



## POST-COVID SYNDROME. OPTIC NERVE LESIONS (Literature Review)

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### SUMMARY

Coronavirus infection COVID19 is an acute respiratory viral disease, which in most cases is severe and leads to the development of various complications known as post-COVID syndrome.

Post-covid syndrome or long-covid syndrome is a consequence of coronavirus infection (COVID-19), while 20% of those who have been ill suffer from long-term symptoms, the duration of which varies greatly and is more than 12 weeks.

According to the WHO, the post-covid syndrome includes 33 symptoms, while in younger people who have been ill, the incidence of this symptom complex is much higher. According to the literature, post-COVID syndrome may reappear 3-6 months after clinical recovery. This condition is characterized by various non-specific symptoms, which can be manifested by dysfunction of individual organs, skin vasculitis, neurological symptoms up to the development of mental disorders.

Summing up, it should be noted that during the pandemic period, certain experience has been accumulated regarding ophthalmic problems. The data obtained are sometimes contradictory, but it is already clear that ophthalmic disorders in COVID-19 can be leading along with damage to other organs. Perhaps a new disease leads to an exacerbation of an existing or manifestation of dormant ophthalmopathology. Regardless of what is the cause, it is necessary to remain vigilant about the state of the organ of vision both in the immediate and long-term period after a new coronavirus infection.

**KEYWORDS.** Postcovid syndrome, optic neuritis, optic vasculitis, anterior ischemic neuropathy

Coronavirus infection COVID19 is an acute respiratory viral disease [1, 2, 3], which in most cases is severe and leads to the development of various complications, known as post-Covid syndrome.

Post-Covid syndrome or Long Covid [2, 4, 6] is a consequence of coronavirus infection (COVID-19), with 20% of recovering individuals suffering from long-term symptoms, the duration of which varies greatly and lasts more than 12 weeks.

According to WHO, post-Covid syndrome includes 33 symptoms, while in younger people who have recovered from the disease, the incidence of this symptom complex is much higher.

It should be noted that the post-Covid syndrome is included in the International Classification of Diseases (ICD-10) [8, 9, 10], category code U09.9 "Condition after COVID-19, unspecified," which also includes the post-Covid condition [11].

According to the literature [8, 9, 10], post-Covid syndrome can reappear 3-6 months after clinical recovery. This condition is characterized by various nonspecific symptoms, which can manifest as dysfunction of individual organs, skin vasculitis, neurological symptoms, and even the development of mental disorders.

According to many authors, the causes of the development of post-Covid syndrome may be hypercoagulation, damage by the virus to cells of various organs, and an inadequate immune response to cells affected by the virus. Thus, the development and spread of these pathological processes can subsequently cause coagulopathy and vasculopathy.

According to the authors, post-Covid syndrome in ophthalmology can manifest itself in the form of uveitis, keratitis, vasculitis,

SARS-CoV-2 infection in the post-Covid period has an impact on both the physical and cognitive and mental health of patients, especially those undergoing treatment in intensive care units. Moreover, it has been shown that the effects of the virus can last for weeks or months. The term "post-COVID syndrome" is commonly used to refer to a variety of physical and psychological symptoms that continue after the acute phase has resolved. This problem is becoming increasingly urgent, the incidence ranges from 10% to 35%, and among patients with a history of hospitalization the rate reaches 85%. This article systematizes the variety of clinical manifestations of post-Covid syndrome, and examines the possible pathogenetic mechanisms of this still poorly understood condition.

According to this author (Zhabura M.O., Shostakovskaya A.S., Yatskov I.A.). The problem of post-Covid complications is as significant for the global medical community as COVID-19 itself. Emerging evidence points to multifactorial pathogenesis, namely inflammation, nervous system dysfunction, endothelial



damage and thromboembolism as the main pathogenic mechanisms. Particular attention should be paid to patients who have comorbid diseases and, accordingly, a higher risk of developing complications. The findings have important prognostic implications, especially for older adults who are more susceptible to severe cognitive outcomes from COVID-19

According to the authors, the growing evidence of the effects of SARS-CoV-2 on the central nervous system raises key questions about identifying factors that determine the risks of subsequent cognitive decline, the development of Alzheimer's disease and other types of dementia, and mood disorders. It is important that patients who have suffered from COVID-19 remain under systematic medical supervision. It is expected that as long-term complications of COVID-19 develop, more data will be available to guide therapeutic management. Further studies are needed to elucidate the incidence, clinical spectrum, pathogenesis and prognosis of this new clinical entity. In the meantime, standardization of definitions and consensus on classification criteria are needed.

