Temporal association of vitreous hemorrhage and hypertension after COVID-19 mRNA vaccines

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Abstract
Vitreous hemorrhage as common eye presentation and hypertension as common systemic presentation are difficult to designate whether they are coincidental or causal in terms of adverse events of COVID-19 vaccinations. Temporal association of hypertension and vitreous hemorrhage was noted in a patient repeatedly after the second and third COVID-19 vaccinations.

KEYWORDS
COVID-19 mRNA vaccine, hypertension, retinal hemorrhage, retinal tear, vitreous hemorrhage

1 | INTRODUCTION
Common manifestations such as retinal and vitreous hemorrhage are difficult to designate whether they are coincidental or causal in relation with COVID-19 vaccinations. Here, we report a patient (one of the authors) who experienced vitreous hemorrhage repeatedly about 2 months after the second and third vaccination for COVID-19.

2 | CASE REPORT
A 60-year-old man, working as an eye doctor (T.M.), had the first and second vaccination for COVID-19 in the interval of 3 weeks (Tozinameran, Pfizer-BioNTech). He had no past history, no medication, and no abnormal findings on the annual health checkups for workers around the same time. He did not smoke, and he had not experienced any allergic reaction to drugs or other vaccines including annual influenza vaccines. The routine annual health checkups consisted of height, weight, and abdominal circumference measurements, inspection and auscultation by an internist, blood pressure measurement, visual acuity testing in each eye, auditory testing in each ear, plain chest X-ray film, electrocardiogram, urine dipstick tests for protein, glucose and occult blood, fecal occult blood test, and blood examinations including hemoglobin, red blood cell count, aspartate aminotransferase (AST), alanine aminotransferase (ALT), γ-glutamyl transpeptidase (γ-GTP), low density lipoprotein (LDL)-cholesterol, high density lipoprotein (HDL)-cholesterol, triglycerides, creatinine, blood glucose, hemoglobin A1c, and quantitative
measurements of hepatitis B surface antigen (HBsAg), hepatitis B surface antibody (HBsAb), and hepatitis C virus antibody (HCV-Ab, third generation).

Two and a half months after the second vaccination, he suddenly noticed black-colored linear flow in the lower visual field of the left eye when he was working in the early morning. A retinal tear with vitreous hemorrhage in the superotemporal midperipheral fundus of the left eye was diagnosed and laser-coagulated by his fellow doctor (H.N.). The vitreous hemorrhage resolved in a few days, but 6 days after the first episode, he experienced another episode of vitreous hemorrhage in the left eye, and this time, his left vision decreased temporarily to hand movement. The vitreous hemorrhage was again spontaneously absorbed in a month (Figure 1B) and the visual acuity in the left eye returned to normal. He underwent the third vaccination for COVID-19, eight months after the second vaccination. He experienced the third episode of vitreous hemorrhage in the left eye 2.5 months after the third vaccination, leading to temporary reduction of the visual acuity to hand movement in the left eye. The vitreous hemorrhage resolved spontaneously in a month. After each vaccination, he experienced general fatigue and pain in the left arm with the vaccinations for a few days but did not develop fever.

At each visit, the patient had clear ocular media in both eyes and showed no retinal hemorrhages in both eyes as a manifestation of hypertensive retinopathy (Figure 1A,B). The retinal arteries in both eyes had no arteriosclerotic changes. The intraocular pressure was 12–15 mmHg in both eyes. Retrospectively, he checked his blood pressure every week and noticed the elevation of diastolic blood pressure in the range of 10–20 mmHg, reaching the level of 80–85 mmHg, in the period of a few months after the second and third vaccination which was the timing for repeat episodes of vitreous hemorrhages. In 5 months after the third vaccination, the blood pressure was 125–145 mmHg in systolic pressure and 65–75 mmHg in diastolic pressure. The best-corrected visual acuity in decimals was 1.2 in each eye.

3 | DISCUSSION

This case represents a common picture of rhegmatogenous vitreous hemorrhage. Rebleeding within a week is also a well-known feature of vitreous hemorrhage of any cause. The third episode of vitreous hemorrhage in this case might be related to residual vitreous gel traction to the retinal artery which passed at the lower edge of the retinal tear (Figure 1B). However, it is somewhat curious to note vitreous hemorrhage many months after laser coagulation around the retinal tear. It is noteworthy in this case to have vitreous hemorrhage repeatedly in the common interval of 2.5 months after the second vaccination and third vaccination for COVID-19. In the long period after COVID-19 vaccinations, retinal and vitreous hemorrhages have been described to occur incidentally in patients with retinal hemorrhage-prone conditions such as diabetic retinopathy and retinal vein occlusion.2,3

In the other aspect of adverse events, hypertension has been recorded to occur after COVID-19 vaccinations.4,5 The present case is unique to show the temporal association between vitreous hemorrhage and diastolic pressure rise repeatedly after the second and third vaccination for COVID-19. Under the circumstances, it is apparently difficult to specify a cause for the elevation of blood pressure since the blood pressure would fluctuate under the influence of many different factors such as physical activity, mental stress, and daily food (salt) intake. It is, at moment, desirable for ophthalmologists to take history of COVID-19 vaccinations and to ask the status of blood pressure.

**FIGURE 1** Wide-view fundus photographs in the right eye (A) with no manifestations and in the left eye (B) with a retinal tear in the superotemporal midperiphery 2 months after laser coagulation. Note that a retinal artery is passing at the lower edge of the tear (arrow in B).
pressure in patients who show rebleeding in the stable condition of diabetic retinopathy and retinal vein occlusion as well as laser-coagulated retinal tears. In addition, it is recommended to think of COVID-19 vaccinations in patients who are diagnosed with uveitis since the uveitis might be vaccine associated.

A major limitation in this study is that a single case is too weak to prove the temporal association of hypertension and vitreous hemorrhage as the concurrent adverse events of COVID-19 vaccinations. Furthermore, only the routine health checkups have been done in this patient, and no systemic investigation in detail has been performed to rule out other etiologies of repeated vitreous hemorrhage. Even with these limitations, the present case would be useful to link hypertension with vitreous hemorrhage, each of which has been reported separately as the adverse event of COVID-19 vaccinations. The generalizability of the present results needs to be investigated in future studies.

AUTHOR CONTRIBUTIONS
T.M. had conception and wrote the manuscript. H.N. treated the patient. All authors approved the final version of the manuscript.

ACKNOWLEDGMENTS
None.

CONFLICT OF INTEREST
The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT
Additional data will be available upon the reasonable request to the corresponding author.

ETHICAL APPROVAL
Ethics committee review was not applicable due to the case report design, based on the Ethical Guidelines for Medical and Health Research Involving Human Subjects, issued by the Government of Japan.

CONSENT
Written informed consent was obtained from the patient to publish this report in accordance with the journal’s patient consent policy.

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