

Unilateral Acute Central Serous Chorioretinopathy with Inactivated Coronavirus Disease 2019 Vaccination: A Case Report and Review of Literature

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Abstract

Purpose: To report unilateral acute-onset central serous chorioretinopathy (CSC) following vaccination with inactivated coronavirus disease 2019 (COVID-19) vaccine in a healthy patient.

Methods: Case report and review of literature.

Results: A 39-year-old male was referred with sudden-onset, painless, unilateral blurred vision in the right eye. His first dose of the Sinopharm vaccine was injected 2 days before. A complete ocular examination revealed central subretinal fluid (SRF) accumulation in favor of CSC in the right eye. Systemic workup disclosed no previous COVID-19 infection or any systemic involvement. After 3 weeks, SRF decreased remarkably without treatment.

Conclusions: It is proposed that CSC development can be an ocular adverse effect of COVID-19 vaccination, although it is infrequent. Ophthalmologists should be aware of the possible association between COVID-19 vaccination and ocular adverse effects, but vaccination is the best effectual measure against COVID-19.

Keywords: Central serous chorioretinopathy, Coronavirus disease 2019, Sinopharm, Vaccination

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INTRODUCTION

Coronavirus disease 2019 (COVID-19) has several ophthalmic manifestations. Early reports were focused on conjunctival and ocular surface presentations. In contrast, reports of different retinochoroidal presentations are ongoing.^{1,2} Besides the preliminary reports on the presence of the virus in the ocular surface and tear film, severe acute respiratory syndrome coronavirus 2 also was found in the retina.³⁻⁶ On the other hand, retinal involvements were numerous as cotton wool spots, retinal hemorrhages, dilated and tortuous vessels, decreased retinal microvasculature, ischemic retinal involvements,

pachychoroid spectrum presentations, chorioretinitis, and optic nerve head involvement.⁷⁻¹³ Retinochoroidal involvement in COVID-19 is possible regarding angiotensin-converting enzyme 2 receptors on several kinds of ocular tissues, including choroid and retina vessels endothelial cells, as well as astrocytes and Müller cells.¹⁴

Ocular manifestations may be associated with direct effects of the virus, immune-mediated reactions, activation of the coagulation pathway, patient comorbidities, and adverse effects of drugs used to manage the disease.¹⁵ Some of

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these mechanisms may be activated with the immunization procedure during vaccination. Manufacturers of vaccines must report possible complications, but some divulge in postmarketing. However, as the most ocular severe adverse effects of vaccination are reported postmarketing, those are rare. It is essential to report them and establish the causality over coincidence; time sequence, biological credibility, and agreement of observations may be tagged with information regarding dose–response relationships to evidence the causality. Nevertheless, these are usually limited in the case of vaccination, especially COVID-19 vaccines. All vaccines' most common ocular adverse effects have been reported as eyelid and conjunctiva reactions, optic neuritis, uveitis, and various retinal inflammatory lesions.¹⁶

Central serous chorioretinopathy (CSC) is a relatively common cause of visual deterioration affecting young men more frequently. It is mainly associated with stress, Type-A personality traits, glucocorticoid use, and catecholamines.¹⁷ Pachychoroid spectrum findings, including CSC, were previously presented in COVID-19. Moreover, the development of CSC has been reported after vaccination for influenza, yellow fever, anthrax, and smallpox.^{18–21} Recently, CSC formation by COVID-19 mRNA vaccine has been reported.²² Herein, we present the development of CSC after the first dose of Sinopharm (Beijing Institute of Biological Products, Sinopharm, Beijing, China) vaccination, an inactivated whole-virus vaccine.²³ Furthermore, we review previously reported ocular complications of COVID-19 vaccines.

CASE REPORT

A 39-year-old otherwise healthy male was referred with a complaint of sudden, painless, blurred vision in the right eye. He had no past medical history and no history of COVID-19 infection. He reported receiving the first dose of Sinopharm COVID-19 vaccine 2 days before developing blurred vision.

