

## COVID-19 and Neuroinvasion

### To the Editor

The pandemic Coronavirus Disease 19 (COVID-19) is rapidly spreading across the world, and the numbers of affected and those deceased are increasing at an alarming rate. COVID-19 is caused by a new zoonotic virus, the severe acute respiratory syndrome coronavirus (SARS-CoV-2). We know Coronavirus (CoV) are a group of RNA viruses causing enteric and respiratory diseases in humans and animals. The symptomatology of the COVID-19 mainly involves the respiratory system and patients present with symptoms of high-grade fever, cough, and dyspnea. There are clinical signs of lung infiltrates and acute lung injury. As neurointensivists, it is imperative for us to know the neurologic consequences of this life-threatening virus. Does this virus affect brain and the central nervous system? What is the mode of its spread to the nervous system?

Some of the neurologic symptoms observed in these patients are headache, nausea and vomiting, loss of smell and taste. It has also been suggested that majority among the severe patients displayed neurologic manifestations including acute cerebrovascular diseases and impaired consciousness.<sup>1</sup> Data from 487 patients in China suggest that older age, male sex, and hypertension are independently associated with severity of the disease.<sup>2</sup> Along with several other risk factors, one can speculate that obesity and existing immune deficiency could possibly be risk factors too.

Experimental studies have demonstrated that transnasal administration of SAR-CoV and Middle East respiratory disease (MER) CoV could enter the brain of transgenic mice. The virus spreads rapidly to thalamus and the brainstem, possibly via the olfactory nerves.<sup>3</sup> Viral antigens have also been detected in the nucleus of solitary tract and nucleus ambiguus.<sup>4</sup> The efferent fibers from the nucleus ambiguus and the nucleus of the solitary tract provide innervation to airway smooth muscle, glands, and blood vessels. Interconnections of such type indicate that the death of infected animals or patients could possibly be due to the dysfunction of the cardiorespiratory center in

the brainstem. There is also an increasing evidence that CoVs may first invade peripheral nerve terminals and then gain access to the central nervous system (CNS) via a synapse-connected route. It has now been reported that encephalitis could be a clinical manifestation of COVID-19.<sup>5</sup> There have been reports emerging about associated neurologic conditions such as stroke, seizures, and acute hemorrhagic necrotizing encephalopathy, in COVID-19-infected patients.

We quote authors Li et al<sup>6</sup> statement that "...awareness of the possible neuroinvasion may have a guiding significance for the prevention and treatment of the SARS-CoV-2-induced respiratory failure." As of now, we know that certain symptoms suggest SARS-CoV-2 might infect neurons, raising questions about whether there could be effects on the brain that play a role in patients' deaths.

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