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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COVID-19 and Cerebral Hemorrhage: Proposed Mechanisms

The coronavirus disease 2019 (COVID-19) outbreak has forced healthcare systems throughout the world to quickly adapt to the sudden surge in demand for the healthcare of infected patients. Being a respiratory pathogen with primarily respiratory symptoms, other non-respiratory symptoms with which patients present may have been easily overlooked, especially at the start of the outbreak. However, an increasing awareness of other systemic manifestations, in particular neurological, has made the management of COVID-19 patients more complex.

The largest series of patients with neurological symptoms was recently published by Mao et al. [1], from Wuhan, the original epicenter of the virus. In their series of 214 patients, 78 (36.4%) had neurological manifestations, including headache, dizziness, impaired consciousness, and acute cerebrovascular diseases. Among the 5 patients with cerebrovascular diseases, only 1 patient had cerebral hemorrhage; this patient later succumbed to respiratory failure. Another study [2] described an elderly male who initially came with typical pneumonia symptoms, later developing confusion and increased intracranial pressure (ICP) symptoms with imaging evidence of massive cerebral hemorrhage associated with intraventricular and subarachnoid components. Craen et al. [3] encountered an elderly female, who was brought in with cardiac arrest after several days of pneumonia. Cranial computed tomography (CT) showed extensive subarachnoid hemorrhage. Poillon et al. [4] described two patients who clinically manifested with headache and eye symptoms, with imaging evidence of cerebral venous thrombosis complicated by hemorrhagic transformation. A group from Italy [5], also once the epicenter of the virus, reported a series of 26 patients presenting to their center with various neurological manifestations, in addition to the respiratory symptoms attributable to COVID-19. In this cohort of patients, 5 had parenchymal hemorrhages involving the frontal (2 patients), hemispheric (1 patient), cerebellar (1 patient), and parietal (1 patient) regions. Four patients were in a coma, while 1 patient only reported headache.

Facilitated entry of COVID-19 into its hosts has been shown to be via the angiotensin-converting enzyme 2 (ACE2) receptors on human cell surfaces, mediated by its S-proteins. Patients with hypertension have reduced ACE2 expression needed to lower blood pressure. The occupancy of COVID-19 onto these receptors further reduces ACE2 expression, increasing the risk of cerebral hemorrhage due to elevated blood pressures [6,7]. This theory has led to the hypothesis that patients with hypertension treated with ACE inhibitors, which are meant to upregulate ACE2 receptors, are prone to developing severe and fatal COVID-19 infection, and complications [8]. However, recent evidence from three studies in different populations has disproved this postulation [9]. Another hypothesis is that patients with COVID-19 often suffer from prolonged prothrombin time and coagulopathy–increasing the risk of secondary cerebral hemorrhage [10,11]. Studies have shown that patients with COVID-19 infection exhibit a distinct form of coagulopathy–increased D-dimer concentration, prolonged prothrombin time, and a modest decrease in platelet count; a pattern different from the disseminated intravascular coagulopathy (DIC) seen in sepsis [12].

Due to its novelty, more research is needed to better understand the behavior and potential damage of COVID-19 to its host. Inevitably, standard of practice will continually evolve based on more recent evidence. The evidence so far suggests a fairly low prevalence of cerebral hemorrhage in infected patients. However, physicians worldwide need to remain vigilant, and consider the possibility of cerebral hemorrhage in patients manifesting with neurological symptoms, to enable prompt institution of therapy. This directly translates to an ever more increasing role of the neuroradiologist in the line of patient care, in this time of crisis.

Disclosure of interest

The author declares that he has no competing interest.

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