On ophthalmic examinations, his best-corrected visual acuity (BCVA) was 20/20 in both eyes, with a +0.5 diopter (D) sphere in the right eye and a –0.5 sphere in the left eye. Anterior segment evaluation revealed normal limit findings. In fundus examination, the right eye showed an absence of the foveal reflex and serous elevation of the retina, especially in the macula, and the left eye was normal [Figure 1a and b]. Enhanced depth imaging optical coherence tomography (EDI-OCT) showed a dome-shaped serous detachment of the macula with significant subretinal fluid (SRF) and pigment epithelial detachments (PEDs) in the superior macula of the right eye [Figure 2a and c]. The left eye EDI-OCT was normal, but some pachyvessels were evident [Figure 2b]. Fundus autofluorescence revealed the absence of normal central hypoautofluorescence in the right eye. There was a hypoautofluorescence area superior to the macula. No other foci of autofluorescence alteration due to previous CSC episodes were found in both eyes [Figure 1c and d]. Fluorescein angiography was normal. In optical coherence

tomography angiography, no abnormal retinal vascular lesion or abnormal flow in choriocapillaris was found.

The right eye acute-onset CSC diagnosis was made based on examination and imaging. The patient was questioned about CSC risk factors and drug history. He had not consumed any drug in the last 3 months, and his past medical history was unremarkable. Except for his sex and age, there was nothing to consider as a modifiable risk factor for CSC development. He declined to receive any kind of treatment and was observed. After 1 week, the right eye vision dropped to 20/40, and the SRF increased. After 4 weeks without treatment, his vision was 20/40 with no further decrease, and SRF dramatically decreased [Figure 2d]. The patient did not come for further follow-up. Consent for publication was acquired from the patient.

DISCUSSION

This report described a 39-year-old male who developed unilateral CSC 2 days after Sinopharm COVID-19 vaccine injection. In thorough evaluations, no known modifiable risk factor for CSC was found. We proposed COVID-19 vaccination as a trigger for CSC development; however, his gender and age were factors that could suggest coincidentally. The pathophysiology of CSC is unclear, and there are some hypotheses about choroidal inflammation. It may cause retinal pigment epithelial (RPE) disturbance and choroidal vasculature changes. The RPE disturbance causes the cross of the choroidal fluid to the sub-RPE space or neurosensory retinal detachment. Another plausible hypothesis is the loss of RPE polarity, which causes reversing the fluid pumping onto the sub-RPE space.²⁴ We think that the induction of inflammation secondary to COVID-19 vaccination could trigger CSC development.

Based on the current literature, COVID-19 vaccination was described to induce different ocular and periocular complications [Table 1]. We found 24 reports of 39 patients who presented ophthalmic complications following injection of available COVID-19 vaccines. The age range of cases was 18–83 years. There were 19 females and 10 males. The gender of 10 cases was not in the reports. Among these cases, the complication occurred after the first vaccination dose in 15 cases, after the second in 14 cases, and after the booster dose in one case. It was unclear for 10 cases. The range of complications presentation was 1–42 days postvaccination (mean: 8.95 days, median: 6.1 days).

The most prevalent side effects of COVID-19 vaccination were acute macular neuroretinopathy (AMN), graft rejection, and eyelid disorders. Fowler *et al.* reported the first case of an ocular complication associated with COVID-19 vaccination. In a 33-year-old male patient, they found a unilateral CSC 3 days after immunization with the first dose of the Pfizer vaccine. He was under observation, and after 3 months, SRF disappeared.²² Our case was the same, and CSC developed very soon after a vaccine injection, but CSC in our case developed with an inactivated whole-virus vaccine.

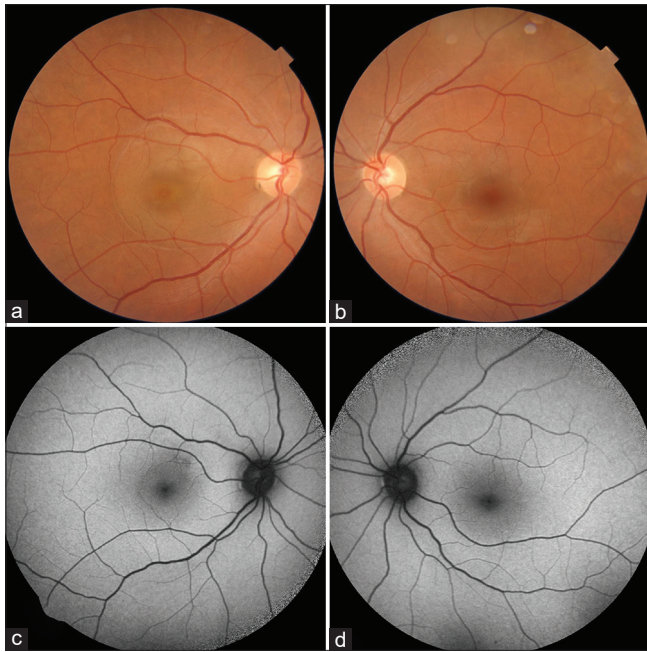


Figure 1: (a) Fundus photograph of the right eye revealed the absence of the foveal reflex and serous elevation of the retina in the macula region. (b) Fundus photograph of the left eye was normal. Fundus autofluorescence (FAF) of the right eye reveals the absence of normal central hypoautofluorescence with a focal area of hypoautofluorescence in the superior macula (c). It is compatible with pigment epithelial detachment, as shown in Figure 2c. The left eye FAF revealed normal findings (d)

