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Case Report

Rapid Progression of Polypoidal Choroidal Vasculopathy following Third BNT162b2 mRNA Vaccination

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Keywords
Coronavirus disease 2019 · Coronavirus disease 2019 vaccine · mRNA vaccine · Polypoidal choroidal vasculopathy · Adverse effects

Abstract
The study aimed to describe a case of rapid progression of polypoidal choroidal vasculopathy (PCV) following the third administration of the Pfizer-BioNTech (BNT162b2) mRNA vaccine. A 79-year-old Japanese man visited our hospital with a 1-week history of blurred vision in the left eye 16 h following the administration of the third BNT162b2 mRNA vaccine. The clinical examinations and imaging tests revealed massive submacular hemorrhage (SMH) and excessive subretinal fluid (SRF), owing to PCV in the left eye. No ocular abnormality was observed in the right eye. His medical history included diabetes and ocular history included cataracts, nonproliferative diabetic retinopathy, glaucoma in both eyes, and irregular retinal pigment epithelium elevation in the left eye. Since he received a single intravitreal injection of aflibercept approximately 2 years ago for the treatment of diabetic macular edema in the left eye, the left eye was stable. We performed an intravitreal injection of bevacizumab and combined phacoemulsification with pars plana vitrectomy with gas, including subretinal injection of tissue plasminogen activator to displace the SMH. Thirteen days after the surgery, the SMH and SRF decreased. Although rare, mRNA COVID-19 vaccine administrations could be associated with PCV deterioration.

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Introduction

COVID-19 vaccine has demonstrated excellent safety and efficacy in phase 3 trials [1]. Meanwhile, recently several literatures have reported ocular adverse effects following the COVID-19 vaccination, including anterior uveitis [2, 3], multiple evanescent white dot syndrome [2, 3], central serous retinopathy [4], acute macular neuroretinopathy [3, 5], Vogt-Koyanagi-Harada disease [3, 6], multifocal choroiditis [7], retinal vein occlusion [3], and quiescent choroidal neovascularization (CNV) activation secondary to myopia or uveitis [3].

Herein, we report a case of rapid progression of polypoidal choroidal vasculopathy (PCV) with submacular hemorrhage (SMH) following the third administration of the Pfizer-BioNTech (BNT162b2) mRNA vaccine. To the best of our knowledge, no reports have demonstrated PCV exacerbation attributed to vaccination.

Case Report/Case Presentation

A 79-year-old Japanese man was referred from another hospital on August 14, 2017, for regular follow-up of cataracts, nonproliferative diabetic retinopathy, and glaucoma in both eyes. Decimal best-corrected visual acuity (BCVA) was 1.2 in the right and 0.9 in the left eye. He had no relevant medical, family, and social history, with the exception of the medication for type 2 diabetes (vildagliptin/metformin hydrochloride combination LD tablet, 2 tablets per day). Diabetes was well controlled (hemoglobin A1c was approximately 6.9%). He was then followed up every 3–4 months at our hospital. On April 9, 2020, diabetic macular edema (central subfield thickness, 327 μm) and irregular retinal pigment epithelium elevation within the macula, which we diagnosed as a precursor lesion of PCV, were observed in the left eye on the optical coherence tomography (OCT) image (shown in Fig. 1a). His decimal BCVA remained 0.9 in the left eye; however, on the same day, he received a single intravitreal injection of 2.0 mg/0.05 mL aflibercept (Eylea®, Regeneron Pharmaceuticals, Inc., South San Francisco, CA, USA) for the treatment of diabetic macular edema. One month after the injection, the macular edema completely resolved and decimal BCVA increased to 1.0. No recurrence of macular edema was observed and decimal BCVA was maintained at 1.0. The precursor lesion of PCV was stable for approximately 2 years following the injection (shown in Fig. 1b, c).