According to the literature, the multidisciplinary COVID-19 clinic at the University of Cincinnati Medical Center in the United States proposed criteria for subtypes of COVID-19 sequelae based on initial symptoms, their duration, rest period, and time of symptom onset [34]. There are five categories of long-term COVID-19 syndrome: – Type 1 – includes patients with varying duration of recovery, which is directly related to the severity of infection, organ damage and comorbidities; – type 2 – symptoms persist for 6 weeks from the onset of the disease; type 3 - characterized by a period of quiescence or near complete recovery after the initial infection, followed by a recurrence of symptoms that persist for at least 3 months (type 3A) or at least 6 months (type 3B); – type 4 – includes patients who are initially asymptomatic at the time of testing positive for SARS-CoV-2, but who develop symptoms after 1–3 months (type 4A) or at least after 3 months (type 4B), persisting over varying periods of time; – Type 5 includes patients who were asymptomatic at the time of testing positive for SARSCoV-2, or who were asymptomatic but died suddenly within the next 12 months [38].

Regarding the prognosis of patients with post-Covid syndrome, other than lingering symptoms, the few published data indicate that most patients have a good prognosis without any further complications or deaths. Post-Covid syndrome, which affects an average of approximately 10% of COVID-19 patients, is not limited to patients with severe acute COVID-19. Symptoms of post-Covid syndrome are usually mild, improve over time, and have no specific predictors. Fatigue, shortness of breath, chest pain, mental health problems, and long-term smell and taste dysfunction are the most common symptoms of post-Covid syndrome. Outpatient services are expected to play a vital role in the rehabilitation of such patients. This review describes the impact of these complex problems on patients with post-Covid syndrome, and the importance of timely diagnosis based on well-described criteria. Patients with post-Covid syndrome should be treated symptomatically, avoiding excessive testing, and pre-existing or new comorbidities should be taken into

account. Guidelines for the diagnosis and treatment of post-Covid syndrome based on established criteria are needed to facilitate and improve the quality of provision of appropriate medical services. In addition, registries are needed to actively and systematically monitor patients with COVID-19 to assess the incidence, clinical spectrum and outcomes of patients with post-Covid syndrome.

Optic neuritis is an inflammatory process, usually unilateral, accompanied by pain and complete or partial loss of vision, which requires pathogenetic treatment, in most cases resolving spontaneously.

Retrobulbar neuritis is an inflammatory lesion of the optic nerve located between the orbit and the optic chiasm. Also accompanied by a decrease in visual acuity, the appearance of loss, limitations of the visual fields, pain when moving the eyeball. It is treated with glucocorticosteroids, antibacterial, antiviral, antihistamines, diuretics, and neuroprotective agents.

Occlusion of the central retinal artery is an acute blockade of the central retinal artery or its branches, leading to circulatory disorders and retinal ischemia. Occlusion of the central nervous system is manifested by sudden loss of vision or sectoral loss of visual fields in one eye.

Optic nerve atrophy is a pathological process that is accompanied by degeneration of the nerve fibers of the optic nerve as a result of their inflammation, swelling, compression, circulatory disorders, and damage.

Optic disc vasculitis is a microthrombovasculitis with predominant damage to the blood vessels of the intraocular part of the microvasculature of the optic nerve, which is accompanied by hyperemia and swelling of the optic disc, expansion and increased permeability of venules and capillaries, hemorrhages, as well as the appearance of remitting microcystic edema in the macula.

To date, the ophthalmological manifestations of COVID-19 have been described in several original studies and clinical cases. In general, eye involvement is rare. In the largest study, W.-J. Guan et al analyzed data from a cohort of 1099 patients with COVID-19 and found conjunctival involvement in only 0.8% of cases. Involvement of the conjunctiva is rather nonspecific and may even be associated with mechanical ventilation, which was used in 6.1% of patients in this study [16].

In another ophthalmology study, P. Wu et al found ocular symptoms in 12 (31.6%) of 38 patients with COVID-19, but SARS-CoV-2 RNA was detected in only 2 (5.2%) of them. Symptoms manifested themselves in the form of hyperemia, chemosis and lacrimation, while the patients had no changes in visual acuity [17].

