Myelin Oligodendrocyte Glycoprotein and Neuromyelitis Optica/Aquaporin-4 Antibody Negative COVID-19-Associated Optic Neuritis

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   COVID-19
   Optic Neuritis
   Autoimmune
A 72-year-old female presented to our service on 12/10/2020 after being referred by ophthalmology for 14 days of bilateral vision loss. Her medical history was notable for essential hypertension, mixed hyperlipidemia, and obesity. Her ophthalmologic history was notable for prior vitrectomy repairing a full thickness macular hole in the left eye in January, 2016 and placement of bilateral intraocular lens implants in December, 2016. Her visual acuity in the left eye was reported to be 20/20 -2 on post-op follow-up in April, 2018.

On 11/16/2020, she presented to the emergency room with a two-week history of bilateral retroorbital headaches, as well as nausea, vomiting, cough and chest discomfort for ten days. She was diagnosed with coronavirus disease 2019 (COVID-19) via positive severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) ribonucleic acid (RNA) by nucleic acid amplification (NAA) test. She subsequently required three days of hospitalization for intractable vomiting. Vision loss began around 10 days after COVID-19 diagnosis, starting with the left eye, then progressing to the right eye a week later. Involvement of the right eye on 12/7/2020 prompted her to seek medical attention. On ophthalmological examination, visual acuity was light perception in both eyes. Her pupils were 3mm with minimal reaction. Fundus examination showed slight optic disk edema of the right eye with disk hemorrhage at 10 o’clock and disk atrophy in the left eye. Magnetic resonance imaging (MRI) of the head with and without gadolinium showed no acute ischemic process, no intracranial contrast enhancement, mild chronic microangiopathic white matter changes not typical of multiple sclerosis (MS), and an empty sella. Orbit MRI showed enhancement of the orbital segments of both optic nerves, right slightly greater than left.(Figure 1A,1B) Optic nerve optical coherence tomography (OCT) showed moderate disc edema of the right eye, with trace disc edema in the left eye.(Table 1) These findings were consistent with the ophthalmoscopic examination of the fundus. Retinal OCT showed substantial ganglion cell loss apparent in the left eye. The right eye did not demonstrate significant cell loss.(Table 1) We attribute the ganglion cell loss in her left eye to prior vitrectomy, as this is a documented
postoperative complication of this procedure. (Reference 1) There was also some chorioretinal atrophy evident in both eyes, but worse in the left. Other imagining included chest X-rays, which demonstrated no radiographic evidence of disease.

Serum laboratory testing including complete blood count and comprehensive metabolic panel were unremarkable. Other serum laboratory results include erythrocyte sedimentation rate 11 mm/hour (0-20 mm/hour), C-reactive protein 1 mg/L (0-8 mg/L), and negative screens for antineutrophil cytoplasmic antibody (ANCA), rapid plasma regain (RPR), *Treponema pallidum* particle agglutination, neuromyelitis optica/aquaporin-4 antibody (NMO/AQP4-IgG), and myelin oligodendrocyte glycoprotein (MOG) antibody. Cerebrospinal fluid (CSF) glucose, protein, culture and cell count were all unremarkable, and CSF NMO/AQP-4-IgG, MOG antibody, MS evaluation, paraneoplastic antibody evaluation, bartonella antibody panel, and venereal disease research laboratory test (VDRL) were negative. Angiotensin converting enzyme in the CSF was 4 U/L (<=15 U/L). SARS-CoV-2 RNA by NAA testing was now negative. The patient was found to have an elevated CSF opening pressure of 27.5 cm. This could explain the patient’s empty sella noted on MRI but was not thought to be etiologically related to her vision loss.

This presentation was consistent with sequential, bilateral optic neuritis, warranting empiric treatment with a 6-day regimen of high-dose IV methylprednisolone followed by an oral prednisone taper. Follow-up with ophthalmology, about 20 days after the initiation of IV steroid treatment, revealed striking recovery of the patient’s vision to 20/30 in each eye with full visual fields. The patient was sent home with a prescription for an oral prednisone refill as precaution for possible recurrence.

We report a case of sequential, bilateral optic neuritis that appears to be a result of SARS-CoV-2 viral infection. There is evidence in the literature that the SARS-CoV-2 virus has the potential to cause new onset or reactivation of autoantibody syndromes including antiphospholipid antibody syndrome,
Guillain-Barré syndrome, and Kawasaki disease. (Reference 2) The virus has also been associated with other autoimmune causes of optic neuritis, including MOG antibody disease and multiple sclerosis. (Reference 2, 3) Thus, the mechanism for COVID-19-related optic nerve inflammation is postulated to be induced production of autoantibodies. As we have been unable to associate the present case with any commonly tested-for serum or CSF autoantibodies, we suspect this may be the first documented instance of NMO/AQP-4-IgG and MOG-IgG negative, COVID-19-induced optic neuritis.

To make this claim, we feel that it is appropriate to discuss other causes of transient vision loss that may mimic the current presentation and respond to treatment with systemic glucocorticoids. Multiple sclerosis (MS), temporal arteritis (TA) and granulomatous disease are three such entities, and we believe that there are details from the current workup that make them all unlikely causes of this patient’s vision loss. First, if affecting the optic nerves, MS generally presents with unilateral optic neuritis. Sequential, bilateral optic neuritis is rare and most often associated with AQP4 and MOG antibody positive disease. (Reference 4) MS CSF laboratory workup was non-revealing, and MS would be less likely to present initially in a patient of this age. (Reference 5) Second, Temporal arteritis (TA) may also present with acute onset vision loss via ischemic optic neuropathy. The patient lacked other symptoms of TA such as jaw claudication, scalp tenderness and malaise. Laboratory workup for TA was normal (CRP, erythrocyte sedimentation rate and platelet count), and we would not expect such a profound recovery of vision after glucocorticoid treatment if vision loss to this degree had already occurred as a result of temporal arteritis. Third, granulomatous disease such as sarcoidosis and granulomatosis with polyangiitis may involve the optic nerves and cause vision loss. Lack of pulmonary or other systemic inflammatory symptomology, normal laboratory workup (CSF ACE, serum ANCA, kidney function and electrolytes), and unremarkable chest X-rays make granulomatous disease another unlikely etiology.
References


Legend

Figure 1A,1B:

Fat saturated, coronal T2 (Figure 1A) and post-gadolinium contrast, fat saturated, coronal T1 (Figure 1B) thin MRI acquisitions demonstrating bilateral enhancement of the orbital segments of the optic nerve. Both nerves are enhancing, with the right more than the left. These findings support the diagnosis of bilateral optic neuritis.
Table 1:

Optical coherence tomography. Optic nerve head (ONH) and retinal nerve fiber layer (RNFL) analysis results, both eyes.

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<tr>
<td>Average RNFL Thickness</td>
<td>137 µm</td>
<td>107 µm</td>
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<tr>
<td>RNFL Symmetry</td>
<td>68%</td>
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<tr>
<td>Rim Area</td>
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<td>1.74 mm²</td>
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<tr>
<td>Disc Area</td>
<td>3.37 mm²</td>
<td>1.74 mm²</td>
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<tr>
<td>Average C/D Ratio</td>
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<td>0.07</td>
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<tr>
<td>Vertical C/D Ratio</td>
<td>0.33</td>
<td>0.05</td>
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<tr>
<td>Cup Volume</td>
<td>0.022 mm³</td>
<td>0.000 mm³</td>
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Statement of Authorship

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