He received the first administration of the BNT162b2 vaccine on May 25, 2021, the second on June 15, 2021, and the third on February 1, 2022. On February 9, 2022, he visited our hospital 8 days following the third vaccination. His last visit to our hospital before the third vaccination was on November 12, 2021 (shown in Fig. 1c). He became conscious of a blurred vision in the left eye since 16 h following the third vaccination. He did not have a history of prior coronavirus infection. Upon examination, decimal BCVA in the left eye decreased from 1.0 to 0.5. In the left eye, slight SMH was detected by slit-lamp examinations and color fundus photography (shown in Fig. 2a). OCT images revealed the following PCV characteristics: a sharp-edged pigment epithelial detachment, polypoidal lesions, double-layer sign, subretinal fluid (SRF), and a thick choroid (shown in Fig. 2b). No other ocular abnormalities, such as keratic precipitates and cells, in the anterior and posterior chamber and vitreous were observed in both eyes. Intraocular pressure of 10 mm Hg was observed in both eyes. In the right eye, no abnormality was observed on the OCT image, and the decimal BCVA remained 1.2.

On February 14, 2022, rapid deterioration of PCV with SMH and SRF were detected on color fundus photography (shown in Fig. 3a) and OCT images (shown in Fig. 3b) in the left eye. Indocyanine green angiography image revealed polypoidal lesions (shown in Fig. 3c). Decimal BCVA decreased to 0.4. He received an intravitreal injection of 1.25 mg/0.05 mL bevacizumab (Avastin®, Genentech, Inc., South San Francisco, CA, USA) in the left eye. The next

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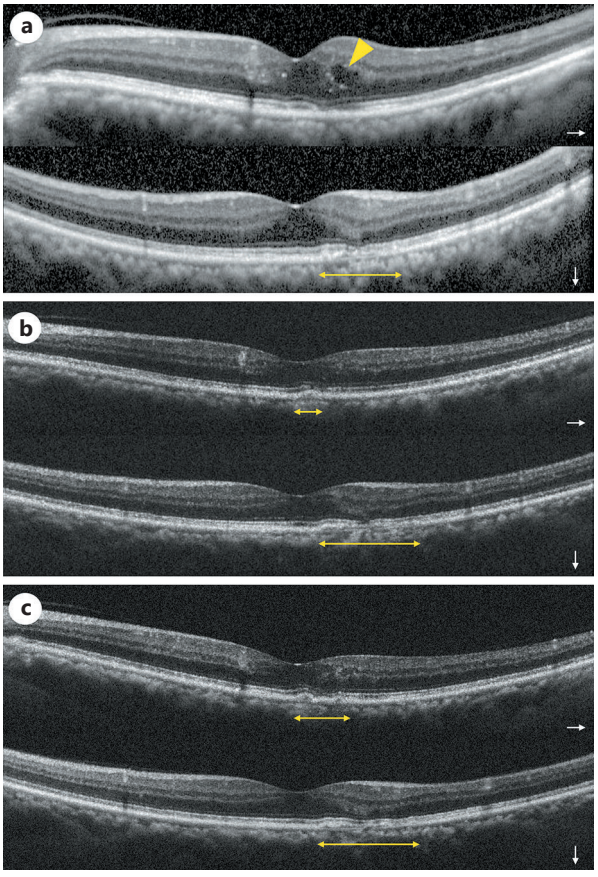

Fig. 1. Quiescent irregular RPE elevation as revealed by cross-sectional OCT images in the left eye before the third Pfizer-BioNTech (BNT162b2) vaccination. **a** Intraretinal fluid (arrow head) owing to diabetic retinopathy and irregular RPE elevation were detected (two-way arrow) on April 9, 2020. On the same day, an intravitreal injection of aflibercept was administered for the treatment of diabetic macular edema. The arrows indicate the OCT scan direction (top, horizontal: bottom, vertical), as well as **b** and **c**. **b**, **c** Irregular RPE elevation was detected (two-way arrows) on July 16, 2021 (7 months before vaccination (**b**)) and on November 12, 2021 (3 months before vaccination (**c**)). No significant change in the irregular RPE elevation was observed. RPE, retinal pigment epithelium; OCT, optical coherence tomography. RPE, retinal pigment epithelium.

