

## Severe and Transient Thrombocytopenia Following the Third Dose of COVID-19 Vaccine (mRNA-1273): A Case Report

Risaburo Akasaka<sup>1,2\*</sup>, Kazuyuki Suzuki<sup>1,2</sup>, Kiyomi Akasaka<sup>3</sup> and Toshiyuki Akasaka<sup>4</sup>

<sup>1</sup>Department of Internal Medicine, Akasaka Hospital, Morioka, Japan

<sup>2</sup>Division of Gastroenterology and Hepatology, Department of Internal Medicine, Iwate Medical University, Yahaba, Japan

<sup>3</sup>Department of Dermatology, Akasaka Hospital, Morioka, Japan

<sup>4</sup>Department of Urology, Akasaka Hospital, Morioka, Japan

### \*Corresponding author:

Risaburo Akasaka,  
Department of Internal Medicine, Akasaka Hospital,  
29-2 Nasukawacho, Morioka, Iwate 020-0116,  
Japan, Tel: +81-19-624-1225,  
Fax: +81-19-623-1825,  
E-mail: akasaka1136@yahoo.co.jp

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## 1. Abstract

Autoimmune thrombocytopenia after coronavirus disease 2019 (COVID-19) vaccination rarely occurs as adverse events and usually occurs after the first or second dose. We report the case of an 89-year-old woman who rapidly developed purpura with severe thrombocytopenia following the third dose of the mRNA-1273 Moderna vaccine. She had no adverse events following the first and second doses of the BNT162b2 Pfizer-BioNTech vaccine, but purpura with petechiae on the left upper chest and both upper and lower extremities appeared the day after the third dose with the mRNA-1273 vaccine. Her platelet counts markedly decreased ( $1.1 \times 10^4/\mu\text{L}$ ) on the fifth day after vaccination but improved spontaneously without any specific treatment, such as administration of glucocorticoids. However, we were unable to confirm whether this case was that of secondary immune thrombocytopenia because of the limited information on biochemical examinations. Careful observation of the appearance of purpura related to thrombocytopenia at an early stage after COVID-19 vaccination is necessary.

## 2. Introduction

Sequential vaccination against coronavirus disease 2019 (COVID-19) has been performed worldwide because of the persistence of the COVID-19 pandemic. COVID-19 is caused by severe acute respiratory syndrome coronavirus 2 infection [1]. The United States Food and Drug Administration issued an Emergency Use Authorization for the use of the COVID-19 vaccine on December 11, 2020. In Japan, three COVID-19 vaccines (BNT162b2 by Pfizer-BioNTech, mRNA-1273 by Moderna, and ChAdOx1 by AstraZeneca) were approved in May 2021, and it was strongly recommended that healthcare workers, elderly persons, and adult patients with chronic underlying diseases, such as diabetes mellitus, chronic pulmonary disease, and chronic heart failure, receive the third dose of the vaccine. Although vaccination against COVID-19 has great advantages in the prevention of COVID-19 and exacerbations in patients with COVID-19, some adverse events are inevitable [2]. Secondary immune thrombocytopenia (ITP) is one of the severe adverse events that occur following COVID-19 vaccination. The majority of cases with secondary ITP following COVID-19 vaccination occur after the first or second dose [3-16]. However, secondary ITP is rare after the third dose of the BNT162b2 vaccine [17]. Herein, we present the case of an elderly woman who developed purpura with severe thrombocytopenia early after the third dose of the mRNA-1273 Moderna vaccine.

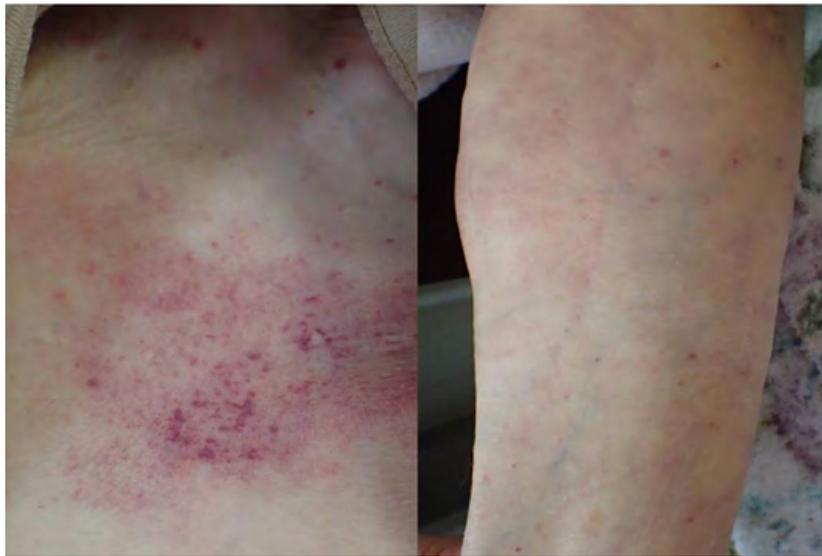
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## 3. Case Presentation

