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COVID-19: Neurological Perspectives of Pathology and Management

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ABSTRACT

The coronavirus disease of 2019 (COVID-19) is an ongoing global pandemic that has so far affected more that 165 million people worldwide across > 200 countries and resulting in more than 3.3 million deaths [1]. The causal virus is the severe respiratory syndrome coronavirus 2 (SARS-CoV-2). Coronaviruses are a group of enveloped viruses with single-stranded positive sense RNA genome. Ultrastructure studies have shown evenly distributed surface projection on the SARS-COV-2 virus giving it the characteristic crown-shaped appearance. This surface protrusion is referred to as the spike protein and it considered the key structure for infectivity and virulence by binding to the receptors on the host cells. The main mode of transmission is contact with respiratory droplets from the infected person and aerosols.

Pathogenicity

The COVID-19 infection manifests as acute pneumonia. The symptoms include fever, dry cough, and shortness of breath. COVID-19 not only causes lung and vascular damage but also causes neural damage. Almost all diagnostic testing for COVID-19 is done using the rRT-PCR. When SARS-COV-2 attaches to the host cells by using host angiotensin-converting enzyme 2 (ACE2) as a receptor [2]. Binding is initiated by the S protein of the SARS-CoV-2 and ACE2 of the host cell. The focus of my review further will be detailing the neuropathological aspects of COVID-19 infection.

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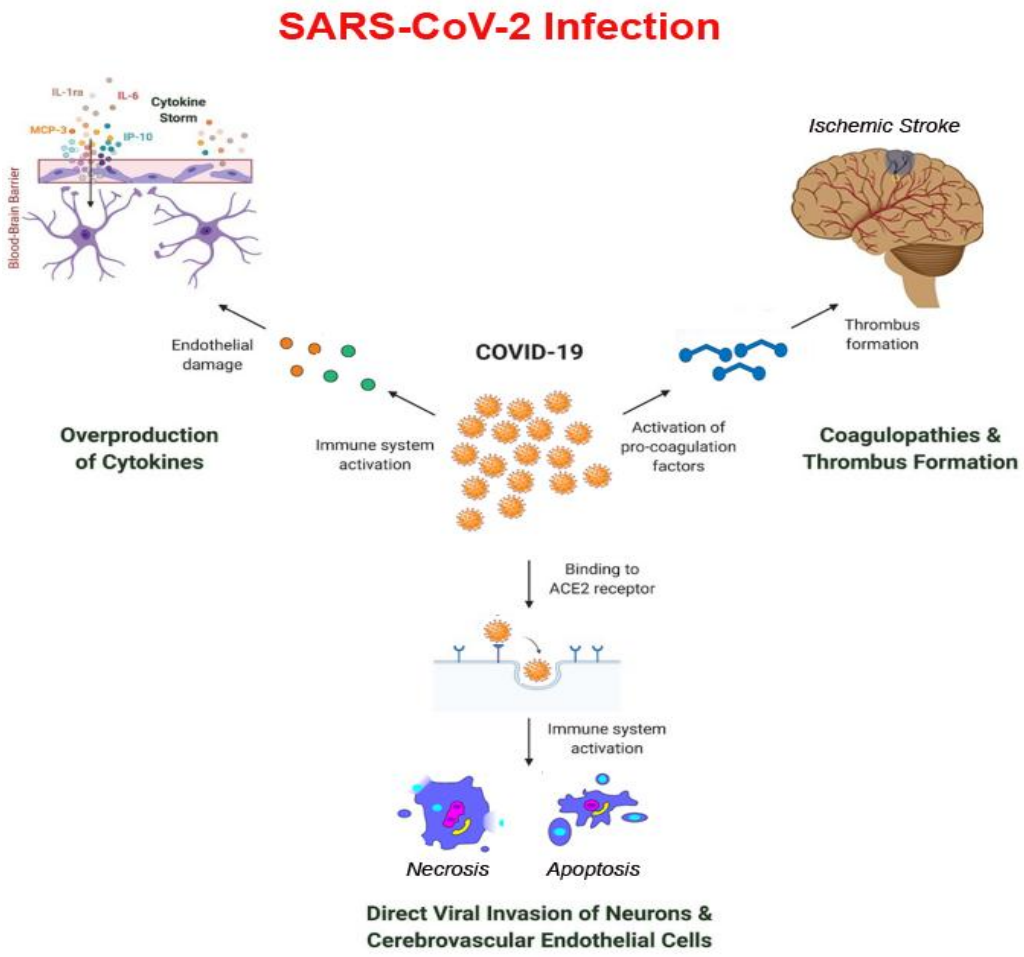

