

# Encephalitis Associated with COVID-19 in a Patient with Multiple Sclerosis

Abdorreza Naser Moghadasi (✉ [abdorrezamoghadasi@gmail.com](mailto:abdorrezamoghadasi@gmail.com))

Multiple Sclerosis Research Center, Neuroscience Institute, Tehran University of Medical Sciences

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## Case Report

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# Abstract

From the beginning of COVID-19 pandemics, the involvement of patient's nervous system with this virus is increasingly reporting. Although various reports are published on affliction of multiple sclerosis (MS) patients with SARS-CoV-2, no report has been published on brain involvement by this virus in MS patients so far. Herein, a 34-year-old patient with MS who experienced the decreased level of consciousness and encephalopathy following COVID-19 involvement has been reported.

# Main Text

From the beginning of COVID-19 pandemics in December 2019, the involvement of patient's nervous system with this virus is increasingly reporting. Accordingly, this involvement is in the form of, encephalitis, acute disseminated encephalomyelitis (ADEM), seizure, stroke, or Guillen-Barre (1). Although various reports are published on affliction of multiple sclerosis (MS) patients with SARS-CoV-2 (2), no report has been published on brain involvement by this virus in MS patients so far. Herein, we reported a patient with MS who experienced the decreased level of consciousness and encephalopathy following COVID-19 involvement.

The patient was a 34-year-old woman with the established MS diagnosis for 15 years. Her disease had been initiated with lower limb paresthesia, and at the beginning, Avonex was prescribed for her. Due to the frequent relapses of the diseases, at first Betaferon, and then dimethyl fumarate were administered, and finally treatment with rituximab was performed. However, despite all these medication changes, her disease has progressed. The brain magnetic resonance imaging (MRI) revealed multiple confluent periventricular lesions with gadolinium enhancement (Figure 1-A, B, C). Lumbar puncture(LP) was performed. Cerebrospinal fluid (CSF) analysis was normal. Oligoclonal bands (OCBs) were present in CSF. Eventually her disease was brought under control using Cyclophosphamide 1 g per month along with 30 mg oral prednisolone. The patient totally received 10 cycles of cyclophosphamide. By passing 25 days from receiving the last dose of injective cyclophosphamide, she complained of fever, coughs, dyspnea, generalized weakness, and nausea. In the first examination, the followings were measured: respiratory rate: 20, pulse rate: 100, temperature: 38 °C, and BP: 100/60. Moreover, O2 saturation was 95% with no oxygen use. Neurologically, the patient had complete time, place, and person orientation. In addition, she had imbalance during walk, and her reflexes had also increased. The muscle power of limbs was 4/5, which had no difference with the examination performed before COVID-19. The chest computed tomography (CT) scan showed bilateral lung involvement especially on the right side (Figure 1-D). So, the patient was hospitalized with COVID-19 diagnosis. In the tests performed, white blood cell (WBC) count was 3100, lymphocyte 20.9%, C-reactive protein (CRP) 62 mg/dl, and *lactate dehydrogenase* (LDH) was 737. Notably, nasopharyngeal and oropharyngeal swab real-time polymerase chain reaction (rt-PCR) test of coronavirus was positive. The patient received **Azithromycin** and **Hydroxychloroquine**. On day 5 of hospitalization, the patient's fever increased up to 40°C, and O2 saturation was 93%. The patient found

diminished consciousness level. Afterward, she was localized in response to painful stimulus, and she also had neck stiffness. Routine tests including blood sugar and biochemistry were normal. Subsequently, ceftriaxone and vancomycin were administered for her, and then emergency MRI was performed. In MRI, numerous old lesions were observed in the periventricular area induced by MS, which had no enhancement in the injected view (Figure 1- E). Moreover, LP was performed for her. The CSF pressure was 10 cm H<sub>2</sub>O. In CSF analysis, glucose was measured as 45, protein: 112, and WBC as 0. CSF smear was negative in terms of bacteria. Furthermore, based on the CSF analysis, the patient's antibiotics were stopped, and by diagnosing COVID-19 associated encephalitis, she received supportive treatment plus intravenous immunoglobulin (IVIG) 25 mg/day for a 5-day period. Complementary tests including tuberculosis, brucellosis, herpes simplex virus (HSV) and human immunodeficiency virus (HIV) were negative, and coronavirus PCR in CSF was also negative. The patient health condition gradually improved as well as her consciousness conditions that returned to normal level. The patient's fever stopped, and she was discharged from the hospital with a good general status.

