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Case Report

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Treatment for Immune Thrombocytopenia in Coronavirus Disease 2019 (COVID-19) Infection after COVID-19 Vaccination: A Case Report

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ABSTRACT

Thrombocytopenia is one of the rare signs of both the coronavirus disease 2019 (COVID-19) and COVID-19 vaccination. An 85-year-old man was diagnosed with immune thrombocytopenia and COVID-19, 7 days after COVID-19 vaccination. The patient was successfully treated with a short course of intravenous immunoglobulin and oral corticosteroids.

Keywords: Coronavirus disease 2019; SARS-CoV-2; COVID-19 vaccines; Vaccine-induced immune thrombocytopenia

INTRODUCTION

The coronavirus disease 2019 (COVID-19) caused the 2020 pandemic, and the World Health Organization declared it as a public health emergency of international concern, the highest level of alarm under international law, in January 2020. Meanwhile, vaccines targeting severe acute respiratory syndrome coronavirus-2 have been developed immediately in response to the pandemic. Several platforms showed high efficacy to prevent COVID-19. However, concerns regarding the adverse effects of vaccines have been raised.

Immune thrombocytopenia (ITP) are rarely reported to be combined to COVID-19 [1]. However, few cases of thrombocytopenia after COVID-19 vaccination also have been reported [2-4]. Although rare, these cases are important because there have been mortality reports due to this hematologic adverse reaction [5]. As the number of people who got vaccinated for COVID-19 increases under one of the global strategies to control the pandemic, cases of COVID-19 infection after vaccination are also expected to increase, and some rare symptoms like thrombocytopenia may need to be considered when approaching whether they are disease-related or vaccination-related. We report a case of ITP with COVID-19 infection after COVID-19 vaccination in the Korea and compared thrombocytopenia caused due to COVID-19 itself with that caused by its vaccination.

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Ethics Statement
This study has been approved by Institutional Review Board of Boramae Medical Center (IRB No.: 20-2021-53). The board waived informed consent due to the retrospective nature of the study and patient anonymization.

Conflict of Interest
No conflicts of interest.

Author Contributions
Conceptualization: EL. Data curation: JHL, SMO. Writing - Original draft: JHL, EL. Writing - Review and edit: JHB, SWP.

CASE REPORT

An 85-year-old man who presented with petechiae on both the legs, oral gum bleeding, fever, cough, and increased sputum was admitted to a hospital for COVID-19 isolation.

He had been diagnosed with gastric cancer, which was successfully treated via total gastrectomy 20 years ago. He had also undergone an appendectomy for acute appendicitis 18 years ago. He was diagnosed with diabetes mellitus 4 months ago and was currently not taking any medication.

He received his first mRNA vaccine BNT162b2 (Pfizer-BioNTech, Mainz, Germany and NY, USA). Seven days after the vaccination, painless and non-pruritic petechiae were observed on his legs. Furthermore, multiple clots were observed in his mouth due to gum bleeding. On the same day, the patient had a fever of 38.3ºC and productive cough. The patient took a routine blood test at a local clinic. The complete blood count showed the platelet count to be 2,000/mm^3. Transfusion was done with 6 packs of platelet concentrations at the clinic. During the transfusion, he tested positive in the COVID-19 test by reverse transcription polymerase chain reaction method (Ct value of RdRP gene: 15.33). He was transferred to a specialized hospital operating respiratory isolation wards for COVID-19.

The patient had a height of 170 cm, and weight of 56.7 kg. His initial vital signs were: blood pressure of 159/99 mmHg, heart rate of 89/min, respiratory rate of 20/min, and body temperature of 37.4ºC. Other symptoms, including gastrointestinal and urinary system, were not reported. Petechiae were observed from the ankle to the knees of both legs. Multiple blood clots were observed in the oral cavity. No other abnormal sign was observed in the thorough physical examination.

The initial blood test showed thrombocytopenia and anemia. Complete blood count revealed a platelet count of 6,000/mm^3. The white blood cell count was 3,160/mm^3, and the hemoglobin was 10.4 g/dL. The segmental Neutrophil was 66.5% and lymphocyte was 19.9%.

Due to the patient's thrombocytopenia and anemia, additional hematologic blood tests were conducted (**Table 1**). Peripheral blood smear showed normocytic and normochromic red blood cells. The white blood cell count was moderately decreased and few atypical lymphocytes were observed (1%). The platelets were significantly decreased, with large platelets observed. Both anti-platelet antibody and platelet associated antibodies were not detected in the blood.

A chest radiography revealed infiltration in both the lung fields. The patient did not complain of shortness of breath nor required oxygenation throughout the hospital stay.