day, we performed combined phacoemulsification with pars plana vitrectomy with gas (1.2 mL of 100% sulfur hexafluoride was injected following fluid-air exchange). During the surgery, approximately 0.2 mL (12.5 μg/0.05 mL) of subretinal injection of tissue plasminogen activator using the MedOne subretinal cannula (25 gauge/38 gauge; MedOne Surgical, Inc., Sarasota, FL, USA) attached to a tuberculin syringe via extension tubing was performed. No complication occurred during the surgery, and the patient was instructed to maintain the prone or left lateral position following the surgery. On February 28, 2022, 13 days after the surgery, decreased SMH was detected on the color fundus photography (shown in Fig. 3d) and the OCT image revealed SMH and SRF reduction (shown in Fig. 3e). Decimal BCVA remained 0.4. We performed two additional intravitreal injections of aflibercept one and 2 months following the surgery. His most recent visit to our hospital was on April 13, 2022. No deterioration of PCV was observed, and there was a tendency of SMH reduction; however, decimal BCVA remained 0.4.

Discussion/Conclusion

We report a case of perceived vision loss following the third BNT162b2 mRNA vaccine administration and rapid PCV progression with massive SMH within 2 weeks following the vaccination. Nevertheless, the lesion was stable for approximately 2 years. Although establishing the mechanism underlying vaccine-associated worsening of PCV in this study is challenging, considering the time between vaccination and the appearance of symptoms, the vaccination

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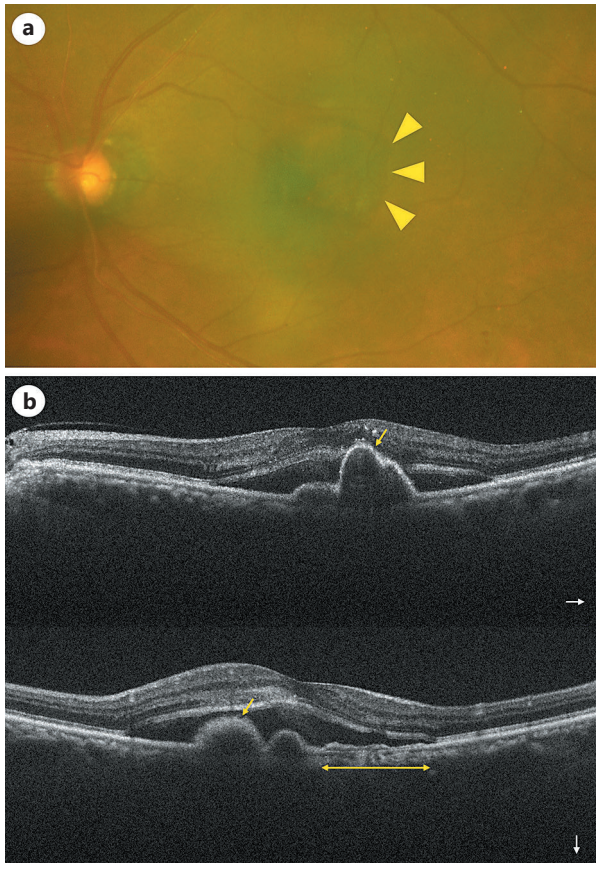

Fig. 2. Deterioration of PCV. **a** Fundus photograph taken 8 days following the third Pfizer-BioNTech (BNT162b2) vaccination (on February 9, 2022). SMH (arrowheads) associated with PCV was observed. **b** Cross-sectional OCT images show multilobular pigment epithelial detachment (yellow arrows), irregular RPE elevation (two-way arrow), and SRF. The white arrows indicate the OCT scan direction (top, horizontal: bottom, vertical). PCV, polypoidal choroidal vasculopathy; OCT, optical coherence tomography; RPE, retinal pigment epithelium.

may have triggered PCV deterioration. To the best of our knowledge, this is the first report of rapid progression of PCV following mRNA COVID-19 vaccination.

To date, several literatures have reported the ocular adverse effects following the COVID-19 vaccination [2–7]. In uveitis, the proposed mechanisms of inflammation may be induced by the adjuvants that are routinely used for enhancing the immunogenicity of the virus [8]. However, in this case, no ocular inflammatory response was observed in both the eyes.

Bolletta et al. [3] reported that an activation of quiescent CNV secondary to myopia in one eye following the BNT162b2 vaccine. The myopic CNV was never treated with intravitreal injections of anti-vascular endothelial growth factor agents. The time interval from the second vaccination to the onset of ocular symptoms was 1 day, which is the similar to this case.

