Ocular involvement

Exposed ocular surfaces are vulnerable to infection by droplets as are other mucous membranes [51]. According to a study in 38 patients, in Hubei, 12 presented ocular symptoms. Ophthalmic manifestations from COVID-19 ranged from conjunctival hyperemia (3 patients), follicular conjunctivitis, chemosis (7 patients), and epiphora (7 patients) [52] to hyperreflective lesions in the ganglion cell and inner plexiform layers of the retina (12 patients, as reported in a study in Sao Paulo) as shown by optical coherence tomography [53]. COVID-19 hypercoagulable states have been correlated with blindness, due to acute ophthalmic artery occlusion [54].

The ocular surface could facilitate the virus to reach the nasopharynx through the nasolacrimal system [55]. Tears have been shown to harbor SARS-CoV-2 thus every healthcare worker needs to take caution as 7% of COVID-19 patients may present the virus in their tears, but be asymptomatic [56] and while studies have shown positive SARS-CoV-2 RT-PCR results from a patient's tears, virus isolation remains difficult [57].

Neurological implications

Human coronaviruses (HCoVs), and other respiratory viruses may enter the central nervous system (CNS) hematogenously or by the ethmoidal cribriform plate by retrograde neuronal route [23, 58]. COVID-19 as a subject infects the blood-brain-barrier's endothelial cells and the blood-cerebrospinal fluid barrier's epithelial cells in the choroid plexus brain's ventricles, or leukocytes that become hematogenous propagation vectors [58].

The critical role of proteins S and E in HCoVs, specifically 0C43, and the slow movement of the blood in the brain's microcirculation, can aid in the interaction of the SARS-CoV-2 S protein with the ACE2 receptor expressed in the capillary endothelium. Viral damage and recruitment of endothelial cells can promote invasion of the CNS by SARS-CoV-2 [23, 59–62].

In the retrograde neuronal route, infection occurs in the body's periphery and axonal transport mechanisms are used to access the CNS [63, 64]. Respiratory viruses use the olfactory, trigeminal, and vagus cranial nerves to access the brain [65–72].

The four endemic HCoVs have associations with extra-respiratory diseases such as myocarditis, meningitis, severe diarrhea, and multi-organ failure [73–78]. There have been reports linking the presence of HCoVs in the human CNS and neurological disorders [79–83]. Identifying the etiology of CNS infections poses a challenge. These difficulties arise due to the spectrum of symptoms that infected patients present and the number of pathogens that can cause them. It is also challenging to differentiate a non-viral etiology from systemic viral infection's symptoms outside of the CNS [84–87].

CNS infections can present as meningitis with fever, neck stiffness, photophobia, and phonophobia. Encephalitis' symptoms may be mild and undiagnosed or attributed to other system's imbalances. Typical encephalitic symptoms such as confusion, altered mental status, personality change, abnormal behavior, movement disorders, and seizures have also been reported [84].

In a case series, in which autopsies were performed and brain specimens collected, histopathological studies showed only hypoxic changes without evidence of viral encephalitis in SARS-CoV-2- exposed patients [88]. However, in a study that involved 153 hospitalized patients, clinical data were available for only 125, which showed that the most common presenting neurological or psychiatric disorder was a cerebrovascular episode in 62% of patients, followed by altered mental status in 31% of patients. The altered mental status' etiology, ranged from encephalopathy (nine patients) to encephalitis (seven patients). The remaining 59% exhibited psychiatric conditions, such as neurocognitive syndrome, psychosis, and affective disorders. Only two patients had exacerbations of pre-existing mental disorders. About 50% of patients with altered mental status were younger than 60 years of age, while 82% of patients with cerebrovascular episodes were over 60 years of age [89].

In 214 hospitalized COVID-19 patients in Wuhan, 36.4% of patients with mild disease had neurological symptoms, and 45.5% presented them, when severely compromised [90]. Symptoms exhibited are seen in Table 3.

A review of literature has shown COVID-19 to be linked with a high number of cases of ageusia and anosmia. It is due to the entry of the COVID-19 virus through the nasal epithelium, which includes respiratory epithelium and olfactory epithelium [91].

Many viruses, including coronaviruses, do induce brief fluctuations in odor acuity due to different inflammatory responses, including cytokine release. Other β-coronaviruses often lead to inflammation, while SARS-CoV-2 does not cause nasal epithelium inflammation. The anosmia caused due to SARS-Cov-2 usually takes weeks for recovery. In contrast,