The patient was diagnosed with ITP for the thrombocytopenia with bleeding sign without any other underlying or suspicious other hematologic diseases. To investigate the cause for ITP, additional blood tests were done. The rheumatoid factor was positive (titer 19.9 IU/mL) whereas the other markers were within normal range and anti-platelet factor 4 antibodies were not detected (**Table 1**). Vaccine-induced thrombotic thrombocytopenia (VITT) was ruled out because he did not show any thrombotic symptom or sign and he received the mRNA vaccine not related with VITT. Moreover, the test result about anti-platelet factor 4 antibodies was negative.

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Table 1. Anemia work up and autoimmune antibodies in a case for immune thrombocytopenia with coronavirus disease 2019 (COVID-19) after COVID-19 vaccination

Variables	On admission	Reference range
Anemia work up		
Platelet antibody	Negative	Negative
Platelet associated antibody	Negative	Negative
Iron (μg/dL)	30	50 - 170
Total iron binding capacity (μg/dL)	273	280 - 400
Ferritin (ng/mL)	60	16 - 400
Folate (ng/mL)	14.8	3.9 - 26.8
Vitamin B12 (pg/mL)	249	197 - 771
Autoimmune antibodies		
Rheumatoid factor (IU/mL)	Positive (19.9)	0.0 - 13.9
Anti-heparin/PF4	Negative	Negative
Anti-nuclear antibody	Negative (<1:80)	Negative (<1:80)
Anti-ds-DNA	3.1	0.0 - 10.0
Anti-CCP	Negative	Negative
Antineutrophil cytoplasmic antibody, MPO	Negative (<0.1)	Negative (<3.5)
Antineutrophil cytoplasmic antibody, PRIII	Negative (<0.1)	Negative (<2.0)

PF, platelet factor; DNA, deoxyribonucleic acid; CCP, cyclic citrullinated peptide; MPO, myeloperoxidase antibodies; PR, proteinase.

Treatment with intravascular immunoglobulin (IVIG, GC Pharma, Yongin, Korea) and oral prednisolone was initiated. IVIG infusion was administered (1g/kg for a total of 57 g) twice on hospital days 2 and 3. Prednisolone was administered twice a day (30 mg total per day) from hospital day 2.

Following IVIG treatment, the petechiae on his legs disappeared. Oral gum bleeding stopped, and the oral cavity blood clots disappeared. The complete blood test revealed a platelet count of 195,000/mm^3 on the hospital day 5.

Other symptoms, such as fever, cough, and sputum production, resolved by hospital day 5. The patient was discharged on hospital day 9, 10 days from the onset of his symptoms and was released from quarantine. Prednisolone was administrated as 15 mg twice a day 7 days after discharge. Further, prednisolone dosage was tapered out for 3 weeks.

DISCUSSION

The necessity to distinguish between ITP due to COVID-19 infection and VITT in patients vaccinated for COVID-19 is that the approach and treatment are different. Attention to hemorrhage and the treatment including platelet transfusion are considered in cases of secondary ITP to COVID-19 infection, whereas considering the thrombotic situation in VITT [3, 4]. Platelet transfusion should not be given, and anticoagulation other than heparin, usually direct oral anti-Xa inhibitors are recommended for treatment of VITT [3, 6]. IVIG is a possible treatment option for both conditions.

The patient's problem was likely ITP rather than VITT. Because he received the mRNA vaccine not related with VITT and the test result about anti-platelet factor 4 antibodies was negative. We had focused on ITP treatment and the outcome was satisfactory.

There are three possible causes of ITP in the patient. First, COVID-19 itself reported to cause ITP [1, 7]. COVID-19-induced ITP is usually accompanied by severe COVID-19 infection.

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However rare cases with mild or asymptomatic COVID-19 infection have also been reported [4]. Second, mRNA vaccine can induce ITP. Although rare, some thrombocytopenic cases after COVID-19 vaccination have been reported [2-4]. There is a previous case report of immune thrombocytopenia after Pfizer-BioNTech BNT16B2b2 mRNA vaccine, reporting multiple petechiae after 3 days of vaccination [8]. Last possible reason is inordinate immune reaction after COVID-19 vaccination. Vaccination against COVID-19 lead to release cytokines which can cause abnormal immune reaction like ITP [9, 10].

COVID-19 itself is a novel infectious disease, and as the vaccination proceeds at a rapid rate, it is inevitable to note the rare adverse reaction. This is the second report on COVID-19-related ITP in the Republic of Korea and the first report of ITP after COVID-19 vaccination. The first case after COVID-19 infection spontaneously improved without treatment [7]. This patient successfully recovered within a short time with treatment. In conclusion, diagnosis according to the clinical characteristics is important and aggressive medical treatment could be helpful for ITP as presented in this case.

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