# COVID-19-associated optic neuritis – A case series and review of literature

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Neuroophthalmic manifestations are very rare in corona virus disease-19 (COVID-19) infection. Only few reports have been published till date describing COVID-19-associated neuroophthalmic manifestations. We, hereby, present a series of three cases who developed optic neuritis during the recovery period from COVID-19 infection. Among the three patients, demyelinating lesions were identified in two cases, while another case was associated with serum antibodies against myelin oligodendrocyte glycoprotein. All three patients received intravenous methylprednisolone followed by oral steroids according to the Optic Neuritis Treatment Trail ptotocol. Vision recovery was noted in all three patients, which was maintained at 2 months of the last follow up visit.

**Key words:** COVID-19, myelin oligodendrocyte glycoprotein, neuroophthalmic manifestation, optic neuritis

COVID-19 infection predominantly causes a respiratory illness, but it can have a myriad of symptoms, affecting almost all organs of the body.[1] Varied ocular manifestations including conjunctivitis, episcleritis, vascular occlusions, dacryoadenitis, mucormycosis, etc., have been reported in COVID-19 infection.[2] Neuroophthalmic manifestations in COVID-19 infection are uncommon, but they can seldom develop either during the active course or the recovery period.[3] Neuroophthalmic manifestations of COVID-19 infection includes optic neuritis, acute transverse myelitis, viral encephalitis, toxic encephalopathy, leukoencephalopathy, acute disseminated encephalomyelitis, diffuse corticospinal tract signs, etc.[4] Only a handful reports of optic neuritis associated with COVID-19 infection with or without demyelinating lesions have been published. Few of them are associated with serum antibodies against myelin oligodendrocyte glycoprotein (MOG).[5-20] In this report, we describe the clinical profile and treatment outcome of three patients who developed optic neuritis during recovery from COVID-19 infection.

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## Case Reports

### Case 1

A 16-year-old boy presented with sudden gross diminution of vision in the left eye (LE) for 3 days with headache and eyepain on extraocular movements. His past history was unremarkable. The patient had tested positive for COVID-19 infection with reverse transcription polymerase chain reaction (RT-PCR) 2 weeks prior to the incident. He was advised home isolation without any supplemental oxygen or steroids. Systemic and neurological examinations were unremarkable. On ocular examination, best-corrected visual acuity (BCVA) was 20/20 in the right eye (RE) and perception of light (PL+) in the LE, with a grade 2 relative afferent pupillary defect in the LE. Fundus examination revealed normal optic discs in both eyes with no evidence of disc edema or hyperemia [Fig. 1a and 1b]. A diagnosis of LE retrobulbar neuritis was made. Laboratory investigations, imaging, treatment received, and disease course are provided in Table 1.

### Case 2

A 35-year-old male presented with sudden vision loss in LE with pain on extraocular movements for 1 week. His past history was unremarkable. He was tested positive for COVID-19 infection with RT-PCR 6 months prior to the vision loss. He was advised home isolation and did not require oxygen or steroids for COVID-19. On ocular examination, BCVA was 20/20 in RE and 20/600 in LE, with grade I RAPD in LE. Fundus examination of the LE revealed edematous disc with blurred margins and peripapillary edema, which was confirmed on optical coherence tomography, while the RE fundus was normal [Fig. 2a and 2b]. A diagnosis of LE papillitis was made. Laboratory investigations, imaging, treatment, and disease course are described in Table 1.

### Case 3

A 38-year-old male presented with sudden gross diminution of vision and pain on extraocular movements in the LE for 5 days. The patient had a similar complaint in the LE 1 month ago. He was treated elsewhere for the same with intravenous methylprednisolone and oral prednisolone. There was symptomatic improvement in the vision within a week following the initiation of treatment. However, he noticed another similar episode of decreased vision in the LE 3 weeks later, when he presented to us. He was tested positive for COVID-19 infection with RT-PCR one-and-half month prior to the current episode. He was advised home isolation, and he also did not require oxygen



