



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

Letter to the Editor

Retinal artery/vein occlusion complicating SARS-CoV-2 vaccinations

Letter to the Editor

We read with interest the review article by Su et al. about central retinal artery/vein occlusion following a SARS-CoV-2 vaccination.¹ Altogether, six patients from 5 articles were retrieved as per the 10th January 2022 upon an appropriate search in the database PubMed.¹ It was concluded that vaccine-related central retinal artery/vein occlusion is a rare complication of SARS-CoV-2 vaccination and that a temporal sequence does not establish a causal link.¹ The study is attractive but raises concerns that should be discussed.

The design of the study does not allow drawing conclusions as presented. At maximum it can be concluded that SARS-CoV-2 vaccination related central retinal artery/vein occlusion is not frequently reported. However, it cannot be concluded that central retinal artery/vein occlusion is a rare complication of vaccinations. Studies with another design (prospective multi-center studies) are required to assess the actual frequency of central retinal artery/vein occlusion after vaccinations. Most likely, the actual frequency is higher as not each case is published.

Matching with this consideration, several other cases of vaccine-related occlusion of the central retinal artery/vein have been reported after the 10th January 2022. Chen et al. reported a 48yo female who developed sudden onset of inferior visual field defects in the left eye four weeks following the first dose of the ChAdOx1 (Astra Zeneca) vaccine (AZV).² Romano et al. reported a 54yo female who developed central retinal vein occlusion 2 days after the second dose of the AZV.³ Retinal vein occlusion was also diagnosed in a 28yo male after the third AZV dose.⁴ In a retrospective study evaluating data between May 1st and October 31st 2021, 14 patients with retinal vascular occlusions after COVID vaccinations were collected.⁵ Two patients with retinal ischemic events after application of the Moderna vaccine (MOV) respectively the Johnson & Johnson vaccine (JJV) have been recently reported.⁶ Kang et al. reported a 64yo male who experienced a branch retinal artery occlusion three days after the first dose of the Biontech Pfizer vaccine (BPV).⁷ A 76yo female developed unilateral, painless visual loss 2 days after the first dose of the AZV.⁸ Four patients experienced branch retinal artery occlusion 22.8 days on the average after the last vaccine dose application.⁹ In a study of 11 patients with visual

complaints after SARS-CoV-2 vaccinations, 5 had retinal artery occlusion and four had retinal vein occlusion.¹⁰ Retinal arteriovenous occlusion was reported one day after the first dose of the AZV in a 77yo male.¹¹ Two days after the second dose of the BPV a 38yo male developed branch retinal vein occlusion in the left eye.¹² A 34yo male presented with right retinal branch venous occlusion two days after the first BPV.¹³ Retinal vein occlusion has been also reported in 5 patients after the AZV (n=3) or the BPV (n=2) respectively.¹⁴ Combined central retinal artery and vein occlusion together with ischemic optic neuropathy was reported in a 34yo male 10 days after the second BPV dose.¹⁵

The authors did not include several reports published before the 10th January 2022.^{16–23} It should be explained why these cases were not included in the review.

No mention is made of Susac syndrome characterised by retinal vascular occlusions, cerebral micro-angiopathy and hypoacusis. Susac syndrome has not only been reported in association with SARS-CoV-2 vaccinations² but also in a patient after smallpox vaccination.²⁴

Hyper-viscosity syndrome (HVS) following SARS-CoV-2 vaccinations was not discussed as possibly pathophysiological mechanism explaining central retinal artery/vein occlusion.²⁵ HVS is related to elevated levels of fibrinogen or immunoglobulins, to dehydration or exsiccosis, oxidative stress, or the inflammatory response to the vaccine.²⁵

Overall, the interesting study has some limitations that call the results and their interpretation into question. Clarifying these weaknesses would strengthen the conclusions and could improve the study. Retinal artery/vein occlusions following SARS-CoV-2 vaccinations is more common than anticipated.

Funding

no funding was received.

Author contribution

JF: design, literature search, discussion, first draft, critical comments, final approval.

Disclosures

The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

1052-3057/\$ - see front matter

© 2022 Elsevier Inc. All rights reserved.

