Ophthalmologists have observed that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) can produce a broad spectrum of ocular manifestations, from anterior segment involvement such as conjunctivitis and anterior uveitis to posterior segment diseases, including retinitis and optic neuritis involving the retina and choroid. Also, several studies reported an association between COVID-19 vaccination and uveitis or graft rejection following endothelial corneal transplant. Uveitis is a collection of diseases characterized by inflammation within the eye, with multifactorial etiology, including autoimmune (60.1%), systemic (30–50%), infectious (30–50%), and idiopathic (20–40%) causes. Uveitis can lead to complications such as cataracts, posterior adhesions, glaucoma, and optic nerve swelling, resulting in decreased or even lost vision. In this retrospective observational study, Chinese authors investigated the association between COVID-19 infection and uveitis, and clinical characteristics of uveitis after COVID-19 infection. A retrospective case series by Korean authors presented the clinical signs, treatment, and outcome of new-onset anterior uveitis that developed after COVID vaccination.

The eye is an immune-privileged organ protected by a blood-retinal barrier, composed of an outer barrier of retinal pigment epithelium and an inner barrier of retinal vascular endothelium. Many infectious agents have been shown to break down a blood-retinal barrier and cause ocular complications. Several respiratory and neurotropic viruses, such as influenza, coronaviruses, Ebola, Zika, and West Nile viruses, have shown ocular tropism and have caused ocular complications in humans. SARS-CoV-2 is known to cause ocular manifestations in COVID-19 patients; its RNA and proteins have been detected in various ocular tissues and fluids.

A study performed in K18-hACE2 mice demonstrated that the intranasal infection with SARS-CoV-2 led to viral positivity in various parts of the eye, including the retina and the anterior segment tissue, as well as in elevated viral titers in the lungs and brain. SARS-CoV-2 induced a hyperinflammatory immune and antiviral response in the retina. Furthermore, long-term exposure to viral spike antigen led to retinal pathologies, including microaneurysm, retinal pigmented epithelium mottling, retinal atrophy, and vein occlusion in mouse eyes.
https://discovermednews.com/retinal-inflammation-after-intranasal-infection-with-sars-cov-2/

Several vaccines were introduced during the pandemic, including messenger RNA (mRNA) vaccines such as mRNA-1273 (Moderna, Inc., Cambridge, MA) and BNT162b1 (Pfizer Inc, BioNTech,), as well as viral vector vaccines such as ChAdOX1 (Oxford-AstraZeneca),

Ad26.COV2.S (Johnson and Johnson), and BBIBP-CorV (Sinopharm, China). The authors noted that a few studies that reported new onset uveitis following the administration of BNT162b2 mRNA vaccines proposed various underlying mechanisms, such as the molecular similarities between uveal self-peptides and vaccine peptides, delayed-type hypersensitivity, immune response to vaccine adjuvants, increased vascular permeability after vaccination affecting the immunologic capability of the cornea, and immune complex deposition in the uvea and iris.

New onset or relapse of uveitis following COVID-19 infection

The study included patients who tested positive for SARS-CoV-2 on reverse transcription polymerase chain reaction and were diagnosed with non-infectious active uveitis according to the Standardization of Uveitis Nomenclature Working Group classification system within one month after the diagnosis of COVID-19. Patients with reactivation of ocular inflammation due to inadequate treatment or discontinuation of medication were excluded.

All patients underwent comprehensive anterior and posterior segment examinations, including best-corrected visual acuity, anterior segment examination with a slit-lamp, intraocular pressure, indirect ophthalmoscopy, and relevant imaging (fundus photography, B-scan ultrasound, indocyanine green angiography, and spectral domain optical coherence tomography). A laboratory workup included routine blood and urine tests, liver and kidney function analysis, and infectious disease investigations (hepatitis, syphilis, and human immunodeficiency virus).

Results

18 patients and 33 eyes were included in the study. 9 patients had newly diagnosed uveitis, and 9 had a relapse of uveitis after COVID-19 infection. Bilateral ocular involvement was diagnosed in 7 of 9 patients with newly diagnosed uveitis and 8 of 9 patients with a relapse of uveitis. The mean age of patients with newly diagnosed uveitis was 37.6 years, and in patients with relapsed uveitis was 39.9 years.

In the group of patients with new-onset uveitis after COVID-19 infection, three patients had Vogt-Koyanagi-Harada syndrome, one sympathetic ophthalmia, four anterior uveitis, and one multiple evanescent white dot syndrome according to the SUN Working Group classification criteria for uveitis. Patients with newly diagnosed uveitis had no history of other systemic or ocular diseases.

In the group of patients with a relapse of uveitis after COVID-19 infection, three cases were diagnosed with Vogt-Koyanagi-Harada syndrome, three with anterior uveitis, two with intermediate uveitis, and one with panuveitis according to the SUN Working Group classification criteria for uveitis.

Local or systemic steroid treatment improved the condition of newly diagnosed or recurrent uveitis with no adverse drug reactions during treatment. In one case of relapsed anterior uveitis after COVID-19 infection, increased intraocular pressure caused permanent vision damage.

