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Case Report

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Simultaneous Encephalitis and Neuroretinitis After COVID-19 in a Young Adult: A Case Report

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Abstract

Coronavirus disease 2019 (COVID-19) pandemic greatly impacted many aspects of life in the world. Both neurological and ophthalmologic presentations after COVID-19 have been reported. Herein, we present a case of both neuroretinitis and encephalitis after COVID-19 in a young adult. Both presentations are among the rare presentations of COVID-19. Similar manifestations were not reported previously. The 18-year-old previously healthy girl initially presented with low-grade fever, nausea, vomiting, body pain, and headache. The patient tested positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by reverse transcriptase-polymerase chain reaction (PCR) by using a nasal swab. Two days after the onset of COVID-19 symptoms, she reported blurred vision in both eyes, progressing to only light perception in 3 days. Based on the ophthalmological evaluation, she was diagnosed with neuroretinitis. A few days later, she gradually became drowsy, so she was referred for neurological evaluation. Brain magnetic resonance imaging (MRI) showed bilateral medial temporal T2 and fluid-attenuated inversion recovery (FLAIR) hyper-signal lesions suggestive of encephalitis. A low-dose steroid was started to treat the neuroretinitis. After about 2 weeks, significant improvement in visual acuity and resolution of retinitis patches were observed. Our case is rare in respect of both neurological and ophthalmic involvement.

Keywords: Neuroretinitis; Encephalitis; COVID-19; SARS-CoV-2

Introduction

Coronavirus disease 2019 (COVID-19) pandemic continues to grow all over the world. There is increasing evidence of neurological manifestations in patients with COVID-19. Besides direct invasion of the virus to the central nervous system (CNS), coronavirus neurotropism was suggested to cause these manifestations [1-5].

In the other aspect, eye involvement in COVID-19 has been reported in several studies. Ocular symptoms are commonly present in patients with severe COVID-19 pneumonia; and it was shown that isolation of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) from the conjunctival sac was feasible in these patients. One of the most common presentations was conjunctivitis [6]. Other ophthalmologic presentations such as retinitis and choroiditis are rare [7, 8].

Herein, we present a case of neuroretinitis and encephalitis post-COVID-19 diagnosis in a young adult. Both presentations are among the rare presentations of COVID-19. The ethical board of Shiraz University of medical sciences approved this study (Approval No: IR.sums.med.rec.1400.144).

Case Report

An 18-year-old previously healthy girl initially presented with low-grade fever, nausea, vomiting, body pain, and headache. The patient tested positive for SARS-CoV-2 by reverse transcriptase-polymerase chain reaction (PCR) using a nasal swab.

Two days after the onset of the COVID-19 symptoms, the patient reported blurred vision, which was progressed to light perception in 3 days in both eyes. The patient was referred to an ophthalmologist. Ophthalmology examination revealed poorly reacting pupils and a positive Marcus gunn (2+) in the left side. Funduscopic examination showed multiple bilateral white-yellowish placoid lesions located at the posterior pole and the mid-peripheral retina. The other findings were papillitis, peripapillary retinal hemorrhage, and edema, especially in the inner retinal layer, and macular edema. All findings were prominent in the left eye. There was no evidence of vitritis, uveitis, peripheral retinal change, or retinal vascular abnormality. In optical coherence tomography (OCT), we observed choroidal folds with an irregular overlying retinal pigment epithelium (RPE) and hyper-reflective spots in the choroid layer. Accordingly, she was diagnosed with neuroretinitis.

For evaluation of neuroretinitis, laboratory examinations including the complete blood cell (CBC) count and examinations for liver, thyroid, renal function, and serum vitamin B12 levels were performed, which showed normal findings. All serology tests for different infections like cat-scratch disease,

