Case Report

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Branch retinal vein occlusion post severe acute respiratory syndrome coronavirus 2 vaccination

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Abstract:

In this article, we report two patients who experienced the first onset of branch retinal vein occlusion (BRVO) 3 days after the administration of the BNT162b2 (Pfizer–BioNTech) severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine. Case 1: A 50-year-old woman without any history of retinal disease developed vision loss in her right eye 3 days after receiving the first dose of the SARS-CoV-2 mRNA vaccine. Case 2: A 56-year-old woman without any history of retinal disease developed vision loss in her right eye 3 days after receiving the first dose of the SARS-CoV-2 mRNA vaccine. Case 1: Temporal superior BRVO and secondary macular edema (ME) were observed in the patient's right eye. Her best-corrected visual acuity (BCVA) was 20/25. Case 2: Temporal inferior BRVO and secondary ME were observed in the patient's right eye. Her BCVA was 13/20. Case 1: Three doses of intravitreal ranibizumab (IVR) were administered. Case 2: Three doses of IVR were administered. Case 1: ME resolved and BCVA improved to 20/20. Case 2: ME resolved and BCVA improved to 20/20. Both the cases showed a possible association between the SARS-CoV-2 vaccination and the first onset of BRVO.

Keywords:

Adverse reactions, branch retinal vein occlusion, coronavirus disease 2019, vaccination

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Introduction

An outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first detected in China at the end of 2019, where many patients suffered an acute respiratory syndrome due to infection with SARS-CoV-2.[1] The respiratory syndrome was given the name coronavirus disease 2019 (COVID-19).[2] Since its initial outbreak, SARS-CoV-2 has been rapidly spreading, therefore, to limit its further spread, vaccination campaigns have been ongoing worldwide.[3] Some of the most commonly reported postvaccination mild reactions include pain, redness, swelling around the injection site, fever, headache, myalgia, and fatigue.[3] On the other hand, severe yet rare reactions such as anaphylaxis, thrombosis, hemorrhage, and myocarditis have also been reported after vaccination.[4-7] Additional postvaccine adverse events affecting the eyes have also been reported, including keratoplasty rejection,[8,9] panuveitis,[10] abducens nerve palsy,[11] episcleritis,[12] anterior scleritis,[12] acute macular neuroretinopathy,[12] paracentral acute middle maculopathy,[12] eyelid localized purpuric and ecchymotic reactions,[13] and subretinal hemorrhage due to age-related macular disease.[14] Moreover, we reported previously two cases with exacerbation of branch retinal vein occlusion (BRVO), implicating a possible association with SARS-CoV-2 vaccination.[15] However, the association between SARS-CoV-2 vaccination and the first onset of retinal vascular occlusion disease remains unclear.

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In this article, we report two cases of individuals without any known history of retinal diseases who developed BRVO 3 days following SARS-CoV-2 vaccination with BNT162b2 (Pfizer–BioNTech).

Case Reports

Case 1

A 50-year-old woman with breast cancer treated with tamoxifen visited our hospital in October 2021 with vision loss in the right eye. She did not have diabetes and hyperlipidemia, which are mentioned as the risk factors for retinal vein occlusion (RVO), or any relevant cardiovascular medical history. She received her first dose of the SARS-CoV-2 mRNA vaccine BNT162b2 (Pfizer–BioNTech) 3 days before her visit. On admission, her blood pressure was 149/87 mmHg, best-corrected visual acuity (BCVA) was 20/25, and ultra-wide-field pseudo-color (UWPC) and optical coherence tomography (OCT) showed a flame-shaped hemorrhage around the temporal superior retinal vein and macular edema (ME) in her right eye [Figure 1a and b]. No avascular area was found on OCT angiography (OCTA). Vitreous cells were not found by fundus examination. With a diagnosis of BRVO and secondary ME, she received three doses of intravitreal ranibizumab (IVR), which resolved her ME [Figure 1c]. Her BCVA improved to 20/20, and no recurrence was detected during the 2-month follow-up.

