Prevalence, pathogenesis and spectrum of neurological symptoms in COVID-19 and post-COVID-19 syndrome

To the Editor: Wesselingh's narrative review[1] is excellent but, in our view, omitted some potentially important points. The spectrum of central and peripheral nervous system complications of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections is probably broader than stated in the review. In addition to the complications listed in the article (eg, headache, peripheral neuropathy, seizures, encephalitis, Guillain–Barré syndrome, movement disorders and cerebrovascular disease), the neurological symptoms of coronavirus disease 2019 (COVID-19) may also include complications such as acute disseminated encephalomyelitis, acute haemorrhagic necrotising encephalitis, acute haemorrhagic leucoencephalitis, acute necrotising encephalopathy, multiple sclerosis, myelin oligodendrocyte glycoprotein-associated disease, pituitary apoplexy, opsoclonus–myoclonus syndrome, cerebellitis, myelitis, myasthenia, myasthenic syndrome, myositis, myopathy and rhabdomyolysis.[2] However, it is important to note that all of these potential complications are derived from observational studies that lacked a control group for comparison.

It has been established that ischaemic stroke associated with SARS-CoV-2 infection can occur between ten and 14 days after the onset of COVID-19.[1] However, there have been reports of several cases of ischaemic stroke associated with SARS-CoV-2 infection occurring just several hours after the onset of COVID-19.[3] Moreover, there are also reported cases of ischaemic stroke associated with SARS-CoV-2 infection occurring more than 14 days after onset of COVID-19.[4]

Furthermore, endotheliitis and coagulopathy might not be distinct pathophysiological mechanisms that explain some of the neurological manifestations of COVID-19,[1] as hypercoagulability/hypocoagulability and endotheliitis could also be explained by the immune response against the virus. Among other things, hypercoagulability can be caused by platelet dysfunction due to antibodies directed against the thrombocyte surface.[5]

There is little evidence that central nervous system complications of SARS-CoV-2 infections are due to generalised hypoxia.[1] Except for cases in which inadequate resuscitation occurred due to pulmonary or cardiac disease caused by SARS-CoV-2 infection, typical hypoxic brain injury has never been reported in patients with COVID-19 with central nervous system involvement. In patients admitted to hospital, oxygenation is usually well monitored, so the development of hypoxia becomes extremely unlikely.

Cardiac involvement should be considered as a pathophysiological mechanism of ischaemic stroke. COVID-19 can be complicated by endocarditis, myocarditis or pericarditis. Moreover, myocarditis, in particular, can be complicated by heart failure, malignant ventricular arrhythmias and atrial fibrillation, with a risk of cardioembolism, which can lead to embolic stroke.

Lastly, D-dimer is not only a biomarker of microangiopathic changes and a biomarker of poor prognosis,[1] it is also an inflammatory marker. Therefore, an elevated D-dimer in patients with COVID-19 might simply reflect the SARS-CoV-2 infection and, in our view, should not be used as a specific biomarker.

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