Development of Branch Retinal Vein Occlusion Following COVID-19 Vaccination and Subsequent SARS-CoV-2 Infection While Taking Oral Contraceptives

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Research Article

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Abstract

Objectives

Oral contraceptive use, vaccination for coronavirus disease 2019 (COVID-19), and the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection are all risk factors for venous thromboembolism (VTE). Although, in general, branch retinal vein occlusion (BRVO) develops during the mid-60s in general, we present a case of BRVO caused by the abovementioned risk factors in a young woman. To the best of our knowledge, this is the first report about BRVO associated with oral contraceptives, COVID-19 vaccination, and SARS-CoV-2.

Case presentation:

A 21-year-old woman was referred to us after experiencing loss of visual acuity in her right eye from 10 days ago. She had been using oral contraceptives for 2 years for paramenia before noticing her ophthalmological symptoms. Despite having received two doses of the mRNA COVID-19 vaccine, she had contracted COVID-19 with fever, sore throat, cough, low back pain, and general malaise about 40 days before the initial visit. However, only the cough persisted for a month. The right eye showed BRVO with macular edema (ME). She did not smoke or have diabetes mellitus or systemic hypertension. The result of blood test was normal, including the cardiolipin antibody IgG. She was treated with an intravitreal aflibercept injection immediately. The right fundus showed rapid improvement in the resolution of ME.

Conclusions

The combination of oral contraceptive use, COVID-19 vaccination, and subsequent SARS-CoV-2 infection could accelerate VTE, thereby leading to BRVO. Given that cases of COVID-19 have increased globally, patients with RVO who use oral contraceptives are likely to be encountered more frequently.

Background

The coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the latest pandemic, which lasted approximately 3 years in Japan. One of the special characteristics of COVID-19 is the propensity to cause venous thromboembolism (VTE) [1], which could lead to fetal complications. In the ophthalmological field, COVID-19 has been reported to cause retinal vein occlusion (RVO) [2–4].

Branch RVO (BRVO) is a major retinal vascular disease and occurs following venous thrombosis at the arteriovenous crossing points. Arteriosclerosis accompanied by hypertension is one of the risk factors for BRVO. Therefore, it predominately affects older people.
BRVO impairs the blood–retinal barrier, and causes macular edema (ME). The photoreceptor cell apoptosis caused by chronic ME is responsible for the reduced vision in patients with BRVO. Therefore, a missing treatment window leads to irreversible loss of vision [5, 6]. Antivascular endothelial growth factor agents are the first-line treatment for ME secondary to BRVO [7].

Over 100 million women worldwide use common contraceptive methods, including intrauterine devices, combined estrogen and progestin oral contraceptives, and progestin -only preparations (oral contraceptives, implants, or injections) [8]. Oral contraceptives contain estrogen, and they increase the risk of VTE because of the activation of blood coagulation. The incidence of VTE caused by oral contraceptives is approximately twice as high as that in the normal population [9]. Generally, the age susceptible to RVO related to oral contraceptives is quite younger than that of typical RVO. As RVO related to oral contraceptives are rare, its clinical features remain unclear compared with typical RVO, such as visual prognosis.

Herein, we present the case of a 21-year-old woman taking oral contraceptives who developed BRVO with ME following COVID-19. To the best of our knowledge, this is the first case report suggesting that the combination of oral contraceptive intake and diagnosis of COVID-19 might be a risk factor for the development of BRVO.

Case Presentation

A 21-year-old woman was diagnosed with polycystic ovary syndrome accompanied by oligomenorrhea at the age of 19 years. Since then, she had been taking oral contraceptives for the improvement of oligomenorrhea. She did not have diabetes, or systemic hypertension or a smoking habit. Furthermore, she had no family history of VTE. Her height, body weight, and body mass index were 162 cm, 52 kg, and 19.8, respectively. Although she had received mRNA COVID-19 vaccine twice, she experienced fever, sore throat, cough, low back pain and general malaise and visited the clinic. Her saliva sample showed a positive reaction to SARS-CoV-2 in the polymerase chain reaction method. Her cough had continued for a month, but the symptoms improved without post-COVID-19 sequelae, such as dysgeusia and dysosmia. Approximately 40 days later, she presented with a decrease in right eye vision following recovery from COVID-19. She was diagnosed with ME secondary to BRVO at the previous eye clinic. On her initial visit to our hospital, the best-corrected visual acuity (BCVA) values were 0.4 in the right and 1.2 in the left eye. The intraocular pressure was normal in both eyes. Slit-lamp biomicroscopy did not detect inflammation in both eyes. Fundus examination revealed retinal hemorrhage in the superior-temporal quadrant of the retina in the right eye (Fig. 1a). Optical coherence tomography demonstrated ME in the right eye (Fig. 1b). Blood test results were within normal limits, including cardiolipin antibody IgG.

