

Case Report

Progressive Central Artery Occlusion, Ophthalmic Artery Occlusion, and Hemispheric Intracranial Thrombosis after COVID-19 mRNA Vaccine Application: Case Report

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Keywords

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Abstract

Thromboembolic events as a result of COVID-19 mRNA vaccination are a rare, though life-threatening complication. In this case report, we describe a 40-year-old female patient who developed central retinal artery and ophthalmic artery occlusion progressing to intracranial thrombosis 3 weeks after vaccination with the Pfizer-BioNTech COVID-19 vaccine. Initially, she presented with progressive acute and painless unilateral vision loss in her left eye. Dilated funduscopy of left eye showed macular whitening with sparing of the area of cilioretinal artery distribution. Labs revealed a normal erythrocyte sedimentation rate, C-reactive protein, and platelet count. Computerized tomography angiography of the head and neck showed an occlusion of the entire left cervical internal carotid artery and occlusion of the origin of the left external carotid artery. Despite treatment with heparin, her vision declined to no light perception. Ten days later, the patient presented with right peripheral vision loss and was found to have a new left posterior cerebral artery/posterior inferior cerebellar artery stroke. Seventeen days later, she presented to the hospital with nausea and vertigo and was found to have a subacute infarction in the left parietal lobe corresponding to left anterior communicating artery/middle cerebral artery watershed territory. Hypercoagulable disorders, vasculitis, cardiac arrhythmias, and intraventricular thrombi were excluded. Fundus fluorescein angiography

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confirmed central retinal artery occlusion and ophthalmic artery occlusion with impressive retina and choroid changes in fluorescein angiography patterns. This complication of mRNA COVID-19 vaccination has not been previously described in the literature and should be considered even weeks after initial presentation.

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Introduction

COVID-19 is an infectious disease caused by SARS-CoV-2 which was first reported in Wuhan, China. Its high mortality and morbidity are resulted from systemic complications, including acute respiratory distress syndrome, cardiac and renal complications, and multiple organ failure [1]. Additionally, ischemic strokes, deep vein thrombosis, and pulmonary embolism (PE) have been reported in COVID-19, which suggest hypercoagulability state in patients with COVID-19 infection [2, 3].

Vaccination against SARS-CoV-2 has played an important role in controlling the COVID-19 pandemic, and it is used extensively in all around the world; however, serious neurologic complications, although unusual, including thromboembolic events have been reported after vaccination [4]. Ischemic stroke after Oxford-AstraZeneca [3], isolated symptomatic carotid occlusion secondary to thrombosis and thrombocytopenia syndrome after Janssen/Johnson & Johnson [5], and malignant cerebral infarction with cerebral venous thrombosis [6] have been recently described in vaccinated patients.

In ophthalmology, bilateral superior ophthalmic vein thrombosis, ischemic stroke, and immune thrombocytopenia after ChAdOx1 nCoV-19 vaccination [7] and central retinal artery occlusion following Oxford-AstraZeneca vaccine administration [8] have been described; however, central retinal artery and ophthalmic artery occlusion with both retina and choroid involvement has not been reported. In this case report, we report a patient who developed unilateral progressive central retinal artery and ophthalmic artery occlusion and hemispheric intracranial thrombosis.

Case Report

A 40-year-old African American female with past medical history of hypertension, tobacco use, and Graves' disease presented to the emergency room with acute painless left eye vision loss for 1 day and 3 weeks after receiving the first dose of the Pfizer-BioNTech (BNT162b2 mRNA) COVID-19 vaccine. Her grandmother has a history of recurrent blood clots on warfarin, and her sister has dermatomyositis with PE. The patient was tested for COVID-19 before and after the vaccination multiple times, and all the results were negative. The patient has a BMI 21, which is within the normal range. She has no history of sleep apnea or dehydration. Three weeks after vaccination, her cholesterol level, TG, HDL were normal; LDL was 125 mg/dL (optimal less than 100). Ten days before her vaccination, in the dental office, her systolic BP was 170 mm Hg and then she was on losartan. She has no history of drug abuse. Patient reported she has smoked 1 pack per day for 15 years. Best-corrected visual acuity was 20/20 and 20/40 in the right and left eyes, respectively. Relative afferent pupillary defect was positive in her left eye. Intraocular pressure was normal in both eyes. Anterior segment examination was normal in both eyes. Dilated fundus examination was normal in the right eye. However, in the left eye, it showed macular whitening with sparing of the area of cilioretinal artery distribution. Labs revealed a



Fig. 1. CTA head and neck with contrast. Left internal and external carotid occlusion. Vessel cutoff notated with arrow.