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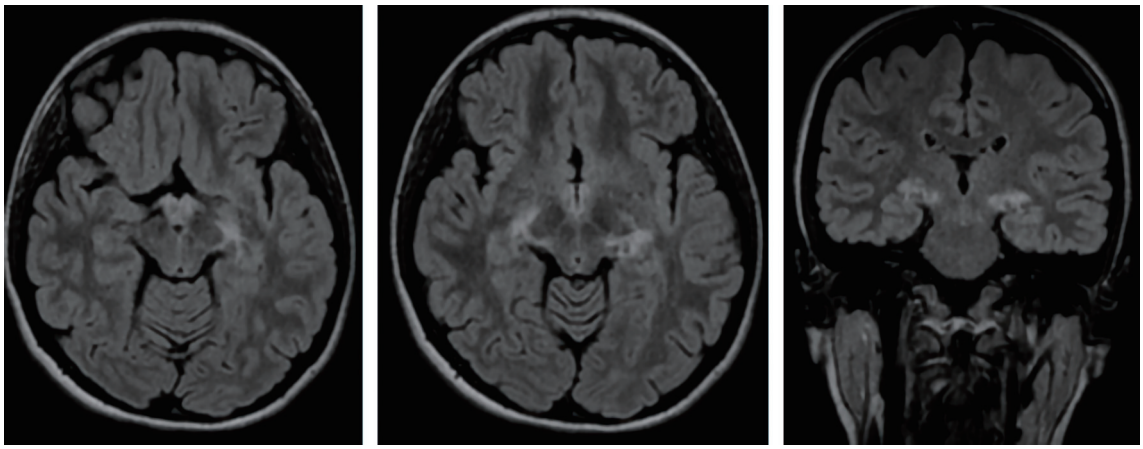

Figure 1. Axial and coronal views of brain MRI show FLAIR increased signal intensity in the cortical and subcortical regions of both mesial temporal lobe and both side hippocampal tails with a relatively symmetrical appearance. MRI: magnetic resonance imaging; FLAIR: fluid-attenuated inversion recovery.

toxoplasmosis, syphilis, Lyme disease, brucellosis, human immunodeficiency virus (HIV), varicella zoster virus (VZV), herpes simplex virus (HSV), cytomegalovirus (CMV), Epstein-Barr virus (EBV), and hepatitis B and C were negative. Angiotensin-converting enzyme (ACE) levels for sarcoidosis and purified protein derivative (PPD) tests were negative. She was also checked for a probable undetected autoimmune disease which was not conclusive (erythrocyte sedimentation rate (ESR), antinuclear antibodies (ANA), double-stranded DNA, C3, and C4). CBC and other biochemistry tests were normal. Therefore, we ruled out systemic autoimmune and infectious processes that could present similar clinical features in this case.

A few days later, she gradually became drowsy; however, clinical seizures, decreased level of consciousness, or behavioral changes were not reported. Due to progressive drowsiness, she was referred to a neurologist for a better neurological evaluation. In neurological examination, she did not have a neurological deficit except for mild drowsiness and minimal delay in mental processing. Brain magnetic resonance imaging (MRI) was performed, which showed evidence of T2 and fluid-attenuated inversion recovery (FLAIR) increased signal intensity in the cortical and subcortical regions of both mesial temporal lobe as well as both side hippocampal tails, with relative symmetrical appearance without evidence of significant enhancement or restricted diffusion in diffusion-weighted imaging (DWI) compatible with viral or autoimmune encephalitis (Fig. 1). Therefore, SARS-CoV-2-associated encephalitis was suggested. The patient and her family disagreed with further investigations and lumbar puncture.

To evaluate COVID-19 involvement of the lung, a high-resolution CT (HRCT) of the chest was performed, which was normal.

Her past medical, drug consumption, and personal histories did not show any significant point.

Drowsiness was recovered in 10 days without treatment, and a low-dose steroid was started for 2 weeks to treat the neuroretinitis. After treatment, significant improvement in visual acuity and resolution of retinitis patches were observed.

Discussion

The present study reported a patient who developed neuroretinitis and encephalitis a few days after being diagnosed with SARS-CoV-2 infection. COVID-19 has a range of clinical presentations from asymptomatic infection to severe respiratory failure and death [5]. Neuro-ophthalmic manifestations are among the less common features. In addition, neurotropism of the virus has been shown. Recently, the viral infection of CNS by SARS-CoV-2 was confirmed by detecting the virus in brain tissues and capillary endothelial cells at autopsy [1].

