

# Post-COVID Neuromyelitis Optica Spectrum Disorder

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## ABSTRACT

After novel coronavirus pandemic that emerged from Wuhan, China in December 2019, several cases of inflammatory and immune-mediated disorders have been reported, thought to be triggered by SARS-CoV-2 infection. Neuromyelitis optica spectrum disorder (NMOSD) is one of the autoimmune demyelinating disorders, which is thought to be triggered by viral infection. Herein, we describe a case of NMOSD in a pediatric patient with a previous SARS-CoV-2 infection, acting as a possible triggering factor.

**Key Words:** Neuromyelitis optica spectrum disorder (NMOSD), Aquaporin 4 (AQP-4), Severe acute respiratory syndrome (SARS).

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## INTRODUCTION

It is reported that coronavirus disease 2019 (COVID-19), a pandemic respiratory infectious disease, can cause autoimmune and inflammatory disorders, which include pediatric inflammatory multisystem syndrome (PIMS), toxic shock syndrome, myocarditis and macrophage activation syndrome in children.<sup>1</sup> Several emerging reports also show that an enhanced immune response in SARS-CoV-2 infection can lead to many autoimmune neurological disorders including Guillain-Barré syndrome (GBS), Miller Fischer syndrome, acute necrotizing encephalitis, myelitis, acute disseminated encephalomyelitis (adem) and myasthenia gravis.<sup>2-4</sup>

Neuromyelitis optica spectrum disorder (NMOSD) is an autoimmune disorder of central nervous system (CNS), which is also known as Devic's disease. It frequently affects optic nerve and spinal cord and clinically presents as optic neuritis, myelitis, area postrema syndrome and acute brainstem syndrome.<sup>3</sup> Pediatric-onset NMOSD accounts for 3-5% of all cases. It is observed that infectious agents, mostly viral infections, are triggers, which play an important role in the development of NMOSD, as 15-35% of cases are preceded by viral infections.<sup>3,5</sup> In this case, we report SARS-CoV-2 infection as a possible triggering agent for the development of NMOSD in a pediatric patient.

## CASE REPORT

A 7.5-year, previously healthy girl, the first-born child of non-consanguineous parents, presented with a 10-day history of difficulty in walking. It was sudden in onset, started with unsteady gait and frequent falls. This was followed by blurring of vision for five days. It was not associated with bladder or bowel dysfunction, backache, or abnormal sensations. There was no preceding history of cough, fever, respiratory difficulty, abdominal pain or diarrhea, but there was a significant history of contact with COVID-19 infection as her grandmother died of SARS-CoV-2 infection three weeks earlier.

On examination, she was alert with normal hearing and speech and cranial nerves. She had ataxia during walking with generalised hypotonia, hyperreflexia, reduced power in lower limbs (MRC Grade 4/5 proximally and 3/5 distally), with bilateral extensor plantar responses and absent superficial reflexes. On visual assessment, she had bilateral normal fundi and light reflex. Visual acuity was 6/36. Rest of the systemic examination was unremarkable.

She was diagnosed as acute transverse myelitis or NMOSD. MRI brain and spinal cord revealed lesions suggestive of NMOSD (Figure 1) that included abnormal signals in optic nerve, brain stem, area postrema, periaqueductal region and spinal cord. Visual evoked potentials (VEPs) revealed bilateral optic pathway dysfunction (Table I).

Immunological workup included serology for aquaporin 4 (AQP-4) antibodies in serum for NMOSD, SARS-CoV-2 IgG antibodies for possibility of post-COVID autoimmune reaction, anti-MOG antibodies for MOG antibody demyelination, and anti-ganglioside antibodies panels for variants of GBS. She had raised acute inflammatory markers that included raised CRP, high serum ferritin of 497 ng/ml (Normal: 13-150), and high LDH of 376 U/L (Normal: 135-214 U/L). She had normal ESR and D-

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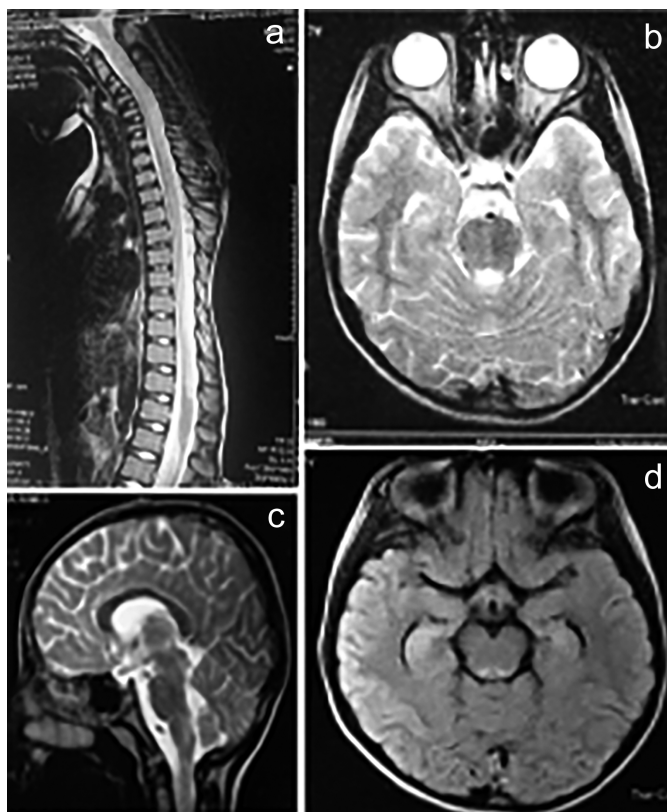
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Dimers of 0.34 µg/ml (Normal: up to 0.50 µg/ml). Among all serological tests, only anti-SARS-CoV-2 antibodies (IgG + IgM) were significantly reactive with a value of 22.41 (Normal value: less than 1.00), rest of the serology for AQP-4 antibodies, anti-MOG antibodies and anti-ganglioside antibodies were negative.