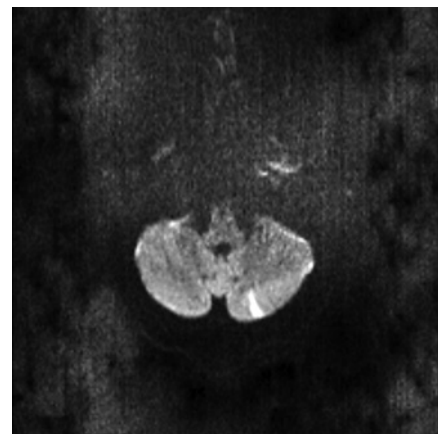


Fig. 2. MRI diffusion-weighted imaging showing left cerebellar ischemic stroke in the posterior inferior cerebellar artery territory.

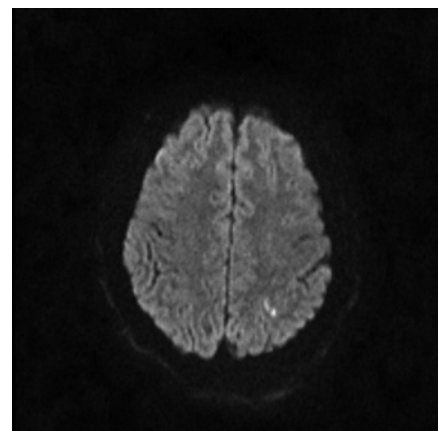


Fig. 3. MRI diffusion-weighted image with high cortical left ACA/MCA watershed infarction.

normal erythrocyte sedimentation rate, C-reactive protein, and platelet count. But before her vaccination, she did have elevated hemoglobin (Hgb) of 18.3 g/dL (normal 12–16 g/dL) and a hematocrit (Hct) level of 52.3% (normal 35–45%). Her D-dimer was 0.5 (normal <0.5 µg/mL), and there was no platelet factor 4 testing.

Computerized tomography angiography of the head and neck showed an occlusion of the entire left cervical internal carotid artery and occlusion of the origin of the left external carotid

