

CASE REPORT

The diagnostic dilemma of bilateral optic neuritis and idiopathic intracranial hypertension coexistence in a patient with recent COVID-19 infection

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Funding information

Qatar National Library funded the open access publication fees of this case

Abstract

Owing to autoantibody production and thrombophilic disorders in COVID-19, physicians must have low threshold to investigate secondary IHH and demyelinating disorders in patients with headache and decreased vision following recent COVID-19 infection.

KEYWORDS

anti-MOG syndrome, coronavirus, COVID-19, neurological manifestations, NMOSD, pseudotumor cerebri, SARS-CoV-2

1 | INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections have presented with numerous neurological manifestations, providing insight into the potential of SARS-CoV-2 virus in triggering autoantibody production and dysregulating the immune system. We report the case of a young obese lady, recently discharged after treatment for COVID-19, who later presented with headache and blurred vision, diagnosed to have pseudotumor cerebri and concurrent bilateral optic neuritis. To the best of our knowledge, this is the first case report to establish concurrent intracranial hypertension, seronegative neuromyelitis optica syndrome disorder (NMOSD), and SARS-CoV-2 infection. The accumulative number of reports of COVID-19 patients with demyelinating manifestations such as bilateral optic neuritis with clinical and

radiological features of NMOSD/anti-MOG syndrome delineate that probable neuro-invasion is a reasonable concern that SARS-CoV-2 is an emerging neuropathogen. Further experimental models and research are warranted to better understand how the acute and chronic course of illness in the context of SARS-CoV-2 could further modulate our approach and treatment.

The first case of COVID-19 emerged in Wuhan, China, in December 2019,¹ following which the surge in COVID-19 cases reached a pandemic proportion by March 2020. Recent reports have demonstrated the plausible neuro-invasive potential of SARS-CoV-2 infection,² and it has also been hypothesized that SARS-CoV-1 may trigger autoantibody production.³ Several cases have also documented the ability of SARS-CoV-2 virus in dysregulation of the immune system, with COVID-19 cases presenting as Guillain-Barré syndrome,⁴ Miller Filler syndrome,⁵ Kawasaki syndrome,⁶

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antiphospholipid antibody syndrome,⁴ and anti-MOG antibody-induced optic neuritis.^{7,8}

2 | CASE PRESENTATION

A 38-year-old female presented to the accident and emergency department in our hospital with history of headache and blurry vision. Her past medical history was significant for diabetes mellitus, obstructive sleep apnea, migraine, gastritis, obesity, and a recent hospitalization for 10 days due to mild COVID-19 and treated as our local guideline with azithromycin, hydroxychloroquine for 7 days, and amoxicillin-clavulanic acid and discharged in good condition. In the 2-week period, she started exhibiting gradually progressive holocephalic headache, described as pulsatile that awakens her from sleep, associated with nausea and importantly was different from her usual migraine episodes. This headache was followed by blurring of vision that worsened gradually over 1 week and difficulty distinguishing colors especially in the left eye as well as painful eye movements. Initial vitals were normal with temperature of 36.8°C, respiratory rate of 19 breaths per minute, blood pressure of 145/80 mm Hg, oxygen saturation of 99%, and weight of 117.3 kg. Ophthalmology examination showed severe optic disk edema on the left and mild on the right side, color vision 1/7 in the left eye and 7/7 in the right. Laboratories were only remarkable for microcytic anemia. COVID-19 PCR was negative on current admission. CT head revealed slightly bulky left optic nerve with/without CT evidence of acute intracranial abnormality. Here, the patient was admitted to the inpatient medical ward with a clinical suspicion of idiopathic intracranial hypertension.

Magnetic resonance image (MRI) head and MR venogram (MRV) showed no intracranial abnormality, and venous system was well opacified without sinus venous thrombosis. Lumbar puncture (LP) revealed an opening pressure of 45 cm H₂O, and 40 mL clear and colorless CSF was drained at this time. With evidence of increased intracranial pressure by LP

findings, acetazolamide 250 mg TID was initiated. After that, the patient reported mild improvement in her headache but her visual acuity remained the same. Due to rapid deterioration in her vision, a therapeutic LP was performed which revealed normal opening pressure of 18 cm H₂O with normal CSF analysis, including no oligoclonal bands. Further imaging of bilateral orbit MRI (Figure 1) revealed effacement of the perioptic optic CSF space, mild diffuse increased T2 signal principally involving bilaterally of optic nerve entire intraorbital segment extending anteriorly to the papilla, with mildly raised optic disk, showing significant diffusion restriction on DWI series and postcontrast optic nerve and perioptic enhancement with mildly raised enhancing papilla/optic nerve insertion.

Above-described appearances raised the suspicion of postinfectious versus demyelinating process (NMOSD/anti-MOG) optic neuritis. There were no findings suggesting ischemic optic neuropathy or increased intracranial pressure.

