• Letter to the Editor •

Phenotypic appearance of central retinal vein occlusion post AstraZeneca vaccine

Peter Cackett[1,2], *Rinoza Bafiq*[1], *Ahmed Ali*[1], *Su Ling Young*[1,2]

[1]Princess Alexandra Eye Pavilion, NHS Lothian, Edinburgh EH3 9HA, United Kingdom
[2]University of Edinburgh, Edinburgh EH16 4SB, United Kingdom
Correspondence to: Peter Cackett. Princess Alexandra Eye Pavilion, 45 Chalmers Street, Edinburgh EH3 9HA, United Kingdom. pdcackett@hotmail.com
Received: 2021-11-14 Accepted: 2022-02-21

DOI:10.18240/ijo.2022.04.24

Citation: Cackett P, Bafiq R, Ali A, Young SL. Phenotypic appearance of central retinal vein occlusion post AstraZeneca vaccine. *Int J Ophthalmol* 2022;15(4):672-673

Dear Editor,

The COVID-19 pandemic has brought about the development of novel vaccines at a rapid pace. The AstraZeneca (AZ) COVID-19 adenovirus vector vaccine has been associated with thrombotic complications, the most serious of which includes cerebral venous sinus thrombosis[1]. However, there are no reports in the literature to date regarding ocular manifestations secondary to the AZ COVID-19 vaccine. We present the cases of two otherwise healthy patients with no significant pre-existing co-morbidities presenting with a central retinal vein occlusion (CRVO) within 1wk following AZ COVID-19 vaccination and describe the typical phenotypic appearances.

The study was conducted in accordance with the principles of the Declaration of Helsinki. The informed consent was obtained from the subjects.

Case 1 A 44-year-old lady presented to eye casualty complaining of two episodes of transient painless blurring of vision in her right eye 5d following her first AZ COVID vaccine. She had no significant past medical or ocular history, was not on any regular medication and was a non-smoker.

On examination Snellen visual acuities were 6/6 right eye and 6/6 left eye. Anterior segments and intraocular pressures were normal bilaterally. Dilated fundal examination of the right eye showed a few scattered flame and blot haemorrhages in all four quadrants (Figure 1). There was no evidence of cystoid macular edema (CME) on optical coherence tomography (OCT) imaging (Figure 2). The left fundus appeared normal. Blood pressure and routine bloods were all essentially normal. A diagnosis of non-ischaemic CRVO in the right eye was made and a 3-month follow up was arranged in the Ophthalmology Clinic. At her 3-month review, the vein occlusion in the right eye had completely resolved and she was discharged.

Case 2 A 49-year-old lady presented to the eye clinic complaining of blurring of vision in her right eye 4d following inoculation with the AZ COVID-19 vaccine. She had no significant past medical or ocular history, was not on any regular medication and was a non-smoker.

On examination Snellen visual acuities were 6/12 right eye and 6/6 left eye. Anterior segments and intraocular pressures were normal bilaterally. Dilated fundal examination of the right eye showed a few scattered blot haemorrhages in all four quadrants with several cotton wool spots (Figure 3). There was no evidence of CME on OCT imaging (Figure 4). The left fundus appeared normal. Blood pressure and routine bloods were unremarkable. A diagnosis of non-ischaemic CRVO in the right eye was made and a 3-month follow up arranged in the Ophthalmology Clinic. At her 3-month review, Snellen visual acuities were 6/6 bilaterally, the vein occlusion in the right eye had completely resolved and she was discharged.

Both of our patients were middle aged females, had no significant ocular or systemic risk factors and presented with a mild non-ischaemic CRVO characterised by a mild amount of haemorrhaging with or without cotton wool spots, and without evidence of CME within 1wk of AZ COVID-19 vaccination.

Traditional methods of vaccination include attenuated vaccines which utilise microorganisms that have had their virulent properties disabled, or inactivated vaccines which contain microorganisms that have been destroyed and are no longer virulent. The AZ COVID-19 vaccine is a genetic vaccine and is in the sub-group viral vector vaccine. These vaccines use a safe virus to insert pathogen genes in the body to produce specific antigens. The AZ COVID-19 vaccine uses a modified version of a chimpanzee adenovirus, known as ChAdOx1, and contains the gene for the coronavirus spike protein. After inoculation with the AZ COVID-19 vaccine, the patient's immune system subsequently becomes primed to the coronavirus spike protein, enhancing the immune response if the patient encounters the COVID-19 virus in the future.

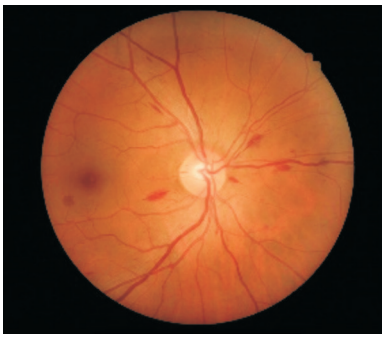

Figure 1 Fundal photo of right eye showing non-ischaemic CRVO.

