Short communication

Causative link between coronavirus disease vaccination and central serous chorioretinopathy: Reality or illusion?

Fatemeh Heidary [1] and Reza Gharebaghi [1]

[1] *International Virtual Ophthalmic Research Center, Austin, Texas, United States*

ABSTRACT

Background: Most COVID-19 vaccines were authorized for emergency use. Despite a large number of vaccines that have been administered, adverse ocular effects have been reported. This paper summarized the reports about central serous chorioretinopathy (CSCR) following coronavirus disease vaccination.

Methods: In this short communication, we have included relevant publications about CSCR after coronavirus disease vaccination from the beginning of the pandemic until January 2022.

Results: The CSCR occurrence after vaccination has been reported for many years. However, a few studies are available about CSCR after coronavirus disease vaccination. Most cases revealed the development of CSCR within one week of vaccination that subsequently resolved.

Conclusions: The timeline of the CSCR diagnosis developing a few days after vaccination suggests a causative link. However, in view of the millions of administered doses of vaccines along with boosters, the causative link between CSCR and vaccines remains uncertain. Additional studies are needed to confirm a causal claim.

KEY WORDS

COVID-19, severe acute respiratory syndrome coronavirus 2, eye, ocular complications, vaccination, vaccine, central serous retinopathy, central serous chorioretinopathy

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 can invade the eye, including the ocular adnexa [1]; therefore, ophthalmologists should be cognizant of coronavirus disease (COVID-19) transmission and take effective measures to prevent it [2]. Ocular and neuro-ophthalmic adverse events after COVID-19 vaccination have been reported in the literature. These effects vary depending on the eyelid, ocular surface, retina, choroid, and involvement of the optic nerve. COVID-19 can affect ocular structures, particularly the retina, even after recovery, possibly through viral invasion or immune-mediated inflammation [3-11]. However, owing to the nonspecific presentation, whether ocular findings after COVID-19 vaccination are associated with vaccination or coincidental remains uncertain.

Central serous chorioretinopathy (CSCR) (Figure 1) is a vision-threatening condition that most commonly occurs in middle-aged working men. The exact mechanisms of CSCR remain unclear; however, the mineralocorticoid pathway may be involved [12]. The major risk factors for CSCR are anxiety, type A

Correspondence: Reza Gharabaghi, International Virtual Ophthalmic Research Center Suite No 4000, 5900 Balcones Drive, STE 100, Austin, Texas, 78731, United States, Tel: +1 (281) 8990369. Email: drgharebaghi@yahoo.com ORCID iD: https://orcid.org/0000-0002-4906-8597

How to cite this article: Heidary F, Gharebaghi R. Causative link between coronavirus disease vaccination and central serous chorioretinopathy: Reality or illusion? Med Hypothesis Discov Innov Optom.2021 Fall; 2(3): 119-123. https://doi.org/10.51329/mehdioptometry135

