LETTER TO THE EDITOR

The Spectrum of Neuro-COVID is Broader than Frequently Anticipated

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Abstract

The spectrum of neuro-COVID is broader than anticipated. Neurological disease in COVID-19 may be due to a direct attack of the virus, due to the immune response against the virus, secondary due to affection of the heart or arteries, or due to side effects from the treatment applied against COVID-19.

Keywords: Brain, Central nervous system, Coronavirus, COVID-19, Critically ill, Nerves, Neurological symptoms, Neurology, SARS-COV-2, Transfer, Transport.

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Dear Editor,

With interest, we read the article by Goel et al. about neurological involvement in seven patients with COVID-19.[1] Patient-1 had hemiparesis due to stroke, patient-2 was unconscious due to stroke, patient-3 was unconscious due to multiple cortical infarcts, patient-4 had altered sensorium and seizures due to central nervous system (CNS) infection, patient-5 had altered sensorium due to cerebral edema, patient-6 had paraparesis due to Guillain-Barre syndrome (GBS), and patient-7 had ascending quadriparesis due to GBS.[1] The study is appealing but raises the following comments and concerns.

The main shortcoming is that the cause of neurological compromise was not entirely identified in each patient. We should be told the type of CNS infection detected in patient-4 and the cause of cerebral edema in patient-5.

A further shortcoming is that neurological manifestations of COVID-19 shown in Figure 1 are incomplete. There is no mention of intra-cerebral hemorrhage (ICH) due to arterial hypertension, hypocoagulability, venous sinus thrombosis (VST), or vasculitis (endotheliitis).[2] Endotheliits is particularly associated with microbleeds.[3] Intra-cerebral hemorrhage can be also due to side effects of anticoagulation for VST, deep venous thrombosis, or pulmonary embolism, increasingly recognized as complications of infection with SARS-CoV-2.[4]

Another neurological complication not discussed is subarachnoid bleeding (SAB). Though only rarely reported, several cases with SARS-CoV-2-associated SAB have been published.[5] The mechanism of SAB in COVID-19 is not fully understood. Only in a few patients has an aneurysm been detected. More likely than aneurysms is endothelial damage (endotheliits).

Nothing is reported about SARS-CoV-2-associated myelitis, a complication increasingly recognized in patients with severe COVID-19. Myelitis in COVID-19 patients may manifest as transverse myelitis or as encephalomyelitis. Cerebrospinal fluid (CSF) investigations in these patients may reveal pleocytosis, and inflammatory biomarkers, but only rarely SARS-CoV-2 virus RNA. Patients with SARS-CoV-2 associated myelitis may profit from methyl-prednisolone or intravenous immunoglobulins (IVIG).

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Acute disseminated encephalomyelitis (ADEM) is another neurological complication of COVID-19 not appreciated in the review. Acute disseminated encephalomyelitis may be even the initial manifestation of a SARS-CoV-2 infection starting prior to the onset of the pulmonary compromise. Cerebrospinal fluid (CSF) investigations in these patients may only show positive oligo-clonal bands but may be otherwise normal. Methyl-prednisolone has been shown beneficial for SARS-CoV-2-associated ADEM.

Discussion about the dissection of cerebral or extra-cranial arteries is missing. Though extremely rare, a few cases with dissection of the internal carotid arteries have been published. The pathophysiology of arterial dissection in SARS-CoV-2 infected patients remains elusive but if it is not coincidental, endotheliitis could play a pathophysiological role.

Another CNS manifestation of COVID-19 not discussed is immune encephalitis. Immune encephalitis is most likely a manifestation of the cytokine release syndrome since CSF investigations for antibodies associated with immune encephalitis are usually negative. Immune encephalitis in COVID-19 patients usually manifests as limbic encephalitis.

Furthermore, the review does not mention reversible cerebral vaso-constriction syndrome as a putative cerebrovascular manifestation of an infection with SARS-CoV-2.

Overall, the interesting study by Goel has several limitations which should be met before drawing final conclusions. The etiology of neurological compromise should be clarified in each of the seven

included patients and the neurological manifestations not included in the review should be discussed.

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