The clinical diagnosis was ME secondary to BRVO after contracting COVID-19. We contacted her gynecologist about the eye condition and oral contraceptives for the improvement of oligomenorrhea were changed to progestational hormone agent (dydrogesterone) only. The patient was treated with an
intravitreal aibercept (Eylea®; Regeneron, Tarrytown, NY, USA) injection. The ME disappeared after 1 month (Fig. 1c) and the BCVA improved to 1.2 in the right eye.

Informed consent was obtained from the patient, and approval from the institutional review board of the Dokkyo Medical University Saitama Medical Center was obtained.

Discussion And Conclusions

The estimated incidence of combined oral contraceptive-related ocular complications is 1 in 230 000, including dry eye symptoms, corneal edema, lens opacities and retinal neuro-ophthalmologic or vascular complications [8]. Sinawat et al. analyzed patients with RVO aged < 50 years and reported that three of 70 patients with central RVO had taken oral contraceptives for 5–6 years and one of 30 patients with BRVO had oral contraceptives for 10 years [10]. As the susceptible age of RVO is the middle of the 60s, the current case is very rare from the standpoint of onset age. According to a 2013 survey regarding VTE, the risk of women who take oral contraceptives is twice as high as that of women not taking oral contraceptives [9]. Lidegaard et al. reported that the VTE risk related to oral contraceptives is 1.0 for women aged 15–19 years, 1.32 for 20–24 years, 1.99 for 25–29 years, 2.91 for 30–34 years, 4.01 for 35–39 years, 5.29 for 40–44 years, and 6.58 for 45–49 years [11]. Therefore, the VTE risk increases with increasing age [11]. Since our patient was 21 years old, the risk for RVO appeared to be low.

Several reports have described that BRVO developed after acquiring SARS-CoV-2 infection [2, 4]. SARS-CoV-2 infection is a high-risk factor of VTE [1]. Pur et al. reported a case of BRVO after mRNA COVID-19 vaccination [12]. They postulated that the vaccine evoked an immunological response, triggering VTE in a healthy patient [12]. Thus, the combination of oral contraceptive intake, SARS-CoV-2 infection, and COVID-19 vaccination could be a risk for the development of RVO.

Independently, oral contraceptive intake, SARS-CoV-2 infection, and COVID-19 vaccination are risk factors of VTE. However, their coexistence may increase the risk of VTE resulting in RVO in the eye. Thus, physicians should pay attention to vision loss as RVO may occur in patients with COVID-19 who are taking oral contraceptives.

Abbreviations


Declarations

Ethics approval and consent to participate

An oral informed consent to participate was obtained from the patient. This study complied with the tenets of the Declaration of Helsinki. IRB approval of the Dokkyo Medical University Saitama Medical
Center was obtained.

**Consent for publication**

An oral informed consent to publish was obtained from the patient.

**Availability of data and materials**

Not applicable.

**Competing interests**

The authors declare that they have no competing interests.

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**Authors’ contributions**

TM wrote the initial manuscript. MS increased resolution of the retinal photo and optical coherence tomography images. SM, SI and KK supervised the manuscript.

YH advised the manuscript from Obstetrics and Gynecology field. All authors read and approved the final manuscript.

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**References**


Figures
Figure 1

a: A retinal hemorrhage is seen in the flow region of the superotemporal vein in the right eye. b: Optical coherence tomography scans suggest the presence of macular edema in the right eye. The white arrows indicate the scanning direction. c: Optical coherence tomography scans show improved macular edema 1 month after intravitreal aflibercept injection in the right eye.