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Neuro-ophthalmologic complications of coronavirus disease 2019 (COVID-19)

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ABSTRACT

Multiple neuro-ophthalmological manifestations have been described in association with COVID-19. These symptoms and signs may be the result of a range of pathophysiological mechanisms throughout the course from acute illness to recovery phase. Optic nerve dysfunction, eye movement abnormalities and visual field defects have been described.

1. Introduction

In December 2019 reports of severe acute respiratory syndrome (SARS-CoV-2) due to coronavirus disease 2019 (COVID-19) causing pneumonia emerged out of Wuhan city in China [1]. The enveloped RNA betacoronavirus is hypothesized to employ the ACE2 binding receptor for infectivity [1,2]. At the time of this article, it was confirmed to have infected nearly 34.5 million people worldwide and caused over 1 million deaths, causing an immense impact on society at large [3].

While the most common symptoms include fever, cough, fatigue, and shortness of breath [1,4], COVID-19 is not purely a respiratory disease; indeed, the virus may produce a vast array of manifestations related to acute cardiac disease, acute kidney injury, vasculopathy, coagulopathy, elevated inflammatory markers, and neurological injury [5]. Presentations vary from completely asymptomatic carriers to severe illness with multiorgan failure and death [5]. Severe cases are typically characterized by a heightened inflammatory and coagulopathic response that is thought to play a prominent role in the pathogenesis and mortality that is associated with this virus [6].

2. Neuro-ophthalmic manifestations

Multiple neuro-ophthalmological manifestations have been described in association with COVID-19. These symptoms and signs may be the result of varying underlying pathophysiological mechanisms including hypoxia, severe hypertension, toxic metabolic processes, ischemic and hemorrhagic strokes along with para-infectious and post-infectious inflammatory processes.

2.1. Optic neuritis

Cases of optic neuritis have been described in patients who had proven COVID-19 infection. In a study examining the neurological complications of COVID-19 admitted to a single hospital in Spain, one case of optic neuritis was observed in the recovery phase [4]. Additionally there have been case reports of MOG antibody positivity in patients with either presumed [7] or confirmed [8] COVID-19 infection. One had bilateral optic nerve abnormalities including peripheral retinal hemorrhages that responded well to intravenous corticosteroids [8]. Presumably the COVID-19 infection triggered an autoimmune response and the production of MOG antibodies. It is unclear whether the patient

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harbored a predisposition to MOG associated disease or if the virus set the process in motion. An additional case of optic neuritis that was associated with other neurological deficits and consistent with acute disseminated encephalomyelitis (ADEM) has also been documented [9].

2.2. Cranial nerve palsies

Both diplopia and ptosis have been described in patients shortly after diagnosis with typical COVID-19 infection. Several patients with ocular motor deficits within days of resolution of typical COVID-19 symptoms have been reported. These ocular motility deficits have been associated with paresthesias and hyporeflexia, suggesting the Miller-Fisher variant of the Guillain Barre syndrome [10–14]. In keeping with this diagnosis, cranial nerve inflammation on MRI has been observed [10].

In another case series, three patients presented with several days of fever and active COVID-19 infection. They did not have sensory complaints, but rather noted generalized fatigability. These patients were assessed with EMG, which showed decremental response on repetitive nerve stimulation and positive acetylcholine receptor antibodies, consistent with a diagnosis of Myasthenia Gravis. Again, the COVID-19 infection may have exposed an unrecognized predisposition to this autoimmune process. The patients in this series recovered with various immunosuppressive agents to treat Myasthenia Gravis [15]. An additional report of an isolated abducens nerve palsy without identifiable lesion on an imaging study and of unclear etiology was described during the height of the pandemic [16].

The hypercoagulable and proinflammatory state triggered by COVID-19 infection has been associated with cerebral venous sinus thromboses that may manifest with confusion and raised intracranial pressure. Increased intracranial pressure may produce a false localizing sixth nerve palsy as well as papilledema [17–19]. Pseudotumor cerebri syndrome has also been reported as a complication of multisystem inflammatory syndrome in children associated with COVID-19 infection [20]. Chemosis has also been described in patients with severe infection and significant ocular exudate [21].

2.3. Eye movement abnormalities and nystagmus

Oscillopsia has been described in several case reports in association with ataxia and myoclonus, usually in the context of encephalopathy and following severe systemic involvement due to COVID-19 infection. These patients were found to have corresponding cerebellar lesions on MRI and bland cerebrospinal fluid [22,23] consistent with a post-infectious immune-mediated rhomboencephalitis. In one case, the MRI did not show any structural lesion, however the time course of presentation, symptoms and bland CSF were felt to be consistent with this process [24]. A single case of opsoclonus myoclonus ataxia syndrome has been reported in a patient five days after resolution of fevers and myalgias typical of COVID-19 symptoms. There were no findings seen on brain MRI, but CT chest showed findings consistent with COVID-19 infection. The patient responded well to treatment with intravenous immunoglobulin and methylprednisolone treating an inflammatory cerebellar syndrome [25]. The authors (SLG personal communication) have also observed a patient with atypical ocular bobbing (slow phase up and fast phase down) in a patient who had transient white matter abnormalities in the bilateral superior cerebellar peduncles.

2.4. Visual field defects

Stroke, especially in the younger population, has been one of the most notable and devastating neurological complications of COVID-19. With involvement of the posterior circulation and occipital lobes, visual field defects and visual snow syndrome have been documented and reported in these patients [26–30]. The entity of posterior reversible vasoconstriction syndrome (PRES) has been another mechanism of injury in COVID-19 and some patients may experience transient visual field defects and MRI abnormalities [31]. There has been one report of hallucinatory palinopsia described in a patient with PRES due to COVID-19 infection with involvement of parieto-occipital lobes on MRI [32].

3. Conclusion

The neuro-ophthalmological symptoms and signs associated with COVID-19 infection are varied and span the course of infection through the recovery phase. The mechanisms of involvement are still in the process of being completely elucidated, however, they tend to fall within three general categories – a post-viral inflammatory syndrome, sequelae of a proinflammatory state with hypercoagulability and "cytokine storm," and the result of systemic abnormalities including hypoxia and severe hypertension. Direct viral invasion seems to be a rare manifestation of COVID-19 and we are unaware of neuro-ophthalmological findings that have been definitively produced by this potential mechanism.

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