Ocular Manifestations with COVID-19 Vaccine

Definition

Ocular manifestations after receiving COVID-19 vaccines may appear on the eyelid, cornea and ocular surface, retina, uvea, nerve, and vessel. The ocular manifestations occurred up to forty-two days after vaccination, and vaccine-induced immunologic responses may be responsible.

1. Eyelid
   - Eyelid swelling

   In a study investigating symptoms after administration of three types of COVID-19 vaccines (Pfizer, AstraZeneca, and Sinopharm), Al Khames Aga et al. reported that two out of 1736 participants had eyelid swelling and severe allergic reaction on the day of vaccination with BNT162b2 COVID-19 vaccine [1].

   - Eyelid purpuric lesions

   In a case series study, Mazzatenta et al. reported that a 44-year-old female and a 63-year-old male had purpuric lesions on the upper eyelids occurring 21–25 days after vaccination with the second dose of BNT162b2 COVID-19 vaccine. The other case was a 67-year-old female who developed ecchymosis on the upper eyelids 10 days after the first dose of BNT162b2 COVID-19 vaccine. All three patients’ purpuric eyelid lesions were asymptomatic and resolved spontaneously after 10–15 days [2].

   - Herpes Zoster Ophthalmicus (HZO)

   Furer et al. conducted a case series on herpes zoster following BNT162b2 COVID-19 vaccination in patients with autoimmune inflammatory rheumatic diseases. One of the six patients had herpes zoster ophthalmicus without corneal involvement. A 56-year-old female with a history of seropositive rheumatoid arthritis developed severe pain in the left eye and forehead four days after the first dose of BNT162b2 COVID-19 vaccine. The accompanying symptoms were hyperemic conjunctivitis of the left eye and a vesicular rash at the left forehead [3].

2. Cornea and Ocular Surface

   Six patients developed corneal and ocular surface manifestations after COVID-19 vaccination. The mean age of these patients was 68.5 (range 56–83) years old. The mean duration between COVID-19 vaccination and onset of ocular symptoms was 14.0 (range 7–21) days. The patients’ characteristics were reviewed in four articles.

   - Corneal graft rejection after penetrating keratoplasty (PKP)

   Ravichandran et al. reported a 62-year-old male with a history of PKP for a corneal scar in his right eye for two years. He had right eye congestion and blurred vision three weeks after the first dose of the ChAdOx1 COVID-19 vaccine. Khodadoust’s rejection line in the center of the endothelium with graft edema and anterior chamber (AC) reaction was noted. Corneal graft rejection of the right eye was diagnosed [4]. Wasser et al. reported two cases of corneal graft rejection after the first dose of BNT162b2 COVID-19 vaccine [5]. A 73-year-old male with a history of PKP in the left eye due to keratoconus and underwent regrafting due to late endothelial failure two years prior. He experienced left eye discomfort 13 days after vaccination. Left eye ciliary injection, corneal edema, Descemet folds, and keratic precipitates (KP) were noted, and corneal graft rejection was diagnosed. The other patient was a 56-year-old male with a history of bilateral keratoconus who underwent PKP 25 and seven years ago in the right and left...
eyes, respectively. Right eye regraft was performed due to late endothelial failure 10 months previously. He developed blurred vision in the right eye 14 days after vaccination. Right eye corneal edema, KPs, and AC cells were noted, and corneal graft rejection was diagnosed [5].

- Corneal graft rejection after Descemet membrane endothelial keratoplasty (DMEK)

Crnej et al. reported a 71-year-old male with a history of endothelial decompensation after phacoemulsification and who underwent DMEK of the right eye for five months [6]. He developed a decrease in vision seven days after the first dose of the BNT162b2 COVID-19 vaccine. A right eye conjunctival injection and corneal edema were noted. The central corneal thickness was 714 μm, and corneal endothelial graft rejection was diagnosed. Phylactou et al. reported two cases with a history of Fuchs endothelial corneal dystrophy who underwent DMEK with acute corneal endothelial graft rejection after administration of BNT162b2 COVID-19 vaccine [7]. A 66-year-old female who underwent DMEK of the right eye 21 days prior developed blurred vision seven days after the first dose of the vaccine. Right eye conjunctival injection, diffuse corneal edema, and fine KPs were noted, and corneal endothelial graft rejection of the right eye was diagnosed. Another 83-year-old female underwent DMEK six and three years prior in the right and left eyes, respectively. She had bilateral blurring of vision, pain, photophobia, and redness three weeks after the second dose of the vaccine. Bilateral circumcorneal injections, KPs, and AC inflammation were also noted. The central corneal thickness was 660 μm and 622 μm in the right and left eyes, respectively. A diagnosis of bilateral simultaneous acute endothelial graft rejection was made.

