The Annals of Internal Medicine

Infection with COVID-19 and Neuropathological Features.

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Received Date : June 11, 2024
Accepted Date : June 13, 2024
Published Date : July 13, 2024

ABSTRACT

The pathophysiology linked to COVID-19 infection is gradually coming to light. Acute airway inflammation and diffuse alveolar injury have been found in recent postmortem examinations; these findings are similar to severe acute respiratory syndromes caused by both SARS-CoV and MERS-CoV outbreaks. While various neuropathologies linked to COVID-19 infection have been noted in recent articles, there is still a dearth of knowledge on this crucial public health issue. Here, we go over how direct viral neuroinvasion and/or cytokine release during the infection could cause COVID-19-related neuroinflammation.

Keywords : COVID-19 infection; neuropathology; autoantibodies; neuroinflammation.

The SARS-CoV-2 virus, a beta coronavirus identified in Wuhan, China towards the end of 2019, is the cause of COVID-19. Reports from China during the outbreak and from other nations subsequently made it abundantly evident that the majority of patients (81%) have Patients with more severe symptoms include 14% who have severe respiratory distress and 5% who have respiratory failure, septic shock, and/or multiple organ failure [1, 2]. moderate symptoms without pneumonia or moderate pneumonia are also included in this category. However, as of right now, we are certain that this virus can infect multiple cell types and organs, resulting in symptoms ranging from neurological to liver, heart, and kidney damage to diarrhea and renal damage [1, 3]. Recent research has demonstrated that the protease TMPRSS2, necessary for cell infection, and ACE2, expressed by both neurons and microglia cells.

Using qRT-PCR, they were able to find viral RNA in 13% of the brain samples from COVID-19-related deaths in the same study [4]. An additional investigation revealed that the virus can infect Within two days of exposure, 3D human brain organoids—or, more accurately, neurons—died [5]. Furthermore, it has previously been reported that SARS-CoV and Middle East respiratory syndrome (MERS)-CoV, which are closely linked to SARS-CoV-2 in terms of evolution, have the potential to be neuroinvasive [6–8]. Apart from these investigations that provide conclusive proof of the virus's existence in the central nervous system, there exist further studies, including a Numerous epidemiological findings suggest that COVID-19 may be linked to a number of neurological conditions, including meningitis, cranial polyneuritis, anosmia, encephalopathy, stroke, Parkinson's disease, Alzheimer's disease, and Guillain-Barré syndrome [9]. According to certain research, COVID-19 and Guillain-Barré syndrome are related. Generally speaking, they explain that neurological symptoms appear seven to ten days following the typical respiratory signs of COVID-19. The SARS-CoV-2 infection linked to autoantibodies is linked to antigens found in certain tissues, such as the brain, where there are significant amounts of autoantibodies in the cerebrospinal fluid that target neural, glial, and endothelial epitopes.

Gangliosides, for example, are one of the antigens linked to the central nervous system. It is unclear, nevertheless, if SARS-CoV-2 infection causes the peripheral nervous system to produce autoantibodies against gangliosides, as is the case with other infections [11–13]. A recent study examined the prevalence of Guillain-Barré cases among 71,904 COVID-19 patients seen in 61 emergency rooms in Spain over the course of the illness' two-month peak. The incidence of Guillain-Barré was found to be 9.44/100,000 inhabitants/year among patients with COVID-19, compared to 0.69/100,000 inhabitants/year among patients without COVID-19 [14]. However, the authors of a different study did not discover a meaningful link between COVID-19 and Guillain-Barré syndrome. In actuality, given that the incidence did not increase.

A significant astrogliosis and microgliosis in the olfactory bulb, most likely brought on by the virus, appears to be linked to the lack of taste (ageusia) and smell (anosmia), which affect nearly 60% of COVID-19 patients [4]. It's thought Since the presence of viral RNA and SARS-CoV S proteins was found in neuroanatomical areas receiving olfactory tract projections, it can be assumed that one of the viral entry pathways is via the neural–mucosal interface by transmucosal entry via

regional nervous structures of the olfactory mucosa, or, more precisely, from axonal transport. The influenza virus is another respiratory virus that can enter the body and infect the central nervous system via this route [16]. Other viral illnesses that harm the olfactory neuroepithelium and impact the upper respiratory tract include influenza. Anosmia may potentially be explained by this [18].

The infection-induced cytokine storm can exacerbate the virus's neurotropism by the central nervous system by starting the process of neuroinflammation.

causing the blood-brain barrier's permeability to rise [19]. Consequently, the resulting neuroinflammatory insult could make people more vulnerable to neurodegenerative illnesses. This injury to brain cells, including astrocytes and microglia, may enhance the release of inflammatory cytokines and ATP. This triggers P2X7 receptor activation, which can then trigger the NLRP3 inflammasome pathway within other pathways [20]. This can lead to diffuse lung edema, immune cell and inflammatory cytokine infiltration, disruption of the blood–brain barrier, and overshooting inflammation with extensive cytokine release. It can also affect coagulation.

It has also been demonstrated that various viral infections can alter the blood-brain barrier, which can lead to the long-term development of neurological disorders like multiple sclerosis, depression, anxiety, and Alzheimer's disease [20]. Changes in blood caused by infections, particularly those involving the cerebral endothelium, can have an impact on the coagulation pathways and may be connected to COVID-19-related stroke occurrences.

According to other patient reports, severe SARS-CoV-2 infections are frequently linked to markedly reduced platelet counts and elevated blood levels of D-dimers, which may help to explain why these patients have an increased risk of cerebrovascular events [21]. Through computed CT, COVID-19-related neurological symptoms were also seen.

Necrotizing hemorrhagic encephalopathy symptoms are evident in the imaging results. This is an uncommon condition that primarily develops from viral brain malfunction and causes seizures, liver issues, and mental disorientation afterward.

infection. The cytokine cascade, particularly IL-6, results in severe encephalopathy and has the potential to cause stroke [22]. greater quantities of antibodies against other The presence of coronaviruses, which cause colds, in the cerebrospinal fluid of Parkinson's disease patients raises the possibility that COVID-19 plays a role in the disease's etiology. Furthermore, SARS-CoV-2's stimulation of the angiotensin system, which is connected to COVID-19 pathophysiology and potentially significant in the neuroinflammatory and neurodegenerative processes seen in Parkinson's disease Other viral infections, such as influenza A, Epstein-Barr, Japanese encephalitis, Coxsackie, West Nile, Western horse encephalomyelitis, and HIV, have also been linked to the onset of temporary or, less frequently, persistent Parkinson's disease. This is mostly because these infections induce neuroinflammation and/or hypoxic brain injury accompanied by basal ganglia structural and/or functional impairment. Furthermore, it has been suggested by conflicting data that prior infections with the herpes simplex 1, Epstein-Barr, chickenpox, zoster, hepatitis C, and influenza A virus may raise the long-term risk of developing Parkinson's disease [23]. Unlike Guillain-Barré, there is currently no substantial correlation between SARS-CoV-2 infection and parkinsonism; to date, only three cases of parkinsonism have been recorded [24–26].

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