There were three cases with extraocular herpes zoster ophthalmicus (HZO) 10–16 days after vaccination. All three cases were old females with a mean age of 71.33 years.²⁵ Another reported periocular complication of vaccination was unilateral transient upper and lower eyelids edema in three cases with a mean age of 39.3 years. It started 1–2 days after vaccination and resolved with observation, antihistamine, and oral steroids for each case after 1–2 days without any sequel.²⁶ Furthermore, regarding the periocular complications, we found a report on three cases with bilateral purpuric and ecchymotic eyelid lesions 10–25 days after vaccination (median 14 days), disappeared without any treatment during 10–14 days.²⁷

Reyes-Capo *et al.* reported a 59-year-old female with unilateral sixth cranial nerve palsy 2 days after Pfizer vaccine injection.²⁸ It was the only report of an extraocular muscle innervation palsy, probably associated with COVID-19 vaccination.

We found two reports of herpes simplex virus (HSV) reactivation as keratitis and keratouveitis, which occurred 1–5 days after vaccination and treated with standard treatment.^{29,30}

Elsheikh *et al.* reported an 18-year-old girl with a history of oligoarticular juvenile idiopathic arthritis who experienced a bilateral anterior uveitis reactivation 5 days after immunization with the second dose of the Sinopharm vaccine, treated with topical steroid successfully.³¹ Furthermore, a case of anterior

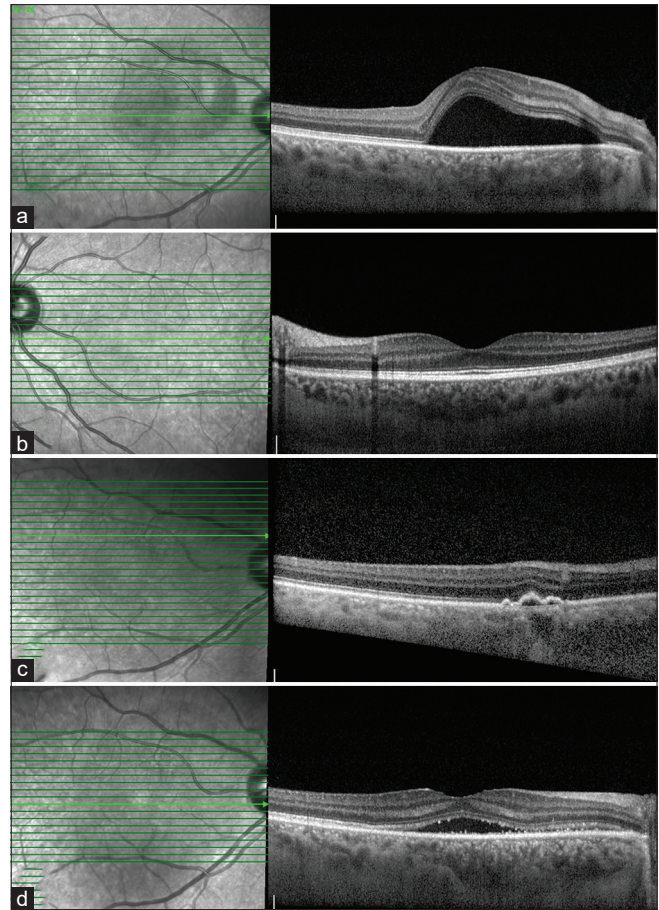


Figure 2: (a) Baseline visit enhanced depth imaging optical coherence tomography (EDI-OCT) showed a dome-shaped serous detachment of the macula with significant subretinal fluid (SRF) in the right eye. (b) EDI-OCT of the left eye showed some pachyvevessels at the temporal and nasal of the macula. (c) EDI-OCT of the superior macula of the right eye revealed a pigment epithelial detachment. (d) Four weeks after vaccination, EDI-OCT of the right eye demonstrated a dramatic decrease in SRF

uveitis was reported in an otherwise healthy young female 2 weeks after the Pfizer vaccine injection.³²

Corneal graft rejection was one of the most reported ocular complications after COVID-19 immunization.^{33–36} Most rejections occurred in endothelial keratoplasty (EK) cases. There were four cases of EK graft rejection, and two of them experienced bilateral graft rejection. There was also a unilateral penetrating keratoplasty (PKP) graft rejection. The cases were old individuals, and the youngest patient was 66 years old. The graft rejection occurred 4–21 days after COVID-19 immunization.