ACE2 expression is reported in several brain areas including the striatum and choroid plexus. Several in vitro studies with induced pluripotent stem cells (hiPSCs) and brain organoids showed that when SARS-CoV-2 is added to them, infection was established resulting in viral proliferation and neuronal cell death. In vivo the possible route of SARS-CoV-2 infection can be blood brain barrier (BBB) and olfactory mucosa. It was reported that subunit S1 of the SARS-CoV-2 S protein reached the brain across mouse BBB. Systemic inflammation caused by COVID-19 can disrupt the BBB and this can become a route for viral invasion. In the olfactory mucosal layer, endothelial tissue and nerve tissue are in proximity allowing a possible route for viral transmission [3]. Neurological manifestations of COVID-19 infection range from headaches, dizziness, nausea and vomiting to loss of consciousness and acute cerebrovascular disorders in severe cases. Respiratory worsening in COVID-19 patients may be explained by an attack of the cardiorespiratory centers such as solitary nuclei. Guillain-Barre syndrome, intraventricular hemorrhage and necrotizing hemorrhagic encephalitis have also been reported. A case series from France reported the presence of corticospinal tract signs and dysexecutive syndrome in patients with

severe COVID-19. A group from Japan reported the first case of CSF-proven SARS-CoV-2 meningonencephalitis. Patients with nervous system symptoms were more likely to have lower lymphocyte and platelet counts, and elevated blood urea nitrogen (BUN) levels.

Management of COVID-19

Cardiovascular comorbidities are prevalent in COVID-19 patients. These comorbidities increase the risk of mortality and morbidity from the infection. With ACE2 serving as the portal for infection, the role of ACE inhibitors (ACEi) or angiotensin receptor blockers (ARB) requires further investigation. A multi-center retrospective trial from China demonstrated reduced COVID-19 mortality in patients taking ACEI/ARB compared to non-ACE1/ARB group. COVID-19 pandemic poses a unique challenge in achieving timely treatment of acute stroke patients with thrombolytics and thrombectomy.

Several therapies targeting viral replication are in investigation. These include Remdesivir 9GS5734), a prodrug of adenosine analog that crosses BBB. Remdesivir has been recently approved for treatment in several countries worldwide for compassionate use. Ribavirin, a guanosine analog usually combined with recombinant interferon. It has shown promising results in vitro although in vivo activity is low. Favipiravir, a viral RNA polymerase inhibitor used to treat influenza, is being tested in Japan in combination with inhaled interferon-α. Oseltamivir, a drug commonly used to treat infleza conditions works by blocking viral neurminidase enzyme, therefore preventing shedding of viral particles in the respiratory tract. Oseltamivir is being studies in clinical trials in combination with famipiravir. Ivermectin, an antiparasitic medication has reported in-vitro activity against multiple RNA viruses. The mechanism of action likely involves blocking entry of viral proteins into the cellular nuclei. Human trials with ivermectin are pending. Immunosuppresive/immunomodulatory therapies with corticosteroids such as methylprednisolone in multivariate regression analysis demonstrated independent association with reduction in reaching primary composite endpoints including mortality, ICU admission and mechanical ventilation in patients receiving steroids after controlling for other risk factors. Toclizumab, a humanized monoclonal antibody targeting IL6 receptors, in studies from China and France demonstrated clinical improvement in patients with severe to critical COVID-19 infection.

Current strain imposed by the COVID-19 pandemic is impacting every aspect of the healthcare and neurology is no exception. While neurologic features appear to be commonly associated with COVID-19, further studies are needed to explain the exact pathophysiology and clinical course. As new data keep emerging, it is paramount to be abreast of these new changes and o adapt to those changes to ensure the best possible care for the patients.

Conflict of interest

No

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