Received: 21 December 2021; Accepted: 18 February 2022

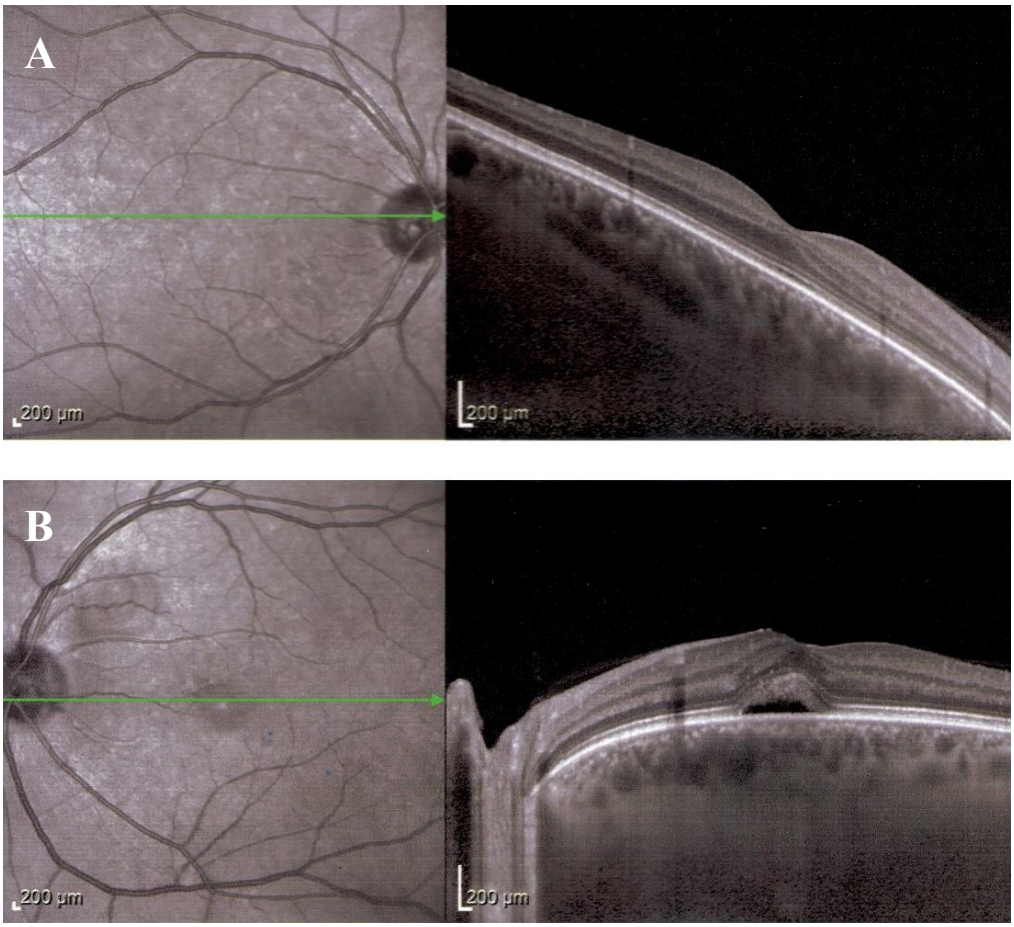

Figure 1. Optical coherence tomography scans in a young male: (A) normal right eye and (B) left eye with central serous chorioretinopathy.

personality, a history of systemic corticosteroids, endogenous Cushing's syndrome, *Helicobacter pylori* infection, collagen vascular disease, and pregnancy. Other risk factors include antibiotics, psychopharmacologic drugs, alcohol consumption, hypertension, and respiratory allergy. Adrenaline, catecholamines, and noradrenaline are elevated in patients with CSCR [13]. Several sporadic cases of familial CSCR have been reported, indicating a genetic component in the pathogenesis of CSCR [12]. During the ongoing COVID-19 pandemic, CSCR has been proposed as an adverse effect of COVID-19 vaccination [9, 14-17]; however, no statistical correlation has been found.

Most COVID-19 vaccines were authorized for emergency use. Despite a large number of vaccines that have been administered, adverse ocular effects have been reported. This paper summarized the reports about central serous chorioretinopathy (CSCR) following coronavirus disease vaccination.

METHODS

In this short communication, we have included relevant publications about CSCR after coronavirus disease vaccination from the beginning of the pandemic until January 2022.

RESULTS

Ocular and neuro-ophthalmic adverse events after COVID-19 vaccination have been determined in recent publications (Table 1).

The development of CSCR after vaccination has been reported for many years. Palacios et al. reported a case of CSCR after influenza vaccination in a 35-year-old woman and proposed the possibility of an immune response [18]. Further, Foster and Agahigian reported a case of CSCR 2 weeks after anthrax vaccination in a 43-year-old woman and discussed anxiety secondary to vaccination as a possible mechanism [19].

Table 1. Ocular and neuro-ophthalmic findings after coronavirus disease vaccination [3-11]

Site	Sign/Diagnosis
Eyelid	Purpura
	Eyelid swelling
	Periocular skin herpes zoster
Ocular Surface	Corneal graft rejection
	Episcleritis
	Keratoconjunctivitis
	Herpetic keratitis
Retina	Central Serous Chorioretinopathy
	Paracentral Acute Macular Neuroretinopathy
	Ophthalmic Vein Thrombosis
	Retinal vein occlusion
	Retinal detachment
	Multiple evanescent white dot syndrome
Uvea and Choroid	Uveitis (anterior, intermediate, or panuveitis)
	Pars planitis
	Reactivation of Vogt-Koyanagi-Harada disease
	Acute zonal occult outer retinopathy
	Choroiditis
Neuroophthalmic manifestations	Optic neuritis
	Ocular myasthenia gravis
	Facial nerve palsy
	Abducens nerve palsy
	Arteritic anterior ischemic optic neuropathy

Table 2. Studies on the development of central serous chorioretinopathy after coronavirus disease vaccination

