A case series of vestibular symptoms in positive or suspected COVID-19 patients

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SUMMARY

Respiratory symptoms are the most common presentation of an acute COVID-19 infection, but thromboembolic phenomena, encephalopathy and other neurological symptoms have been reported.
With these case series, we present multiple presentations of COVID-19 induced vestibular symptoms namely dizziness, vertigo and nystagmus. The patients reported in this case series are from different parts of the world, belong to different age groups and had manifested these symptoms in different periods of the pandemic.

The pathophysiology of vestibular neuritis induced by COVID-19 is similar to any other viral infection. Whether in the inpatient or outpatient settings, COVID-19 should be considered in the differential diagnosis for patients presenting with these symptoms, irrespective of the presence of respiratory symptoms or hypoxia.

Keywords: COVID-19, vestibular neuritis, vertigo, dizziness.

INTRODUCTION

The Covid-19 pandemic outbreak still remains a major global challenge for physicians and patients. The spectrum of the disease and organ involvement is still not fully known and evolving. The symptoms vary between asymptomatic to severe multiorgan complications [1].
Vestibular neuritis is an inner ear disorder associated with symptoms such as sudden, severe vertigo, dizziness, balance problems, nausea and vomiting. It is a result of 8th cranial nerve disorder following a viral infection leading to inflammatory changes of the nerve [2]. It is a benign condition and usually self-limiting but the recovery time can vary from days to months. Diagnosis is usually based on symptomatology seldom requiring imaging to be supported with exclusion of other similar disorders [3].
The accumulating evidence from Wuhan published case series confirmed 8% of COVID-19 patients reported dizziness. Another study from Wuhan reports 16.8% confirmed cases of COVID-19 causing vestibular symptoms [2, 4]. Though the mechanism by which COVID-19 causes vestibular neuritis is unclear, it could be due to its effect on individual cranial nerves similar to its pathogenesis in causing anosmia, optic neuritis or a result of vasculitis or vasculopathy.
We compiled a case series of six patients who had distinct symptoms of different severities diagnosed eventually with vestibular neuritis. Some of the neurological manifestations that have already been identified are delirium, anosmia, headache, corticospinal tract signs, dizziness, stroke, encephalopathy, encephalitis but as described in our case series vestibular neuritis can also be their initial presentation [5-7]. The participant in case 2 was admitted and treated by the

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primary author in Delaware, United States. The participant in case 4 is an American female but on an extended trip to Europe (country was kept anonymous per her request). Rest of the participants are from Iran, Brazil, Canada and Switzerland and they volunteered to discuss their clinical presentation through a telephone interview.

Case 1

A 31-year-old Persian female, resident of Iran presented with runny nose, sweating, fever and lethargy. She did not report shortness of breath, loss of taste or loss of smell. She had a known exposure to a COVID-19 contact. Diagnosis of COVID-19 infection was confirmed with PCR of nasal swab. She received symptomatic treatment and was advised home quarantine.

About thirteen days after the initial infection, she developed dizziness and vertigo that worsened on any head movement and would get better on lying still. The symptoms were associated with lack of appetite and fatigue. She denied earache, tinnitus, hearing loss or unsteady gait. She denied any other history of similar illness, recent upper respiratory tract infection or recent trauma.

She seeked medical attention due to worsening symptoms. On examination her vital signs were within normal limits, systemic examination and neurological examination by her physician did not reveal any abnormalities. Audiometric examination and Magnetic Resonance Imaging (MRI) scan of the brain did not reveal any underlying pathology. A diagnosis of COVID-19 induced vestibular neuritis was made after excluding other diagnoses. She was prescribed dimenhydrinate but her symptoms still persisted despite conservative measures. Subsequently she was given 60 mg prednisone that was tapered over the next ten days. With this therapy, her symptoms improved and gradually resolved over the next six weeks.

Case 2

A 29-year-old Hispanic female residing in Delaware, USA, presented to the emergency room in April 2020 with sudden onset of severe vertigo, nausea and vomiting two days prior to arrival. She was working at a chicken plant in the local rural community, which had a huge cluster of COVID-19 infections. She denied tinnitus, hearing loss or unsteady gait. She described the vertigo at rest and it worsened with any type of movement. She described it as "persistent" vertigo in every position, though she was not able to explain the direction in which movement made it worse.

She seemed to be in severe distress from her nausea, non-bilious non bloody vomiting, and severe vertigo. Nystagmus, positioning maneuvers like Dix Hallpike, gait could not be attempted because of her distress. The cranial nerve exam did not show defects.

Her urine toxicology and rest of the laboratory parameters were completely within normal limits. Computed Tomography (CT) scan of the head showed no acute pathology. A CT chest/abdomen and pelvis without contrast showed multifocal, bilateral, peripheral, ill-defined, ground-glass opacifications, features consistent with acute COVID-19 pneumonia. Acute cerebrovascular attack was also considered a differential but the MRI of the brain did not show any acute findings.