Compliance with Ethics Guidelines

This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

Josef Finsterer,
Neurology and Neurophysiology Center, Postfach 20, 1180
Vienna, Austria
E-mail address: fipaps@yahoo.de

<https://doi.org/10.1016/j.jstrokecerebrovasdis.2022.106617>

References

- Su CK, Au SCL. Isolated and combined unilateral central retinal artery and vein occlusions after vaccination. A review of the literature. *J Stroke Cerebrovasc Dis* 2022;31(8):106552. <https://doi.org/10.1016/j.jstrokecerebrovasdis.2022.106552>.
- Chen PJ, Chang YS, Lim CC, Lee YK. Susac syndrome following COVID-19 vaccination: a case report. *Vaccines (Basel)* 2022;10(3):363. <https://doi.org/10.3390/vaccines10030363>.
- Romano D, Morescalchi F, Romano V, Semeraro F. COVID-19 adenoviral vector vaccine and central retinal vein occlusion. *Ocul Immunol Inflamm* 2022;1-3. <https://doi.org/10.1080/09273948.2022.2079534>.
- Dutta Majumder P, Prakash VJ. Retinal venous occlusion following COVID-19 vaccination: Report of a case after third dose and review of the literature. *Indian J Ophthalmol* 2022;70(6):2191-2194. https://doi.org/10.4103/ijoo.IJO_592_22.
- Vujosevic S, Limoli C, Romano S, Vitale L, Villani E, Nucci P. Retinal vascular occlusion and SARS-CoV-2 vaccination. *Graefes Arch Clin Exp Ophthalmol* 2022;1-10. <https://doi.org/10.1007/s00417-022-05707-5>.
- Priluck AZ, Arevalo JF, Pandit RR. Ischemic retinal events after COVID-19 vaccination. *Am J Ophthalmol Case Rep* 2022;26:101540. <https://doi.org/10.1016/j.ajoc.2022.101540>.
- Kang MS, Kim SY, Kwon HJ. Case report: recanalization of branch retinal artery occlusion due to microthrombi following the first dose of SARS-CoV-2 mRNA vaccination. *Front Pharmacol* 2022;13:845615. <https://doi.org/10.3389/fphar.2022.845615>.
- Abdin AD, Gärtner BC, Seitz B. Central retinal artery occlusion following COVID-19 vaccine administration. *Am J Ophthalmol Case Rep* 2022;26:101430. <https://doi.org/10.1016/j.ajoc.2022.101430>.
- Ishibashi K, Yatsuka H, Haruta M, Kimoto K, Yoshida S, Kubota T. Branch retinal artery occlusions, paracentral acute middle maculopathy and acute macular neuroretinopathy after COVID-19 vaccinations. *Clin Ophthalmol* 2022;16:987-992. <https://doi.org/10.2147/OPHT.S357359>.
- Silva LSCD, Finamor LPS, Andrade GC, Lima LH, Zett C, Muccioli C, Sarraf EP, Marinho PM, Peruchi J, Oliveira RDL, Giralt L, Charcan I, Fonollosa A, Diaz JD, Davis JL, Nascimento H, Belfort Jr. R. Vascular retinal findings after COVID-19 vaccination in 11 cases: a coincidence or consequence? *Arq Bras Oftalmol* 2022;85(2):158-165. <https://doi.org/10.5935/0004-2749.20220071>.
- Groselli S, Gabka K, Bechstein L, Ulbig M. Retinaler arteriovenöser Gefäßverschluss nach COVID-Impfung mit Vaxzevria® (AstraZeneca) – Eine Impfkomplication oder nicht? [Retinal arteriovenous vascular occlusion after COVID vaccination with Vaxzevria® (AstraZeneca)-A complication of vaccination or not?]. *Ophthalmologe* 2022;1-5. <https://doi.org/10.1007/s00347-022-01598-3>. German.
- Sugihara K, Kono M, Tanito M. Branch retinal vein occlusion after messenger RNA-based COVID-19 vaccine. *Case Rep Ophthalmol* 2022;13(1):28-32. <https://doi.org/10.1159/000521838>.