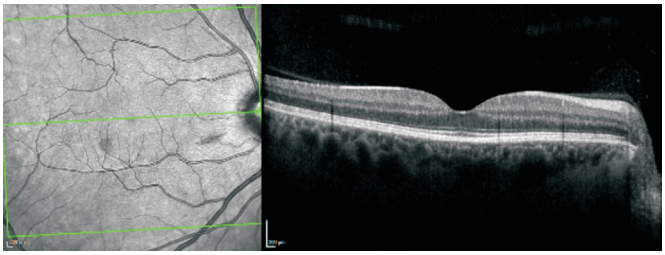

Figure 2 OCT of right macula showing absence of CME.

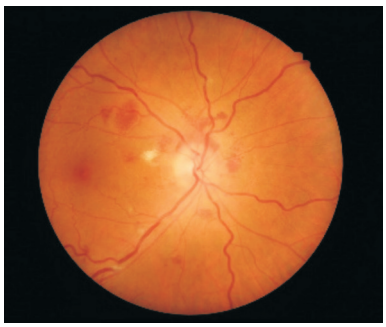

Figure 3 Fundal photo of right eye showing non-ischaemic CRVO.

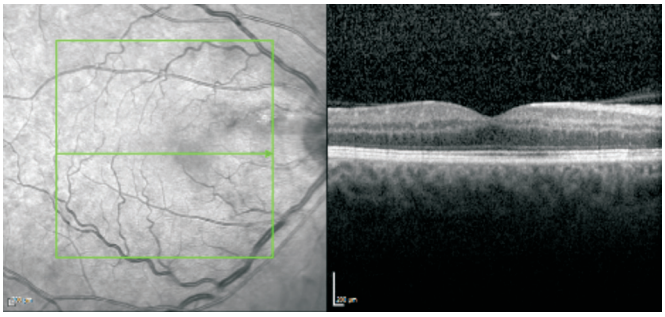

Figure 4 OCT of right macula showing absence of CME.

There appears to be increasing evidence in the literature suggesting a possible association between the AZ COVID-19 vaccine and thrombotic events. Pottegård *et al*[1] reported a standardised morbidity ratio of 1.97 (1.50 to 2.54) and 11 (5.6 to 17.0) excess venous thromboembolic events per 100 000 vaccinations, with an excess of 2.5 (0.9 to 5.2) cerebral venous thrombotic events per 100 000 observed. This possible association has been recognized by European Medicines Agency[2] and United Kingdom Medicines and Healthcare Products Regulator[3].

The proposed mechanism of action of AZ COVID-19 related blood clots is an immune response that resembles a rare reaction to the drug heparin, called heparin-induced thrombocytopenia and is referred to as vaccine-induced immune thrombotic thrombocytopenia (VITT)[4-5]. This disorder clinically resembles heparin-induced thrombocytopenia, which is a prothrombotic state caused by platelet-activating antibodies that recognise and bind to complexes of cationic platelet factor 4 (PF4) and anionic heparin. It has been recognised that other triggers apart from heparin can cause this reaction and it is believed that the AZ COVID-19 vaccine does so in this case. It is thought that interactions between the vaccine and platelets or between the vaccine and PF4 may play a role, but the exact pathogenesis still remains unclear[4].

The occurrence of CRVO shortly after the mRNA COVID-19 vaccine has been reported previously[6], however our two cases represent the first documented reports of CRVO in association with the AZ COVID-19 vaccine. We hypothesize that the AZ COVID-19 vaccine predisposes to the development of CRVO with the VITT mechanism of action described in the two New England Journal of Medicine papers[4-5]. From our two cases, CRVO occurring secondary to AZ COVID-19 vaccination appears to be non-ischaemic and relatively benign in nature, resolving rapidly without complications or requirement for any intervention. Further work in identifying cases may lead to improved understanding of the pathophysiology underlying this phenomenon of thrombosis secondary to AZ COVID-19 vaccination and verification of the VITT mechanism of action which has been proposed.

ACKNOWLEDGEMENTS

Conflicts of Interest: Cackett P, Honoraria from Bayer, Allergan, Novartis, Roche and Travel Grants from Bayer, Allergan and Novartis; **Bafiq R,** None; **Ali A,** None; **Young SL,** Travel Grant from Bayer.

REFERENCES

1 Pottegård A, Lund LC, Karlstad Ø, *et al*. Arterial events, venous thromboembolism, thrombocytopenia, and bleeding after vaccination with Oxford-AstraZeneca ChAdOx1-S in Denmark and Norway: population based cohort study. *BMJ* 2021;373:n1114.

2 European Medicines Agency 2021. https://www.ema.europa.eu/en/news/astrazenecas-COVID-19-vaccine-ema-finds-possible-link-very-rare-cases-unusual-blood-clots-low-blood

3 Public Health England 2021. https://www.gov.uk/government/publications/COVID-19-vaccination-and-blood-clotting/COVID-19-vaccination-and-blood-clotting

4 Greinacher A, Thiele T, Warkentin TE, Weisser K, Kyrle PA, Eichinger S. Thrombotic thrombocytopenia after ChAdOx1 nCov-19 vaccination. *N Engl J Med* 2021;384(22):2092-2101.

5 Schultz NH, Sørvoll IH, Michelsen AE, *et al*. Thrombosis and thrombocytopenia after ChAdOx1 nCoV-19 vaccination. *N Engl J Med* 2021;384(22):2124-2130.

6 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.