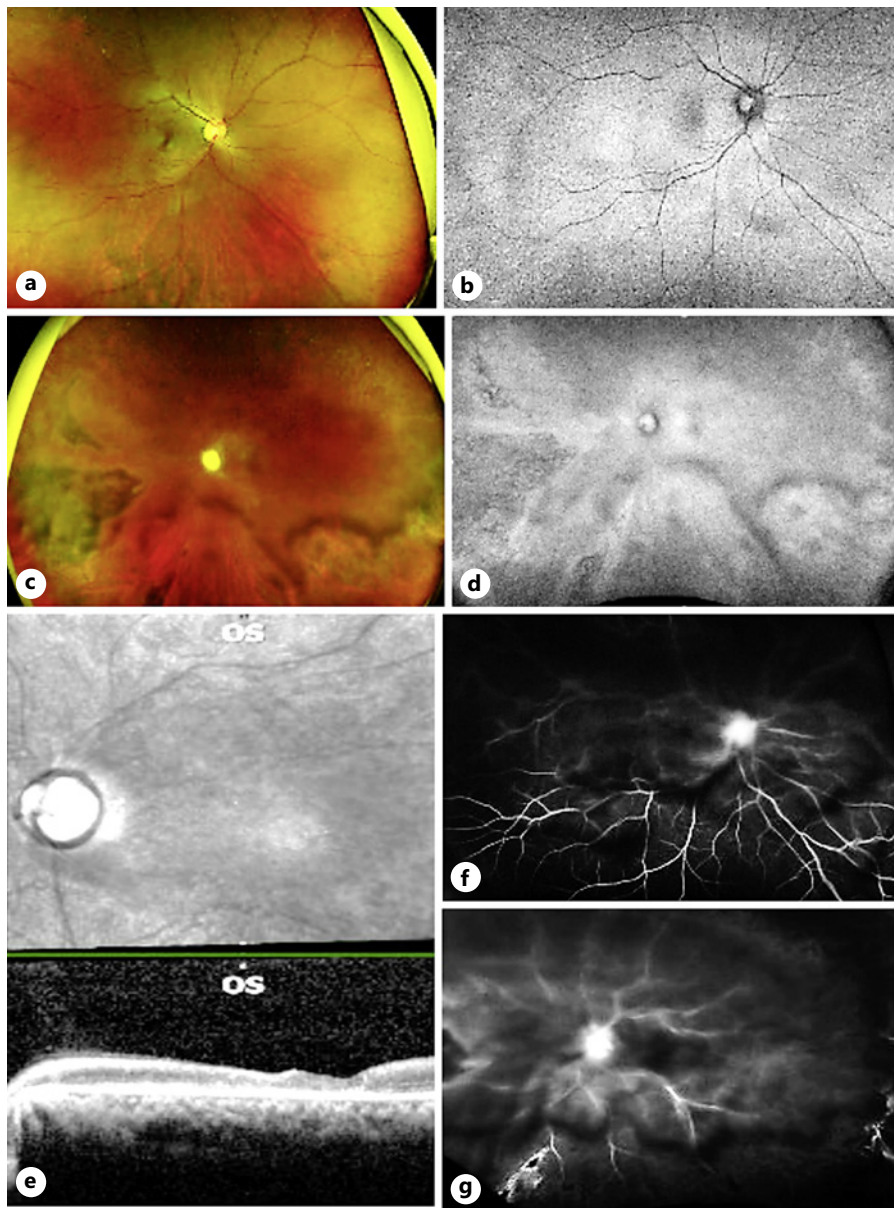


Fig. 4. **a** Multicolor fundus photography of the right eye. **b** Fundus autofluorescence of the right eye. **c** Multicolor fundus photography of the left eye 1 month after the first presentation shows optic nerve atrophy, impressive arterial narrowing, atrophic retina, and extensive retinal pigment epithelium (RPE) and choroid changes, especially inferiorly. **d** Fundus autofluorescence of the left eye 1 month after the first presentation depicts extensive hypo- and hyper-autofluorescence changes 1 month after the first presentation. **e** Optical coherence tomography image of the left eye shows diffused thinning of both inner and outer retinal layers. Fluorescein angiography and ICGA of the left eye 1 month after the first presentation show impressive arterial narrowing with retina hypoperfusion (**f**) and hypoperfusion of choroid (**g**). ICGA, indocyanine green angiography.

artery (Fig. 1). There was a small amount of adherent thrombus within the distal aortic arch and left subclavian artery origin. Despite treatment with heparin, her vision declined to no light perception. Ten days later, the patient presented with right peripheral vision loss and was found to have a new left posterior cerebral artery/posterior inferior cerebellar artery stroke (Fig. 2). Seventeen days later, she again presented to the hospital with nausea and

vertigo and was found to have a subacute infarction in the left parietal lobe corresponding to left anterior communicating artery/middle cerebral artery watershed territory (Fig. 3). In addition to her arterial thromboses, she also was noted to have a distal left internal jugular vein occlusion. Extensive workup revealed a Hgb of 21.8/Hct of 62.8 on admission, suggesting polycythemia vera. Other hypercoagulable labs, including factor V Leiden, antiphospholipid syndrome, lupus anticoagulant (LA), antithrombin III, and protein C/S deficiency, were negative. Hgb electrophoresis showed 97.3 Hgb A and 2.7 Hgb A2. The erythropoietin level was low. She was treated with hydroxyurea and serial phlebotomy; however, JAK2 mutation resulted negative. Other blood tests showed that ANA IgG was detected <1:80 and RF was negative. The neurologic workup did not reveal any other causes for stroke including arrhythmia, atrial fibrillation, cardiac intraventricular thrombus (on TTE and TEE), patent foramen ovale, or signs of atherosclerosis of the intracranial vessels. The workup was also negative for vasculitis based on CTA head/neck. She was continued on aspirin 81 mg daily and fondaparinux. Six weeks after her initial presentation at the emergency room, she presented to our eye clinic for follow-up when the exam showed diffused wedge-shaped pigmentation, optic disc pallor, and significant attenuation of retinal vessels in the left eye. Her vision was still no light perception. Fundus fluorescein angiography, indocyanine green angiography (ICGA), and macular optical coherence tomography were obtained and confirmed central retinal artery and ophthalmic artery occlusion with atrophic retina (Fig. 4).

Discussion

The patient has a genetic predisposition for infarcts because her grandmother has a history of recurrent blood clots on warfarin, and her sister has dermatomyositis with PE. The patient also had elevated Hgb, Hct, and D-dimer levels. It is possible that the vaccine is a trigger for a hidden disorder and not the direct cause of her thromboembolic events.

It is hypothesized that acute ischemic stroke secondary to SARS-CoV-2 infection is caused by hypoxemia and excessive secretion of inflammatory cytokines with prothrombic/procoagulant effects [9]. Additionally, inflammation itself plays an important role in cardiovascular disease due to acceleration of atherosclerosis process and atherosclerotic plaque instability [9].