Our case report demonstrated rapid deterioration following the third booster vaccination. The third booster immunization could have been an ultimate trigger contributing to the deterioration of the fragile retinal pigment epithelium, a pre-PCV lesion.

This single case report has a major limitation since establishing a causal relationship between the mRNA COVID-19 vaccination and rapid progression of PCV in this patient is challenging. Accumulation of further cases is warranted to elucidate the mechanism of PCV deterioration following mRNA COVID-19 vaccination.

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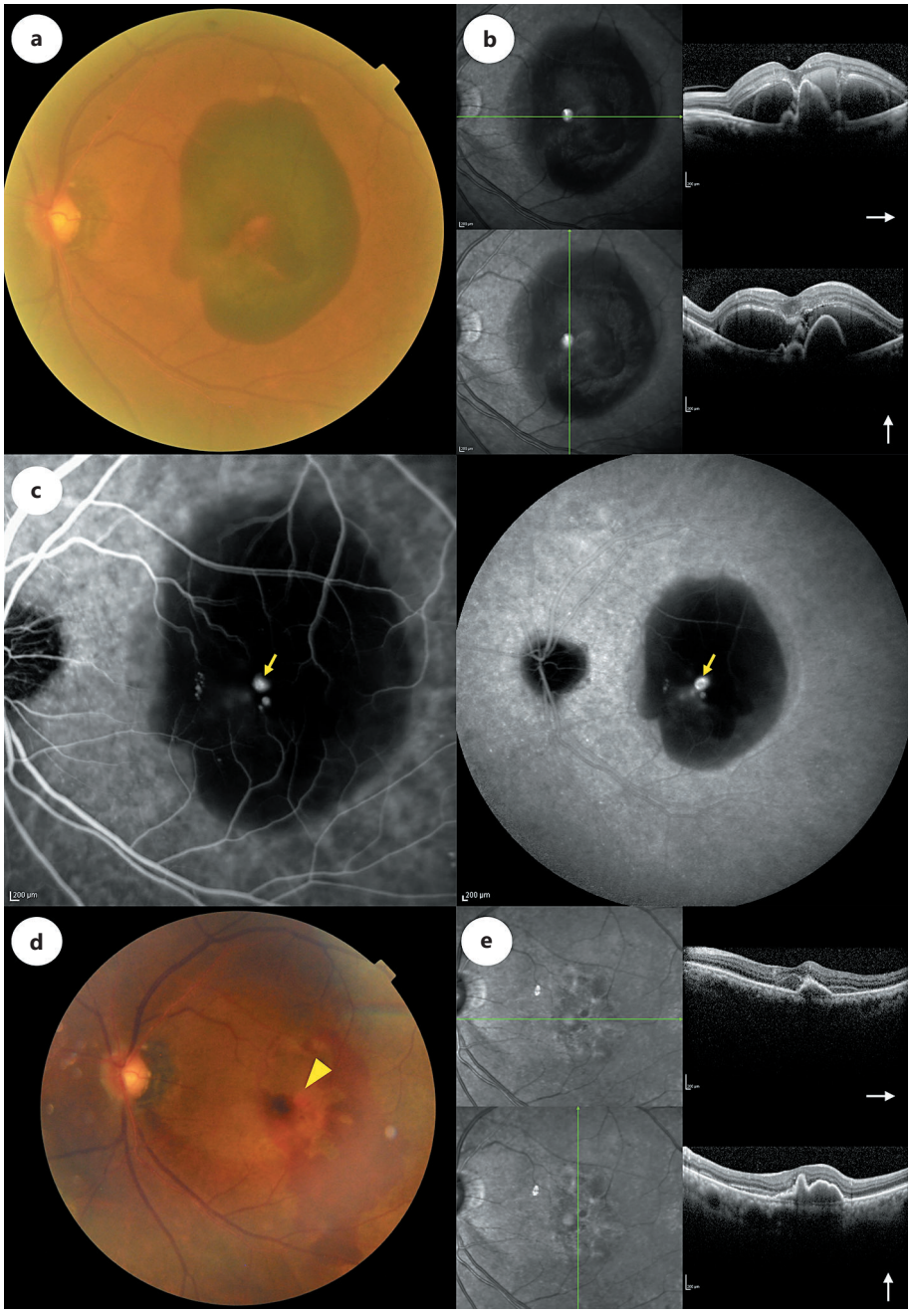