3. Retina

There were seven patients who had retinal manifestations. The mean age of these patients was 24.7 (range 20–33) years old. The mean duration between COVID-19 vaccination and onset of retinal symptoms was 4.0 (range 1–15) days. The patients’ characteristics were reviewed in five articles.

- Acute Macular Neuroretinopathy (AMN)

Bøhler et al. reported a 27-year-old female who took oral contraceptives and developed an acute paracentral scotoma after receiving the first dose of the ChAdO×1 COVID-19 vaccine [8]. Fundoscopy of the left eye revealed a delicate teardrop-shaped macular lesion located nasally with respect to the fovea. Ocular coherence tomography (OCT) demonstrated slight hyperreflectivity of the outer nuclear and plexiform layers and disruption of the ellipsoid zone. Thus, AMN of the left eye was diagnosed. Gabkak et al. reported a 20-year-old female with a history of oral contraceptives and with bilateral flickering scotoma after administration of the ChAdO×1 COVID-19 vaccine [9]. Fundoscopy revealed subtle brightening around the fovea. OCT showed hyperreflective plaques and disruption of the ellipsoid junction. Therefore, bilateral AMN was diagnosed. Book et al. reported a previously healthy 21-year-old female with bilateral paracentral scotomas three days after receiving the first ChAdO×1 COVID-19 vaccine [10]. Infrared reflectance imaging showed bilateral circumscribed paracentral dark lesions that matched outer plexiform layer thickening and discontinuity of the ellipsoid band on OCT. A diagnosis of bilateral AMN was made. Mambretti et al. reported a 22-year-old female and a 28-year-old female who were on long-term oral contraceptives they developed acute onset of paracentral scotoma two days after receiving the ChAdO×1 COVID-19 vaccine. Multimodal retinal imaging was consistent with AMN in both cases [11].

- Central serous retinopathy

Fowler et al. reported a 33-year-old male who did not take any medications. He developed blurred vision and metamorphopsia in his right eye 69 h after receiving the BNT162b2 COVID-19 vaccine. OCT of the right eye showed serous macular detachment of the neurosensory retina. On fluorescein angiography (FA), a single point of leakage was noted following the ink-blot pattern. He was diagnosed with central serous retinopathy in the right eye [12].

- Retinal detachment
Subramony et al. reported a 22-year-old female with myopia but had no ocular trauma or any major past medical history. She developed vision loss in her right eye 15 days after the second dose of the mRNA-1273 COVID-19 vaccine. Fundoscopy revealed bilateral retinal detachment (macula-off in the right, macula-on on the left) despite having no vision loss in her left eye [13].

4. Uvea

There were seven patients with uveal manifestations. The mean age of the patients was 35.2 (range 23-43) years old. The mean duration between COVID-19 vaccination and onset of uveitis symptoms was 15.2 (range 3-42) days. The patients’ characteristics were reviewed in six articles.

- **Acute anterior uveitis**

Renisi et al. reported that a 23-year-old male who had no significant medical history developed ocular symptoms after receiving the BNT162b2 vaccine. He developed unilateral periocular erythema, with involvement of the left eyelid 5 h after the first dose of the vaccine. The symptoms resolved 72 h after topical glucocorticoid administration. However, he developed blurred vision, red eye, and conjunctival hyperemia of the left eye 14 days after the second dose of the vaccine. Left eye posterior synechiae, AC cells, and KPs were noted. Funduscopic examination and autoimmune or infection lab screening did not reveal any alterations. A diagnosis of left eye acute anterior uveitis was made [14].

