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Neurological Complications of COVID-19: A Rare Case of Bilateral Blindness

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Abstract—Background: There are growing reports of the neurological involvement among patients with coronavirus disease 2019 (COVID-19). Headache, confusion, and anosmia after olfactory nerve disruption are the most prevalent presentation of the neurological involvement related to COVID-19. However, small numbers of the central nervous system involvement have been reported. Case Report: A 49-year-old man was referred to our hospital with abrupt vision loss. Three weeks earlier he was admitted to the hospital based on his respiratory symptoms and was diagnosed with COVID-19 infection. Initial brain magnetic resonance imaging indicated diffuse restricted bilateral foci in both parietal and occipital lobes in favor of acute infarction. Diffuse weighted imaging demonstrated restricted bilateral hyperintense signals in parietal and occipital region. Occipital cortex biopsy showed brain tissue with focal infiltration of foamy macrophages mixed with reactive astrocytes and no plasma cell infiltration. Considering all of the evidence, post–COVID-19 encephalitis diagnosis was considered for the patient, and methyl prednisolone pulse therapy and intravenous immunoglobulin were initiated. Why Should an Emergency Physician Be Aware of This?: Although there are growing reports of neurological involvement among patients, blindness is rarely observed as a complication of post–COVID-19 encephalitis. To our knowledge, this is the first case of post–COVID-19 encephalitis that presented with bilateral vision loss primarily. This case may raise physicians’ awareness of neurological complications of COVID-19.

Keywords—COVID-19; SARS-CoV-2; encephalitis; blindness; neurology

Introduction

During the current pandemic, novel severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection has led to a surge in respiratory tract infection in the world. However, there are growing reports of the neurological involvement among patients (1). Headache, confusion, and anosmia after olfactory nerve disruption are the most prevalent presentation of the neurological involvement related to coronavirus disease 2019 (COVID-19). However, infinitesimal numbers of the central nervous system (CNS) involvement have been detected recently (2).

Despite the importance of neurological manifestations, data about the neurological involvement of SARS-CoV-2 infection are scarce (3). We report a rare case of post–COVID-19 encephalitis presenting with bilateral blindness in a male patient.

Case Report

A 49-year-old man was referred to our hospital with abrupt complete vision loss in his right eye and visual
impairment in the left eye. Three weeks earlier, he was admitted to the hospital based on his respiratory symptoms and was diagnosed with COVID-19 infection (confirmed with polymerase chain reaction [PCR] test). Four days after he was discharged, he noticed a sudden vision loss in his right eye and a mild visual impairment in his left eye. In addition, he reported moderate headache. His medical history was significant for diabetes controlled by pioglitazone (30 mg twice daily) and gliclazide (80 mg daily).

In the physical and neurological examination, he was afibrile, awake, oriented, and speech was normal. Both pupils were symmetric and mid-sized on the first day of admission. The right pupil was nonreactive and the left pupil was reactive. Visual acuity on the first day was measured as 0/10 for the right eye (no light perception) and 5/10 for the left one. The fundoscopy of the both eyes were normal. In addition, all of the cranial nerves, sensory, motor, deep tendon, plantar reflex and cerebellar examinations, and mental status examination were normal.

Spiral chest computed tomography (CT) scan indicated ground-glass, patchy infiltrations in sub-pleural area, which were attributed to the former COVID-19 infection. Both abdominopelvic ultrasound and CT scan were normal, and no abnormalities were detected in temporal artery biopsy and ultrasound. Also, no evidence of mucormycosis infection was observed in paranasal sinus CT scan. Brain magnetic resonance imaging (MRI) indicated diffuse restricted bilateral foci in both parietal and occipital lobes in favor of acute infarction. Diffuse weighted imaging demonstrated restricted bilateral hyperintense signals in parietal and occipital region (Figure 1). Cervical spine MRI was also normal.

Laboratory tests revealed normal complete blood count and biochemical tests. Moreover, interferon-gamma release assay, anti-MOG and anti-NMDA receptor antibodies, vasculitis tests, viral infection tests, and current SARS-CoV-2 PCR were reported as negative. Lumbar puncture was performed and the results showed negative anti–herpes simplex virus 1 and 2, varicella zoster IgM antibodies, and SARS-CoV-2 PCR in the cerebrospinal fluid (CSF). According to the initial findings, antiplatelet therapy (aspirin) was initiated for the patient.

Two days after admission, visual acuity of the left eye deteriorated into complete vision loss, similar to the right eye (no light perception).

According to the deteriorating state of the patient, cerebral angiography was done in order to rule out reversible cerebral vasoconstriction syndrome and other cerebral vessels involvements. In spite of normal cerebral angiography findings, nimodipine was administered for the patient (10 mL infused in 10 min). In addition, based on cardiology consult, bridging anti-anticoagulant therapy (heparin and then warfarin) was initiated because of a moderate to large patent foramen oval.

