

## Case Report

# Demyelinating solitary lesion of the central nervous system associated with COVID-19: a case report and literature review

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**Received:** 11 October 2020

**Revised:** 10 November 2020

**Accepted:** 11 November 2020

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### ABSTRACT

In December 2019, coronavirus disease (COVID-19) emerged in China and rapidly spread to the world to become the largest pandemic since the 1918 influenza. The disease has been identified as a severe acute respiratory syndrome caused by a novel coronavirus-2 (SARS-CoV-2). Although the typical presentation is respiratory symptoms, reports of neurological involvements are increasing, as more than one-third of patients with COVID-19 develop neurological manifestations. The most frequently reported neurological manifestations in COVID-19 patients were headache, dizziness, taste, and smell impairments, and altered level of consciousness. More specific neurological complications were also reported in literature including acute cerebrovascular complications, seizures, meningoencephalitis, and Guillain-Barré syndrome. Very few studies have shown CNS demyelinating lesions as complications of COVID-19. Current report described a case of a COVID-19 patient with an acute solitary demyelinating lesion in the central nervous system. I also reviewed and summarized the available related cases.

**Keywords:** Demyelinating diseases, Myelitis, Encephalomyelitis, COVID-19

### INTRODUCTION

In December 2019, coronavirus disease (COVID-19) emerged in China and rapidly spread to the world to become the largest pandemic since the 1918 influenza. The disease has been identified as a severe acute respiratory syndrome caused by a novel coronavirus-2 (SARS-CoV-2).

Although the typical presentation is respiratory symptoms, reports of neurological involvements are increasing, as more than one-third of patients with COVID-19 develop neurological manifestations.<sup>1</sup> The most frequently reported neurological manifestations in COVID-19 patients were headache, dizziness, taste and smell impairments, and altered level of consciousness.<sup>1,2</sup>

More specific neurological complications were also reported in literature including acute cerebrovascular complications, seizures, meningoencephalitis, and Guillain-Barré syndrome.<sup>3,4</sup> The most believed neuroinvasive mechanism of SARS-CoV-2 is similar to other coronavirus, as these viruses reach the brain through the olfactory tract. It was suggested that coronavirus strains can initiate an immunological process leading to demyelination lesions in the central nervous system.<sup>5</sup>

Very few reports were published about the demyelinating event in the central nervous system in the context of recent symptoms typical of COVID-19. This article is a retrospective case report of an acute solitary demyelinating lesion with COVID-19.

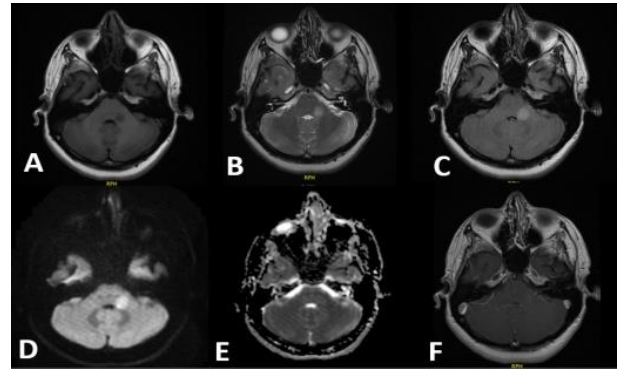
## CASE REPORT

A previously healthy 34 year old female, right handed, presented to the emergency room with 3 days history of slowly progressive unsteadiness, and left sided facial weakness. She reported high fever two weeks ago subsided with simple analgesia; she denies any history of cough, chills, sore throat, headache, hyposmia, or hypogeusia. No previous history of dry eyes, dry mouth, hair loss, facial/skin rash, joints pain, weight loss, mouth/genital ulcers, or abortions. No clear history of recent contact with sick patients in the past few weeks. She denies any history of drinking unpasteurized milk or recent travel. On examination, her blood pressure was 118/85 mmHg, and her pulse was 93 beats per minute. Her temperature was 37.9°C, her respiratory rate 18 per minute, and her oxygen saturation 94% while she was breathing ambient air. The patient was alert and orientated to time, place, and person, fluent, and comprehended. There was no evidence of meningeal irritation signs. Cranial nerve examination revealed left lower motor neuron facial weakness. Power 5/5 with normal tone and deep tendon reflexes. Sensory examination was normal. The cerebellar exam showed left side cerebellar tremor, incoordination, and ataxic gait. MRI brain with contrast showed a well defined rounded lesion at the left middle cerebellar peduncle, demonstrating hypointense signal on T1, hyperintense signal on T2/flair, with high DWI signal and normalized ADC map value in addition to a faint blush of contrast enhancement. No other lesions identified through the brain. MRI cervical spine with contrast was unremarkable. Initial laboratory findings were normal, including white blood cell count, hemoglobin, platelet, erythrocyte sedimentation rate, C reactive protein, alanine transaminase, aspartate aminotransferase, alkaline phosphatase, albumin, HIV, and hepatitis B serology. Brucella workup was negative including standard tube agglutination (STA) tests, brucella IgG and brucella antibody. A COVID-19 nasopharyngeal swab test was positive.