There are some reports on COVID-19-induced encephalitis (3, 4). Although in our patient, the CSF PCR of coronavirus was negative, based on ruling out the other causes as well as the improvement of patient through supportive treatments and IVIG, the best diagnosis can be COVID-19 associated encephalitis. In this regard, COVID-19 disease can cause brain involvement in different ways. Firstly, coronavirus is a neurotropic virus, and through attaching to angiotensin converting enzyme (ACE)2 receptor, which is located on cells surface such as astrocytes, can cause direct brain involvement. Moreover, another route of involvement is through olfactory nerve and bulb. Eventually, the hyper-inflammation induced by COVID-19 can cause ADEM-like involvement in patients with COVID-19 (5). Whether the MS disease itself or the drugs consumed (such as immunosuppressive drugs) can increase the chance of developing brain involvement of COVID-19 is something that needs to be further explored. Nevertheless, one cannot overlook is the effect of cyclophosphamide as an immunosuppressive drug on developing COVID-19 associated encephalitis in patients.

## Declarations

**Contributors' statement:** ANM contributed to conception and design, described the case study, analyzed data and prepared the manuscript

**Conflict of interest:** The author declares there is no conflict of interest

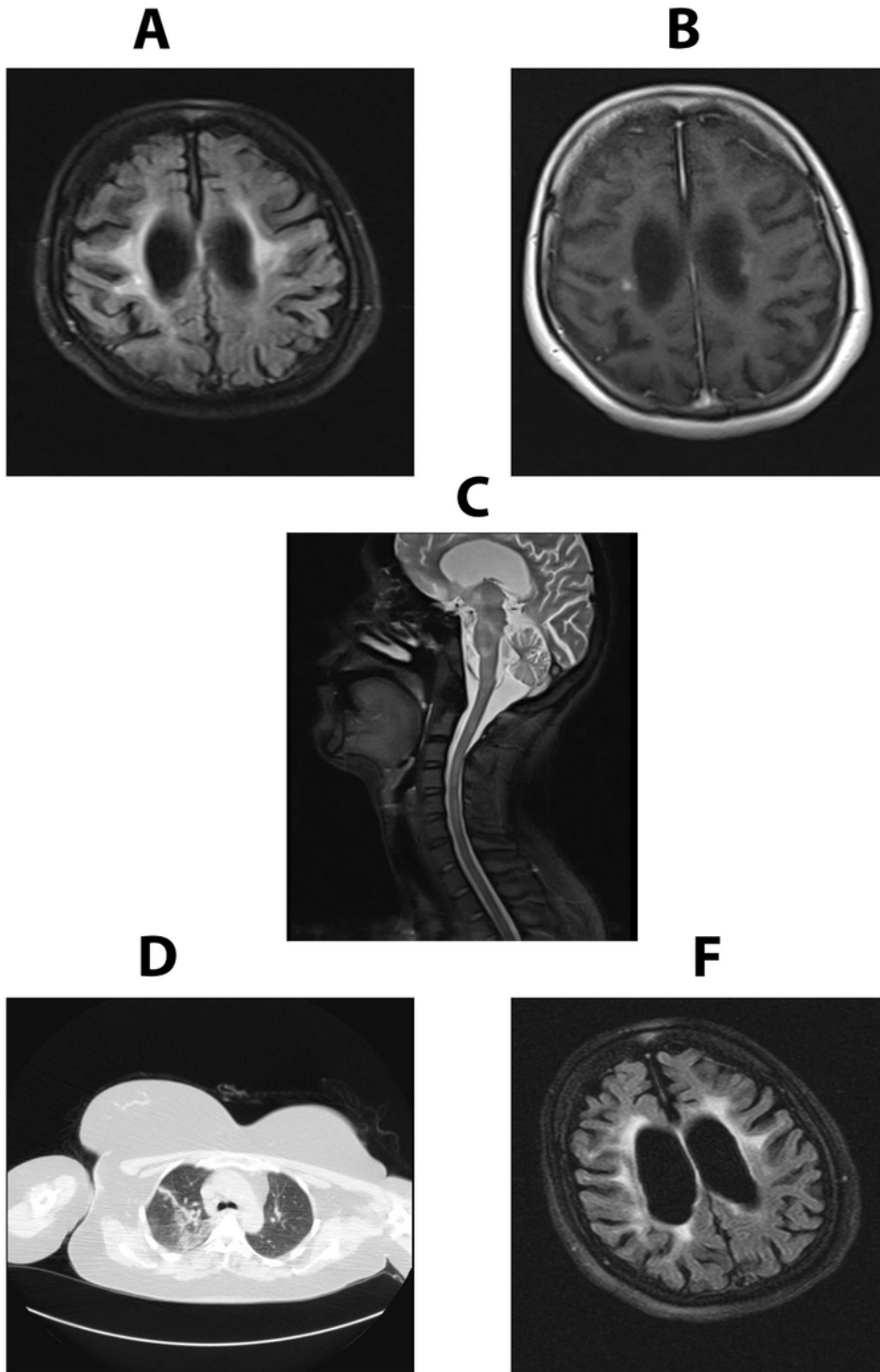
**Consent:** The patient consented to publish their case, clinical data, and images .

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## Figures



**Figure 1**

A. Brain MRI multiple confluent lesions. B. with gadolinium enhancements. C. Cervical and brain stem involvements were seen in Cervical MRI. D. Chest CT scan revealed lung consolidation. E. Numerous old lesions were observed in the new brain MRI