We found AMN as the most reported complication.^{37–41} There were seven AMN cases and one paracentral acute middle maculopathy (PAMM) case. All patients were in the third decade of their life, and AMN/PAMM occurred only 2–3 days after vaccination in all cases. Five cases were female, and the rest of the patients' gender was unclear. There was also a case of bilateral AMN.⁴⁰ Four cases experienced AMN after

Table 1: Patient demographics and clinical information on complications associated with coronavirus disease 2019 vaccination

Studies	Country	Age (years)	Female/ male	Vaccine brand	Vaccine dose	Complication	Presentation of complications after vaccination (days)
Papasavvas <i>et al.</i> ²⁵	Switzerland	73	Female	Pfizer	Booster	HZO	16
		69	Female	Pfizer	1 st	HZO	10
		72	Female	Moderna	1 st	HZO	13
Austria <i>et al.</i> ²⁶	USA	Mean: 39.3	NA (3 patients)	Pfizer	1 st and 2 nd	Unilateral transient eyelid edema	1-2
Mazzatenta <i>et al.</i> ²⁷	USA	44	Male	Pfizer	2 nd	Bilateral eyelid purpuric lesions	21-25
		63	Male	Pfizer	2 nd	Bilateral eyelid purpuric lesions	21
		67	Female	Pfizer	1 st	Bilateral eyelid ecchymotic lesions	10
Reyes-Capo <i>et al.</i> ²⁸	USA	59	Female	Pfizer	NA	Unilateral abducens nerve palsy	2
Herbert Jr. and Papasavvas ²⁹	Switzerland	53	Male	Moderna	2 nd	Unilateral HSV keratouveitis	5
Richardson-May <i>et al.</i> ³⁰	UK	40	Male	AstraZeneca	1 st	Unilateral HSV keratitis	1
Elsheikh <i>et al.</i> ³¹	Egypt	18	Female	Sinopharm	2 nd	Bilateral anterior uveitis	5
Renisi <i>et al.</i> ³²	Italy	23	Male	Pfizer	2 nd	Unilateral anterior uveitis	14
Rallis <i>et al.</i> ³³	UK	68	Female	Pfizer	1 st	Unilateral PKP rejection	4
Abousy <i>et al.</i> ³⁴	USA	73	Female	Pfizer	2 nd	Bilateral EK rejection	14
Phylactou <i>et al.</i> ³⁵	UK	66	Female	Pfizer	1 st	Unilateral EK rejection	7
		83	Female	Pfizer	2 nd	Bilateral EK rejection	21
Crnej <i>et al.</i> ³⁶	Lebanon	71	Male	Pfizer	1 st	Unilateral EK rejection	7
Fowler <i>et al.</i> ²²	Mexico	33	Male	Pfizer	1 st	Unilateral central serous chorioretinopathy	3
Valenzuela <i>et al.</i> ³⁷	USA	20	Female	Pfizer	2 nd	Unilateral AMN	2
Mambretti <i>et al.</i> ³⁸	Italy	22	Female	AstraZeneca	1 st	Unilateral AMN	2
		28	Female	AstraZeneca	1 st	Unilateral AMN	2
Böhler <i>et al.</i> ³⁹	Norway	27	Female	AstraZeneca	1 st	Unilateral AMN	2
Book <i>et al.</i> ⁴⁰	Germany	23	Female	AstraZeneca	1 st	Bilateral AMN	3
Pichi <i>et al.</i> ⁴¹	UAE	Mean±SD: 41.4±9.3	NA (7 patients)	Sinopharm	NA	Episcleritis (1 case) Anterior scleritis (2 cases) AMN (2 cases) PAMM (1 case) Subretinal fluid (1 case)	5.2 (range: 1-10)
Koong <i>et al.</i> ⁴²	Singapore	54	Male	Pfizer	1 st	VKH	NA
Saraceno <i>et al.</i> ⁴³	Brazil	62	Female	AstraZeneca	NA	VKH	2
Papasavvas and Herbert Jr. ⁴⁴	Switzerland	43	Female	Pfizer	2 nd	VKH reactivation	42
Maleki <i>et al.</i> ⁴⁵	USA	79	Female	Pfizer	2 nd	Bilateral AAION	2
		33	Female	Moderna	2 nd	Bilateral AZOOR	10
Goyal <i>et al.</i> ⁴⁶	India	34	Male	AstraZeneca	2 nd	Bilateral multifocal choroiditis	9
Mishra <i>et al.</i> ⁴⁷	India	71	Male	Covaxin	1 st	Unilateral ARN (VZV)	10