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**Table 1: Investigation and treatment details of all cases**

| Age/ sex | COVID-19 disease course | Duration between COVID-19 positivity and ocular symptoms | Lab investigations | Imaging and VEP | Diagnosis | Management | Disease course and final Outcome |
|---|---|---|---|---|---|---|---|
| 16Yr/M | Mild, Home Isolation | 2 weeks | Hematology normal except high ESR (43 mm/h)<br>Infectious etiology panel screening including HIV, syphilis, toxoplasma, rubella, and tuberculosis were negative<br>Immunology screening for ANA, ANCA were also negative<br>Biochemical analysis of the cerebrospinal fluid (CSF) was normal, absence of anti-aquaporin-4 IgG antibodies in the CSF and serum. Serum antibodies against myelin oligodendrocyte glycoprotein (anti-MOG IgG) was also negative | MRI brain and spine were within normal limits, while MRI orbit showed hyperintensity in the intraorbital and intracanalicular part of the left optic nerve [Figure 1c]<br>Pattern visual evoked potential (VEP) done 1 week after presentation showed increased latency and decreased amplitudes in left eye [Figure 1d] | LE retrobulbar neuritis | ONTT protocol[15] IVMP X 3 days →1 mg/kg oral steroids×11 days and tapering over the next 3 days) | Improvement in vision noted after IVMP treatment Vision improved to 20/120 on day 7, 20/60 on day 21, and finally improved to 20/32 after 2 months of follow- up |
| 35 Y/M | Mild, Home isolation | 6 months | Blood investigations showed elevated WBC (15430 cells/ $mm^3$) and raised ESR counts (38 mm/h). Serum inflammatory markers (ANA, ANCA) were within normal limits<br>Infectious etiology panel screening was negative<br>CSF analysis was within normal limits. Anti-aquaporin-4 IgG antibodies were not detected in serum and CSF. Serum anti MOG-IgG was also negative | MRI brain, spine, and orbits were within normal limits [Figure 2c]<br>Pattern visual evoked potential performed 2 weeks postrecovery showed minimal increased latency with decreased amplitudes in the left eye [Figure 2d] | LE Papillitis | Intravenous methylprednisolone (1 gm/day for 3 days) followed by tapering doses of oral prednisolone according to ONTT protocol [22] | LE BCVA improved to 20/120 at 2 weeks, BCVA remained the same at 2 months |
| 38 Y/M | Mild, Home isolation | 6 weeks | Hematological investigations, infectious profile, immunology screening were unremarkable. CSF analysis showed no evidence of oligoclonal bands; serum myelin oligodendrocyte glycoprotein (MOG) antibody was found to be positive<br>Serum anti Aquaporin-4 IgG antibodies were absent | MRI of the brain and spine were normal MRI of the orbits showed hyperintense lesions along both optic nerves suggestive of demyelination [Figure 3c] Pattern Visual evoked potential could not be done due to poor vision at presentation; flash VEP showed normal N2P2 latency with decreased amplitudes in both eyes [Figure 3d] | LE Myelin oligodendrocyte glycoprotein (MOG)-associated retrobulbar neuritis | Intravenous methylprednisolone (1g/day for 3 days) followed by oral prednisolone as per ONTT protocol | BCVA improved to 20/20 in LE on day 7 Vision maintained at 2 months of follow-up with no further recurrence |

**Table 2: Summary of all the published studies**

| Study | Age/ Sex | Duration between COVID-19 positivity and ocular symptoms (weeks) | COVID-19 disease | Signs and Symptoms | Diagnosis | Management | Outcome |
|---|---|---|---|---|---|---|---|
| Sawalha *et al*.[5] | 44/M | 2 weeks | Mild, Home isolation | RE 20/200, LE 20/20, RE RAPD, superior arcuate VF defect, brain MRI showed enhancement in the right more than the left optic nerve | OU Optic neuritis Myelin oligodendrocyte glycoprotein (MOG) | IVMP 1 g daily for 5 days, followed by oral in tapering doses | Remarkable improvement in VA in OD, complete recovery in OS |
| Zhou *et al*.[6] | 26/M | Concurrent | Mild, Home isolation | OU vision loss, OD HM, OS 20/250, disc edema, retinal hemorrhage | MOG-Ab associated ON in the setting of COVID19-parainfectious demyelinating | IVMP, oral steroids | 3 weeks- dramatic improvement in vision, resolution of disc edema |
| Benito-Pascual *et al*.[7] | 60/F | Concurrent | Moderate, Hospitalization, Hydroxychloroquine, lopinavir-ritonavir | OS vision loss, OD 20/20, OS 20/200 with RAPD, panuveitis, with 3+cells in the AC and vitreous cells | OS optic neuritis with panuvetis | Oral and topical steroids | 2 weeks - VN improved OS 20/40 |
| Parvez[8] | 10/F | Concurrent | Mild | OS vision loss, no neurological impairment, orbit MRI showed mild enlargement and slight T2 hyperintensity of theintracanalicular and intraorbital segment of the left optic nerve | OS Optic neuritis | IVMP followed by oral steroids | Visual recovery after 3 days of IVMP |
| Catharino *et al*.[9] | 64/M | Concurrent | Mild | OS visual loss, MRI brain showedleft optic nerve hypersignal in the STIR-weighted sequence - suggestive of optic neuritis | OS optic neuritis | IVMP for 5 days followed by oral steroids | Partial recovery of vision after 5 days of IVMP |
| Žorić *et al*.[10] | 63/M | 4 weeks | Mod, Hospitalization, O2 supplementation, antibiotics, anticoaqulant | OD vision loss, VN OD 20/630, OS 20/20, RAPD, MRI orbits were normal | MOG-Ab- associated ON | IVMP for 5 days followed by oral steroids | OS VN improved to 20/63 after 5 days of IVMP |
| Rodríguez-Rodríguez *et al*.[11] | 55/F | Concurrent | Mod, Hospitalization | Headache, OS eye pain with vision loss, vision OD 20/40, OS 20/200 with RAPD, MRI of the orbit showed mild increased thickness and signal in the left optic nerve | OD optic neuritis | IVMP for 5 days followed by oral steroids | Eye pain reduced, no improvement in vision, optic atrophy after 3 months |
| Kogure *et al*.[12] | 47/M | Concurrent | Close contact with family member, home isolation | OS pain and an upper visual field defect, with RAPD, MRI orbits showed T1-weighted fat-suppressed MRI revealed the bilateral (but left-dominant) uniform enhancement along with optic nerve sheaths | MOG antibody - positive optic neuritis | IVMP for 3 days followed by oral steroids | Eye pain reduced, vision improved after 10 days of therapy |