Publication	Patient's Characteristics	Laterality	Timeline	Follow-up
Bolletta et al. [9]	34-year-old male	Bilateral	Thirteen days after second dose	Resolved
Delbarre et al. [14]	38-year-old male	Left eye	Seven days after first dose	Subretinal fluid persisted despite treatment
Fowler et al. [15]	33-year-old male History: unremarkable	Right eye	Three days after first dose	Resolved
Pichi et al. [16]	Seven patients with post-vaccination ocular complications.	Case 3: History of CSCR in both eyes, left eye had post-vaccination serous PED with AMN.	Five days after first vaccination	Resolved
		Case 6: Bilateral shallow areas of SRF, no choroidal thickening, an associated hypertrophy of the photoreceptor overlying the fluid suggestive of a forme fruste of CSCR.	A mean of 6 days after the first vaccination	Not mentioned
Lee et al. [17]	41-year-old female. History: unremarkable	Right eye optic disc edema	Two days after first dose	Resolved
		Left eye CSCR		

Abbreviations: CSCR, central serous chorioretinopathy; PED, pigment epithelial detachment; AMN, acute macular neuroretinopathy; SRF, subretinal fluid.

The timeline of the diagnosis emerging a few days after vaccination suggests a causative link between vaccination and CSCR. However, most publications were case reports instead of controlled trials; therefore, the causative link cannot be concluded [9, 14-17]. Table 2 summarizes the studies on CSCR following COVID-19 vaccination.

When rare signs appear in association with more common events, such as COVID-19 vaccination, the findings may be unassociated [20]. Furthermore, several vaccines against COVID-19 with different mechanisms have been administered worldwide. Considering the millions of administered doses of vaccines along with boosters, the causative link between ocular events and vaccines remains uncertain [20].

CONCLUSIONS

The development of CSCR after vaccination has been reported for many years. The timeline of the diagnosis emerging a few days after COVID-19 vaccination suggests a causative link between vaccination and CSCR. However, most publications were case reports instead of controlled trials; therefore, the causative link cannot be concluded. Therefore, the coincidental onset of CSCR should be investigated in studies with a large sample size. The development of CSCR triggered by COVID-19 vaccination is plausible; however, symptoms resolve within a few months. Ultimately, vaccines provide protection against life-threatening conditions, and plausible side effects should not lead to vaccine hesitancy.

ETHICAL DECLARATIONS

Ethical approval: No ethical approval was required.
Conflict of interests: Dr. Fatemeh Heidary was assigned as Editor in Chief of Medical hypothesis, discovery & innovation in optometry.

FUNDING

None.

ACKNOWLEGEMENTS

Articles submitted by the board, staff, and Editor-in-Chief at this journal will also be subjected to peer review. These types of papers have been handled by another person on the editorial board (without conflicts of interest), and in all processes, those who have a conflict of interest will not be involved.

