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LETTER TO THE EDITOR

COVID-19 vaccination-related intraocular inflammation in Japanese patients

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Key messages

- COVID-19 vaccination-related intraocular inflammation in Japanese appears to include Vogt-Koyanagi-Harada disease at rates higher compared to initial reports from countries with predominantly Caucasian populations.
- Of 10 such patients presenting to the Kyorin Eye Center, 4 had Vogt-Koyanagi-Harada disease and 1 had the related disorder of sympathetic ophthalmia.
- All patients with COVID-19 vaccination-related intraocular inflammation responded well to standard treatment.

Dear Editor,

Large-scale vaccination campaigns to prevent coronavirus disease 19 (COVID-19) started earlier in Europe and the USA compared to most of Asia, and therefore, early reports of new-onset or relapse of intraocular inflammatory disease after vaccination came from populations with low proportions of Asians. The data for these reports was gathered in the spring to summer of 2021 and revealed high rates of anterior uveitis (61.9% and 58.6% for 2 representative multicenter studies, the latter study included scleritis) [1, 2], a type of uveitis known to be common in Caucasians. In contrast, our experience with post-COVID-19 vaccination intraocular inflammation differed greatly to those early reports, prompting the current study.

Medical records were retrospectively reviewed of 10 consecutive patients (6 women and 4 men, mean age 44.6 years, all of Japanese ethnicity) presenting to the Kyorin Eye Center, Tokyo, between June and August of 2021 with new-onset or acutely worsening/relapsing intraocular inflammation within 1 month of vaccination with either BNT162b2 (Pfizer/BioNTech) or mRNA-1273 (Moderna), the only two COVID-19 vaccines offered to the general Japanese population to date. The present study was conducted in accordance with the tenets of the Declaration of Helsinki and was approved by the Kyorin University Hospital Research Ethics Committee.

Of 7 patients with new-onset disease, 4 were diagnosed with Vogt-Koyanagi-Harada (VKH) disease, and of 3 patients with worsening/relapsing disease, 1 had sympathetic ophthalmia that had been under long-standing good control on adalimumab and cyclosporine with excellent visual acuity in the sympathizing eye (Table 1). Only 1 patient (10%) had anterior uveitis. All patients received standard treatment for their condition and achieved usual clinical outcomes for their disease (Table 2).

A rapid survey was conducted by the Japanese Ocular Inflammation Society from February through December 2021, and results tabulated from 14 responding institutions revealed that of 35 patients with new-onset or recurrent uveitis presenting within 2 weeks of COVID-19 vaccination, only 6 (17.1%) had anterior uveitis, while an astonishing 17 (50%) had VKH disease [3]. A Japan nationwide

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Table 1 Clinical characteristics of patients with intraocular inflammation after COVID-19 vaccination

Patient no	Age[a]/gender	Vaccine used	Onset of symptoms after vaccination[b]	Diagnosis (eye(s) involved)
New-onset cases				
1	53/M	BNT162b2 (Pfizer/BioNTech)	10 days after vaccination #2	VKH disease (both eyes)
2	45/F	BNT162b2 (Pfizer/BioNTech)	12 days after vaccination #2	VKH disease (both eyes)
3	29/M	mRNA-1273 (Moderna)	14 days after vaccination #2	VKH disease (both eyes)
4	52/F	BNT162b2 (Pfizer/BioNTech)	6 days after vaccination #1	VKH disease (both eyes)
5	38/M	BNT162b2 (Pfizer/BioNTech)	1 day after vaccination #1	multifocal choroiditis (right eye)
6	64/F	mRNA-1273 (Moderna)	13 days after vaccination #2	Undifferentiated panuveitis (left eye)
7	16/F	BNT162b2 (Pfizer/BioNTech)	16 days after vaccination #1	Autoimmune retinopathy (right eye)
Worsening/relapsing cases				
8	66/F	BNT162b2 (Pfizer/BioNTech)	11 days after vaccination #1	AZOOR (left eye)
9	30/F	BNT162b2 (Pfizer/BioNTech)	1 day after vaccination #2	Anterior uveitis (both eyes)
10	53/M	BNT162b2 (Pfizer/BioNTech)	23 days after vaccination #2	Sympathetic ophthalmia (both eyes)