*Contd...*

**Table 2: Contd...**

| Study | Age/ Sex | Duration between COVID-19 positivity and ocular symptoms (weeks) | COVID-19 disease | Signs and Symptoms | Diagnosis | Management | Outcome |
|---|---|---|---|---|---|---|---|
| Sardar *et al.*[13] | 38/F | 2 weeks | Mild, hospitalization, antibiotics, hydroxychloroquine | Headache, OS pain, OS vision loss, severe optic disk edema on the left and mild on the right side, MRI brain and venogram normal, lumber puncture revealed high opening pressure, MRI orbits showed signs of optic neuritis | Post COVID-19 Optic neuritis OS with intracranial hypertension | IVMP for 5 days follwed by sterods but minimal improvement | IVIG trial for 5 days showed improvement in VN |
| de Ruijter *et al.*[14] | 15/M | 2 weeks | Close contact, mild disease, home isolation, both parents became postive subsequently | Vision loss OU, OD 1/300, OS 1/70, bilarateral papilary edema, MRI orbits showed bilateral edematous optic nerve lesion (OD > OS), suggestive of bilateral optic neuritis serum anti-AQP4-IgG negetive, but anti MOG-IgG positive | MOG-ab-associated Bilateral optic neuritis is a presumed COVID-19 infection | IVMP for 3 days | Significant improvement after 2 weeks of treatment |
| Al-Salihi *et al.*[15] | 33/F | 1 week | Mild disease associated with pituitary macroadenoma | Bilateral vision loss (L>R); MRI brain revealed enlarged pituitary gland, MRI orbit showed enhancing patch over the retrobulbar segment of optic nerve on both sides; aquaporin 4 antibodies and anti-MOG antibodies were negative | Bilateral optic neuritis associated with COVID-19 infection | IVMP for 5 days | Significant improvement in vision after 3 weeks of treatment |
| Sinha *et al.*[16] | 13Y/M | Concurrent | COVID-19-associated multisystem inflammatory syndrome in children (MIS-C) | Bilateral vision loss (OU vision 3/60); sluggish pupils; fundus examination revealed bilateral optic disc edema with hyperaemic discs, blurring of disc margins, and obliteration of the physiological cups | Bilateral optic neuritis-associated with COVID-19 | IVMP | Complete restoration of vision |
| Deane *et al.*[17] | 21Y/F | 1 week | Mild disaese No respiratory symptoms | Severe loss of vision in LE (HM+); MRI orbits showed abnormal T2 flair with hyperdense signals in the left optic nerve suggestive of acute optic neuritis | Unilateral optic neuritis | IVMP | Improvement in vision after 5 days |
| Azab *et al.*[18] | 32Y/M | 10 days | Severe disease, ICU admission | Loss of vision in LE; fundus examination revealed mild disc swelling only in the left eye; MRI orbit showed left side optic nerve swelling of the retrobulbar intraorbital segment. | Left optic neuritis | IVMP for 3 days followed by oral steroids | Vision improved to 20/40 |

