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Uveal effusion syndrome following COVID-19 vaccination

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ABSTRACT

Purpose: To report a rare case of uveal effusion syndrome following COVID-19 vaccination.
Observation: A 71-year-old Asian man presented to his ophthalmologist with blurred vision and noticing distorted lines in his left eye two weeks after the first dose of COVID-19 vaccination. Examination revealed choroidal detachment and he was advised systemic corticosteroids. The symptoms were ignored and the second vaccine dose was taken. After five months, he presented to our clinic with persistent visual complaints. He also had a history of COVID-19 infection three months prior to vaccination. Ocular examination revealed a quiet anterior chamber with annular choroidal detachment consistent with the diagnosis of Type 3 uveal effusion syndrome. B-scan ultrasonography revealed increased choroidal thickness with detachment. Optical coherence tomography showed subretinal fluid with retinal pigment epithelium and choroidal folds. Ultrasound biomicroscopy revealed all around supraciliary effusion in the left eye. The patient was treated with oral prednisolone and mycophenolate mofetil which resulted in complete resolution of uveal effusion and improvement in visual acuity.
Conclusions and importance: Uveal effusion syndrome is a rare ocular disease, however it may manifest following COVID-19 vaccination. Our case highlights the importance of a complete ophthalmic examination in patients with ocular symptoms after vaccination.

1. Introduction

As of January 2023, WHO has reported over 750 million cases of coronavirus disease 2019 (COVID-19) which resulted in nearly 6.8 million deaths across the globe; over 13 billion vaccine doses have been administered since the approval for emergency use in various countries and these vaccines include Moderna (mRNA-1273), Pfizer-BioNTech (BNT162b2), Oxford/AstraZeneca (ChAdOx1-S), Sinopharm, Sinovac-CoronaVac, Covaxin (BBV152), Novavax and others.[1]

Besides the beneficial effects of these vaccines, there have been various systemic side effects reported following vaccination, including headache, fever, chills, myalgia, arthralgia and rashes.[2] Also, there have been many ocular associations like episcleritis, scleritis, uveitis, central serous chorioretinopathy, Vogt Koyanagi Harada disease (VKH), multifocal choroiditis, anterior ischemic optic neuropathy (AION), Graves' disease, herpes zoster ophthalmicus (HZO), central retinal vein occlusion and acute retinal necrosis reported in the literature following the administration of COVID-19 vaccines.[3,4] Uveal effusion syndrome (UES) is a rare syndrome presenting as exudative detachments of the choroid, ciliary body and retina. It is thought to arise due to a primary abnormality of the choroid or sclera, which results in fluid retention in the suprachoroidal and supraciliary space. The etiology is not well defined, although various inflammatory and hydrostatic conditions can cause uveal effusion.[5,6] We report the first case of UES-Type 3 in a patient who was immunized with a whole inactivated virus-based COVID-19 vaccine.

2. Case report

A 71-year-old Asian Indian male, presented initially to an outside ophthalmologist with blurred vision and noticing distorted lines in his left eye, two weeks after the administration of the first dose of COVID-19 vaccine (Covaxin BBV152). Examination revealed choroidal detachment in the left eye and he was advised systemic corticosteroids. However, that was ignored and the second vaccine dose was taken as per the schedule at one month. He continued to be visually symptomatic and five months later presented to our clinic. He had undergone uneventful phacoemulsification with intraocular lens implantation in the left eye two years ago elsewhere. He was a known hypertensive and diabetic under medication. He also had a history of COVID-19 infection three

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months prior to taking vaccination. There was no prior history of uveitis or trauma. The best corrected visual acuity (BCVA) was 20/20, N6 in the right eye and 20/40, N10 in the left eye. The intraocular pressure was 14 mmHg and 12 mmHg in the right and the left eye, respectively. Anterior segment examination did not reveal any abnormality.