[a]Age given in years

[b]For onset after the second vaccination, the same vaccine was used for both first and second vaccinations. The interval between vaccinations was 3 weeks for the BNT162b2 (Pfizer/BioNTech) vaccine and 4 weeks for the mRNA-1273 (Moderna) vaccine as per Japanese Ministry of Health and Welfare guidance

Abbreviations used: *M*, male; *F*, female; *VKH*, Vogt-Koyanagi-Harada; *AZOOR*, acute zonal occult outer retinopathy

Table 2 Treatment used and visual outcomes in patients with COVID-19 vaccination-related intraocular inflammation

Patient no	Diagnosis (eye(s) involved)	BCVA[a] initial (right eye/left eye)	Initial treatment[b]	BCVA[a] at 3 months (right eye/left eye)
New-onset cases				
1	VKH disease (both eyes)	0.5/0.6	Methylprednisolone IV (two pulses[c]), corticosteroid eyedrops	1.2/1.2
2	VKH disease (both eyes)	1.0/1.2	Methylprednisolone IV, corticosteroid eyedrops	1.2/1.2
3	VKH disease (both eyes)	0.8/1.2	Methylprednisolone IV, corticosteroid eyedrops	1.2/1.2
4	VKH disease (both eyes)	1.0/1.2	Methylprednisolone IV, corticosteroid eyedrops	1.2/1.2
5	Multifocal choroiditis (right eye)	0.5 1.2	Oral prednisolone 50 mg/day, anti-tubercu-losis therapy[d]	1.2/1.2
6	Undifferentiated panuveitis (left eye)	1.2/0.5	Oral acetazolamide, corticosteroid eyedrops	1.2/0.8
7	Autoimmune retinopathy (right eye)	0.6/1.2	None	1.2/1.2
Worsening/relapsing cases				
8	AZOOR (left eye)	1.2/1.2	None	1.2/1.2
9	Anterior uveitis (both eyes)	0.9/0.7	Corticosteroid eyedrops	0.9/0.7
10	Sympathetic ophthalmia (both eyes)	1.0/0.02	Methylprednisolone IV, corticosteroid eyedrops (continuation of adalimumab IM 40 mg/2 weeks)	0.8/light perception

[a]Visual acuities were measured using metric Landholt rings

[b]Following methylprednisolone IV (1000 mg/day for 3 days), patients received oral prednisolone at a dose of 0.8 mg/kg/day tapered over 9 to 12 months. Other medications were also tapered and discontinued as appropriate for clinical findings

[c]Patient 1 received two pulses of methylprednisolone IV, with oral prednisolone at 0.8 mg/kg/day for 1 week between pulses. The other 3 patients with VKH disease received only one pulse of methylprednisolone IV

[d]Concomitant anti-tuberculosis therapy was used in patient 5 due to positive results on both tuberculin skin test and interferon-gamma release assay. Subsequent chest computed tomography revealed old tuberculosis scarring, however the patient had no signs or symptoms of active tuberculosis

Abbreviations used: *BCVA*, best-corrected visual acuity; *IV*, intravenous; *VKH*, Vogt-Koyanagi-Harada; *AZOOR*, acute zonal occult outer retinopathy; *IM*, intramuscular

retrospective multicenter study conducted prior to the COVID-19 pandemic of consecutive new patients presenting to uveitis specialty clinics over a 1-year period (not including scleritis) reported anterior uveitis as an anatomical type in 36% of patients and VKH disease and/or sympathetic ophthalmia in 8.2% [4]. While VKH disease and sympathetic ophthalmia share similar pathogenic mechanisms involving immune reaction against melanocyte-related antigens, it is unclear why these diseases would be preferentially triggered after COVID-19 vaccination. VKH or VKH-like disease has also been reported in association with intradermal vaccination for other infectious pathogens including hepatitis B virus and human papilloma virus [5]. We wonder whether the intradermal and/or intramuscular site (but still near the dermis) of vaccination may be playing a contributory role to triggering this particular vaccine-related adverse effect.

Declarations

Competing interests The authors declare no competing interests.

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