ARTYKUŁ PRZEGLĄDOWY REVIEW ARTICLE
DOI: 10.24292/01.OT.201221

Special report

Ocular manifestations of COVID-19 infection

Ada Pandey[1], Justyna Gugnowska[1], Angelika Kruszyńska[1], Kinga Czarnacka[1], Małgorzata Gawlak[1], Katarzyna Sajak-Hydzik[1, 2], Ilona Pawlicka[1, 2], Maciej Kozak[1, 2]

[1] Faculty of Medicine and Health Sciences Andrzej Frycz Modrzewski Krakow University
Dean: Prof. Filip Gołkowski, MD, PhD

[2] Clinical Department of Ophthalmology, Provincial Ophthalmology Hospital, Krakow
Head: Katarzyna Sajak-Hydzik, MD, PhD

HIGHLIGHTS

COVID-19, although often associated only with pulmonary symptoms, can also manifest as ocular symptoms, which are often overlooked, and can lead to serious consequences.

ABSTRACT

The most common eye disease associated with SARS-CoV-2 infection is conjunctivitis. COVID-19 also predisposes to other manifestations and complications in the organ of vision, often very unusual or not suspected of viral etiology. Since patients infected with SARS-CoV-2 have a higher risk of thromboembolic complications, they may experience such far-reaching consequences as, for example, occlusion of a vein or central retinal artery. The paper presents cases of SARS-CoV-2 infection with ophthalmic symptoms.

Key words: COVID-19, SARS-CoV-2, ocular manifestations of SARS-CoV-2

INTRODUCTION

The COVID-19 pandemic has been an intrinsic element of our reality since December 2019. The spectrum of the disease is still partly a mystery to scientists and physicians. Widely available studies mainly report on respiratory, cardiovascular, or psychiatric disorders. However, a study conducted by the Polyclinical Hospital of the University of Messina also highlighted the high prevalence of mild ocular symptoms in patients with COVID-19 [1]. The following article reviews the ocular disorders caused by SARS-CoV-2 virus.

CONJUNCTIVITIS

Among the numerous scientific papers on the effects of coronavirus on the human body, there are reports of conjunctival diseases [2]. According to Sindhuja, conjunctivitis is the most common documented ocular symptom in COVID-19 patients, with redness of one or both eyes and conjunctival congestion being the most common symptoms reported by patients [3]. Chen, in a study involving 535 patients, provides the contact route (hand-eye) as the reason for infection [4]. Coronavirus patients with ocular symptoms mostly report them between 7 and 14 days after the onset of systemic symptoms. However, there are reports that present conjunctivitis as the first manifestation of COVID-19 infection. It is possible that the virus is present in the conjunctival sac before the onset of systemic symptoms [5]. Cases of COVID-19 manifestation as conjunctivitis are presented below. A 53-year-old patient, described by Guo et al, was admitted to Zhejiang University Hospital because of fever (up to 38°C) and increasing dyspnea (SARS-CoV-2 positive test result) that had persisted for 6 days. Ten days after the first symptoms, conjunctivitis of the left eye developed (main symptoms: eye discomfort and stabbing pain, no deterioration of visual acuity). The smear was positive from the left conjunctiva. The patient was treated with levofloxacin, and sodium hyaluronate solution 0.1% drops. The patient improved within 7 days, but relapsed within 5 days, this time in both eyes. Smears for SARS-CoV-2 from the conjunctiva of both eyes were negative; however, IL-6 levels were elevated 10-fold in the left eye. Suspecting autoimmune conjunctivitis and keratitis, fluorometholone 0.1% steroid drops were used with very good results [6].

A case of a 63-year-old man with severe COVID-19 infection was reported in France. He was admitted to the intensive care unit 2 days after the onset of flu-like symptoms. On day 17, the first ocular symptoms appeared in the form of conjunctival congestion and the presence of clear discharge. The eye smear was negative. The patient was moistened with saline solution, artificial tears were administered and eyelid hygiene was maintained. On day 19, the clinical symptoms worsened and new ones appeared in the form of vesicles, petechiae on the choroid conjunctiva and swelling of the conjunctiva – hemorrhagic and pseudomembranous conjunctivitis was diagnosed. The patient was given azithromycin (twice daily for 3 days), with low doses of dexamethasone drops. From day 21 to day 26, ocular symptoms regressed, with no corneal complications. A repeat test for COVID-19 from the conjunctiva was negative [7]. Based on previous studies, it is highly likely that SARS-CoV-2 has low conjunctival replication. At the same time, it is speculated that the virus infects the conjunctiva through still unidentified receptors [8].