Patients with ocular symptoms had higher white blood cell and neutrophil counts, as well as higher levels of procalcitonin, C-reactive protein, and lactate dehydrogenase. Because these markers have been found to be highly correlated with disease severity, the possible association between the presence of



ocular symptoms and moderate to severe disease should be explored in further studies. In this report, approximately 30% of patients with COVID-19 had ocular abnormalities, which often occurred in patients with more severe COVID-19. Although SARS-CoV-2 is rarely found in tears, it can be transmitted through the ocular surface [18].

A study by I. Seah et al found similar symptoms in 1 (5.8%) of 17 patients who had conjunctival injection and chemosis [9]. The same clinical picture was described by L. Chen and co-authors, noting the presence of redness, foreign body sensation and lacrimation in the patient. In addition, the authors found follicles on the conjunctiva of the lower eyelid. Symptoms appeared on the 13th day of the disease, and the condition improved on the 15th day, and all symptoms completely disappeared on the 19th day [19]. The work of M. Cheema et al found similar signs of conjunctivitis, but the authors also noted the presence of eyelid edema, follicles and keratitis with subepithelial infiltrates and epithelial defects [7].

A review by I. Seah and R. Agrawal regarding the pathogenicity of coronaviruses in general indicates that conjunctivitis, anterior uveitis, retinitis and optic neuritis are characteristic in experimental models in cats and mice [20]. To date, it is essentially unclear whether SARS-CoV-2 can cause more severe ocular pathology beyond keratoconjunctivitis. However, since ACE-2 is present in the retina and vitreous, uveitis or damage to the posterior pole of the eye may occur, especially with increased viral load [21]. It should be noted that patients with high viral loads are also more likely to develop severe or critical disease, so vision problems may go largely undetected as these patients are often treated in intensive care units for much more severe, life-threatening conditions.

A.A. Ryabtseva and co-authors observed 23 patients within 44-85 days from the onset of symptoms. Observations showed that in the late period of convalescence complaints of dry eyes and impaired color perception persisted with unchanged visual acuity. Optical coherence tomography (OCT) of the peripapillary retina revealed small hyperreflective foci in the inner layers. According to the authors, changes in the organ of vision in patients who have had COVID-19 are mainly associated with the condition of the ocular surface, impaired color perception and changes in the architectonics in the inner layers of the retina, which can persist for a long time during the period of convalescence [22].

In the literature described multiple neuro-ophthalmological manifestations in patients with COVID-19. These symptoms and signs may result from a variety of pathological conditions, including hypoxia, hypertension, ischemic and hemorrhagic strokes, and parainfectious and postinfectious inflammatory processes. To date, the development of these pathological processes in the post-Covid period has not been studied. Cases of optic neuritis have been described in patients with confirmed COVID-19 infection. A study examining the neurological complications of COVID-19 describes one case of optic neuritis in the convalescent phase. In addition, there are case reports of the presence of antibodies in patients with suspected or confirmed COVID-19 infection and optic neuritis. One patient

had bilateral optic nerve abnormalities, including peripheral retinal hemorrhages, which were successfully treated with intravenous corticosteroids. A case of optic neuritis has been reported that was associated with other neurological disorders and consistent with acute disseminated encephalomyelitis [33]

According to the authors, all cranial nerves can be involved in COVID-19, but cranial nerves VII, VI and III are most commonly involved. Cranial nerve involvement in COVID-19 can occur with or without Guillain-Barré syndrome. As of the end of January 2021, 32 patients with isolated cranial nerve injury and 24 patients with GBS and cranial nerve injury were enrolled. Brain imaging is important in patients with cranial nerve injury because it can show damage not only to clinically affected but also to clinically healthy cranial nerves. In patients with cranial nerve damage, COVID-19 infections are usually mild. Isolated cranial nerve palsy without GBS usually responds well to steroid treatment. GBS with cranial nerve involvement will benefit from IVIG.

To summarize, it should be noted that during the pandemic, certain experience has been accumulated regarding ophthalmological problems. The data obtained are sometimes contradictory, but it is already clear that ophthalmological disorders in COVID-19 can be leading along with damage to other organs. Perhaps a new disease leads to an exacerbation of an existing or manifestation of dormant ophthalmopathy. Regardless of what the cause is, it is necessary to remain vigilant regarding the condition of the organ of vision both in the immediate and long-term period after suffering a new coronavirus infection.

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