The virus can penetrate CNS via trigeminal (signal changes seen in the brainstem and thalamus) and olfactory (increased FLAIR signal in the medial temporal lobe) nerve endings [9, 10]. The other possible route of entry may increase the permeability of the blood-brain barrier (BBB) due to high pro-inflammatory cytokines in the cerebrospinal fluid (CSF) during infection [11]. Thus, encephalitis and meningoencephalitis following COVID-19 may be caused by the entrance of the virus via these routes of invasion, which has been reported in several case reports [5, 12].

In COVID-19, involvement of both the brain and ophthalmic tissues is rare. One possible explanation may be the role of the ACE2 receptor, a functional receptor for SARS-CoV-2. ACE2 receptor has a high expression in the conjunctiva and endothelium of the brain vessels like lung mucosa and gastrointestinal duct [13]. Thus, the virus can enter the cells via these receptors.

On the other hand, ophthalmologic presentations after COVID-19 are less frequent than neurological presentations. Among ophthalmologic manifestations, conjunctivitis is the most common presentation [6].

From the beginning of the pandemic, direct or indirect contamination of the conjunctival epithelium with infectious droplets was suggested as a possible route of transmission of COVID-19 [14]. The ocular surface can serve as a reservoir for SARS-CoV-2. The eye can be contaminated with SARS-CoV-2 by hand-eye contact and aerosols, and then the virus

Table 1. Clinical Presentations of Retinal Involvement After COVID-19

No.	Author	Age/sex of the patient	Clinical presentations	Diagnosis	Outcome
1	Hosseini et al, 2021 [24]	37/M	Bilateral severe vision loss	Bilateral retinitis and panuveitis	Significant improvement after treatment
2	Goyal et al, 2021 [25]	32/M	Bilateral paracentral and triangular negative scotoma	Acute macular neuroretinopathy (AMN) and paracentral acute middle maculopathy (PAMM)	No change in vision
3	Liu et al, 2021 [23]	Elderly/F	Monocular blindness	Retinitis and optic neuritis	N/A
4	Mahendradas et al, 2021 [26]	49/F	Sudden-onset painless loss of vision in both the eyes	Bilateral post fever retinitis with retinal vascular occlusions	Improvement in vision after treatment
5	Our patient	18/F	Bilateral severe vision loss	Bilateral neuroretinitis	Significant improvement after treatment

Similar presentation (bilateral involvement) was seen in three cases; in most of these patients significant improvement was seen after treatment (similar as our patient). COVID-19: coronavirus disease 2019; M: male; F: female; N/A: not applicable.

can transfer to other systems through the nasolacrimal route and hematogenous metastasis [15]. Eye involvement after other types of coronavirus infection has been evaluated several times. For example, in animal models, anterior uveitis, choroiditis, vasculitis, and retinitis were reported in other types of coronavirus infection [16]. However, in SARS-CoV-2, these types of involvements are not frequent [6].

Ophthalmic tissue involvement and visual impairment in SARS-CoV-2-infected patients might be associated with several underlying pathophysiologies, including infection of lacrimal glands (dacryoadenitis), conjunctivitis choroiditis, tonic pupils, vitritis, central retinal artery/vein occlusion (CRAO/CRVO), retinitis, retinal bleeding (in some reports bilateral retinal hemorrhages), panuveitis, anterior ischemic optic neuropathy (AION), optic neuritis, optic perineuritis, optic nerve stroke, or occipital ischemic stroke. Interestingly, it was shown that visual impairment could be the initial manifestation of COVID-19 [17-21].

Sim et al [22] reported retinal microvascular changes on ocular imaging of the patients with COVID-19, even in asymptomatic patients. They suggested that these retinal microvascular signs could be related to underlying cardiovascular and thrombotic alternations related to COVID-19.

Overall, retinal involvement after COVID-19 was reported only in few case reports (Table 1) [23-26]. Liu et al reported acute viral retinitis in patients with COVID-19 and severe acute monocular blindness [23].

Hosseini et al reported bilateral neuroretinitis and panuveitis in a 37-year-old male patient with a history of recovered COVID-19. This patient had similarities with our patient regarding bilateral involvement; however, encephalitis was not reported in this case [24].

