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EDITORIAL

COVID-19: A primer for Neuroradiologists

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Abstract

The potential for central nervous system (CNS) involvement in coronavirus disease 2019 (COVID-19) is a matter of grave concern and there is a relevant body of evidence in the basic sciences to support this possibility. A neuroradiologist should be aware of the potential mechanisms involved in the neuropathogenesis of this virus, as we begin to see cases with abnormal brain scans emerging from all parts of the world.

Keywords COVID-19 · CNS · ANEC · ACE2 · Stroke

The potential for central nervous system (CNS) involvement in coronavirus disease 2019 (COVID-19) is a matter of grave concern and there is a relevant body of evidence in the basic sciences to support this possibility. Numerous animal coronaviruses, which are molecularly similar to human coronaviruses, have been shown to invade (neuroinvasion), infect (neurotropism), and induce neurological disease (neurovirulence) in animal models [1, 2]. A neuroradiologist should be aware of the potential mechanisms involved in the neuropathogenesis of this virus, as we begin to see cases with abnormal brain scans emerging from all parts of the world.

The causative agent severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) utilizes the Angiotensin Converting Enzyme 2 receptor (ACE2) for entry into host cells, and causes a severe clinical syndrome manifested primarily as a respiratory tract infection [3]. However, patients are also known to demonstrate adverse neurological symptoms in the form of anosmia, dysgeusia, headache, nausea and vomiting [4]. ACE2 is widely expressed throughout the human brain, mostly in the glial cells, but also in the brainstem nuclei that regulate the cardiorespiratory systems, the reticular activating system, and in the motor cortex [1]. The propensity for accumulation in the nucleus solitarius and nucleus ambiguus, both of which play a key role in the modulation of respiratory function, is of research interest in its contribution to the severe respiratory dysfunction [5].

Proposed routes of CNS migration include haematogenous dissemination of infected leukocytes through compromised endothelial cells of the blood-brain barrier as well as retrograde peripheral nerve propagation with subsequent neuron-to-neuron propagation within the brain [6]. In the case of SARS-CoV-2, retrograde propogation along the olfactory tract may explain the unique feature of anosmia in affected patients [6, 7].

Once within the CNS, a viral-induced dysregulated host immune response has been shown to produce a ‘cytokine storm’ [8]. This cytokine storm and the direct cytopathic damage by the virus particles may lead to neurological disease such as encephalitis, acute flaccid paralysis, or acute necrotising encephalopathy (ANE) in susceptible individuals.

In a recent case report published by Poyiadji et al. [9], the authors describe a female COVID-19 patient in her late fifties presenting with altered sensorium and neuroimaging features typical of ANE. Cytokines are known to have a central role in the pathogenesis of acute necrotising encephalopathy [10]. This case highlights a possible association between COVID-19 and ANE. Interestingly, there is another form of ANE, referred to as ANE1 which has very similar imaging

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characteristics. ANE1 is associated with an underlying RAN binding protein 2 (*RANBP2)* mutations. *RANBP2* is a protein present on the nuclear pore and facilitates cellular traffic of proteins and energy balancing [11]. A mutation of this gene makes individuals susceptible to the effects of viral infections. While the imaging manifestations of ANE 1 are similar to that provided in the case, it would be highly atypical for the initial manifestation of ANE 1 to occur in a patient of this age. However, as we continue to learn more about the COVID-19, one needs to keep an open mind about underlying genetic susceptibilities irrespective of the COVID-19 status of the patient. Further, raised CSF protein (>0.45 g/L) in the absence of CSF pleocytosis and the presence of external capsular involvement on imaging would also satisfy screening criteria for *RANBP2* [11, 12].

There have also been reported cases of arterial and venous thromboembolic phenomena in the severely ill COVID-19 patients [13], typically as a result of disseminated intravascular coagulation (DIC). Nevertheless, one may see a rise in stroke presentations in association with COVID-19.

Much is still speculative about the neurovirulent potential of the novel SARS-CoV-2. The discerning clinician (and neuroradiologist) must however consider the possibility of CNS migration and its clinical sequelae in patients with COVID-19 who present with neurological signs. Para- and post-infectious phenomena, stroke-like episodes, and a generalized brainstem syndrome can be expected in affected patients. It would also be prudent to screen where appropriate for any underlying genetic or other predisposition before labelling any case as a primary COVID-19 driven pathology in the age of precision genomic medicine.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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Informed consent NA

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