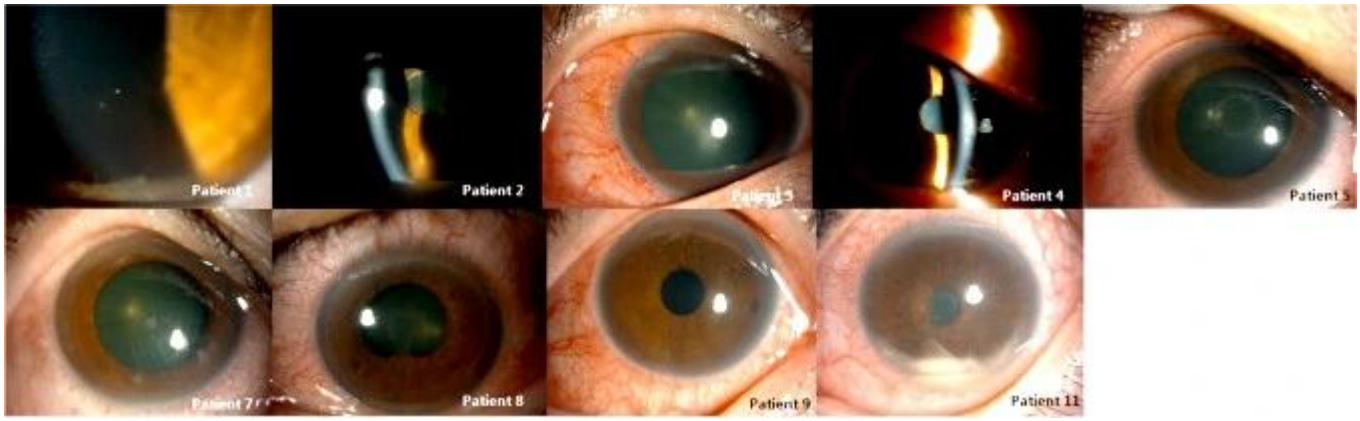
New-onset uveitis after COVID vaccination

This case series included patients who developed a new-onset anterior uveitis within a month of receiving mRNA COVID vaccines (BNT162b1) or virus vector COVID vaccines (ChAdOX1 or Ad26.COV2.S). Patients with a history of uveitis, ocular surgery within 90 days before the diagnosis of uveitis, abnormal laboratory findings suggestive of uveitis-related systemic disease, and involvement of the posterior segment, such as Vogt-Koyanagi-Harada syndrome, white dot syndrome, and retinal vasculitis were excluded from the study.

All patients underwent comprehensive ocular examination, including slit-lamp examination, fundus examination, non-contact tonometry, optical coherence tomography, and best-corrected visual acuity. Laboratory analysis included complete blood cell count, electrolytes, CRP level, serology, rheumatoid factor, human leukocyte antigen-B27, antistreptolysin O, antinuclear antibodies (ANA), anti-neutrophil cytoplasmic antibodies (ANCA), and tests for infectious diseases (toxoplasmosis, toxocariasis, and Cytomegalovirus).

Results

11 patients who experienced the first episode of anterior uveitis after COVID vaccination and had no abnormal laboratory findings were included in the study. All participants with new-onset uveitis after COVID vaccination had unilateral manifestations. The mean age was 51.8 years (ranging 21-72 years).



Clinical presentation of acute uveitis at the initial visit: slit-lamp photography of patients 1–5, 7–9, and 11

In all patients, uveitis occurred shortly after vaccination. The mean period between COVID vaccination and the onset of uveitis was 8.3 days (ranging from 2 to 14 days).

All patients received two doses of COVID vaccines, and 4 of 11 received a third dose. None of the participants developed acute uveitis after the first dose. Most patients (64%) developed uveitis after receiving the second dose (five patients after the second dose of BNT162b1, one after the second dose of ChAdOX1, and one after the second dose of Ad26.COV2.S). 36% of patients developed uveitis after receiving the third dose (three patients after the third dose of BNT162b1, and one after the second vaccination with ChAdOX1, and the third vaccination with BNT162b1).

Younger patients tended to have more severe anterior chamber inflammation and vitritis. A 21-year-old woman had the shortest uveitis development and the most severe anterior chamber inflammation with hypopyon and vitritis. The second youngest patient (32-year-old) also had signs of positive anterior chamber inflammation and vitritis.

Although initially severe, all patients responded well to topical and systemic steroid therapy without vision-threatening complications.

Conclusion

The first study found an association between COVID-19 infection and newly diagnosed or recurrent uveitis within one month of the onset of infection. The authors concluded that these results should prompt ophthalmologists to recognize uveitis developing as a possible

ocular complication after infection with SARS-CoV-2.

The second study presented patients who developed active anterior uveitis shortly after COVID-19 vaccination. The mean time between vaccination and the onset of uveitis was 8.3 days. Most patients developed uveitis after the second dose of the mRNA COVID vaccine. The authors concluded that anterior uveitis should be investigated in all patients complaining of congestion or impaired vision after COVID vaccination, especially in those who received the second dose.

Journal References

Ha Eun Sim, Je Hyung Hwang. New onset of acute uveitis following COVID 19 vaccination. Graefe's Archive for Clinical and Experimental Ophthalmology (2023) 261:555–560. (Open Access) https://doi.org/10.1007/s00417-022-05798-0

Feng, H., Zhao, M., Mo, J. *et al.* New onset or recurrence of uveitis following COVID-19 infection. BMC Ophthalmol 2024; 24, 23. (Open Access) https://doi.org/10.1186/s12886-024-03289-w