In light of the MRI orbit findings, with normal CSF parameters, including negative oligoclonal bands, raised our suspicion of post-COVID-19 optic neuritis. She was started on a course of pulsed methylprednisolone for 5 days, and acetazolamide dose was increased to 500 mg BID. Aquaporin-4 antibodies and oligoclonal bands were negative. Despite a 5-day course of steroids, the patient reported only mild improvement in vision. Hence, we proceeded with plasma exchange; however, she developed anaphylactic reaction, and thus, plasma exchange was discontinued. Serum IgA level was normal, and she was commenced on a trial of intravenous immunoglobulin (IVIG) for 5 days after which she reported significant improvement in her visual acuity and she was discharged home.

3 | DISCUSSION

Since March 2020, the World health organization (WHO) declared the SARS-CoV-2 infections to have reached pandemic proportions, with over 63.9 million reported cases to

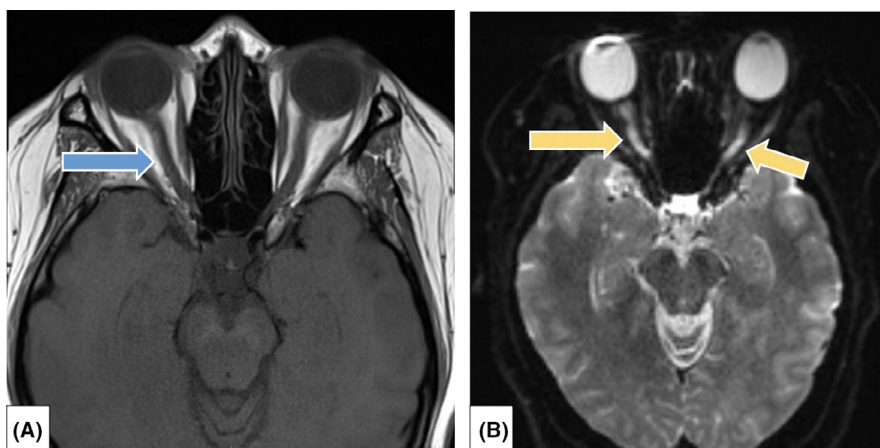


FIGURE 1 MRI orbit showing effacement of the perioptic-optic CSF space, mild diffuse increase in T2 signal involving the optic nerve, entire intraorbital segment extending anteriorly to the papilla, with significant diffusion restriction on DWI series and postcontrast optic nerve and perioptic enhancement

date. The virus is well known with its portentous respiratory system involvement, and compelling evidence from experimental study and case reports points toward its potential neurotropism.^{9,10}

Severe acute respiratory syndrome coronavirus 2 has demonstrated a wide array of manifestations and its potent ability to ignite a profound host immune response.¹¹ Multiple neurological manifestations are well recognized which could be gauged on a spectrum of severity, from anosmia, to stroke syndromes, encephalitis, and demyelination in close proximity to the illness.¹⁰ V. Montalvan in May 2020 published a systematic review highlighting the possible neuro-pathogenicity of the virus. It proposed possible invasion of cerebral circulation endothelium via hematogenous spread of SARS-CoV-2 from systemic circulation and potential viral propagation through the cribriform plate and olfactory bulb.⁹ COVID-19-associated demyelination is hypothesized to be attributed to the cytokine storm due to IL-1, IL-6, and TNF- α , which may subsequently activate the glial cells and thereby cause demyelination.¹² Another possible hypothesis is ascribed to SARS-CoV-2-triggered production of antiglial cell antibodies in the parainfectious or postinfectious state, thereby leading to demyelinating pathologies such as acute or subacute disseminated encephalomyelitis (ADEM),¹³ acute hemorrhagic leukoencephalitis with MRI features of concentric demyelination pattern,¹⁴ acute transverse myelitis,^{15,16} and neuromyelitis optica as witnessed in our case.

Neuromyelitis optica spectrum disorder (NMOSD) and antimyelin oligodendrocyte glycoprotein (anti-MOG) syndromes are two distinct demyelinating conditions owing to their proposed pathophysiology, and diagnostic antibodies yet have compelling and overlapping features.¹⁷ It is estimated that NMOSD holds a prevalence of 0.5-10 per 100 000, with well-recognized ethnic and geographical discrepancies.^{18,19} The hallmark of NMOSD is severe visual loss at onset with bilateral involvement of the optic nerves or optic chiasm optic nerve seen in 42% of patients according to clinical analysis of the largest international cohort to date published of AQP4-seropositive NMOSD.²⁰⁻²³

Anti-MOG syndromes are defined as AQP4-seronegative patients with a phenotype of NMOSD.^{18,20,21} In 2017, a large cross-sectional study of 132 patients with non-MS demyelinating disease estimated that 73% fulfilled the diagnostic criteria of 2015 International Panel for NMO diagnosis have aquaporin-4 antibodies (AQP4-IgG), around 11% were MOG-IgG seropositive, and 16% remained seronegative.²²

Despite the overlapping features between NMOSD and anti-MOG syndrome, optic neuritis in the latter rarely has chiasmal involvement, which could help us distinguish it from optic neuritis in AQP4-IgG NMOSD and MS.^{20,23} In an observational study by Chen et al²⁴, 86% of studied patients were found to have optic disk edema in the setting of anti-MOG antibody-positive optic neuritis.