Various types of thrombotic syndromes have been reported after the use of the Oxford-AstraZeneca COVID-19 vaccine [4, 6]. They were first described in April 2021 and were named vaccine-induced thrombotic thrombocytopenia (VITT) [10]. These syndromes include cerebral venous sinus thrombosis, limb ischemia, pulmonary artery thrombosis, and splanchnic vein thrombosis [11]. The mechanism of these thrombotic syndromes is similar to heparin-induced thrombosis and thrombocytopenia with producing antibodies against platelet factor 4. VITT has been also reported with CoronaVac [11] and Janssen/Johnson & Johnson [12] COVID-19 vaccines.

Jampol et al. [13] described the abnormalities in the retina after COVID-19 infection and COVID-19 vaccination. They reported an unpublished case with remote branch retinal artery occlusion and acute macular neuroretinopathy after Johnson & Johnson/Janssen COVID-19 vaccination. They hypothesized various immunity mechanisms and side-effect profiles among different types of COVID-19 vaccines. They also discussed SARS-CoV-2 S immunogen in the AstraZeneca COVID-19 vaccine as an important factor to induce a proinflammatory/procoagulant response and damage to endothelial cells [13].

Since none of the COVID-19 vaccines contain the intact virus, the mechanisms of ocular involvement tend to be immunologic rather than infectious, and it is closely related with the components of the vaccines. Molecular mimicry theory can also contribute in the pathogenesis of retinal pathologies [13].

Abdin et al. [8] reported a case of central retinal vein occlusion after vector-based AstraZeneca COVID-19 vaccine administration. Similar to the study by Jampol et al. [13], they hypothesized activation of a prothrombotic vascular endothelial microenvironment and increased hypercoagulability as mechanisms for developing central retinal artery occlusion in their patient [8]. It is important to note that the median time period between vaccination and arterial thrombotic events is similar in various types of vaccines (2 days); however [14], the range varies between COVID-19 vaccines. The range is between 0 and 52 days for BioNTech-Pfizer, between 0 and 63 days for Moderna, and between 0 and 38 days for AstraZeneca [14].

To the best of our knowledge, this patient is the first reported case with ophthalmic artery occlusion after mRNA COVID-19 vaccination (BioNTech-Pfizer) in the literature. She also had a unique course of central retinal artery occlusion with cilioretinal artery sparing, which progressed to ophthalmic artery occlusion, and eventually hemispheric intracranial thrombosis. The interval between vaccination and thrombotic event was also longer than previously reported in the study by Abdin et al. [8], which may be explained by less immunogenicity of the mRNA COVID-19 vaccine; however, this hypothesis should be investigated further in more potent studies. We believe that our patient had VITT despite her normal platelet count (near the lower limit of normal range) since it dropped from an average of 2.7×10^5 prior to vaccine injection to an average of 1.6×10^5 after vaccine injection. This is a 40% decrease in platelet count with a borderline increase in D-dimer. Given this explanation in patients with thrombosis syndrome after COVID-19 vaccination, a significant drop in the platelet count after vaccination should be considered seriously, especially in the early course of a thrombotic event.

It is important to note that despite the low incidence of thromboembolic events, COVID-19 vaccination is strongly recommended due to its efficacy in preventing the infection, reducing the rate of hospitalization, and decreasing mortality and morbidity. The strengths of our case report are that a thorough workup including laboratory and multiple imaging tests supported our diagnosis. The limitations associated with this case report include that the patient has a family history of development of blood clots and she had high blood pressure.

Conclusion

Progressive central retinal artery occlusion, ophthalmic artery occlusion, and hemispheric intracranial thrombosis may be rare thrombotic events and complications triggered by COVID-19 mRNA (BioNTech-Pfizer) vaccination. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see www.karger.com/doi/10.1159/000529770).

Statement of Ethics

This study was performed in accordance with the Declaration of Helsinki and was compliant with the Health Insurance Portability and Accountability Act. Information revealing the subject's identity was avoided. This study protocol was reviewed, and the need for approval was waived by the Ethics Committee of the University of Florida. Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

J.C., C.P., and E.D.S. participated in data gathering, data analysis, writing the draft, and final revision of the manuscript. B.B. participated in data gathering, data analysis, writing the draft, final revision of the manuscript, and neurologic image interpretation. A.M. participated in data gathering, data analysis, writing the draft, final revision of the manuscript, fluorescein angiography interpretation, and indocyanine green angiography interpretation.

Data Availability Statement

All available data were included in the manuscript.

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