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.

Letter to the Editor Regarding "Neurological Impact of Coronavirus Disease (COVID-19): Practical Considerations for the Neuroscience Community"

Letter:

We read with much interest the article "Neurological Impact of Coronavirus Disease (COVID-19): Practical Considerations for the Neuroscience Community" by Werner et al.[1] The authors have described the various neurologic details of COVID-19 in detail.[1] We think this topic is important and is continuously evolving. We have the following comments as an addition to the article.

Symptomatic patients with COVID-19 can present with mild, moderate, or severe illness. Across all studies, patients with severe illness have multiorgan involvement. Patients with severe disease are prone to develop acute respiratory distress syndrome (ARDS), acute cardiac injury, acute renal failure, and acute liver dysfunction.[2] Although several patterns of central nervous system involvement have been reported among these patients, diffuse central nervous system (CNS) involvement has been reported to be higher.[3]

Multiple mechanisms could contribute to the initiation and progression of CNS injury in patients with COVID-19. They are described as follows.

1. Cytokine storm, defined as dysfunctional, uncontrolled, continuous activation of inflammation, has been consistently reported across all studies. This exaggerated inflammation has been postulated to contribute to ARDS, myocardial injury, renal failure, severity of illness, requirement of intensive care unit admission, requirement of mechanical ventilation, and mortality. This has been diagnosed with an elevated level of inflammatory markers including C-reactive protein, leukocytes, procalcitonin, proBNP, ferritin, interleukins, and various other inflammatory markers. Although diffuse CNS involvement is noted to be higher among patients with severe illness, a temporal association between inflammatory markers and CNS dysfunction has not yet been shown.[4,5]
2. Autopsy studies on patients with COVID-19 have been limited. Direct viral invasion has been reported in various organs including lung, liver, and heart. However, no reports have yet identified the virus, or viral particles in the brain.[6]
3. Hypoxia-induced apoptosis and ischemia, have also been reported, presenting in most patients as multiorgan dysfunction.[7]
4. Prothrombotic state has also been reported, secondary to endothelial injury, thrombocytopenia, deranged coagulation parameters as evident from the raised D-dimer, fibrinogen, and prothrombin time.[6,8]
5. Embolic events secondary to myocardial dysfunction, have been reported, with increased risk of arrhythmia. This has been supported by the presence of several raised cardiac markers including high-sensitivity troponins and D-dimer.[6,8,9]
6. Among patients with severe illness, multiple other contributors of CNS dysfunction requiring consideration are 1) prolonged requirement of CNS depressing agents including benzodiazepines (diazepam and midazolam), opioids (fentanyl and morphine), anesthetic agent (propofol), and neuromuscular blocking agents to achieve better ventilation goals in patients with severe ARDS, 2) prolonged intensive care unit stay, 3) presence of cardiogenic and septic shock, and 4) CNS side effects of other medications including corticosteroid, antibiotics, and so forth.[6,9-11]

Finally, cerebrovascular injury is being commonly reported in patients with COVID-19. Studies have shown that patients with severe COVID-19 have higher cardiocerebrovascular comorbidities including older age, hypertension, diabetes mellitus, hyperlipidemia, heart failure, coronary artery disease, and cerebrovascular disease.[12,13] A recent study also showed that patients with severe COVID-19 had higher cerebrovascular events compared with patients without severe Illness.[3] We agree with the authors that future studies will be instrumental in clarifying patterns, predictors, and outcome of COVID-19–related neurologic injury.

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