood count was conducted once petechia purpura was diagnosed, which displayed thrombocytopenia. After the peripheral thrombocyte count was found to be low, which supported the blood count test results, secondary thrombocytopenia symptoms were eliminated and the patient was diagnosed with ITP.

Pain, swelling or a rash around the vaccinated area are all reported side effects of vaccination with the Pfizer-BioNTech mRNA vaccine, as well as fever, weakness, headache, muscle pain, nausea, vomiting, itching, trembling, arthralgia, and rarely, anaphylactic shock. According to reports from the American Society of Hematology, there are also thrombocyte-related side effects associated with the ChAdOx1 nCov-19 (AstraZeneca) vaccine: Antibody production against platelet factor 4 in 4–30 days; medium to heavy thrombocytopenia; production of thrombosis in atypical zones, such as the splenic vein and cerebral venous sinus; and vaccine-induced immune thrombotic thrombocytopenia. Welsh et al. studied the thrombocytopenia induced by mRNA vaccines and reported that the Pfizer-BioNTech vaccine resulted in 15 cases in 18 million doses and that the Moderna COVID-19 vaccine resulted in 13 cases in 16 million doses. Thrombocytopenia can arise as a result of reduced platelet production owing to bone marrow suppression, increased platelet breakdown due to platelet usage in vascular thrombosis and immunological such as ITP, and increased platelet storage in the spleen and dilution. Age of the patient, basal platelet count, history of operation, bleeding-thrombosis status, drug use history, family history, laboratory, and physical examination findings should be investigated. Vaccine-induced thrombocytopenia may be due to increased B cell function, cellular immunity due to the effect of cytokines on CD4+ T-cells. After FDA approval, the Pfizer-BioNTech mRNA vaccine became the most used vaccine in the world and ITP cases have been reported in the form of case reports. Recently, vaccination has been continuing rapidly in Turkey, and this case report presents the first vaccine-induced ITP case in Turkey.

**Conclusion**

Since COVID-19 is untreatable and pandemic-related mortality rates are increasing globally, vaccines have...
been determined to be the most effective solution for controlling the pandemic. Despite COVID-19 vaccine-related thrombocytopenia cases being reported, the incidence is lower than ITP incidence. Therefore, this side effect should not be considered as a reason to halt vaccination.

Author contributions statement
MSI: writing-original draft, conceptualization, MD: writing-original draft, review and editing, BBU: software, formal analysis, review and editing, MG: methodology, writing-original draft, review and editing.

Conflicts of interest
None Declared.

Consent for publication
Written informed consent was obtained from the patient for the publication of this case report. A copy of the written consent is available.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

Financial support and sponsorship
None.

References
1. Aleem A, Nadeem AJ. Coronavirus (COVID-19) vaccine-induced immune thrombotic thrombocytopenia (VITT). In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2021. Available from: https://www.ncbi.nlm.nih.gov/books/NBK570605/. [Last updated on 2021 Jul 18].
2. Dooling K, Gargano JW, Mouia D, Wallace M, Rosenblum HG, Blain AE, et al. Use of Pfizer-BioNTech COVID-19 vaccine in persons aged ≥16 years: Recommendations of the advisory committee on immunization practices – United States, September 2021. MMWR Morb Mortal Wkly Rep 2021;70:1344-8.
3. Welsh KJ, Baumblatt J, Chege W, Goud R, Nair N. Thrombocytopenia including immune thrombocytopenia after receipt of mRNA COVID-19 vaccines reported to the Vaccine Adverse Event Reporting System (VAERS). Vaccine 2021;39:3329-32.
4. Lambert MP, Gernsheimer TB. Clinical updates in adult immune thrombocytopenia. Blood 2017;129:2829-35.
5. Lakshmanan S, Cuker A. Contemporary management of primary immune thrombocytopenia in adults. J Thromb Haemost 2012;10:1988-98.
6. Miller E, Waithg P, Farrington CP, Andrews N, Stowe J, Taylor B. Idiopathic thrombocytopenic purpura and MMR vaccine. Arch Dis Child 2001;84:227-9.
7. Bhattacharjee S, Banerjee M. Immune Thrombocytopenia Secondary to COVID-19: a Systematic Review. SN Compr. Clin. Med. 2, 2048-2058 (2020). https://doi.org/10.1007/s42399-020-00521-8.
8. Pfizer BioNTech. Pfizer BioNTech COVID 19 Vaccine Briefing Document, Vaccines and Related Biological Products Advisory Committee Meeting December 10, 2020 https://www.fda.gov/media/144245/download.
9. Meo SA, Bukhari IA, Akram J, Meo AS, Klonoff DC. COVID-19 vaccines: Comparison of biological, pharmacological characteristics and adverse effects of Pfizer/BioNTech and moderna vaccines. Eur Rev Med Pharmacol Sci 2021;25:1663-9.
10. Smock KJ, Perkins SL. Thrombocytopenia: An update. Int J Lab Hematol 2014;36:269-78.
11. Pasin F, Calabrese A, Pelagatti L. Immune thrombocytopenia following COVID 19 mRNA vaccine: Casuality or causality? Intern Emerg Med 2021 Jun 7;3-3. doi: 10.1007/s11739-021-02778-w.
12. Ganzel C, Ben-Chetrit E. Immune thrombocytopenia following the Pfizer-BioNTech BNT162b2 mRNA COVID-19 vaccine. Isr Med Assoc J 2021;23:341.
13. Fueyo-Rodriguez O, Valente-Acosta B, Jimenez-Soto R, Neme-Yunes Y, Inclán-Alarcon SI, Trejo-Gonzalez R, et al. Secondary immune thrombocytopenia supposedly attributable to COVID-19 vaccination. BMJ Case Rep 2021;14:e242220.
14. Al-Maqbali JS, Al Rasbi S, Kashouh MS, Al Hinaai AM, Farhan H, Al Rawahi B, et al. A 59-year-old woman with extensive deep vein thrombosis and pulmonary thromboembolism 7 days following a first dose of the Pfizer-BioNTech BNT162b2 mRNA COVID-19 vaccine. Am J Case Rep 2021;22:e932946.
15. Tarawneh O, Tarawneh H. Immune thrombocytopenia in a 22-year-old post COVID-19 vaccine. Am J Hematol 2021;96:E133-4.