Occipital cortex biopsy showed brain tissue with focal infiltration of foamy macrophages mixed with reactive astrocytes and no plasma cell infiltration (Figure 1). No evidence of vasculitis or granuloma were detected. The immunohistochemistry study demonstrated positivity of CD68 and scattered CD3+ cells.

Brain MRI after deterioration revealed extension of infarct lesions to the left cerebellar hemisphere, bilateral frontoparietal lobes, splenium of corpus callosum, and anterior aspect of the pons.

Considering all of the evidence, post–COVID-19 encephalitis diagnosis was considered for the patient. In accordance with infectious disease consult, our patient underwent methyl prednisolone pulse therapy (1 g/d) for 3 days, and then prednisolone (1 mg/kg/d) as a maintenance therapy was initiated. Later, the patient was confused with right hemiparesis. Therefore, intravenous immunoglobulin (IVIg) (25 g/d for 5 days) was initiated for the patient, which resulted in the improvement of both mental state and clinical symptoms. The patient was then discharged; however, both eyes remained blind (no light perception). Right lower-extremity muscle force was recorded as 1/5, and others were observed as 4/5. Patient was advised to use prednisolone (60 mg/kg) and warfarin (5mg/d).

After 3 months of clinical follow-up, the patient was still blind (no light perception) without pupillary light reflex. Muscle forces returned to normal; nevertheless, a wide-based gait was still observed (which was not reliable due to blindness). MRI also showed no new lesions. Prednisolone was tapered (10 mg/d) and patient received warfarin (international normalized ratio 2.2).

**Discussion**

We described a rare case of post–COVID-19 encephalitis, which led to bilateral blindness 3 weeks after COVID-19 infection. To our knowledge, this is the first case of post–COVID-19 encephalitis that presented with bilateral vision loss primarily.

It should also be maintained that retrobulbar optic neuritis may be another differential diagnosis justifying the patient’s blindness. However, MRI evaluation did not reveal any abnormalities in the optic nerve, but it cannot be ruled out. Atypical optic neuritis has also been reported as a rare complication after COVID-19 (4).

The possible mechanisms of neurological sequelae attributed to COVID-19 infection could be either direct invasion of the virus from nasopharyngeal route or increasing inflammatory factors due to the severe infection, which can decrease the function of blood-brain barrier (5,6). These theories can be classified into two groups,
para-infection encephalitis and post-infection encephali-
tis (7). In our patient, PCR of SARS-CoV-2 in the CSF was negative and COVID-19 symptoms had improved 3 weeks earlier. However, according to previous studies, negative SARS-CoV-2 PCR of the CSF cannot rule out direct invasion of the virus to the brain (8). Curiously, the manifestation of encephalitis 3 weeks after COVID-19 in-
fection might highlight the pivotal role of inflammatory factors after the infection rather than direct invasion of the

Discovering the exact mechanism of encephalitis could help to recognize the best management for these patients. In previous reports, corticosteroid has been suggested as an appropriate treatment for post-infection immune-
mediated encephalitis through reducing the level of inflam-
matory factors, and there are some reports of COVID-
19 patients with encephalitis whose clinical course improved after administration of corticosteroid (3,9). Fur-
thermore, IVIg has been reported as a safe and effective choice for COVID-19–associated encephalopathy (10). In

Figure 1. Brain magnetic resonance imaging (MRI) performed on the first day of admission. (A) T2-weighted, (B) fluid-attenuated inversion recovery (FLAIR), (C) diffusion-weighted imaging, (D) apparent diffusion coefficient: diffuse restricted bilateral foci are observed in both parietal and occipital lobes (green arrows) in favor of acute infarction. Brain MRI performed after deterioration (E, F) T2-weighted, (G, H) FLAIR, (I, J) T1-weighted, (K, L) T1-weighted post-contrast: extension of infarct lesions to the left cerebellar hemisphere, bilateral frontoparietal lobes, splenium of corpus callosum and anterior aspect of the pons (hypersignal area in T1 sequence is attributable to brain biopsy). Brain biopsy of the lesions (M, N, O, P): brain biopsy of occipital lesion revealed astrogliosis with slight edema, mild perivascular lymphocytic infiltration, and foamy macrophages infiltration.
our case, however, it is unclear whether receiving steroid pulse therapy led to improvement or IVIg was the effective treatment. More studies are required in order to define best treatment options for patients with post-COVID-19 encephalitis.

Why Should an Emergency Physician Be Aware of This?

Although there are growing reports of neurological involvement among patients, blindness can be observed rarely as a complication of post–COVID-19 encephalitis. To our knowledge, this is the first case of post–COVID-19 encephalitis that presented with bilateral vision loss primarily. This case should raise physicians’ awareness of neurological complications of COVID-19.

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