Case 2

A 56-year-old woman visited our clinic in October 2021 with vision loss in the right eye. She did not have diabetes and hyperlipidemia, which are mentioned as the risk factors for RVO, or any relevant cardiovascular medical history. She received her first dose of the SARS-CoV-2 mRNA vaccine BNT162b2 (Pfizer–BioNTech) 3 days before her visit. On admission, her blood pressure was 102/65 mm Hg. BCVA in the right eye was 13/20. UWPC and OCT images showed a flame-shaped hemorrhage around the temporal inferior retinal vein and ME in the right eye [Figure 2a and b]. No avascular area was found on OCTA. Vitreous cells were not found by fundus examination. With a diagnosis of BRVO and secondary ME, she received three doses of IVR, which resolved her ME [Figure 2c]. Her BCVA had improved to 20/20. No recurrence was detected during the 2-month follow-up.

Discussion

In this article, we report two cases of BRVO development 3 days after SARS-CoV-2 vaccination.

Since early 2021, several published reports, including ours, have supported the risk of vascular disease that results from abnormal coagulation after the administration of COVID-19 vaccines. In this context, Pottegård *et al*.[5] reported that the rates of developing venous embolus, thrombocytopenia, abnormal coagulation, and other types of bleeding within 28 days after the administration of the adenovirus vector vaccine ChAdOx1-S (AstraZeneca plc) SARS-CoV-2 vaccination were significantly higher than the expected rates based on age- and sex-specific incidence rates among the general population. Furthermore, See *et al*.[6] reported 12 cases of cerebral venous sinus thrombosis with thrombocytopenia within 15 days after the administration of the adenovirus vector vaccine, Ad26.COV2.S (Johnson & Johnson K. K.) SARS-CoV-2 vaccination. The authors considered the pathogenesis of venous thrombosis to be similar to that of autoimmune heparin-induced thrombocytopenia. In addition, Smadja *et al*.[16] reported that venous thromboembolism disorders such as lower-limb thrombosis and pulmonary embolism could develop after the administration of any of the following COVID-19 vaccines: BNT162b2, mRNA-1273, and AZD1222. In fact, they suggested that although the mechanisms of abnormal coagulation might be different between ChAdOx1-S and Ad26.COV2.S, abnormal coagulation could occur after the administration of BNT162b2 and other SARS-CoV-2 mRNA vaccines. Similarly, we recently reported two

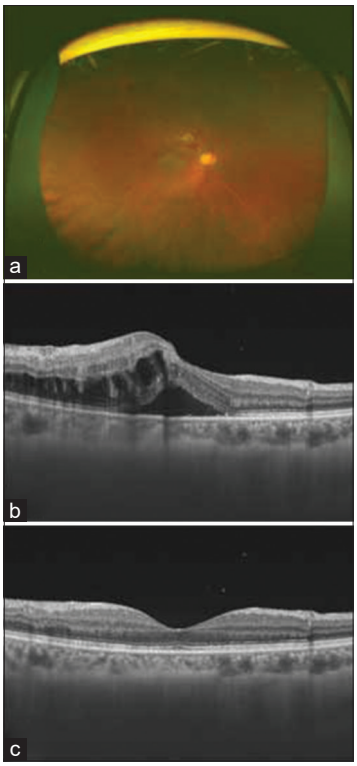

Figure 1: UWPC and sagittal OCT images of the right eye in case 1. (a and b) UWPC and sagittal OCT images at initial presentation. Temporal superior branch retinal vein occlusion (a) and ME in the fovea (b). Sagittal OCT images after 3 times of intravitreal ranibizumab treatment 3 times. ME disappeared (c). UWPC = Ultra-wide-field pseudo-color, OCT = Optical coherence tomography, ME = Macular edema

