

We need well-designed multicenter studies to investigate neurologic manifestations of coronavirus disease 2019

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Early reports of coronavirus disease 2019 (COVID-19) infection from China and other parts of the world emphasized that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) primarily infected the respiratory system leading to serious cardiorespiratory complications such as acute respiratory distress syndrome (ARDS). However, according to recent reports, coronaviruses could involve the central nervous system (CNS) and peripheral nervous system (PNS).¹⁻⁵ Both acute and chronic infections with SARS-CoV-2 could affect the nervous system. Encephalitis, acute reactive seizures and status epilepticus, acute disseminated encephalomyelitis (ADEM), and Guillain-Barre syndrome (GBS) have been reported as neurologic

manifestations of coronavirus infection. After infection by the Middle East respiratory syndrome-related coronavirus (MERS-CoV), a number of neurologic complications such as mental status changes, ataxia, focal motor deficits, and Bickerstaff encephalitis have been described. In children, seizures and meningoencephalitis have been reported after infection with human coronaviruses.¹⁻⁶

On March 11, 2020, the World Health Organization (WHO) declared a pandemic by SARS-CoV-2 and the disease named COVID-19. SARS-CoV-2 is the seventh strain of human

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coronaviruses that the first infected cases by this virus were reported from Wuhan, China. It was cleared that this infection had high morbidity and mortality. The main manifestation of this infection is respiratory manifestation and many patients will die because of ARDS. In addition, a large number of patients with COVID-19 have shown non-specific neurologic manifestations such as headache and a few patients developed severe neurologic complications like seizures and stroke.²

A number of investigators have tried to describe the neurologic manifestations of COVID-19. However, these reports are scarce and have low quality. In one report, 25% of patients with COVID-19 developed CNS problems and 9% had PNS symptoms such as neuropathy and muscle disorders. The most common CNS complaints were dizziness and headache. The most PNS problems were taste impairment and anosmia. They also reported severe neurologic complications such as stroke.² In one report from the United States (US), a case of acute necrotizing hemorrhagic encephalopathy has been reported and SARS-CoV-2 has been confirmed as the etiology.³ In one case report, a 61-year-old woman with GBS associated with COVID-19 has been described from China. Interestingly, this patient did not have any respiratory symptoms.⁵ In another report, 5 cases of GBS after COVID-19 disease have been described.⁴ In all of them, COVID-19 has been confirmed using culture or serologic tests. There is an interesting report from Iran of a patient with COVID-19 that presented by repeated generalized tonic-clonic seizures (GTCs).¹ In addition, reports from European countries have described neurologic manifestations like sedation, agitation, inattention, disorientation, and poorly-organized movements in response to commands. Also, there are reports of cerebrospinal fluid (CSF) abnormalities such as positive oligoclonal bands (OCBs), elevated CSF immunoglobulin G (IgG), and protein. Magnetic resonance imaging (MRI) studies have shown ischemic strokes and

leptomeningeal enhancement.⁶

Interestingly, children experienced a lower rate of COVID-19 infection with mild signs and symptoms. Although, until now, no serious neurologic manifestations have been reported in children, it seems logical that children could potentially develop serious neurologic manifestations, especially those with underlying diseases. Some of the reported neurologic disorders of COVID-19 in adults such as acute necrotizing encephalopathy (ANE) are more common in infants and children.

In conclusion, SARS-CoV-2 infection is a leading cause of serious respiratory complications in adults and elderly and early reports inadvertently missed many neurologic manifestations in these patients. The neurologic manifestations have been reported in the previous endemic and epidemic diseases with coronaviruses. Recently, different reports from various parts of the world have indicated that SARS-CoV-2 infection could potentially involve the nervous system and lead to a number of neurologic complications from a mild headache to serious and potentially lethal generalized seizures and cerebrovascular disorders. Therefore, we need well-designed multicenter studies from different parts of the world that closely monitor (using CSF studies, neuroimaging, and neurophysiologic studies) different neurologic manifestations of this infection. A number of these serious neurologic complications might be treatable such as non-convulsive seizures (NCSs) that lead to disturbed mentation and without continuous electroencephalography (EEG) monitoring could not be diagnosed.

Conflict of Interests

The authors declare no conflict of interest in this study.

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References

1. Karimi N, Sharifi Razavi A, Rouhani N. Frequent convulsive seizures in an adult patient with COVID-19: A case report. *Iran Red Crescent Med J* 2020; 22(3): e102828.
2. (2) Mao L, Jin H, Wang M, Hu Y, Chen S, He Q, et al. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. *JAMA Neurol* 2020; 77(6): 683-90.
3. (3) Poyiadji N, Shahin G, Noujaim D, Stone M, Patel S, Griffith B. COVID-19-associated acute hemorrhagic necrotizing encephalopathy: Imaging features. *Radiology* 2020; 296(2): E119-20.
4. (4) Toscano G, Palmerini F, Ravaglia S, Ruiz L, Invernizzi P, Cuzzoni MG, et al. Guillain-Barre syndrome associated with SARS-CoV-2. *N Engl J Med* 2020; 382(26): 2574-6.
5. (5) Zhao H, Shen D, Zhou H, Liu J, Chen S. Guillain-Barre syndrome associated with SARS-CoV-2 infection: Causality or coincidence? *Lancet Neurol* 2020; 19(5): 383-4.
6. (6) Helms J, Kremer S, Merdji H, Clere-Jehl R, Schenck M, Kummerlen C, et al. Neurologic features in severe SARS-CoV-2 infection. *N Engl J Med* 2020; 382(23): 2268-70.