**Table I: Visual evoked potentials.**

Pattern shift technique				
Sides	Latency (ms)			Amplitude (µV)
	N75	P100	N195	P100
Right	119.1	173.1	21.9	1.40
Left	93.9	152.7	210.0	1.47



**Figure 1: MRI images: (a) Sagittal T2-weighted (T2W) MRI of cervico-dorsal spine showing long segment myelitis (arrows). (b) MRI brain T2W images with axial view showing hyperintense signals in brainstem (bilateral pons and midbrain). (c) T2W sagittal brain images showing hyperintense signals in area postrema of brainstem (arrows). (d) Axial FLAIR brain images showing hyperintense signals in midbrain periaqueductal region.**

Considering all above findings and investigations, we made our final diagnosis of seronegative NMOSD as our patient had clinical, radiological, serological and electrophysiological features of seronegative NMOSD, according to international panel for NMO diagnosis (IPND) criteria, secondary to previous SARS-CoV-2 infection.<sup>5</sup> After making final diagnosis of post-COVID NMOSD, she was treated with IV methylprednisolone (MP) 30 mg/kg/day for five days by consultant pediatric neurologist along with supportive care and involvement of multidisciplinary team. She did not show improvement. Then, a course of IVIG was given with dose of 2 g/kg over three days,

and no appreciable clinical response was observed. Later, after detailed parental counselling and informed consent, five cycles of plasma exchange (PLEX) over 10 days were carried out. She was discharged on maintenance therapy of low dose steroids and azathioprine. She is improving gradually and on close follow-up, while receiving maintenance treatment.

## DISCUSSION

It is well known that acute inflammatory autoimmune demyelinating disorders can be caused by murine corona virus.<sup>1</sup> Other common viruses, which are reported as triggering agents in case of NMOSD, are VZV, mumps, HIV and Epstein Barr viruses.<sup>1,2</sup> The possible mechanism by which viral infections activate autoimmune reaction in NMOSD is damage to AQP4-rich tissue, which provokes activation of B-cells to form AQP4-specific antibodies and molecular mimicry.<sup>4</sup> This case was diagnosed by application of IPND criteria, that unify term NMOSD, which further include serology testing (with or without AQP4-IgG).<sup>5</sup> As serology for AQP-4 antibodies was negative but specific areas of brain were involved that fulfill diagnostic requirement, we finally diagnosed it as AQP-4 negative NMOSD.<sup>5</sup> Out of all laboratory investigations done in this case, only SARS-CoV-2-IgG were significantly raised even on repeat testing. The specificity of SARS-CoV-2-IgG for COVID-19 patient is 96.5%, but specificity of both IgG and IgM is 100%.<sup>4</sup> It is also reported that SARS-CoV-2 cell lysate for the ELISA to detect SARS-CoV-2 antibodies could lead to false positive reaction or cross reaction of SARS-CoV antibodies in non-SARS and healthy contacts.<sup>4</sup>

Since she did not show a dramatic response to IV MP, IVIG, and PLEX, as one would have expected, but showed a slow delayed recovery, the possibility of other mechanisms/neurotropic factors associated with SARS-CoV-2 may have been responsible. Further studies over the next few years may clarify this in future.

Considering all the above evidence and the presence of high serum level of SARS-CoV-2 antibodies, this NMOSD may represent an autoimmune reaction, triggered by preceding SARS-CoV-2 infection.

## PATIENT'S CONSENT:

Informed consent was obtained from patient's parents to publish the data concerning this case.

## CONFLICT OF INTEREST:

The authors declared no conflict of interest.

## AUTHORS' CONTRIBUTION:

SR: Data compilation and interpretation, literature review and writing the case.

AW: Data collection and provision of text.

TS: Basic concept, structure and final diagnosis.

AA: Performance of electrophysiological study, help in making final diagnosis and proofreading.

## REFERENCES

1. Galeotti C, Bayry J. Autoimmune and inflammatory diseases following COVID-19. *Nat Rev Rheumatol* 2020; **16(8)**: 413-4. doi: 10.1038/s41584-020-0448-7
2. Llorente Ayuso L, Torres Rubio P, Beijinho do Rosário R, Giganto Arroyo M, Sierra-Hidalgo F. Bickerstaff encephalitis after COVID-19. *J Neurol* 2020; **3**:1-3. doi: 10.1007/s00415-020-10201-1.
3. Seah I, Agrawal R. Can the coronavirus disease 2019 (COVID-19) Affect the eyes? A review of coronaviruses and ocular implications in humans and animals. *Ocular Immunol Inflammation* 2020; **28(3)**:391-5. doi: 10.1080/09273948.2020.1738501.
4. Vojdani A, Kharrazian D. Potential antigenic cross-reactivity between SARS-CoV-2 and human tissue with a possible link to an increase in autoimmune diseases. *Clin Immunol* 2020; **217**:108480. doi: 10.1016/j.clim.2020.108480.
5. Hamid S, Elson L, Mutch K, Solomon T, Jacob A. The impact of 2015 neuromyelitis optica spectrum disorders criteria on diagnostic rates. *Multiple Sclerosis J* 2016; **23(2)**:228-33. doi: 10.1177/1352458516663853.

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