Balance disorders and vertigo as a complication of COVID-19

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Summary COVID-19 is a disease caused by a new type of SARS virus. COVID-19 clinical symptoms are primarily related to the respiratory system but may also be involved in many others, including the nervous system. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) can be an aetiological factor responsible for balance disorders. Symptoms such as vertigo may coexist with other symptoms or be an isolated manifestation of the disease. Among other balance dysfunctions associated with COVID-19 are BBPV (benign paroxysmal positional vertigo), vestibular neuritis, acute labyrinthitis, acute cerebellitis, as well as Ménière's disease. MRI, Videonystagmographic (VNG) and the Dix-Hallpike test are used to make a diagnosis. Improvements were observed after treatment with oral corticosteroids and vestibular physiotherapy along with intratympanic injection of dexamethasone. Antiemetics, antihistamines, anticholinergics and benzodiazepines drugs may be helpful in relieving symptoms. In addition, drugs used in scheduled treatment of COVID-19, such as azithromycin and hydroxychloroquine, may cause balance disorders due to their potential side effects. The following article presents cases of COVID-positive patients with balance disorders. The aim of this article was to raise awareness that nonspecific symptoms such as balance disorders may be the only manifestation of COVID-19, which is important due to early diagnosis and administration of treatment.

Data sources: PubMed, Web of Science, Thieme MedOne, Otolaryngology, Embase, UpToDate, Scopus, Access Medicine.

Review methods: A systematic review of literature was performed according to 2020 PRISMA guidelines.

Key words: dizziness, vertigo, labyrinthitis, Ménière disease, nystagmus, pathologic.

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Background

In February 2020, the World Health Organization (WHO) named the coronavirus disease COVID-19 [1]. COVID-19 caused by the SARS-CoV-2 virus was first reported in December 2019 in Wuhan, China. Most patients affected by the infection are asymptomatic [2]. The most common symptoms include dry cough, fever, muscle ache and general weakness. Some patients develop taste and smell disorders, as well as gastrointestinal and neurological disorders [3], and in some cases, this can progress to pneumonia, acute respiratory distress syndrome and multiorgan dysfunction [2]. New variants of the virus are emerging, so new potential signs of infection should be observed. The cases and analyses present in literature point to a possible aetiology of SARS-CoV-2 virus in balance disorders.

The results of some studies suggest that vertigo/dizziness should be included among the main symptoms of COVID-19 [2]. The aim of this review article was to gather information on the probable role of the virus in the pathogenesis of balance disorders.

Balance disorders due to COVID-19 infections

The balance disorders caused by SARS-CoV-2 may manifest as, benign paroxysmal positional vertigo, dizziness vestibular neuritis, acute labyrinthitis, acute cerebellitis [3-6] COVID-19 infection may be accompanied by the development of Ménière's disease [2, 7].

COVID-19 infection may present as isolated balance disorders [8]. Dizziness or vertigo may be the only symptom of the disease though may also be a complication of the disease [3, 9, 10]. Simultaneously, it may be accompanied by hearing loss, tinnitus or headache [2, 8, 11].

SARS-CoV-2 virus can cause degeneration of the otolith membrane of the lamina propria and disruption of otolith movement in the semi-circular canals leading to BBPV (benign paroxysmal positional vertigo) [2, 12].

It is possible for the virus to infect the cochlear branch of the vestibulocochlear nerve leading to the labyrinthitis, which can in turn lead to a combination of vertigo and unilateral hearing loss [2].

There is a possible connection between COVID-19 infection and the pathogenesis of Ménière's disease, where inflammation can result in the production of autoantibodies against the endolymphatic sac [2].

Neuroinflammatory processes induced by SARS-CoV-2 can lead to brainstem dysfunction and vestibular dysfunction. Some patients who had COVID-19 infections developed acute vestibular neuritis, and the main symptoms were dizziness, nausea and vomiting. Vascular damage and ischemia of inner ear structures can lead to balance disorders [13]. The virus can be found in oral swabs, nasopharyngeal swabs, as well as in CSF [4, 14, 15]. The probable harmful effects of drugs found in scheduled of treatment COVID-19, such as azithromycin and hydroxychloroquine, should be taken into consideration [9].

Discussion

Viral infections are a known cause of balance disorders. Herpes simplex virus (HSV), cytomegalovirus, Epstein-Barr virus, adenovirus, varicella zoster virus (VZV) and HIV are among the known viruses that can cause this condition [2, 8].

There are several theories to explain the mechanism of balance disorders due to SARS-CoV-2 infection. Results show that the viral protein "spike" binds to ACE2 receptors and is processed by serine protease type II (TMPRSS2), which is necessary for the fusion of the viral cell membrane and the host cell membrane [16]. Recent studies have demonstrated the presence of the ACE2 receptor in the brainstem [13]. The virus binds to the receptors: ACE2, basigin (BSG) or neuropilin-1 (NRP-1) on brain microvascular endothelial cells and enters the brain via transcytosis [16]. It has been shown that the virus can bind to haemoglobin and enter erythrocytes, causing deoxygenation of erythrocytes and resulting in hypoxia and further damage to the inner ear [13].