Since the early 1790s, an etiologic correlation between prodromal viral illness and parainfectious or postinfectious demyelinating syndromes is well recognized,^{8,25,26} with the description of a 23-year-old woman developed encephalomyelitis 1 week after a measles rash.²⁷ Anti-MOG syndromes, Guillain-Barré syndromes, and NMOSD in SARS-CoV-2 infection are well reported in a number of cases, with one for the prevailing mechanism of injury is likely to involve molecular mimicry; with various viral antigens, trigger an immune response toward endogenous CNS myelin proteins, including MOG.^{11,28}

Recent evidence has linked interleukin-6 (IL-6) to disease activity in NMOSD by mechanism of promoting survival of plasmablasts, stimulation of AQP4-IgG secretion, altering integrity and functionality of BBB, and increasing differentiation and activation of proinflammatory T-lymphocytes. In patients with NMOSD, IL-6 levels in the serum and CSF are significantly increased.²⁹ Interlinking this to elevated IL-6 levels in SARS-CoV-2 infection may explain the underlying pathophysiology for occurrence of NMOSD in cases of recent COVID-19 infection. Post-COVID-19 bilateral optic neuritis has been reported recently in November 2020 by Sawalha et al³⁰

On the other hand, idiopathic intracranial hypertension (IIH) constitutes a constellation of signs and symptoms of raised intracranial pressure with fulfillment of modified Dandy's criteria. IIH has an annual incidence of 19.3 per 100 000 in those who weigh 20% or more than their ideal body weight, with 90% affecting females.³¹ Different types of pathophysiology varying from vascular, hormonal, and increased CSF outflow resistance have been proposed, which could be directly linked to common risk factors.³¹

Our patient's constellation of symptoms of pulsatile headache, optic disk edema, and high opening pressure on LP made the diagnosis of optic neuritis challenging. Her MRI head was unremarkable. Lumbar puncture (LP) showed high opening pressure (45 cm H₂O) and normal CSF analysis, with headache that improved with therapeutic LP and acetazolamide. Fulfilling modified Dandy's criteria for IIH. However, MRI orbits were pursued due to further deterioration of her vision, which showed bilateral extensive retrobulbar optic neuritis with postcontrast optic nerve and perioptic enhancement, thereby raising the suspicion of optic neuritis due to anti-MOG syndrome or NMOSD in correlation with her recent SARS-CoV-2 infection. With use of pulsed high dose 1000 mg methylprednisolone and multiple sessions of IVIG, her visual acuity gradually improved.

She was discharged home, on acetazolamide and topiramate for IIH, with regular follow-up in our general neurology clinic and showed improvement in her headache and vision. A 4-month neuro-ophthalmology assessment showed resolution of optic disk edema, normal color vision, and visual acuity.

4 | CONCLUSION

COVID-19-associated neurological manifestations are widely reported, with some rare instances of anti-MOG syndrome in coexistence with SARS-CoV-2 infection. We report the first case of concurrent NMOSD and IHH in the context of COVID-19 infection. While the propensity for triggering autoantibody production and thrombophilic disorders is prevalent in COVID-19, physicians and neurologists must be vigilant with low threshold to further investigate the possibility of secondary idiopathic intracranial hypertension and demyelinating disorders in patients presenting with headache and rapid deterioration in visual acuity following recent COVID-19 infection.

ACKNOWLEDGMENTS

None.

CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

SS, AS, and LO: Writing the initial draft of the manuscript. NS and GA: Conceptualization and supervision. SS, AS, NS, GA: Medical management of the case. SS, AS, LO, NS, and GA: Critical manuscript revision and literature review.

ETHICAL APPROVAL

The publication of this case report was approved by local medical research committee/institutional review board.

CONSENT

Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editor in Chief of this journal.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from authors, SS and AS, upon reasonable request.

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How to cite this article: Sardar S, Safan A, Okar L, Sadik N, Adeli G. The diagnostic dilemma of bilateral optic neuritis and idiopathic intracranial hypertension coexistence in a patient with recent COVID-19 infection. *Clin Case Rep*. 2021;9:e04347. <https://doi.org/10.1002/ccr3.4347>