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LETTER TO THE EDITOR

Presentation and pathophysiology of neuro-COVID

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Abstract

Letter to the Editor commenting on Orsucci D, Caldarazzo Ienco E, Nocita G, Napolitano A, Vista M. Neurological features of COVID-19 and their treatment: a review. *Drugs Context*. 2020;9:2020-5-1. https://doi.org/10.7573/dic.2020-5-1

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Citation

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With interest we read the review article by Orsucci et al. about the neurological implications in COVID-19.[1] The authors concluded that COVID-19 patients should be referred to the neurologist and that neurologists should stay alert for neurological compromise due to infection with SARS-CoV-2.[1] The review is appealing but has several limitations, which raise the following comments and concerns.

We do not agree with the statement that SARS-CoV-2-associated acute, inflammatory, demyelinating polyneuropathy (AIDP) is rare.[1] In a recent review of SARS-CoV-2-associated Guillain–Barre syndrome, 118 patients with AIDP had been reported by the end of December 2020.[2] The age range of patients with AIDP was 11–94 years, 71 patients were male, and onset of Guillain–Barre syndrome ranged from 0 to 35 days after infection. A spinal tap did not detect the virus in the cerebrospinal fluid of any patient. A total of 107 patients received intravenous immunoglobulins, 10 patients underwent plasmaphereses and 1 patient received steroids. Finally, 21 patients recovered completely, 88 patients recovered partially and 5 died.[2]

The pathophysiological mechanisms of neuro-COVID (neurological involvement in COVID-19), which are particularly relevant in patients with severe COVID-19 requiring ICU treatment and not addressed in the review, are complications of ICU treatment. Patients with severe COVID-19 requiring short-term or long-term artificial ventilation may develop critical illness neuropathy or critical illness myopathy. Artificial ventilation may be also complicated by pressure palsies due to extreme or long-term bedding or, rarely, compartment syndrome.[3] Additionally, long-term artificial ventilation may be complicated by cerebral hypoxia. If patients are superinfected due to suppression of the immune system by the virus, sepsis may develop and may be complicated by septic encephalopathy.

Not sufficiently addressed as a pathophysiological mechanism in the review is the neurotoxicity or myotoxicity of anti-COVID-19 drugs. The possibility of adverse reactions is known for several compounds used in the treatment of COVID-19, which in turn may cause neurological compromise. Potentially neurotoxic drugs frequently used in the treatment of COVID-19 include daptomycin, linezolid, lopinavir, ritonavir, hydroxychloroquine, cisatracurium, clindamycin, tocilizumab and glucocorticoids.[4] Potentially myotoxic drugs administered to COVID-19 patients include chloroquine (causes myopathy or myasthenia), remdesivir/lopinavir (cause rhabdomyolysis), azithromycin (causes myasthenia or myasthenic crisis), tocilizumab (causes pyomyositis) and steroids (cause mitochondrial myopathy).

Not addressed in the review were the cerebral complications from cardiac involvement in COVID-19. Cardiac disease due to a SARS-CoV-2 infection includes arterial hypertension, myocarditis, Takotsubo syndrome, sudden death or autonomic neuropathy.[5] These conditions may be associated with supra-ventricular or ventricular arrhythmias or heart failure and systolic dysfunction, which itself may be complicated by various neurological abnormalities, such as cerebral hypoperfusion and

thus hypoxia, thromboembolism, or impaired autoregulation of the cerebral perfusion, possibly leading to ischaemic stroke, intracerebral bleeding, posterior reversible encephalopathy syndrome or cerebral vasoconstriction syndrome. Myocarditis may be caused by the invasion of the virus into myocardiocytes. Myocardial ischaemia may be caused by invasion of the virus into endothelial cells of coronary arteries. Arterial hypertension may be caused by autonomic dysfunction. Takotsubo syndrome may be triggered by mental or physical stress from the viral infection and its treatment.

Overall, the interesting review has several limitations, which challenge the results and their interpretation. All limitations should be addressed to strengthen the conclusions.

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