An interesting theory states that the virus infects monocytes, leukocytes and granulocytes and, together with them, crosses the blood-brain barrier, entering the brainstem and vestibular system, called the Trojan Horse mechanism [16, 17]. It is possible to invade the olfactory epithelium, where the virus enters the CNS through olfactory sensory neurons [16].

Cases reported in literature and studies suggest the role of SARS-CoV-2 in balance disorders. In a large study led by Alde et al. [2], patients were evaluated based on the criteria: adults, confirmed SARS-CoV-2 infection and mild to moderate disease severity. They abstracted 1,512 patients, and 30 of them reported vertigo, with females having a higher prevalence of vertigo.

In another study, Viola et al. [8] also noted that out of 185 COVID(+) patients, 32 reported dizziness, and 2 reported an acute attack of vertigo.

Mao et al. [1] analysed a total of 216 patients and revealed that apart from respiratory and general symptoms, 36.4% of patients with COVID-19 had neurological symptom and was first to note that 16.8% with CNS symptoms reported dizziness.

Malayala and Raza [18] described a 29-year-old female patient who presented to hospital due to severe vertigo, nausea and vomiting with generalised fatigue without any additional symptoms that could suggest COVID-19 infection. They suspected vestibular neuritis. After CT scan and the change in lungs, a COVID-19 PCR test was performed, which came back positive. Symptomatic treatment, such as antiemetics, antihistamines, anticholinergics and benzodiazepines, was introduced along with vestibular physiotherapy and intravenous corticosteroids. This case may suggest possible COVID-19-induced acute vestibular neuritis.

Perret et al. [5] described the case of an 84-year-old patient with symptoms of vertigo, vestibular nystagmus and acute vomiting and hearing loss. Brain magnetic resonance imaging showed no lesion of neurovascular origin. Vestibule, right semicircular canals and cochlear FLAIR hypersignals were shown, leading to the diagnosis of right labyrinthitis. A nasopharyngeal swab confirmed SARS-CoV-2 infection. It is possible that COVID-19 infection led to labyrinthitis. Oral corticotherapy and physiotherapy rehabilitation was suggested for treatment, along with intratympanic injection of dexamethasone, which resulted in some patients improving in health.

In a study by Fadakar et al. [4], the SARS-COV-2 RNA virus was detected in the CSF fluid of a 47-year-old male, and after

neurological examination and MRI imaging, cerebellar dysfunction was revealed, which manifested as vertigo, ataxia and headache. Vertigo was not accompanied by nausea, vomiting, tinnitus or hearing loss, nor any loss of taste and smell. Improvement was noted after 14 days of treatment with lopinavir and ritonavir [16].

Kong et al. [19] described a patient who presented with sudden dizziness for 3 days who did not report any other symptoms. Interestingly, there were no changes in the CT scan of the lungs on the day of admission but only the next day. It was decided to perform a SARS-CoV-2 PCR test, which came back positive. The patient was treated with antiviral oseltamivir and moxifloxacin, and the symptoms resolved, which may suggest the effectiveness of this treatment.

The next cases described by Maslovar and Košec [3] were patients who, one month after COVID-19 infection, began to have symptoms of circular dizziness when they got out of bed or turned their head to the right side. After referral to an otolaryngologist, they were diagnosed with BBPV after a positive Dix-Hallpike test. After applying the Epley manoeuvre, the symptoms resolved. Interestingly, patients during COVID-19 infection did not report typical symptoms of infection such as sudden loss of taste and smell, fever, cough and shortness of breath.

As regards treatment, antiemetics, antihistamines and sedatives drugs may be helpful in the symptomatic treatment of vertigo in COVID-19 patients [3].

The clinical study described by Pazdro-Zastawny et al. [20] presented 58 patients between 23 to 75 years of age with vertigo 6 months after COVID-19. The patients were subjected to an examination consisting of anamnesis, otorhinolaryngological evaluation and Videonystagmography (VNG). VNG showed spontaneous nystagmus with closed eyes in 8 patients (13.8%), positional nystagmus was observed in 15 patients (24.1%), and asymmetrical optokinetic nystagmus was observed in 18 patients (31%). This study showed that COVID-19 infection can affect long-term complications in balances.

The above cases strongly suggest the probable role of SARS-CoV-2 virus in the pathogenesis of balance disorders and vertigo; however, there is a need for studies providing evidence to confirm this association.

Physicians in various specialties, especially otolaryngologists, should pay attention to unusual symptoms such as vertigo, as these may be the only symptoms of SARS-CoV-2 infection. There is a need for screening and otoneurological assessment in order to recognise balance disorders and introduce effective treatment.

Conclusions

Balance disorders and vertigo may be the only manifestation of COVID-19 infection. The most important causes of these symptoms in the course of COVID-19 include vestibular nerve inflammation and cerebellitis. Balance disorders and vertigo require multidisciplinary diagnostics, even for infectious diseases such as COVID-19.

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