CONJUNCTIVITIS IN CHILDREN

In Italy, a 30-fold increase in the incidence of an illness similar to Kawasaki disease in children has been reported – pediatric inflammatory multisystem syndrome associated with COVID-19 (PIMS). Ophthalmic manifestations in this syndrome mainly manifested as bilateral conjunctivitis. It is suspected to be a manifestation of a delayed immune response to COVID-19. Treatment consists of glucocorticosteroids, intravenous immunoglobulins (IVIG), biologics and, due to an increased risk of venous thromboembolism, acetylsalicylic acid (ASA) [9].

EPIDURAL INFLAMMATION

Otaif et al. described a case of epidural inflammation as the initial manifestation of COVID-19 in a 29-year-old man. The patient reported a history of redness and a foreign body sensation in his left eye that occurred 2 days before consultation. He had no symptoms in the other eye or any systemic symptoms. External examination of the left eye revealed conjunctivitis and epiphora. Three days after the onset of ocular symptoms, the patient developed a mild viral infection with flu-like symptoms. The PCR test was positive for COVID-19. The patient was admitted for observation and supportive therapy was started. After 5 days, his condition improved and he was discharged from the hospital with the recommendation of isolation at home for 14 days [10].

According to Mangana et al., most cases of epidural inflammation are idiopathic and self-limiting. Almost one-third of them may be associated with viral infections, including ebola, HSV (*Herpes simplex virus*) and hepatitis C, and now possibly SARS-CoV-2 virus [11].

CREEPING CHOROIDOPATHY

Creeping choroidopathy is a rare, usually bilateral, chronic inflammation of the choroid and retinal pigment epithelium of unknown etiology. The course is progressive with multiple recurrences, leading to potentially significant vi-

sion loss. A sudden, painless deterioration of central vision in one eye may be the first noticeable sign of the disease. In most cases, peripheral vision remains normal.

Choroidopathy reactivation after SARS-CoV-2 infection has been reported in a patient with a previously diagnosed episode of choroiditis. There are also unpublished cases of creeping and multifocal choroiditis in patients with a positive history of COVID-19. It is difficult to determine whether this is the onset of new inflammation or reactivation of previous inflammation. As a result of the observations made, autoimmunity activated by SARS-CoV-2 is thought to play a key role [12].

CENTRAL RETINAL VEIN OCCLUSION

COVID-19 infected are at higher risk of thromboembolic complications, especially with severe disease [13]. Besides, occasional hypoxia in patients with pneumonia (also as a result of SARS-CoV-2) can activate endothelial cells to release tissue factors, as well as the extrinsic pathway of the coagulation cascade [14].

Due to increased thromboembolic complications, central retinal vein occlusion (CRVO) and branch retinal vein occlusion (BRVO) are among the many vascular manifestations of COVID-19. Studies (fluorescein angiography [FA]) and optical coherence tomography [OCT]) have shown no differences between patients with CRVO without COVID-19 and those with CRVO and COVID-19. Treatment consists of local laser therapy and anti-VEGF injection. Thromboprophylaxis should be considered in patients with severe COVID-19 [14].

CENTRAL RETINAL ARTERY OCCLUSION

In situations of sudden vision loss, central retinal artery occlusion (CRAO) may be suspected. The cases of patients described in the articles highlight elevated inflammatory markers including IL-6, CRP, ferritin, fibrinogen, and D-dimers in the setting of severe coronavirus infection resulting in vascular occlusion [15, 16]. In the case presented by Dumitrascu, incomplete occlusion of the ocular artery occurred despite the use of enoxaparin due to deep vein thrombosis [16]. However, according to Sunny and Callie, most cases of CRAO in COVID-19 are due to the coincidence of the disease and other CRAO risk factors present in the patients described, such as hypertension, hyperlipidemia, coronary artery disease, and smoking, and further reports on this topic should be closely followed [17].

ACUTE ISOLATED DETERIORATION OF NEAR VISION

Umapathi et al. observed accompanying deterioration of near vision with accommodative impairment in patients with COVID-19 infection. The first patient, a 46-year-old man, noted that he had difficulty reading documents regarding his quarantine rules. He had no neurologic symptoms. The pupils were equal (3 mm) and responded well to light, but the pupillary response to an approaching object was impaired („reversed" Argyll-Robertson sign). The patient was treated with vision correction with satisfactory improvement. The second patient described was a 40-year-old man who developed anisocoria and problems with near vision on day 6. The diameter of the right pupil was 2.5 mm and the left pupil was 2 mm. Several days later, the left pupil changed its shape, described as „eccentric" with positive Argyll-Robertson sign. There were no neurological symptoms. The patient was treated with +1.00 D vision correction with satisfactory results. On Day 18, ophthalmologic examination showed no change. Further observation of the patient was recommended [18].

CONCLUSIONS

In SARS-CoV-2 infections, attention should be paid to ocular symptoms, which may be a manifestation of the infection. Patients most commonly report complaints such as burning eyes, foreign body sensation, tearing, photophobia, and conjunctival swelling. These symptoms, although appearing mild, can lead to serious complications or make it difficult to link them to COVID-19 infection. The long-term effects of SARS-CoV-2 infection and their impact on the eye are still the subject of much research and debate.