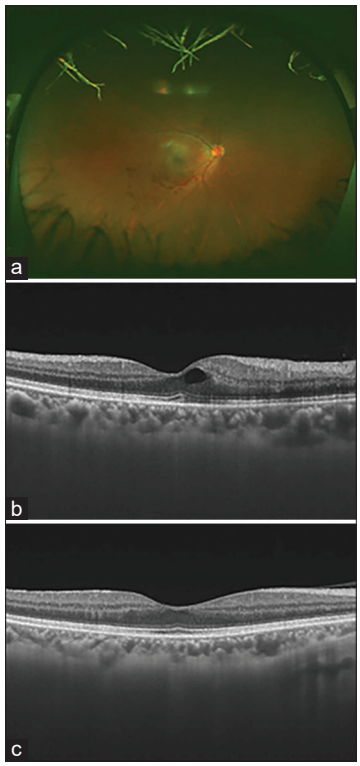

Figure 2: UWPC and sagittal OCT images of the right eye of case 2 patient. (a and b) UWPC and sagittal OCT images at initial presentation. Temporal inferior branch retinal vein occlusion (a) and ME in the fovea (b) were shown. Sagittal OCT images after 3 times of intravitreal ranibizumab. ME disappeared (c). UWPC = Ultra-wide-field pseudo-color, OCT = Optical coherence tomography, ME = Macular edema

cases with a history of BRVO, who experienced a recurrence and exacerbation of BRVO after receiving the SARS-CoV-2 vaccination, suggesting that SARS-CoV-2 vaccination has likely triggered the recurrence of BRVO, taking into consideration the inflammatory response that occurred in the process of the acquisition of immunity and potential hypercoagulability after SARS-CoV-2 vaccination.[15] In parallel, Lee and Huang[17] hypothesized that antibodies against proteins generated by translating the SARS-CoV-2 mRNA vaccine and mRNA caused cross-reactions with tissues such as uvea, Schwann cells, and vascular endothelium, which resulted in inflammation and microvascular disorders. Similar case studies have shown ophthalmic microvascular disorders possibly induced by the COVID-19 vaccine. Mazzatenta *et al*.[13] reported three cases of purpuric lesions on the eyelids after receiving SARS-CoV-2 mRNA vaccination. Although many of these adverse events were inflammation flare-ups, such problems could be considered common postvaccine complications. Therefore, it is highly possible that microvascular disorders induced by the SARS-CoV-2 mRNA vaccine may also occur in the retinal vein.

In this report, case 1 was treated with tamoxifen, a selective estrogen receptor modulator, and a drug intended for chemotherapy to treat estrogen-dependent breast cancer. Treatment with tamoxifen has been associated with an increase in the relative risk of systemic deep venous thrombosis and secondary pulmonary embolism in several studies,[18,19] suggesting it to be the reason for the hypercoagulable state of the patient. Several ophthalmic studies have also indicated an association between tamoxifen and the development of BRVO and superior ophthalmic vein thrombosis.[20-22] Systemic vascular diseases, including hypertension, are strongly associated with BRVO.[23] These reports suggested that the tendency to develop venous thrombosis with tamoxifen could affect systemic and ophthalmic diseases. Nevertheless, SARS-CoV-2 vaccination may trigger an inflammatory response, microvascular disorders, and hypercoagulability, resulting in the development of BRVO.

In addition, case 2 had no history of cardiovascular disease, hypertension, diabetes mellitus, or any other condition that might have led to the development of BRVO. Endo *et al*.[24] reported the case of a 52-year-old man who developed BRVO 15 days after receiving SARS-CoV-2 vaccination, knowing that no recent condition related to developing RVO was present. In a similar case series study, Park *et al*.[14] also reported 11 cases of subretinal hemorrhage and RVO after receiving SARS-CoV-2 vaccination. This report suggests that RVO onset after SARS-CoV-2 vaccination could occur with or without a related medical history and across any type of vaccine formulation. In this respect, and similar to our case, it is likely that SARS-CoV-2 vaccination generated an inflammatory response and abnormal coagulation, which might have triggered BRVO development.

Therefore, the onset of BRVO in the two case studies in the present report may also be related to SARS-CoV-2 vaccination.

Conclusion

We report two cases of first-onset BRVO immediately after SARS-CoV-2 vaccination. Health-care professionals promoting SARS-CoV-2 vaccination should be aware that vaccination may increase the risks of the first onset of BRVO and exacerbation in patients with a history of BRVO. More studies are needed to determine whether BRVO leading to ME is a potential risk factor for this vaccine.

Acknowledgments

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Data availability statement

All data relevant to the study are included in this article.

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Nil.

Conflicts of interest

The author declares that there are no conflicts of interests of this paper.

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