Fundus examination with indirect ophthalmoscopy showed asteroid hyalosis, fine folds in the posterior pole and annular choroidal detachment in the left eye (Fig. 1 A). The right eye was normal with few drusen in the foveal area. B-scan ultrasonography revealed diffusely thickened choroid with 360° choroidal detachment in the left eye (Fig. 1 B). The peripapillary choroidal thickness was raised (2.13mm OD and 2.41mm OS). Axial length was 20.69 mm OD and 21.43 mm OS. Fundus fluorescein angiography (FA) and indocyanine green angiography (ICGA) showed the presence of disc staining with peripheral effusion in the left eye. (Fig. 1C–F) An ancillary imaging study of the right eye showed signs of mild diabetic retinopathy without any inflammation or effusion. Ultrasound biomicroscopy revealed all-around supraciliary effusion in the left eye. (Fig. 1G) Swept-source optical coherence tomography SS-OCT (Topcon Atlantis DRI OCT-1 system, Topcon Medical Systems, Paramus, NJ, USA) showed the presence of subfoveal retinal fluid extending superior and inferior to the fovea, subretinal precipitates, cystic spaces, increased retinal thickness, retinal pigment epithelium and choroidal folds with internal limiting membrane wrinkling in the left eye. (Fig. 1H) SS-OCT in the right eye was normal. Foveal thickness was 219μ (OD) and 348μ (OS), and subfoveal choroidal thickness was 259 μ OD and 436 μ OS.

Following this, a diagnosis of type 3 uveal effusion syndrome in the left eye was made. A thorough systemic evaluation including tuberculin skin test (TST), serum angiotensin-converting enzyme, interferon-gamma release assay (IGRA), rapid plasma reagin (RPR), treponema pallidum haemagglutination assay (TPHA), toxoplasma serology, high resolution computed tomography (HRCT) chest was non-contributory. He was started on mycophenolate mofetil (MMF) 1 gm twice daily and oral prednisolone 60mg/day (1mg/kg body weight) in slow tapering doses. The patient was followed up periodically, and there was complete resolution of the subfoveal fluid and cilio-choroidal effusion at one year (Fig. 2 A,B). Visual acuity in the left eye improved to 20/20, N6 in the left eye. At the last follow-up after 18 months, there was no recurrence, and the patient has maintained on MMF 500mg twice daily.

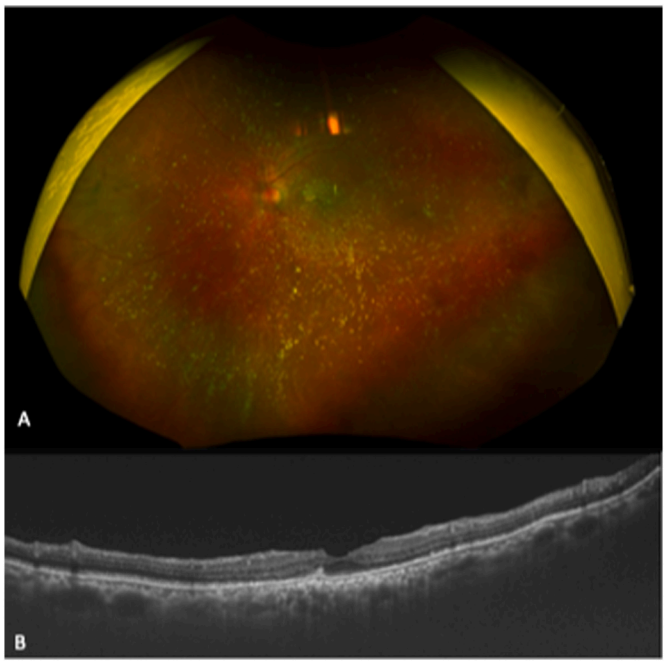

Fig. 2. At 1 year post treatment, complete resolution of choroidal effusion in the left eye. (A). Optical coherence tomography showing no subretinal fluid or choroidal and retinal pigment epithelium folds.(B).