- **Panuveitis**

Mudie et al. reported a 43-year-old female who developed decreased vision three days after the second dose of the BNT162b2 COVID-19 vaccine. On examination, anterior chamber and vitreous inflammation were noted. However, she was also diagnosed with asymptomatic COVID-19 shortly after the onset of ocular symptoms [15].

- **Multifocal Choroiditis**

Goyal et al. reported a 34-year-old man had vision loss one week after receiving the second dose of the COVID-19 vaccine. On examination, serous detachment of the macula in the right eye and severe choroidal thickening noted on ultrasonography in both eyes were noted. A bilateral multifocal choroiditis was diagnosed [16].

- **Acute zonal occult outer retinopathy (AZOOR)**

In a case report on ocular inflammatory side effects after administration of COVID-19 vaccine, Maleki et al. reported a 33-year-old previously healthy female who developed progressive nasal field defect in her left eye and flashes in both eyes. Her symptoms occurred 10 days after receiving the second mRNA-1273 COVID-19 vaccine. Laboratory investigations demonstrated high erythrocyte sedimentation rate and C-reactive protein levels. On examination, there was no inflammation in either the anterior or vitreous cavities. OCT on both eyes showed a segmented and disrupted ellipsoid zone in the right eye and a very thin ellipsoid zone in the left eye. Multi-luminance-flicker electroretinogram revealed defective areas in the inferotemporal macula and temporal macula in the right and left eyes, respectively. A bilateral AZOOR was diagnosed [17].

- **Reactivation of Vogt-Koyanagi-Harada (VKH) Disease**

Papasavvas et al. reported that a 40-year-old female taking infliximab for VKH disease for six years had reactivation six weeks after the second dose of BNT162b2 COVID-19 vaccine. On examination, AC inflammation, mutton-fat KPs, retinal folds, subretinal fluid, and increased choroidal thickness were noted [18].

- **Uveitis**
Furer et al. conducted a multicenter observational study on the immunogenicity and safety of the BNT162b2 vaccine in adult patients with autoimmune inflammatory rheumatic diseases. The results showed that, among 686 cases, one case developed uveitis several weeks after the first dose of the vaccine and two cases developed uveitis after the second dose of the vaccine \[^{19}\].

### 5. Nerve

There were three patients who developed neural manifestations. The mean age of the patients was 59.3 (range 40–79) years old. The mean duration between COVID-19 vaccination and onset of neural symptoms was six (range 2-14) days. Patients’ characteristics were reviewed in three articles.

- **Optic neuritis**
  
  Helmchen et al. reported a 40-year-old female with a history of relapsing-remitting multiple sclerosis (MS) and developed bilateral blurring of vision that rapidly progressed to blindness two weeks after the first dose of the ChAdOx1 COVID-19 vaccine. Other symptoms include paraparesis that deteriorated to paraplegia, with absent tendon reflexes in the legs, incontinence, and a sensory deficit for all modalities below Th5 (thoracic spine). Brain magnetic resonance imaging (MRI) revealed numerous old white matter lesions compatible with MS and increased signal intensity in the chiasm and part of the adjacent optic nerves and tracts. Spinal MRI revealed myelitis at Th7-10, while aquaporin-4 (AQP4) was negative in serum and cerebrospinal fluid. Optic neuritis with AQP4-antibody negative neuromyelitis optica spectrum disorders-like syndrome was diagnosed \[^{20}\].

- **Arteritic anterior ischemic optic neuropathy (AAION)**
  
  Maleki et al. reported a 79-year-old previously healthy female who had a sudden bilateral loss of vision two days after the second dose of BNT162b2 COVID-19 vaccine. Laboratory examination revealed a very high erythrocyte sedimentation rate and C-reactive protein level. There was a 3+ afferent pupillary defect in the right eye. Fundoscopy revealed complete pallor of the optic nerve head in the right eye and segmental pallor in the left eye. OCT showed ganglion cell complex thinning, and the retinal nerve fiber layer appeared normal in both eyes. The visual field in the right eye showed severe generalized depression, and the left eye depicted a superior altitudinal defect. A right temporal artery biopsy was compatible with AAION, and bilateral AAION was diagnosed \[^{17}\].

