Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Editorial

Special issue Editorial: Neurologic manifestations of the Covid-19 pandemic

Samuel R. Daly, Anthony V. Nguyen, Yilu Zhang, Dongxia Feng *, Jason H. Huang *

Department of Neurosurgery, Baylor Scott and White Health, Scott and White Medical Center, Temple, TX, USA

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The World Health Organization reports that as of October 2021, the Coronavirus disease (Covid-19) pandemic has been responsible for the death of nearly 5 million people worldwide. Despite the development of safe and effective vaccines, many areas around the world continue to experience infection rates that put strain on available healthcare resources. Covid-19 is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and it primarily affects the pulmonary and cardiac systems. However, the virus can exert devastating effects on multiple organ systems, including the central nervous system (CNS). This special issue of *Brain Hemorrhage* aims to increase awareness and understanding of the CNS manifestations of Covid-19 as well as the rare CNS hemorrhagic complications of SARS-CoV-2 mRNA vaccines.

The prevailing mechanistic theory on how SARS-CoV-2 infiltrates the CNS is via endothelial angiotensin converting enzyme-2 (ACE-2) receptors. ACE-2 receptors are also present in corneal and conjunctival tissue, and Hassan, et al. propose that the ocular surface may be one mode of viral CNS infiltration.[1] To support this, the authors present a case of Covid-19 in which SARS-CoV-2 RNA was detected in the patients tear samples up to 28 days after symptom onset. They conclude that eye protection should be standard personal protective equipment.

There is evidence that active or recent Covid-19 infection is associated with intracranial hemorrhage (ICH). Dr. Huang and colleagues provide an extensive review of nearly 100 PubMed indexed articles on the incidence and types of ICH that occur during or immediately after Covid-19 infection.[2] The authors highlight several categories of ICH that have been associated with Covid-19 in the literature, including subarachnoid hemorrhage, intraparenchymal hemorrhage, hemorrhage related to ischemic infarct and venous thrombosis, and subdural hematoma.

While there does appear to be an inherent risk of ICH during active Covid-19 infections, cases are commonly confounded by simultaneous anticoagulation treatment. There may also be an association between ICH and other Covid-19 therapies that modulate coagulation, such as baricitinib. Dr. Finsterer and colleagues present a case of an elderly female undergoing treatment for Covid-19, which included baricitinib.[3] The patient unfortunately developed a temporal lobe intracerebral hemorrhage, and while the patient recovered, the authors raise an important consideration regarding the etiological complexity of ICH related to Covid-19.

Cerebral venous sinus thrombosis (CVST) has been recognized as an uncommon complication of Covid-19. Athar, et al. describe a case of a 30-year-old male, who presented with Covid-19 and seizures, and was found to have a CVST that extended through the superior sagittal sinus, the vein of Galen, the bilateral transverse

* Corresponding authors at: 2401 S 31st Street, MS-01-610A, 254-724-5390, Temple, TX 76508, USA.

E-mail addresses: Dongxia.Feng1@BSWHealth.org (D. Feng), Jason.Huang@BSWHealth.org (J.H. Huang).

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sinuses, and the left proximal sigmoid sinus.[4] The authors discuss various routes of entry of the virus into the CNS as well as possible biological mechanisms mediated by SARS-CoV-2 that lead to the development of CVST.

A second case of CNS thrombosis is presented by Mobeen et al. of a middle-aged woman, who developed cavernous sinus thrombosis associated with sino-orbital Mucormycosis in the weeks after recovering from Covid-19.[5] She required aggressive treatment, including ocular enucleation. The authors conclude that her risks for this severe infection included both potential nosocomial exposure and the immune system inhibitors that she received as treatment for Covid-19. They recommend continued surveillance in patients that have recovered from Covid-19, in order to detect delayed complications such as this.

Hassan, et al. chronicle a series of six patients that presented to their institution with neurologic manifestations of Covid-19.[6] The present a case of Guillain-Barre Syndrome during active Covid-19 infection, two cases of devastating ischemic infarcts, two cases of encephalitis with evidence of CSF invasion of the virus, and a case of a young patient, who developed post-infection myositis. The authors call for enhanced basic science research efforts focused on understanding the mechanisms of how SARS-CoV-2 causes neurologic dysfunction.

Vaccines for Covid-19 have been developed and have been determined to be both safe and highly effective. However, there are rare CNS hemorrhagic complications associated with the mRNA vaccines. Finsterer, et al. discuss a case of a patient on aspirin with a recent myocardial infarction that developed aphasia one week after the second dose of a mRNA vaccine.[7] The patient was found to have a left temporal lobe intracerebral hemorrhage with no associated vascular abnormalities. The authors conclude that although the patient did have pre-existing risk factors for ICH, a causal relationship between the vaccine and the hemorrhage cannot be ruled out. In response to this article, Sookaromdee, et al. suggest that the mechanism of post-vaccine ICH may be due in part to alterations in blood viscosity.[8]

A possible risk factor for developing intracranial hemorrhage following the mRNA vaccine is an existing CNS lesion. Dr. Finsterer and Dr. Redzic describe a case of a man in his 60′s, who presented with neurologic symptoms and was found to have a subacute hemorrhage in an existing cerebellar peduncle cavernoma.[9] The bleed was presumed to be mediated by vaccine-induced immune thrombocytopenia, and the authors call for urgent research into the underlying pathology of this reaction.

This special issue of *Brain Hemorrhage* highlights CNS manifestations of Covid-19 infections as well as CNS hemorrhagic complications of the SARS-CoV-2 mRNA vaccines. While CNS complications are rare, it is necessary to keep them in mind in order to provide comprehensive care for patients during this prolonged pandemic.

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