3. Discussion

Uveal effusion syndrome (UES), a rare disease entity characterised by serous detachment of the choroid, retina and ciliary body, was first reported by Schepens and Brockhurst in 1963.[5] It is classified into three types: Type 1 in nanophthalmic eyes, Type 2 in non-nanophthalmic eyes

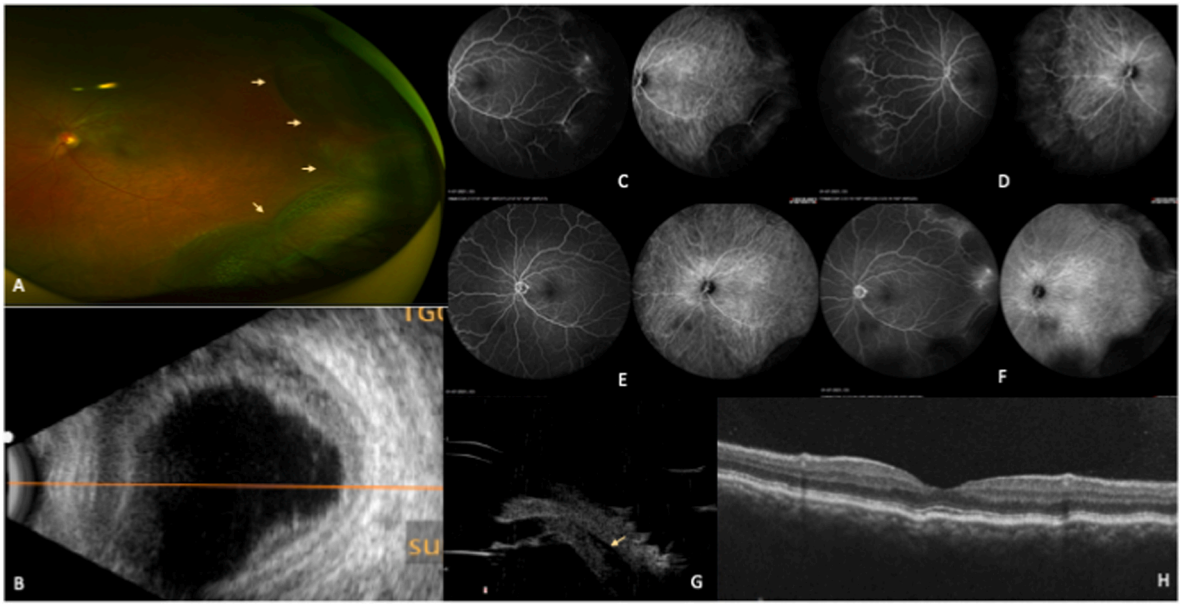

Fig. 1. A – Widefield fundus photograph of the left eye showing annular choroidal detachment suggestive of uveal effusion syndrome.
B – B-scan ultrasonography showing diffuse choroidal thickening and detachment with no T sign.
C–F – Fluorescein angiography showing disc hyperfluorescence and peripheral effusion.
G - Ultrasound biomicroscopy demonstrating supraciliary effusion in the left eye.
H – Retinal pigment epithelium and choroidal folds seen in optical coherence tomography.

with the abnormal sclera, and Type 3 in non-nanophthalmic eyes with the normal sclera. The pathogenesis of UES is still unclear. However, scleral abnormality, vortex vein compression, increased choroidal vessel permeability, chronic choroidal inflammation, and hypotony have been the key factors resulting in uveal effusion. Abnormal sclera impedes the transscleral outflow of intraocular protein and fluid. It compresses the vortex veins, accumulating fluid in the choroidal space, leading to ciliochoroidal detachment, retinal pigment epithelial decompensation and exudative retinal detachment.[5,6] The diagnosis of UES is challenging due to its similarities with other causes of uveal effusion like uveitis, scleritis, neoplasms, drug-induced, trauma, central serous chorio-retinopathy and intraocular surgery.