- **Abducens nerve palsy**
  
  Reyes-Capo et al. reported that a 59-year-old previously healthy female had acute horizontal diplopia two days after receiving the BNT162b2 COVID-19 vaccine. On examination, right esotropia of 25 diopters in primary gaze, 30 diopters in the right gaze, 10 diopters in the left gaze, and a severe abduction limitation of the right eye were noted. MRI of the brain and orbit was unremarkable. The patient was diagnosed with right abducens nerve palsy \[^{21}\].

### 6. Vascular Thrombosis

There were eight patients with vascular thrombosis and related ocular manifestations. The mean age of the patients was 42.9 (range 18–60) years old. The mean duration between COVID-19 vaccination and onset of ocular symptoms was 8.1 (range 2-13) days. The patients’ characteristics were reviewed from eight articles.

- **Superior ophthalmic vein (SOV) thrombosis**
  
  Panovska-Stavridis et al. reported a 29-year-old previously healthy female with blurring of vision of the left eye nine days after receiving the first dose of the ChAdOx1 COVID-19 vaccine. The accompanying symptoms were severe headache, left eye swelling with proptosis, limited ocular motility, and diplopia at the vertical gaze. Laboratory investigations revealed thrombocytopenia and high D-dimer levels. IgG enzyme-linked immunosorbent assay (ELISA) for platelet factor 4 (PF4)-heparin complex antibodies was
positive. MRI demonstrated left SOV thrombosis with widening SOV and filling defects. On the other hand, Bayas et al. reported a 55-year-old previously healthy female who developed conjunctival congestion, retro-orbital pain, and diplopia 10 days after receiving the first dose of ChAdOx1 COVID-19 vaccine. Laboratory investigations revealed thrombocytopenia. IgG-ELISA for PF4-heparin complex antibodies was negative. MRI showed SOV thrombosis with no contrast filling.

- **Cerebral venous sinus thrombosis (CVST)**

Castelli et al. reported that a 50-year-old previously healthy male developed slight visual impairment 11 days after receiving the first dose of the ChAdOx1 COVID-19 vaccine. He also had severe headache, slight deviation of the right buccal rim, loss of strength in the right lower limb, and unstable walking. Laboratory investigations revealed decreased platelet count and lack of fibrinogen. Computed tomography (CT) angiography showed multiple parenchymal hemorrhage and thrombosis of the left transverse and sigmoid sinuses. Wolf et al. reported a 46-year-old previously healthy female who developed headache, hemianopia to the right, and aphasia 13 days after receiving the ChAdOx1 COVID-19 vaccine. Laboratory examination revealed thrombocytopenia. IgG-ELISA for the PF4-heparin complex antibody was positive. MRI showed thrombotic occlusion of the superior sagittal sinus and the left-hand transverse sinus and sigmoid sinus. Left occipital intracerebral hemorrhage was also noted. Suressh et al. reported a 27-year-old male who developed headache associated with eye floaters and vomiting 48 h after receiving the first dose of the ChAdOx1 COVID-19 vaccine. Laboratory investigations revealed elevated D-dimer levels, low platelet counts, and fibrinogen levels. IgG-ELISA for the PF4-heparin complex antibody was positive, while CT venogram showed CVST. However, the headache worsened, and new homonymous hemianopia occurred the following day. Repeat CT showed right parietal lobe hemorrhage.

- **Thrombocytopenia with acute ischemic stroke and bleeding**

Blauenfeldt et al. reported that a 60-year-old female with a history of Hashimoto thyroiditis and hypertension developed abdominal pain seven days after receiving the first dose of the ChAD0x1 COVID-19 vaccine. Laboratory investigations showed thrombocytopenia, raised D-dimer, and she was positive for PF4 antibodies. Abdominal computed tomography (CT) revealed bilateral adrenal hemorrhages and a subcapsular renal hematoma. The following day, she developed left-sided weakness and eye deviation to the right. MRI revealed a complete infarction in the entire area supplied by the right middle cerebral artery. The patient died on the sixth day of hospitalization.

References


Keywords
COVID-19; vaccine; Ocular; eye

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