REFERENCES

1. Bernabei F, Versura P, Rossini G, Re MC. There is a Role in Detection of SARS-CoV-2 in Conjunctiva and Tears: a comprehensive review. New Microbiol. 2020;43(4):149-155. pmid: 33135085
2. Pei X, Jiao X, Lu D, Qi D, Huang S, Li Z. How to Face COVID-19 in Ophthalmology Practice. Med Hypothesis Discov Innov Ophthalmol. 2020; 9(3):164-171. doi: 10.51329/mehdiophthal1406
3. Ng XL, Betzler BK, Testi I, Ho SL, Tien M, Ngo WK, et al. Ocular Adverse Events After COVID-19 Vaccination. Ocul Immunol Inflamm. 2021;29(6):1216-1224. doi: 10.1080/09273948.2021.1976221 pmid: 34559576
4. Lee YK, Huang YH. Ocular Manifestations after Receiving COVID-19 Vaccine: A Systematic Review. Vaccines (Basel). 2021;9(12):1404. doi: 10.3390/vaccines9121404 pmid: 34960150
5. Testi I, Brandão-de-Resende C, Agrawal R, Pavesio C; COVID-19 Vaccination Ocular Inflammatory Events Study Group. Ocular inflammatory events following COVID-19 vaccination: a multinational case series. J Ophthalmic Inflamm Infect. 2022;12(1):4. doi: 10.1186/s12348-021-00275-x pmid: 34982290
6. Pang K, Pan L, Guo H, Wu X. Case Report: Associated Ocular Adverse Reactions With Inactivated COVID-19 Vaccine in China. Front Med (Lausanne). 2022;8:823346. doi: 10.3389/fmed.2021.823346 pmid: 35111790
7. Galassi G, Rispoli V, Iori E, Ariatti A, Marchioni A. Coincidental Onset of Ocular Myasthenia Gravis Following ChAdOx1 n-CoV-19 Vaccine against Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). Isr Med Assoc J. 2022;24(1):9-10. pmid: 35077038
8. Eleiwa TK, Gaier ED, Haseeb A, ElSheikh RH, Sallam AB, Elhusseiny AM. Adverse Ocular Events following COVID-19 Vaccination. Inflamm Res. 2021;70(10-12):1005-1009. doi: 10.1007/s00011-021-01506-6 pmid: 34561753
9. Bolletta E, Iannetta D, Mastrofilippo V, De Simone L, Gozzi F, Croci S, et al. Uveitis and Other Ocular Complications Following COVID-19 Vaccination. J Clin Med. 2021;10(24):5960. doi: 10.3390/jcm10245960 pmid: 34945256
10. Sanjay S, Agrawal S, Jayadev C, Kawali A, Gowda PB, Shetty R , et al. Posterior segment manifestations and imaging features post–COVID-19. Med Hypothesis Discov Innov Ophthalmol. 2021; 10(3): 95-106. doi: 10.51329/mehdiophthal1427
11. Mazzatenta C, Piccolo V, Pace G, Romano I, Argenziano G, Bassi A. Purpuric lesions on the eyelids developed after BNT162b2 mRNA COVID-19 vaccine: another piece of SARS-CoV-2 skin puzzle? J Eur Acad Dermatol Venereol. 2021;35(9):e543-e545. doi:

10.1111/jdv.17340 pmid: 34048614
12. Daruich A, Matet A, Dirani A, Bousquet E, Zhao M, Farman N, et al. Central serous chorioretinopathy: Recent findings and new physiopathology hypothesis. Prog Retin Eye Res. 2015;48:82-118. doi: 10.1016/j.preteyeres.2015.05.003 pmid: 26026923
13. Liew G, Quin G, Gillies M, Fraser-Bell S. Central serous chorioretinopathy: a review of epidemiology and pathophysiology. Clin Exp Ophthalmol. 2013;41(2):201-14. doi: 10.1111/j.1442-9071.2012.02848.x pmid: 22788735
14. Delbarre M, Maréchal M, Froussart-Maille F. Central serous chorioretinopathy following Pfizer-BioNTech COVID-19 vaccine: A case report. J Fr Ophtalmol. 2022;45(1):e1-e2. doi: 10.1016/j.jfo.2021.11.003 pmid: 34949501
15. 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;23:101136. doi: 10.1016/j.ajoc.2021.101136 pmid: 34151047
16. Pichi F, Aljneibi S, Neri P, Hay S, Dackiw C, Ghazi NG. Association of Ocular Adverse Events With Inactivated COVID-19 Vaccination in Patients in Abu Dhabi. JAMA Ophthalmol. 2021;139(10):1131-1135. doi: 10.1001/jamaophthalmol.2021.3477 pmid: 34473209
17. Lee DY, Wu HJ, Cheng KC, Chang YC. Disc edema in one eye and central serous chorioretinopathy in the other eye shortly after AstraZeneca COVID-19 vaccination. Kaohsiung J Med Sci. 2021:10.1002/kjm2.12473. doi: 10.1002/kjm2.12473 pmid: 34783448
18. Palacios AI, Rodríguez M, Martín MD. Coriorretinopatía serosa central de etiología inusual: a propósito de dos casos [Central serous chorioretinopathy of unusual etiology: A report of 2 cases]. Arch Soc Esp Oftalmol. 2014;89(7):275-8. Spanish. doi: 10.1016/j.oftal.2013.04.007 pmid: 24269442
19. Foster BS, Agahigian DD. Central serous chorioretinopathy associated with anthrax vaccination. Retina. 2004;24(4):624-5. doi: 10.1097/00006982-200408000-00023 pmid: 15300091
20. Jampol LM, Tauscher R, Schwarz HP. COVID-19, COVID-19 Vaccinations, and Subsequent Abnormalities in the Retina: Causation or Coincidence? JAMA Ophthalmol. 2021;139(10):1135-1136. doi: 10.1001/jamaophthalmol.2021.3483 pmid: 34473193