The cerebrospinal fluid analysis showed normal proteins (400 mg/l), CSF/blood glucose ratio, and lactate dehydrogenase (LDH) levels. White blood count was 2; cultures for bacteria, virus, fungi, acid fast bacilli culture, and acid-fast bacilli DNA amplification were negative, as well as PCR for SARS-Cov-2 and CMV. Brucella IgG antibody, CSF, and brucella total antibody, CSF were normal. Oligoclonal band (OCB) in CSF was negative. The patient was treated with 1 gram of IV methylprednisolone daily for 5 days with good improvement in her coordination and ataxia. Unfortunately, there was no significant improvement in facial weakness.

The published literature was reviewed with search via PubMed on articles published between December 2019 and August 05, 2020, using the following strategy and key words; COVID-19 (title/abstract) or (SARS-CoV-2

(title/abstract) or coronavirus (title/abstract) and demyelinating (title/abstract). Studies published in English related to SARS-CoV-2 in adults were reviewed.



**Figure 1: MRI brain with contrast, (A) axial T1 sequence demonstrates left middle cerebellar peduncle hypointensity, (B) axial T2 sequence demonstrates hyperintense signal, (C) axial flair sequence demonstrates hyperintense signal, (D) DWI sequence demonstrates high signal, (E) ADC sequence demonstrates a normalized map, (F) Faint blush of contrast enhancement.**

## DISCUSSION

The typical presentation of COVID-19 is respiratory symptoms that may lead to respiratory failure and death. However, reports of neurological involvements are increasing, as more than one-third of patients with COVID-19 develop neurological manifestations.<sup>2</sup>

Many possible mechanisms were suggested to explain the neuroinvasive and neurotropic characteristics of coronavirus, these mechanisms include; direct central nervous system injury via blood or nasal epithelium, unpredictable effects of the host immune response leading to nervous tissue damage, indirect injury of the central nervous system due to systemic disease, and overactivation of the immune response, which results in a cytokine storm.<sup>3,6</sup>

The most common neurological manifestations of COVID-19 are non-specific, this include; headache, dizziness, taste and smell impairment, or impaired level of consciousness.<sup>1</sup> However, accumulating reports highlights specific neurological complications like acute cerebrovascular complications, seizures, meningoen- cephalitis, and Guillain-Barré syndrome.<sup>3</sup> WHO provisional case definitions of probable association of COVID-19 with neurological include; neurological disease onset within 6 weeks of COVID-19, either SARS-CoV-2 RNA detected from any sample or antibody evidence of acute SARS-CoV-2 infection and no evidence of other commonly associated causes.<sup>7</sup> The WHO provisional case definitions were established for meningitis, encephalitis, myelitis, or CNS vasculitis, ADEM, GBS, neuropathy, and stroke. Moreover, there

are no provisional case definitions for demyelinating disease with COVID-19, so this association is being extrapolated from these other provisions.

The incidence of acute/subacute demyelinating lesions associated with COVID-19 infection is unknown. A few case reports show that SARS-CoV-2 has been associated with demyelinating lesions like acute disseminated encephalomyelitis (ADEM) and acute transverse

myelitis.<sup>1,8-12</sup> ADEM is a rare acute inflammatory demyelinating disease that affects the brain and spinal cord, usually occurs in children. Both ADEM and acute transverse myelitis may follow viral infections. Moreover, a recent report revealed delayed central nervous system demyelinating events following COVID-19.<sup>9</sup> Nevertheless, it is still debatable whether these lesions occur directly from the viral infection or as autoimmune sequelae.<sup>13</sup>