Fig. 3. Deteriorated PCV before and after treatments. **a** Fundus photograph taken 13 days following the third Pfizer-BioNTech (BNT162b2) vaccination (on February 14, 2022). Extensive SMH was observed. **b** Cross-sectional OCT images show multilobular pigment epithelial detachment, SMH, and SRF. The white arrows indicate the OCT scan direction (top, horizontal: bottom, vertical). **c** Mid- (left, 225 s) and late-phase (right, 21 min) ICGA images. The images present the polypoidal lesion (arrows). **d** Fundus photograph taken 13 days following the surgery (on February 28, 2022). Orange nodule (arrowhead) is consistent with the polypoidal lesion on the ICGA images. **e** Cross-sectional OCT images show decreased SMH and SRF. The white arrows indicate the OCT scan direction (top, horizontal: bottom, vertical). PCV, polypoidal choroidal vasculopathy; SMH, submacular hemorrhage; OCT, optical coherence tomography; SRF, subretinal fluid; ICGA, indocyanine green angiography.

Statement of Ethics

The Ethics Committee of Shinseikai Toyama Hospital waived the need for approval of this study that involved a retrospective review of medical records. This report adhered to the tenets of the Declaration of Helsinki 1964. Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Hirofumi Sasajima treated the patient. Hirofumi Sasajima and Rio Maeda collected the clinical data. Hirofumi Sasajima, Masahiro Zako, and Yoshiki Ueta analyzed the findings and provided critical suggestions. Hirofumi Sasajima contributed to the original draft preparation. Masahiro Zako reviewed and edited the manuscript. Hirofumi Sasajima, Masahiro Zako, Rio Maeda, and Yoshiki Ueta agreed to be accountable for all aspects of work. Hirofumi Sasajima, Masahiro Zako, Rio Maeda, and Yoshiki Ueta approved the final version of the manuscript for publication.

Data Availability Statement

All data analyzed in this study are included in this article. Further inquiries can be directed to the corresponding author.

References

1 Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. N Engl J Med. 2020 Dec;383:2603–15.
2 Rabinovitch T, Ben-Arie-Weintrob Y, Hareuveni-Blum T, Shaer B, Vishnevskia-Dai V, Shulman S, et al. Uveitis after the BNT162b2 mRNA vaccination against SARS-CoV-2 infection: a possible association. Retina. 2021 Dec 1; 41:2462–71.
3 Bolletta E, Iannetta D, Mastrofilippo V, Simone LD, Gozzi F, Croci S, et al. Uveitis and other ocular complications following COVID-19 vaccination. J Clin Med. 2021;10:5960.
4 Fowler N, Mendez Martinez NR, Pallares BV, Maldonado RS. Acute-onset central serous retinopathy after immunization with COVID-19 mRNA vaccine. Am J Ophthalmol Case Rep. 2021 Dec 19;23:101136.
5 Mambretti M, Huemer J, Torregrossa G, Ullrich M, Findl O, Casalino G. Acute macular neuroretinopathy following coronavirus disease 2019 vaccination. Ocul Immunol Inflamm. 2021 May 19;29(4):730–3.
6 Koong LR, Chee WK, Toh ZH, Ng XL, Agrawal R, Ho SL. Vogt-Koyanagi-Harada disease associated with COVID-19 mRNA vaccine. Ocul Immunol Inflamm. 2021 Aug 18;29(6):1212–5.
7 Goyal M, Murthy SI, Annum S. Bilateral multifocal choroiditis following COVID-19 vaccination. Ocul Immunol Inflamm. 2021 May 19;29(4):753–7.
8 Watad A, Quaresma M, Brown S, Cohen Tervaert JW, Rodríguez-Pint I, Cervera R, et al. Autoimmune/inflammatory syndrome induced by adjuvants (Shoenfeld's syndrome): an update. Lupus. 2017 May 19;26:675–81.

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