To the best of our knowledge, we report the first case of unilateral UES following COVID-19 vaccination (Covaxin BBV152) in an Asian Indian man. He also had a previous history of COVID-19 infection and developed ocular symptoms two weeks following his first dose of the vaccine. It has also been reported in a study by Tissot et al. that vaccine recipients with pre-existing COVID-19 immunity had more frequent reactogenicity symptoms after the first dose as compared to naïve individuals.[7] Benage and Fraunfelder also described that the median time from vaccination to onset of uveitis was 16 days (range one day – 6 years), as was seen in our patient.[8] The etiology of UES is still unknown. However, Mansour et al., in their study, have reported uveal effusion syndrome in seven patients following H1N1 influenza infection.[9] Lee et al. have also described a case of UES precipitating three weeks post herpes zoster ophthalmicus. Uveal effusion resolved in four weeks with oral corticosteroids and systemic antiviral agents.[10] Although our patient developed unilateral UES following COVID-19 vaccination, several autoimmune disorders, such as thyroid eye disease, myasthenia gravis, scleritis, granulomatosis with polyangiitis, and optic neuritis due to multiple sclerosis, may affect only one eye.

Ocular adverse events following COVID-19 vaccination have been mainly reported following mRNA vaccines (Pfizer-BioNTech BNT162b2, Moderna mRNA-1273) and adenovirus vector vaccines (Oxford/AstraZeneca ChAdOx1-S). However, there have been reports of multiple evanescent white dot syndrome (MEWDS), juvenile idiopathic arthritis (JIA) associated - uveitis and hypopyon anterior uveitis following inactivated whole virus vaccines (CoronaVAC, Sinopharm, Covaxin).[11–13] Different hypotheses have been suggested for vaccine-induced uveitis, including molecular mimicry, antigen-mediated cellular/humoral immune response, and adjuvant-mediated inflammation.[14] Vaccination triggers both innate and adaptive immune responses in the recipient, requiring a pathogen-specific immunogen and adjuvant. Although an optimal adjuvant stimulates innate immunity without inducing systemic inflammation, it may still cause the autoimmune inflammatory syndrome, also known as Shoenfeld's syndrome, characterised by arthralgia, myalgia and fatigue.[15] In the Hepatitis A vaccine (inactivated), an aluminium-containing adjuvant has been suggested to cause an inflammatory response, as seen in uveitis.[8] Covaxin also contains inactivated viruses mixed with the aluminium-based adjuvant Alhydroxiquim-II, which might have triggered our patient's abnormal immune response, resulting in uveal effusion. The patient responded well to oral corticosteroids and immunosuppressives, thus strengthening this hypothesis. Although the most common treatment of UES has been sclerectomy with sclerotomy,[16–18] medical treatment with corticosteroids also shows a good therapeutic response.[16,19] Uyama et al. described that sclerectomy was effective in only Types 1 and 2 UES and not in Type 3 with no detectable scleral abnormality.[20] Shields et al., in their recent study of 59 eyes with uveal effusion syndrome, also reported complete resolution of effusion in over 95% cases with combined corticosteroid therapy (oral, periocular and topical).[19]

Given the acute onset of ocular symptoms and uveal effusion following vaccination, our case suggests the temporal association and not the causative association with the COVID-19 vaccination. Using the Naranjo algorithm,[21] our case reflects a possible association between the adverse event and vaccine administration.

4. Conclusions

Uveal effusion syndrome is a rare ocular disease which may manifest following COVID-19 vaccination. Our case highlights the importance of a complete ophthalmic examination in patients with ocular symptoms after vaccination. Ophthalmologists must be aware of the potential risk of UES following COVID-19 vaccination.

Patients consent

Availed.

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Authorship

All authors attest that they meet the current ICMJE criteria for authorship.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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None.

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