Neurological Manifestations of COVID-19

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Abstract

Coronavirus disease 2019 (COVID-19) is defined as illness caused by a novel coronavirus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2; formerly called 2019-nCoV), which was first identified amid an outbreak of respiratory illness cases in Wuhan City, Hubei Province, China [1]. It was initially reported to the WHO on December 31, 2019. On January 30, 2020, the WHO declared the COVID-19 outbreak a global health emergency [2, 3]. On March 11, 2020, the WHO declared COVID-19 a global pandemic, its first such designation since declaring H1N1 influenza a pandemic in 2009 [4].

Keywords: COVID-19,
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Introduction

Most patients infected by SARS-CoV-2 have presented with a mild clinical course: beginning with fever and dry cough, progressing to a form of mild or moderate respiratory disease, and resolving without specific treatment [5]. Serious complications of the infection, however, remain a central concern. Acute respiratory distress syndrome, acute heart injury or failure, acute kidney injury, sepsis, disseminated intravascular coagulation, and life-threatening metabolic derangements have all been reported in COVID-19 patients, particularly among those with underlying comorbidities or advanced age [6, 7].

Coronaviruses are not always confined to the respiratory tract, and under certain conditions they can invade the central nervous system and cause neurological pathologies. The potential for neuro invasion is well documented in most human coronaviruses (OC-43, 229E, MERS and SARS) [8].

Neurological manifestations of SARS-CoV-2

More than 80 percent of hospitalized patients may have neurologic symptoms at some point during their disease course [9].

In a local retrospective study which is considered to be the first in Qatar, neurologic manifestations (48.5%) were reported in hospitalized COVID-19 patients. Patients with COVID-19 are at high risk of developing neurological manifestations. The most common COVID-19-related acute neurological manifestations were myalgia, headache, dizziness, and acute ischemic stroke. Prompt recognition, early diagnosis, and appropriate management of these manifestations could potentially lead to better patient outcomes in COVID-19 patients (10).

Two large cohort-based studies on neurological manifestations of COVID-19 have been reported so far. In a study done in Wuhan, China, Mao et al. [11] noted neurological manifestations in 36.4% of 214 COVID-19 patients and these were significantly more common in patients with severe disease. Central nervous system (CNS) and peripheral nervous system manifestations were seen in 24.8% and 8.9%, respectively. In a study conducted in France, Helms et al. [12] found 84% of 58 patients admitted to the intensive care unit because of acute respiratory distress syndrome due to COVID-19 had neurological signs. The differences in percentage between the two studies may be because the second study focused on more severely affected COVID-19 patients. Table 1 summarizes the common neurological manifestations in COVID-19.

Smell and taste disorders:

Anosmia and dysgeusia have been reported as common early symptoms in patients with COVID-19, occurring in greater than 80 percent of patients in one series [13]. In a meta-analysis of 83 studies involving more than 27,000 patients, olfactory dysfunction was reported in 48 percent [14].

Dizziness

Numerous studies, appearing daily from various parts of the world, have revealed vertigo as one of the significant clinical manifestations of COVID-19. One of them cites vertigo as the most common neurological manifestation of COVID-19, thought to follow the neuro invasive potential of the virus [15]. Some researchers hypothesized that the virus enters neuronal tissue from the circulation and binds angiotensin-converting enzyme 2 receptors (ACE2), which are located in the capillary endothelium. Other mechanisms that lead to dizziness during COVID-19 infection are direct inflammatory action of the virus on nervous tissue, indirect immune response, hypoxia, and hypercoagulopathy [15].

Cerebrovascular disease

Li et al.,(16) who analyzed the cohort of patients described by Mao et al. and seven more, found 5% to have acute ischemic stroke. Stroke was also reported in five patients younger than 50years from New York(17). Based on brain magnetic resonance imaging (MRI) findings from 13 of their 58 patients, Helms et al.(18) reported two to have acute cerebral ischemic stroke and one to have subacute cerebral ischemic stroke. In a retrospective cohort-based study from New York, 0.9% had imaging-proven acute ischemic stroke and most (65%) strokes were cryptogenic, possibly related to an acquired hypercoagulability(19). A recent systematic review showed the incidence of acute ischemic stroke in COVID-19 to be 0.9% to 2.7% with a mortality rate of 38%(20). The CVD in COVID-19 may be due to high levels of inflammation and/or a hypercoagulable state. Raised serum interleukin and C-reactive protein concentration have been reported, and coagulation abnormalities are increasingly noted with raised D-dimer concentration pointing to a poorer prognosis(21).

Delirium:

Delirium for patients with COVID-19 has been especially common. Rarely it is present at onset and typically associated with sepsis, but it is otherwise seen in the critical care setting where causes are multifactorial. In one series 84 % of COVID-19 patients in the ICU had delirium with a combination of acute attention, awareness, and cognition disturbances [22].

Table 1. Cohort studies on neurological manifestations in COVID-19

Cohort studies on neurological manifestations in COVID-19.

Study	N	Headache (%)	Dizziness (%)	Impaired consciousness (%)	Acute cerebrovascular disease (%)	Skeletal muscle injury (%)	Ataxia (%)	Seizure (%)
Li et al.[8]	221	NA	NA	NA	5.8	NA	NA	NA
Mao et al.[6]	214	13.1	16.8	7.5	2.8	10.7	0.5	0.5
Qin et al.[9]	452	11.4	8.1	NA	NA	NA	NA	NA
Helms et al.[7]	58	NA	NA	NA	23 (3/13)[a]	NA	NA	NA
Wang et al.[10]	138	6.5	9.4	NA	NA	34.5[b]	NA	NA

COVID-19: coronavirus disease 2019; N: number of patients; NA: not analyzed (all studies were conducted in 2020); MRI: magnetic resonance imaging.

[a]Brain MRI scans were done in 13 patients and cerebral ischemic stroke was identified in three.

[b]Only myalgia was considered.

Outside of a true encephalitis, delirium in the ICU may arise from medications including sedative-hypnotics, anticholinergics, and corticosteroids; from the prolonged course of many COVID-19 sufferers' needs for mechanical ventilation; and from isolation. This latter component is especially challenging for patients. As with any respiratory virus setting, both the physical barriers of personal protection equipment and the limited contact with the medical team can lead to prolonged periods of isolation in the ICU. And because of social distancing requirements and many hospitals' need to restrict visitors, critically ill COVID-19 patients are almost always isolated from loved ones as well. The combination of these factors have been especially challenging for patients and it is not uncommon to hear stories of post-ICU trauma and anxiety that arise and persist well past the critical phase of illness (23).

Seizures and status epilepticus

Seizures and status epilepticus have been reported in patients with severe COVID-19 infection [24,25]. In one series of 32 patients with COVID-19 who presented to the hospital with seizures, 40 percent had no history of epilepsy or other central nervous system diagnoses [26]. In rare instances, seizures have been the presenting symptom for patients without signs of infection who have tested positive for COVID-19 [26,27]. A systematic review of case series and reports identified 47 patients with COVID-19 who developed status epilepticus [28].

Conclusion

The nervous system may also be affected via indirect methods such as hypoxia, inflammation or an immune-mediated damage. Future studies using brain imaging, EEGs, CSF analysis and histopathology would provide a clearer understanding of the effect of SARS-CoV-2 on the nervous system (29).

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