An 89-year-old woman with severe dementia and Parkinson's disease had been living in a nursing home since October 2018. She received the first dose of the BNT162b2 Pfizer-BioNTech vaccine on June 2, 2021 and the second dose on June 23, 2021. She did not experience any adverse events after the vaccinations. She received the third dose of the mRNA-1273 vaccine by Moderna on February 16, 2022. The next day, nurses noticed punctate, nonpal-

pable purpura scattered on both the upper and lower extremities of the patient. On February 21, 2022, because of the new purpura that appeared on the left upper chest, she visited our dermatology outpatient clinic. No fever had occurred after the vaccination up to the day of the dermatology consultation. Physical examination revealed purpura with petechiae on the left upper chest and both upper and lower extremities (Figure 1). Laboratory test data showed a platelet count of  $1.1 \times 10^4/\mu\text{L}$ . The prothrombin time international normalized ratio and activated partial thromboplastin time were 1.0 and 36.6 s, respectively. Liver and renal function test results were normal. The serum C-reactive protein level was slightly elevated (0.52 mg/dL). Serum autoimmune antibodies, in-

cluding antinuclear and anti-dinucleotide antibodies, were negative. The serum antibody for protein-bindable immunoglobulin G, which is an anti-platelet antibody and was measured by a mixed passive agglutination method, was negative. She had no history of additional medications associated with drug-induced dermatitis and/or thrombocytopenia before the vaccination. Therefore, vaccine-related ITP was strongly considered. Fortunately, her purpura did not spread, and the platelet counts increased rapidly ( $8.9 \times 10^4/\mu\text{L}$  on February 24,  $25.2 \times 10^4/\mu\text{L}$  on February 28, and  $23.2 \times 10^4/\mu\text{L}$  on April 4) without administration of either glucocorticoids or intravenous immunoglobulin G. Based on her medical records, her platelet counts in May 2019, before vaccination, were  $34.9 \times 10^4/\mu\text{L}$ .



**Figure 1:** Purpura with petechiae on the left upper chest (left) and petechiae on the right lower extremity (right).

#### 4. Discussion

Several cases of secondary ITP following the first and second doses of COVID-19 vaccinations have been reported [3-16]. However, cases of ITP after the third dose of the BNT162b2 Pfizer-BioNTech vaccine are rare [17]. Moreover, we did not find any case report of ITP following the third dose of the mRNA-1273 vaccine by Moderna. in the literature related to the vaccine and its side-effect profile until the end of March 2022. In this case, although purpura appeared the next day, thrombocytopenia was confirmed 5 days after the COVID-19 vaccination. Previous reports have shown that the number of days from vaccination to the confirmation of thrombocytopenia ranges from 1 to 21 days [3-16]. In this case, purpura appeared very early after the vaccination, suggesting a side effect of the vaccine. In addition, the purpura may have occurred due to an autoimmune mechanism. However, the diagnosis of ITP could not be confirmed because platelet-associated immunoglobulin G (PA-IgG), protein-bindable IgG, and platelet factor 4 levels were not measured. In Japan, the interval between the administration of the first and second doses of COVID-19 vaccines is 2 weeks, and the third dose of the COVID-19 vaccine is usually administered over 5 months after the second COVID-19 vaccination. This pro-

gram was followed in this case. Although thrombocytopenia with purpura following the third vaccination was reported in this case, there is a possibility that mild thrombocytopenia without purpura might have occurred after the first and/or second dose of COVID-19 vaccine, and severe thrombocytopenia with purpura appeared only after the third COVID-19 vaccination. Moreover, the Pfizer-BioNTech vaccine was used for the first and second vaccinations in our patient, whereas the Moderna vaccine was used for the third vaccination. An autoimmune reaction might have been triggered following the administration of a different vaccine. The reporting rate of secondary ITP following both COVID-19 vaccines (Pfizer-BioNTech and Moderna) is almost the same (0.80 per million doses), and the incidence rate of ITP following the administration of these mRNA COVID-19 vaccines is not greater than the expected number of ITP cases [3]. Furthermore, Crickx et al. suggested that administration of BNT162b2, ChAdOx1, and mRNA-1273 vaccines is generally safe in adult patients with primary ITP and ITP relapses after mRNA vaccination are rare [18]. However, two cases of primary ITP with exacerbations after the Pfizer-BioNTech COVID-19 vaccination have been reported [19, 20]. To determine the prevalence of secondary ITP after the ad-

ministration of these mRNA COVID-19 vaccines, it is necessary to routinely assess laboratory examinations, including platelet counts, early after vaccination. However, this program is unrealistic in clinical settings. People with severe dementia, such as in our case, cannot quickly recognize adverse events following vaccination themselves. Therefore, it is necessary to carefully observe the appearance of purpura associated with thrombocytopenia at an early stage after COVID-19 vaccination. More recently, a fourth dose of the COVID-19 vaccine has been initiated in Japan for people over 65 years of age with any chronic diseases. Further information on cases with secondary ITP following COVID-19 vaccination is necessary.

## 5. Authorship

Contribution: R. Akasaka supported the medical care of this patient and wrote part of the manuscript; K. Suzuki designed the study and wrote the manuscript; K. Akasaka first examined this case and made the diagnosis; and T. Akasaka supervised and read the final draft of this paper. All authors reviewed and approved the final version of the manuscript.

## 6. Conflict of Interest

All authors state no conflicts of interest for the submission of this case report.

## 7. Funding Statement

This research did not receive any external financial support.

## 8. Patient Consent Statement

Written consent for the publication and use of personal data and pictures was obtained from the patient's family because she was unable to speak, write, or understand the situation owing to her severe dementia.

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