*Contd...*

**Table 2: Contd...**

| Study | Age/ Sex | Duration between COVID-19 positivity and ocular symptoms (weeks) | COVID-19 disease | Signs and Symptoms | Diagnosis | Management | Outcome |
|---|---|---|---|---|---|---|---|
| Rojas-Correa *et al.*[19] | 69 Y/M | 2 weeks | Mild disease antibiotics home isolation | Bilateral loss of vision; fundus examination revealed bilateral disc oedema; MRI orbits showed extensive and uniform contrast enhance- ment of both optic nerves; MOG-IgG was positive | MOG Ab-associated optic neuritis | IVMP for 5 days followed by oral sterods | Vision improved |
| Wodhall *et al.*[20] | 39Y/F | Concurrent | Mild disease Old case of MOG-associated disease | Bilateral visual disturbance; MRI orbit was suggestive of bilateral optic neuritis; MOG Ab was positive | Myelin Oligodendrocyte Glycoprotein Antibody-associated Relapse with COVID-19 | IVMP for 5 days and plasma exchange | Vision improved |

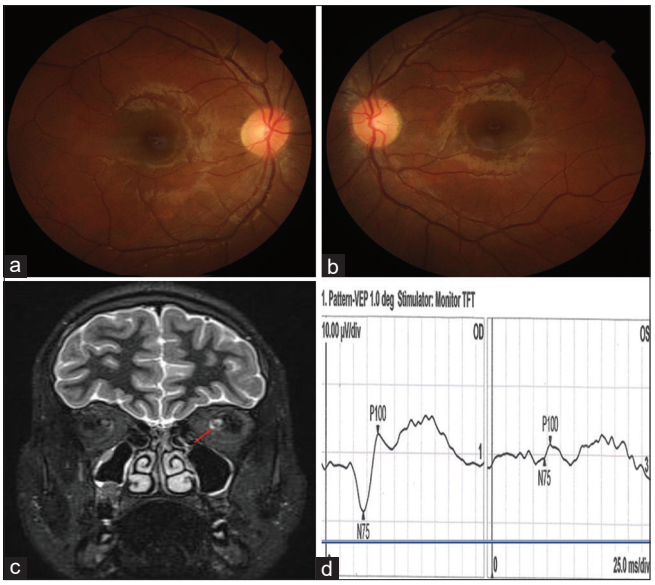


**Figure 1:** Fundus images of both eyes at presentation showing normal disc and macula (a and b), magnetic resonance imaging of the orbits at presentation (c) showing hyperintense lesion in the left optic nerve (red arrow), and pattern visual evoked potential at 1 week (d) showing increased latency and decreased amplitudes in the left eye

or steroids for COVID-19 infection. Systemic examination was unremarkable. On ocular examination, BCVA was RE 20/20 and LE hand movements (HM+), with grade III RAPD in the LE. Fundus examination showed normal discs in both eyes [Fig. 3a and 3b]. A diagnosis of LE retrobulbar neuritis was made. Laboratory investigations, imaging findings, treatment, and disease course are described in Table 1.

## Discussion

Optic neuritis is an inflammatory demyelinating optic neuropathy causing acute uniocular or binocular loss of vision.[21] Optic neuritis is mainly a clinical diagnosis based on history and examination findings. Investigations like magnetic resonance imaging, lumbar puncture, and antibodies against AQP4 and MOG help in finding the association and cause of vision loss.[21] Once the diagnosis is established, treatment is done based on optic neuritis treatment trial (ONTT) protocol.[22]

Neurotropism of the virus was postulated as one of the mechanisms for neuroophthalmic manifestations.[2] Another mechanism involves molecular mimicry where the viral antigens trigger host immune response directed toward the CNS myelin proteins.[4,6] All the three cases reported by us had viral prodromes and positive COVID-19 infection. It is interesting to note that all three cases had mild COVID-19 infections with no oxygen requirement or steroid use, and their recoveries were uneventful. Vision loss in all the three cases happened during the recovery period of the infections and dramatic response to steroids points toward an inflammatory disorder triggered by the viral antigen. In the third case, the patient had two similar episodes of vision loss in 2 months after the COVID-19 infection. He was tested positive for MOG antibody. MOG antibody-associated optic neuritis usually has good visual recovery with good response to steroids but shows bilaterality and recurrence. Our case also showed initial good response to systemic steroids with recurrence within 2 weeks