Moreover, optic neuritis has been reported in COVID-19 patients and may occur with or without affection of other cranial nerves [27, 28].

Burgos-Blasco et al [29] reported that SARS-CoV-2 might affect the optic nerve and cause changes in the retinal layers even at the stage in which the infection has resolved. As such, in patients with COVID-19 and decreased vision, before diagnosing SARS-CoV-2-associated optic nerve involvement, other differentials need to be excluded [28]. It has been reported that SARS-CoV-2 may cause endothelial damage, thrombus formation, and thromboembolism; accordingly, ophthalmologic vascular complications such as AION, CRAO and CRVO [30-36]. Therefore, they should be considered in the differential diagnoses list in the cases of vision loss after SARS-CoV-2 infection [28].

Despite these ophthalmic and neurological presentation reports, the coincidence of neurological presentations and ophthalmic presentations after COVID-19 is rare [37].

Other neurological manifestations such as headache and ocular and periocular pain have been described in cases with ophthalmic presentations [38]. However, it should be considered that headache is a prevalent clinical presentation in COVID-19 and may be seen in several patients [9]. In some case reports, third nerve palsy and sixth nerve palsy with peripheral neuropathy suggestive of Miller Fisher syndrome were reported with COVID-19 [39]. However, the coincidence of encephalitis and neuroretinitis after COVID-19 is very rare.

This rare coincidence (encephalitis and neuroretinitis) was reported in the other viral infections too. There are reports of similar presentation in the patients infected with HSV [40], VZV [41], Japanese encephalitis (JE) virus [42], pseudorabies virus [43], and Rift Valley fever virus (RVFV) [44].

Interestingly, during the COVID-19 pandemic, besides reports of neuroretinitis after SARS-CoV-2, there were also reports of reactivation of acute retinal necrosis due to HSV after COVID-19 in few cases [45, 46].

In our patient, the eye might have been contaminated with SARS-CoV-2 through hand-eye contact and aerosols and then transferred to the CNS through the nasolacrimal route [15]. Involvement of both medial temporal lobes may show this transmission via the olfactory nerve. Ocular involvement may occur in the mid-phase of COVID-19 illness. Viral SARS-CoV-2 ribonucleic acid (RNA) was detected in conjunctival swabs of the patients even without ocular manifestations, after resolution of conjunctivitis, and even after nasopharyngeal swabs turned negative, and in the retina of deceased COVID-19 patients [38].

Lacks of CSF evaluation and PCR from the vitreous sam-

ple were the most important limitations in this study, excluding other possible etiology in this patient.

In the aspect of MRI findings related to encephalitis after COVID-19, several patterns of MRI were reported. Temporal lobe encephalitis (which was seen in our patient) was among the most common MRI presentations in these patients. As mentioned before, this finding may relate to the route of entry of the virus in these patients [47].

In conclusion, the ocular surface remains a potential transmission route for the virus to other people and other organs, such as the brain of the patients themselves [39]. Therefore, we recommend that all health care providers get familiarized with SARS- CoV-2 infection complications, particularly neurological involvement in the presence of acute ophthalmologic presentations with or without systemic symptoms [38].

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None to declare.

Conflict of Interest

The authors declare that they have no relevant conflict of interest to report.

Informed Consent

Informed consent was obtained from the patient.

Author Contributions

All authors have contributed to data collection, data analysis and writing of the manuscript.

Data Availability

The authors declare that data supporting the findings of this study are available within the article.

Abbreviations

PCR: polymerase chain reaction; MRI: magnetic resonance imaging; COVID-19: coronavirus disease 2019; CNS: central nervous system; OCT: optical coherence tomography; RPE: retinal pigment epithelium; CBC: complete blood cell; ACE: angiotensin-converting enzyme; ESR: erythrocyte sedimentation rate; ANA: antinuclear antibodies; DWI: diffusion-weighted imaging; CRAO: central retinal artery occlusion; CRVO: central retinal veins occlusion; AION: anterior ischemic optic neuropathy; HIV: human immunodeficiency virus; CMV: cytomegalovirus; EBV: Epstein-Barr virus; PPD: purified protein derivative; JE: Japanese encephalitis; RVFV: Rift Valley fever virus

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