CORRESPONDENCE
Ada Pandey
31-510 Kraków, ul. Rakowicka 20B/36
phone: 531 53 15 68
e-mail: adapandey.ap@gmail.com

ORCID
Ada Pandey – ID – http://orcid.org/0000-0001-9467-1005
Justyna Gugnowska – ID – http://orcid.org/0000-0002-2649-3531
Angelika Kruszyńska – ID – http://orcid.org/0000-0003-3567-9079
Kinga Czarnacka – ID – http://orcid.org/0000-0002-6889-6507
Małgorzata Gawlak – ID – http://orcid.org/0000-0003-4573-1379
Maciej Kozak – ID – http://orcid.org/0000-0001-7993-2588
Ilona Pawlicka – ID – http://orcid.org/0000-0003-1556-7678
Katarzyna Sajak-Hydzik – ID – http://orcid.org/0000-0002-1973-2717

References

1. Meduri A, Oliverio GW, Mancuso G et al. Ocular surface manifestation of COVID-19 and tear film analysis. Sci Rep. 2020; 10: 1-7.
2. Amesty M, Alio del Barrio J, Alio J. COVID-19 Disease and Ophthalmology: An Update. Ophthalmol Ther. 2020; 9: 415-26.
3. Sindhuja K, Lomi N, Asif MI et al. Clinical profile and prevalence of conjunctivitis in mild COVID-19 patients in a tertiary care COVID-19 hospital: A retrospective cross-sectional study. Indian J Ophthalmol. 2020; 68: 1546-50.
4. Chen L, Deng C, Chen X et al. Ocular manifestations and clinical characteristics of 535 cases of COVID-19 in Wuhan, China: A cross--sectional study. Acta Ophthalmol. 2020; 98: 951-9.
5. Nayak B, Poddar C, Panigrahi MK et al. Late manifestation of follicular conjunctivitis in ventilated patient following COVID-19 positive severe pneumonia. Indian J Ophthalmol. 2020; 68: 1675-7.
6. Guo D, Xia J, Wang Y et al. Relapsing viral keratoconjunctivitis in COVID-19: a case report. Virology Journal. 2020; 17: 1-7.
7. Navel V, Chiambaretta F, Dutheil F. Haemorrhagic conjunctivitis with pseudomembranous related to SARS-CoV-2. Am J Ophthalmol Case Rep. 2020; 19: 100735.
8. Bertoli F, Veritti D, Danese C et al. Ocular Findings in COVID-19 Patients: A Review of Direct Manifestations and Indirect Effects on the Eye. J Ophthalmol. 2020; 2020: 4827304.
9. Danthuluri V, Grant M. Update and recommendations for ocular manifestations of COVID-19 in adults and children: A narrative review. Ophthalmol Ther. 2020; 9: 853-75.
10. Otaif W, Al Somali AI, Al Habash A. Episcleritis as a possible presenting sign of the novel coronavirus disease: A case report? Am J Ophthalmol Case Rep. 2020; 20: 100917.
11. Mangana C, Kargacin A, Barraquer R. Episcleritis as an ocular manifestation in a patient with COVID-19. Acta Ophthalmol. 2020; 98: 1056-7.
12. Providência J, Fonseca C, Henriques F et al. Serpiginous choroiditis presenting after SARS-CoV-2 infection: A new immunological trigger? Eur J Ophthalmol. 2020; 1120672120977817.
13. Tarmey T, Cullen G, Patel T et al. Thromboembolic Disease in COVID-19. J Clin Imaging Sci. 2021; 11(16): 1-5.
14. Invernizzi A, Pellegrini M, Messenio D et al. Impending central retinal vein occlusion in a patient with coronavirus disease 2019 (COVID-19). Ocul Immunol Inflamm. 2020; 28: 1290-2.
15. Acharya S, Diamond M, Anwar S et al. Unique case of central retinal artery occlusion secondary to COVID-19 disease. IDCases. 2020; 21: e00867.
16. Dumitrascu O, Volod O, Bose S et al. Acute ophthalmic artery occlusion in a COVID-19 patient on apixaban. J Stroke Cerebrovasc Dis. 2020; 29(8): 104982.
17. Sunny C, Callie K. Prevalence of SARS-CoV-2 among central retinal artery occlusion patients: A case series-HORA study report No. 3. J Acute Dis. 2021; 10(4): 147-9.
18. Umapathi T, Li K, Chin C et al. Acute Isolated Near Vision Difficulty in Patients With COVID-19 Infection. J Neuroophthalmol. 2021; 41(3): 279-82.

Authors' contributions:
All authors have equal contribution to the paper.

Conflict of interest:
None.

Financial support:
None.

Ethics:
The content presented in the article complies with the principles of the Helsinki Declaration, EU directives and harmonized requirements for biomedical journals.