- Pur DR, Catherine Danielle Bursztyn LL, Iordanous Y. Branch retinal vein occlusion in a healthy young man following mRNA COVID-19 vaccination. *Am J Ophthalmol Case Rep* 2022;26:101445. <https://doi.org/10.1016/j.ajoc.2022.101445>.
- Peters MC, Cheng SSH, Sharma A, Moloney TP. Retinal vein occlusion following COVID-19 vaccination. *Clin Exp Ophthalmol* 2022. <https://doi.org/10.1111/ceo.14056>.
- Lee S, Sankhala KK, Bose S, Gallemore RP. Combined central retinal artery and vein occlusion with ischemic optic neuropathy after COVID-19 vaccination. *Int Med Case Rep J* 2022;15:7-14. <https://doi.org/10.2147/IMCRJ.S328931>.
- Shah PP, Gelnick S, Jonisch J, Verma R. Central retinal vein occlusion following BNT162b2 (Pfizer-BioNTech) COVID-19 messenger RNA vaccine. *Retin Cases Brief Rep.* 2021. <https://doi.org/10.1097/ICB.0000000000001214>.
- Bolletta E, Iannetta D, Mastrofilippo V, De Simone L, Gozzi F, Croci S, Bonacini M, Belloni L, Zerbini A, Adani C, Fontana L, Salvarani C, Cimino L. Uveitis and other ocular complications following COVID-19 vaccination. *J Clin Med* 2021;10(24):5960. <https://doi.org/10.3390/jcm10245960>.
- Sonawane NJ, Yadav D, Kota AR, Singh HV. Central retinal vein occlusion post-COVID-19 vaccination. *Indian J Ophthalmol* 2022;70(1):308-309. https://doi.org/10.4103/ijoo.IJO_1757_21.
- Tanaka H, Nagasato D, Nakakura S, Tanabe H, Nagasawa T, Wakuda H, Imada Y, Mitamura Y, Tabuchi H. Exacerbation of branch retinal vein occlusion post SARS-CoV2 vaccination: Case reports. *Medicine (Baltimore)* 2021;100(50):e28236. <https://doi.org/10.1097/MD.00000000000028236>. PMID: 34918688; PMCID: PMC8677974.
- Sacconi R, Simona F, Forte P, Querques G. Retinal vein occlusion following two doses of mRNA-1273 (Moderna) immunization for SARS-Cov-2: a case report. *Ophthalmol Ther* 2022;11(1):453-458. <https://doi.org/10.1007/s40123-021-00441-3>.
- Ikegami Y, Numaga J, Okano N, Fukuda S, Yamamoto H, Terada Y. Combined central retinal artery and vein occlusion shortly after mRNA-SARS-CoV-2 vaccination. *QJM* 2022;114(12):884-885. <https://doi.org/10.1093/qjmed/hcab287>. PMID: 34791479; PMCID: PMC8689963.
- Endo B, Bahamon S, Martínez-Pulgarín DF. Central retinal vein occlusion after mRNA SARS-CoV-2 vaccination: A case report. *Indian J Ophthalmol* 2021;69(10):2865-2866. https://doi.org/10.4103/ijoo.IJO_1477_21.
- Bialasiewicz AA, Farah-Diab MS, Mebarki HT. Central retinal vein occlusion occurring immediately after 2nd dose of mRNA SARS-CoV-2 vaccine. *Int Ophthalmol* 2021;41(12):3889-3892. <https://doi.org/10.1007/s10792-021-01971-2>.

24. Landa G, Marcovich A, Leiba H, Springer A, Bukelman A, Pollack A. Multiple branch retinal arteriolar occlusions associated with smallpox vaccination. *J Infect* 2006;52(1):e7-e9. <https://doi.org/10.1016/j.jinf.2005.04.019>.
25. Al-Kuraishy HM, Al-Gareeb AI, El-Bouseary MM, Sonbol FI, Batiha GE. Hyperviscosity syndrome in COVID-19 and related vaccines: exploring of uncertainties. *Clin Exp Med* 2022:1-10. <https://doi.org/10.1007/s10238-022-00836-x>.