COVID-19 for neurologists

Coronaviruses interfere with target cells by membrane-bound spike proteins. Angiotensin-converting enzyme 2 was identified as an input receptor for SARS-CoV-2. Due to its wide pattern of expression, COVID-19 was shown to affect several organs, including the central nervous system, where the receptor is mainly expressed as neurons.

In the current pandemic, there is a rising number of global infections, the aim of this case to increase the awareness about SARS-CoV-2 possible complications, even if there are possible further mutations for the virus, especially in the central nervous system [1].

It is associated with an increased risk of long-term cognitive decline in the elderly population. COVID-19 patients, especially severe patients, should be intensively monitored for post-infection cognitive decline [2] [3]

Several neurological complications of the central and peripheral nervous systems following SARS-CoV-2 infection have gained clinicians' attention. Encephalopathy, stroke, encephalitis/meningitis, Guillain-Barré syndrome, andmultiple sclerosis are considered probable neurological signs of COVID-19. The virus may invade the nervous system directly or induce a massive immune-inflammatory response via a “cytokine storm.” Specific antiviral drugs are still under study. To date, immunomodulatory therapies and supportive treatment are the predominant strategies. In order to improve the management of COVID-19 patients, it is crucial to monitor the onset of new neurological complications and to explore drugs/vaccines targeted against SARS-CoV-2 infection [4].

A cross-sectional exploratory prospective biomarker cohort study of 21 patients with COVID-19 neurological syndromes (Guillain Barre Syndrome [GBS], encephalitis, encephalopathy, acute disseminated encephalomyelitis [ADEM], intracranial hypertension and central pain syndrome) and 23 healthy COVID-19 negative controls. Ziff et al. measured cerebrospinal fluid (CSF) and serum biomarkers of amyloid processing, neuronal injury (neurofilament light), astrocyte activation (GFAp) and neuroinflammation (tissue necrosis factor [TNF] α, interleukin [IL]-6, IL-1β, IL-8). Patients with COVID-19 neurological syndromes had significantly reduced CSF soluble amyloid precursor protein (sAPP)-α ($p = 0.004$) and sAPPβ ($p = 0.03$) as well as amyloid β (Aβ) 40 ($p = 5.2\times10\text{-}8$), Aβ42 ($p = 3.5\times10\text{-}7$) and Aβ42/Aβ40 ratio ($p = 0.005$) compared to controls. Patients with COVID-19 neurological syndromes showed significantly increased neurofilament light (NfL, $p = 0.001$), and this negatively correlated with sAPPα and sAPPβ. Conversely, GFAp was significantly reduced in COVID-19 neurological syndromes ($p = 0.0001$) and this positively correlated with sAPPα and sAPPβ. COVID-19 neurological patients also displayed significantly increased CSF proinflammatory cytokines and these negatively correlated with sAPPα and sAPPβ. A sensitivity analysis of COVID-19 associated GBS revealed a non-significant trend towards greater impairment of amyloid processing in COVID-19 central than peripheral neurological syndromes. This pilot study raises the possibility that patients with COVID-19 associated neurological syndromes exhibit impaired amyloid processing. Altered amyloid processing was linked to neuronal injury and neuroinflammation but reduced astrocyte activation [5].

Dolatshahi et al. provided evidence to critically discuss the claim that the survived patients could possibly be at increased risk for neurodegenerative diseases via various mechanisms. This virus can directly invade the brain through the olfactory bulb, retrograde axonal transport from peripheral nerve endings, or via hematogenous or lymphatic routes. Infection of the neurons along with peripheral leukocyte activation results in pro-inflammatory cytokine increment, rendering the brain to neurodegenerative changes. Also, occupation of the Angiotensin-converting enzyme 2 (ACE2) with the virus may lead to a decline in ACE-2 activity, which acts as a neuroprotective factor. Furthermore, acute respiratory distress syndrome (ARDS) and septicemia induce hypoxemia and hypoperfusion, which is locally exacerbated due to the hypercoagulable state and micro-thrombosis in brain vessels, leading to oxidative stress and neurodegeneration. Common risk factors for COVID-19 and neurodegenerative diseases, such as metabolic risk factors, genetic predispositions, and even gut microbiota dysbiosis, can contribute to a higher occurrence of neurodegenerative diseases in COVID-19 survivors. However, it should be considered that the severity of the infection, the extent of neurologic symptoms, and the persistence of viral infection consequences are major determinants of this association. Importantly, whether this pandemic will increase the overall incidence of neurodegeneration is not clear, as a high percentage of patients with a severe form of COVID-19 might probably not survive enough to develop neurodegenerative diseases [6].

COVID-19 and Guillain-Barré Syndrome

see COVID-19 and Guillain-Barré Syndrome.

Acute ischemic stroke in COVID-19 pandemic

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SARS-CoV-2 associated viral encephalitis

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