**Table 1: Summary of the demyelinating lesions of the CNS related complications of COVID-19.**

Ref. no.	Age (years), sex	SARS-CoV-2		Neurological presentation	MRI	Other results
		Nasal swab	CSF			
7	21, M	Negative	Negative	Progressive weakness and paresthesia of the lower limbs, urinary retention, followed by progressive upper limbs weakness.	Bilateral posterior internal capsule lesions extending to the pons. Cervical and thoracic longitudinally extensive transverse myelitis, non enhancing lesions.	Spinal tap; cloudy CSF, leukocytes; 150, 60% lymphocytes. CSF protein 281 mg/dl, and the glucose level was 34 mg/dl, with a serum glucose level of 110 mg/dl concomitantly. Gram stain and culture were negative. PCR panel for viral meningoence-phalitis were negative. AQP4 and MOG antibodies were negative. Serologic COVID-19 IgM was negative, but the IgG level was 1.6 (positive >1.1).
8	51, F	Positive	Negative	Coma, impaired oculocephalic response to one side.	scattered hyperintense lesions on flair imaging in deep hemispheric and juxtacortical white matter. hyperintense on DWI, with few lesions showed restricted diffusion on ADC. Small IVH in the occipital horns of both lateral ventricles.	CSF analysis; 1 WBC, 2095 RBC with xanthochromia, 62 mg/dl protein, 56 mg/dl glucose. Bacterial culture, fungal culture, and a PCR panel (including HSV, VZV, EBV, and CMV) were negative. SARS-CoV-2 negative.
9	54, F	Positive	Negative	Impaired level of consciousness, seizures, anosmia and ageusia.	periventricular confluent white matter lesions and multiple high signal cord lesions from bulbo-medullary junction to T6 level with no gadolinium enhancement.	CSF: normal WBC, protein and glucose.
10	32, M	Positive	NA	Acute lower limbs weakness.	Extensive diffuse cervical, dorsal and lumbar spine hyperintense signal with mild enlargement and swelling of the cervical cord.	Lumbar puncture was not done.

Continued.

Ref. no.	Age (years), sex	SARS-CoV-2		Neurological presentation	MRI	Other results
		Nasal swab	CSF			
11	60, M	Positive	Negative	Bladder dysfunction and progressive lower limbs weakness.	T2 hyperintensity of the thoracic spinal cord at Th9 with normal brain MRI.	CSF analysis; lymphocytic (Contd.) pleocytosis (16/ $\mu$ l), elevated protein level (793 mg/l). Oligoclonal bands were negative.
14	54, W	Positive	Negative	Impaired level of consciousness, right sided hemiplegia.	Multiple lesions in white matter bilaterally involving the periventricular and corpus callosum, punctiform and tumefactive lesions with mass effect on the left lateral ventricle. Bilateral globus pallidus lesions with hyperintensity on flair and restricted diffusion.	CSF analysis; unremarkable.
15	60, M	Positive	Negative	Bilateral lower limb weakness, urinary retention, and constipation.	Hyperintense T2 signal centrally from T7 to T10.	CSF analysis; elevated protein count with normal glucose and white blood cell count.

**Table 2: Summary of diagnosis and treatment outcomes of the demyelinating lesions of the CNS related complications of COVID-19.**

Ref. no.	Diagnosis	Treatment and outcome
7	Possible atypical demyelinating event of the CNS.	Empirical treatment with IV meropenem, vancomycin, and acyclovir. At the end of the second week, the upper limbs weakness improved, the lower limbs power was 3+5.
8	Acute disseminated encephalomyelitis.	High-dose steroids followed by IVIG. The patient Improved over weeks.
9	Acute disseminated encephalomyelitis.	Treated with antiretrovirals and HCQ. High dose dexamethasone. After one month Improved. No sensorimotor deficit.
10	Acute transverse myelitis.	Pulse steroid, acyclovir and enoxaparin. Significant improvement.
11	Acute transverse myelitis.	Methylprednisolone was started on day 7 at a dose of 100 mg/d. The patient improved, discharged with a mild spastic paraparesis and hypesthesia normal bladder function.
14	Demyelination or small-vessel vasculitis.	Treated with HCQ, azithromycin and amoxicillin/clavulanic acid.
15	Acute transverse myelitis.	Pulse methylprednisone with significant neurological improvement.

PCR; polymerase chain reaction, AQP4; aquaporin-4, MOG; myelin oligodendrocyte glycoprotein, CSF; cerebrospinal fluid, WBC; white blood cell, RBC; red blood cells, CNS; central nervous system, IV; intravenous, DWI; diffusion weighted imaging, ADC; apparent diffusion coefficient, IVH; intraventricular hemorrhage, IVIG; intravenous immunoglobulin, HCQ; hydroxychloroquine.

In the present study, the clinical presentation and the radiological finding are suggestive of post viral demyelination disease. The subacute unsteadiness and facial weakness with positive SARS-CoV-2 nasal swab and the focal neurological deficit with left lower motor neuron facial weakness, left cerebellar tremor, and ataxic

gait are consistent with a subacute pathological process like a demyelinating disease. The MRI showed left middle cerebellar peduncle solitary faintly enhancing lesion in late subacute age, in keeping with a demyelinating lesion in a patient with COVID-19.

## CONCLUSION

This article is a retrospective case report of a demyelinating event in the central nervous system in the context of recent symptoms typical of COVID-19 and a positive COVID-19 nasopharyngeal swab at the time of neurologic presentation. This case and the listed cases help to expand our understanding of the potential neurologic sequelae of COVID-19, adding to the very limited body of literature associating COVID-19 with demyelinating events.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: Not required*

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**Cite this article as:** Alqwaify M. Demyelinating solitary lesion of the central nervous system associated with COVID-19: a case report and literature review. *Int J Adv Med* 2020;7:1884-8.