Disease of the Year: COVID-19 and Its Neuro-ophthalmic Complications

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We are living through times of tremendous change in many spheres of our lives, unfolding against the backdrop of COVID-19, the deadliest pandemic in living memory. As such, COVID-19 does not really need an introduction but rather demands a reckoning of how profoundly this disease has affected all areas of medical practice. Neuro-ophthalmology is no exception, and as such, we are dedicating the next *Journal of Neuro-Ophthalmology* Disease of the Year section to COVID-19.

A variety of ophthalmic and neurologic manifestations of COVID-19 continue to be described. An initial study of neurologic manifestations of COVID-19 from China described a high prevalence of neurologic symptoms, 30.2% overall, including nonspecific viral symptoms such as myalgias but also vision changes (1). It is not yet clear whether these reported visual symptoms originated from the anterior visual pathways or the cortex. Headache and especially eye pain are common symptoms and, importantly, may be early manifestations of COVID-19 that develop before any respiratory symptoms or CT chest abnormalities are present (1). Acute cerebrovascular disease appears to be the most common severe neurologic manifestation, occurring in 2.8% of patients, mostly primarily ischemic stroke but intracerebral hemorrhages and venous sinus thromboses also occur. Some of these cases have been associated with homonymous vision loss or eye movement deficits. Several reports of Guillain–Barre syndrome and Miller Fisher syndrome have emerged, pointing to a postinfectious, antibody-mediated mechanism for associated cranial neuropathies. Most of these cases have been associated with atypically short latency between respiratory symptoms and neurological symptoms, likely owing to the well-described presymptomatic phase of COVID-19. One case of bilateral optic neuritis associated with myelin oligodendrocyte glycoprotein antibodies has been reported in the setting of COVID-19, also pointing to the generation of autoantibodies provoked by this novel virus. Both acute disseminated encephalomyelopathy and the more severe acute hemorrhagic necrotic encephalopathy have been described in association with COVID-19, postinfectious complications that may also affect vision. Furthermore, the newly described pediatric inflammatory syndrome associated with COVID-19 bears a resemblance to Kawasaki disease, which may rarely lead to disc edema. As more cases of this complication emerge, neuro-ophthalmic manifestations may be observed. It is likely that the pandemic will lead to a greater-than-expected incidence of such inflammatory syndromes, which may also create an opportunity to closely examine the mechanisms by which infection triggers parainfectious and postinfectious neurologic disease. The large number of clinical cases in the era of the Internet also opens up new avenues for the study of patient symptoms and epidemiology, such as for instance analysis of search engine data sets and metadata.

Three main putative mechanisms of neurological injury have been proposed: direct viral central nervous system invasion, endothelial dysfunction, and a neurotoxic effect from excessive inflammation and cytokine release. However, the relative importance of these mechanisms remains to be elucidated. In early clinical reports, data on brain and eye pathology were sparse, but more information will hopefully become available that can shed light on the pathogenesis of the neurologic complications. A great number of clinical trials have been launched, and some of these involve medicines familiar to neuro-ophthalmologists, such as the interleukin 6 inhibitor tocilizumab, studied in the hope that it may dampen the exuberant "cytokine storm" of severe COVID-19. Data from these drug trials could shed light on mechanisms of infection and immune response that may be relevant to the neuro-ophthalmology of COVID-19. Others such as hydroxychloroquine also have potential for retinal toxicity. In addition,

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many inflammatory neuro-ophthalmic disorders such as demyelinating diseases, myasthenia, and temporal arteritis are treated with various levels of immune suppression, and we must carefully examine the effects these treatments may have on morbidity and mortality related to COVID-19 and adjust our treatment algorithms accordingly.

COVID-19 poses particular risks of infection to health care providers, and this risk may be especially great for eye care providers, who sit face to face mere inches away from patients at the slit lamp. The ocular surface is believed to be a site of COVID-19 disease, and direct contact of virus-containing droplets or aerosolized particles with mucous membranes, including the eye, is a suspected route of transmission (2–4). In fact, one of the first physicians to raise concerns regarding the spread of a novel coronavirus was Dr. Li Wenliang, MD, an ophthalmologist, who later died of COVID-19 and was believed to have contracted the virus from an asymptomatic glaucoma patient in his clinic. In addition, risk of nosocomial spread of the disease must be minimized in all clinical settings. As a consequence, medical care in the era of COVID-19 has been profoundly altered, creating particular difficulties for the traditionally physical examination–based practice such as neuro-ophthalmology. We are also being challenged to innovate in the area of resident and fellow training during a pandemic. Many physicians have suffered financial losses. However, these challenges also create opportunities for innovation in virtual health and telemedicine in neuro-ophthalmology and for the use of smartphone and video technology. Online visual field testing, for example, has accelerated in heavily hit regions. It is to be hoped that in the future these technological advances can be levied to expand access to neuro-ophthalmology services, especially in underserved areas.

By engaging directly with both the challenges and innovations in the field of Neuro-ophthalmology in the era of COVID-19, we hope to showcase and promote the growth of our field in these particularly challenging times.

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