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SevereandTransientThrombocytopeniaFollowingtheThirdDoseofCOVID-19 Vaccine (mRNA-1273): A Case Report

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1. Abstract

Autoimmune thrombocytopenia after coronavirus disease 2019 (COVID-19)vaccinationrarelyoccursasadverseeventsandusu- ally 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 andseconddosesoftheBNT162b2Pfizer-BioNTechvaccine,but purpurawithpetechiaeontheleftupperchestandbothupperand lower extremities appeared the day after the third dose with the mRNA-1273vaccine.Herplateletcountsmarkedlydecreased(1.1 × 10^4/μL) on the fifth day after vaccination but improved spontaneously without any specific treatment, such as administration of glucocorticoids.However,wewereunabletoconfirmwhetherthis case was that of secondary immune thrombocytopenia becauseof 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 oftheCOVID-19pandemic.COVID-19iscausedbysevereacute respiratory syndrome coronavirus 2 infection [1]. The United States Food and Drug Administration issued an Emergency Use AuthorizationfortheuseoftheCOVID-19vaccineonDecember 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.

3. Case Presentation

An89-year-oldwomanwithseveredementiaandParkinson'sdisease had been living in a nursing home since October 2018. She receivedthefirstdoseoftheBNT162b2Pfizer-BioNTechvaccine 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 February16,2022.Thenextday,nursesnoticedpunctate,nonpal-

pable purpura scattered on both the upper and lower extremitiesof 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 × 10^4/μL. The prothrombin time internationalnormalizedratioandactivatedpartialthromboplastin time were 1.0 and 36.6 s, respectively. Liver and renal function test results were normal. The serum C-reactive protein level was slightlyelevated(0.52mg/dL).Serumautoimmuneantibodies,including antinuclear and anti-dinucleotide antibodies, were negative.Theserumantibodyforprotein-bindableimmunoglobulinG, which is an anti-platelet antibody and was measured by a mixed passive agglutination method, was negative. She had no historyofadditionalmedicationsassociatedwithdrug-induceddermatitis and/or thrombocytopenia before the vaccination. Therefore, vaccine-relatedITPwasstronglyconsidered.Fortunately,herpurpura didnotspread,andtheplateletcountsincreasedrapidly(8.9×10^4/ μLon February 24, 25.2 ×10^4/μLon February 28, and 23.2 ×10^4/ μLonApril 4) without administration of either glucocorticoids or intravenousimmunoglobulinG.Basedonhermedicalrecords,her platelet counts in May 2019, before vaccination, were 34.9 ×10^4/ μL.

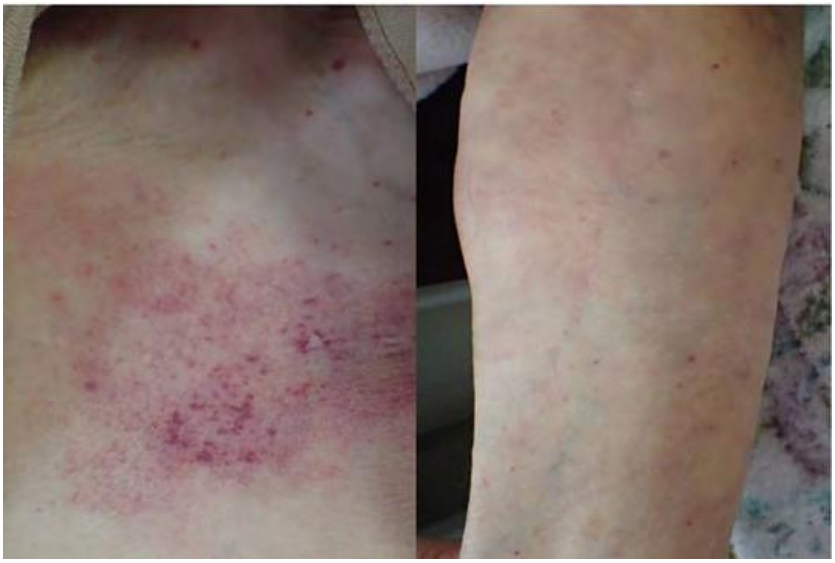

Figure1: Purpura with petechiaeon the left upper chest(left) and petechiae onthe right lower extremity (right).

4. Discussion

SeveralcasesofsecondaryITPfollowingthefirstandseconddosesofCOVID-19vaccinationshavebeenreported[3-16].However,casesofITPafterthethirddoseoftheBNT162b2Pfizer-BioNTechvaccinearerare[17].Moreover,wedidnotfindanycasereportofITPfollowingthethirddoseofthemRNA-1273vaccineby Moderna.intheliteraturerelatedtothevaccineanditsside-effect profileuntiltheendofMarch2022.Inthiscase,althoughpurpura appeared the next day, thrombocytopenia was confirmed 5 days aftertheCOVID-19vaccination.Previousreportshaveshownthat thenumberofdaysfromvaccinationtotheconfirmationofthrombocytopeniarangesfrom1to21days[3-16].Inthiscase,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 ITPcould not be confirmed because platelet-associated immunoglobulin G (PA-IgG), protein-bindable IgG, and platelet factor 4 levels were notmeasured.InJapan,theintervalbetweentheadministrationof the first and second doses of COVID-19 vaccines is 2 weeks, and the third dose of the COVID-19 vaccine is usually administered gramwasfollowedinthiscase.Althoughthrombocytopeniawith over5monthsafterthesecondCOVID-19vaccination.Thispro-

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 COV- ID-19 vaccine, and severe thrombocytopenia with purpura ap- peared only after the third COVID-19 vaccination. Moreover, the Pfizer-BioNTechvaccinewas usedfor thefirst andsecondvacci- nations 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 vac- cines (Pfizer-BioNTech and Moderna) is almost the same (0.80 permilliondoses),andtheincidencerateofITPfollowingthead-ministration of these mRNA COVID-19 vaccines is not greater than the expected number of ITP cases [3]. Furthermore, Crickxetal.suggestedthatadministrationofBNT162b2,ChAdOx1,and mRNA-1273 vaccines is generally safe in adult patients with pri- mary ITPand ITPrelapses after mRNAvaccination are rare [18]. However, two cases of primary ITP with exacerbations after the Pfizer-BioNTech COVID-19 vaccination have been reported [19, 20].TodeterminetheprevalenceofsecondaryITPafterthead-

ministration of these mRNACOVID-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 vaccinationthemselves.Therefore,itisnecessarytocarefullyobserve theappearanceofpurpuraassociatedwiththrombocytopeniaatan 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 caseandmadethediagnosis;andT.Akasakasupervisedandread thefinaldraftofthispaper.Allauthorsreviewedandapprovedthe final version of the manuscript.

6. ConflictofInterest

Allauthorsstatenoconflictsofinterestforthesubmissionofthis case report.

7. Funding Statement

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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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