USA: United States of America, UK: United Kingdom, UAE: United Arab Emirates, NA: Not applicable, HZO: Herpes zoster ophthalmicus, HSV: Herpes simplex virus, PKP: Penetrating keratoplasty, EK: Endothelial keratoplasty, AMN: Acute macular neuroretinopathy, PAMM: Paracentral acute middle maculopathy, AAION: Arteritic anterior ischemic optic neuropathy, AZOOR: Acute zonal occult outer retinopathy, ARN: Acute retinal necrosis, VZV: Varicella-zoster virus, SD: Standard deviation, VKH: Vogt-Koyanagi-Harada

immunization with the first dose of the AstraZeneca vaccine. Five patients did not experience decreased vision, and their BCVAs were 20/20. One patient with AMN in the left eye had a 20/400 BCVA at presentation, but it improved to 20/30 after 2 months.

Pichi *et al.* reported nine cases with ocular complications after vaccination with Sinopharm.⁴¹ There was one case of episcleritis, two cases of anterior scleritis, two cases of AMN,

one case of PAMM, and one case with SRF forme fruste of CSC. The mean age of cases was 41.4 ± 9.3 years, and the meantime of complication presentation was 5.2 days after vaccination.

We found three reports on Vogt-Koyanagi-Harada (VKH) disease development associated with COVID-19 vaccination.⁴²⁻⁴⁴ One case experienced VKH reactivation after 6 years, 6 weeks after immunization with the second dose of

Pfizer.⁴⁴ It was the latest onset complication associated with COVID-19 immunization. Previously, the VKH development after immunization was reported with Bacille Calmette-Guérin, influenza, hepatitis B, and yellow fever vaccines.⁴⁸⁻⁵⁰

Other posterior segment complications were bilateral arteritic anterior ischemic optic neuropathy (AAION), bilateral acute zonal occult outer retinopathy (AZOOR), bilateral multifocal choroiditis, and unilateral acute retinal necrosis (ARN) due to varicella-zoster virus.⁴⁵⁻⁴⁷ These complications occurred 2–10 days after vaccination.

In summary, Pfizer and Moderna vaccines, which are COVID-19 mRNA vaccines, are suspected to be associated with ophthalmic complications such as CSC, HZO, transient eyelid edema, eyelid purpuric and ecchymotic lesions, abducens nerve palsy, HSV keratouveitis, anterior uveitis, EK and PKP graft rejection, AMN, VKH, AAION, and AZOOR. The AstraZeneca vaccine is a viral vector vaccine, and its probable ophthalmic complications are reported as HSV keratitis, AMN, VKH, and multifocal choroiditis. Finally, the inactivated whole virus vaccines, Sinopharm and Covaxin, are associated with anterior uveitis, episcleritis, anterior scleritis, AMN, PAMM, CSC, and ARN.

In all these cases we reviewed, localized activation of inflammatory process secondary to COVID-19 vaccination might be induced, which prepared the condition for activating immune reactions, coagulation mechanisms, and microbial agent activity. However, whether the association between these complications and COVID-19 vaccination is factual or just a co-incident is unclear. It emphasizes the importance of further and precise evaluation and investigation of the vaccinated population. The roles of infection in inciting autoimmune disorders have been explained as molecular mimicry, epitope spreading, bystander activation, and polyclonal activation.⁵¹ The immune response to the vaccine can involve every host cell in the body and result in complications with autoimmune etiology. The most probable mechanism for increasing the risk of thrombosis in patients with COVID-19 infection is an inflammatory reaction that causes microvascular damage and leads to a hypercoagulation state.⁵² As it is known, the vaccine is an induced infection for activating the immune system response against a pathogen, so the vaccine can play the role of the actual infection for disturbing the body systems, especially the coagulation systems.

In conclusion, any COVID vaccines can be associated with some vision or nonvision-threatening ocular complications. We strongly recommend COVID-19 vaccination for all individuals irrespective of previous ocular diseases despite the abovementioned ocular complications. However, it is of paramount importance for the ophthalmologist to be familiar with and deal with ocular adverse events of COVID-19 vaccination.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his

consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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