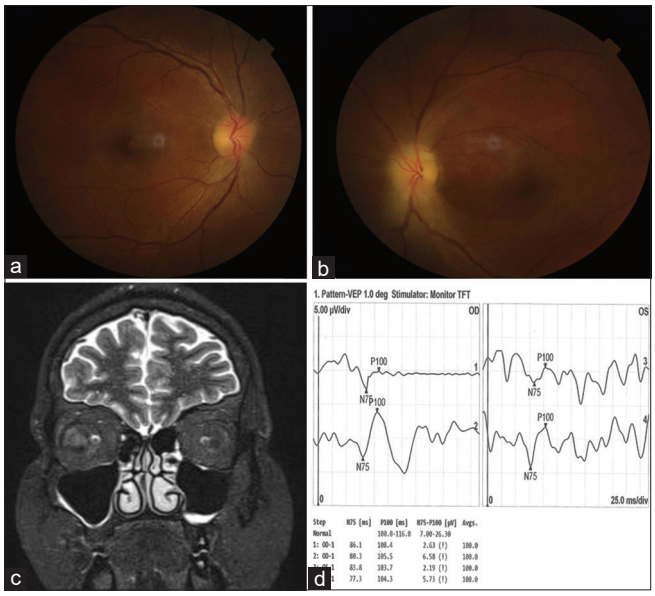


**Figure 2:** Fundus image of RE (a) showing normal disc and macula and LE (b) showing an edematous disc with blurred margins and peripapillary edema, magnetic resonance imaging of the orbits (c) showing normal findings; visual evoked potential performed 2 weeks after presentation (d) showed minimally increased latency with decreased amplitude in the left eye

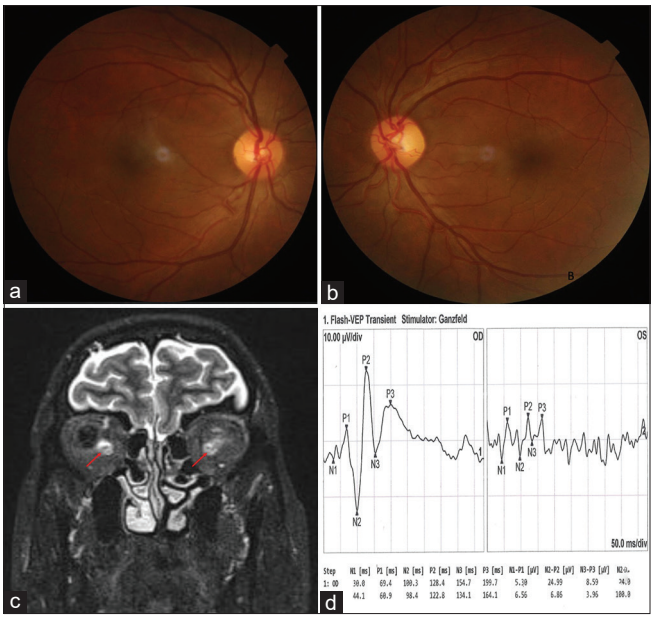


**Figure 3:** Fundus image of both eyes (a) & (b) showing normal disc and macula, magnetic resonance imaging of the orbits (c) showing hyperintense lesion in the optic nerves of both eyes (red arrows), and flash VEP (d) showed normal N2-P2 latency with decreased amplitudes in both the eyes

of discontinuation of steroids. MOG antibody-associated optic neuritis in COVID-19 infection has been reported by Zhou *et al*.,[6] Zoric *et al*.,[10] Kugure *et al*.,[12] Sawalha *et al*.,[5] de Ruijter *et al*.,[14] Rojas-Correa *et al*.[19]. Table 2 describes the details of all cases of COVID-19-associated optic neuritis. Due to the ongoing COVID-19 pandemic, we can expect more similar cases in future. So, prospective studies are warranted to establish the relationship between the viral antigen, severity of COVID-19 infection, and associated optic neuritis.

## Conclusion

Neuro-ophthalmic manifestations are rare in COVID-19 infection, and can be seen either during the active disease phase or the recovery phase.[3] Optic neuritis is one such rare manifestation. The three cases of optic neuritis being reported by us had mild COVID-19 infection. Two cases developed ocular symptoms and signs within the first six weeks of recovery while another case developed ocular manifestations six months after recovery from COVID-19. All the three cases showed good response to systemic steroids with significant visual recovery. Keeping the ongoing pandemic in perspective, we should, therefore, be vigilant in identifying the neuro-ophthalmic features of COVID-19 infection to prevent irreversible vision loss.

### Statement of ethics

Written assent for publication (including clinical information and the images) from patient 1 and consent from the parent have been obtained. Written informed consents have also been obtained from patient 2 and patient 3. All procedures carried out were in accordance with the tenets of the Declaration of Helsinki. Institute Ethics Committee approval is not required for a case report according to Indian council of medical research guidelines.

### Presentation

The article has not been presented in any conference.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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### Conflicts of interest

There are no conflicts of interest.

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