She was admitted to the hospital with acute vestibular neuritis as the admission diagnosis and she was offered symptomatic management with anti-emetics and meclizine as needed. When she was found to be positive for COVID-19 infection through a nasal Polymerase Chain Reaction (PCR), she was started on oral hydroxychloroquine and azithromycin (which was the standard of treatment for acute COVID-19 infection). The acute phase reactants, coagulation parameters and other inflammatory markers were within normal limits.

With no improvement in the symptoms, she was subsequently treated with intravenous steroids. She also required vestibular rehabilitation from physical and occupational therapy while she remained inpatient. The symptoms were quite persistent and refractory to this treatment and it took almost a week for her to recover and become asymptomatic. She was eventually discharged home after a prolonged eight-day stay in the hospital.

Case 3

A 63-year-old Caucasian female with a known medical history of aplastic anemia, mitral valve prolapse with regurgitation, celiac disease, and motion sickness, presented with a runny nose and would feel out of breath with activity. She did not report fever, chills, cough, wheezing or chest pain. Given the past history of aplastic anemia, she took over-the-counter iron pills for shortness

of breath with no improvement. She is a resident of the United States but in Europe on a trip when the symptoms developed. The symptoms developed in March 2020 when there were no reported COVID-19 cases.

Due to lack of improvement despite a few days of symptomatic management, the PCR on nasal swab for the SARS-CoV-2 test was performed in an ambulatory setting. It was positive for COVID-19 and she was advised home quarantine.

About four weeks after the initial episode, she developed twitching of her left eye and left cheek, non-bloody diarrhea, generalized weakness, palpitations, sleep disturbances, decreased appetite, skin rash, anosmia, and dysgeusia. The twitching was involuntary, initially involving the left eye which then progressed to the left side of the face. No pain, loss of sensation or numbness were reported. There were 8 to 10 painful, red skin lesions around 3 mm in size over perioral area. She was clinically diagnosed with herpes labialis. She also developed purple discoloration at the base of her fingers and whitish discoloration at her fingertips with temperature changes. She continued conservative management with ample hydration, antipyretics, and over-the-counter aspirin, multivitamins, and calcium supplements. She gradually had some clinical improvement over a 4-week period. She was tested for COVID-19 every week until she was negative on the 58th day.

A week post being tested negative for COVID-19, she suddenly developed chills and vomiting. She woke up in the middle of the night with dizziness, a sense of the room spinning and an unsteady gait. She did not have tinnitus or hearing loss.

She immediately sought medical attention and the physical examination showed a strong nystagmus to the right. Dix-Hallpike maneuver was performed, and she was confirmed to have vertigo and was diagnosed with post-viral vestibular neuritis. She was treated initially with meclizine, antiemetics, and Cawthorne vestibular rehabilitation exercises. Due to lack of symptomatic improvement she was subsequently given 60 mg prednisone with a gradual taper over the next 10 days. On the 10th day of prednisone, the patient noticed a sudden onset of flashes and floaters in the left eye. A slit-lamp examination diagnosed Posterior Vitreous Detachment (PVD) of the left eye. PVD was attributed to an increase in intraocular pressure with the use of steroids. There was a slight improvement in her vision post cessation of steroids.

Several weeks later, she developed a high-grade fever, pain and swelling of her joints and a non-itchy erythematous rash all over her chest and abdomen eight hours following the intake of 2 g amoxicillin/clavulanic acid for a dental procedure. Tmax was 102F, not associated with chills and rigors. She did not report lymphadenopathy or pedal edema. Symptoms self-resolved after 48hrs. Five months after her positive COVID-19 test, she was tested for COVID-19 immunoglobulin G (IgG) antibodies and was found to be negative.

Case 4

A previously healthy 35-year-old Canadian female presented to the hospital with a 4-day history of dizziness, lightheadedness and loss of balance describing it as a "drunk like feeling". She works as a television producer and reportedly worked with people on a cruise ship during the COVID-19 outbreak in March 2020. She started noticing the symptoms a week after that. Her symptoms were aggravated with caffeine intake and staring at laptop screens and alleviated by lying down. These symptoms were associated with fatigue, nausea, crackling sound like perception with loud voices in the right ear. She denied fever, headache, vomiting, diarrhea and earache. No abnormalities in facial sensations were reported.

She sought medical attention due to worsening of symptoms. On examination her vitals were within normal limits, systemic examination and neurological examination did not reveal any abnormalities. No abnormalities were revealed on routine blood tests. However, she was never tested for COVID-19 infection as she did not meet the "testing criteria" around that time, as she was not hospitalized. She was treated with betahistine and vestibular therapy but her symptoms persisted even after that for a while. Her symptoms gradually improved over the next 10 weeks. She was tested for COVID-19 antibodies (IgG and IgM) in September which turned out to be negative.

Case 5

A 71-year-old Brazilian female with a history of obesity developed sudden onset lightheadedness, a sense of loss of balance between May 24th 2020 and May 31st 2020. The severity of symptoms had

progressively worsened and the episodes would last her about 15 to 20 minutes. She also developed nausea and could perceive a white noise resembling sound. On 1st June she was evaluated by her primary care physician who advised admission to the hospital for further testing. On June 2nd 2020 she tested negative for COVID-19 via nasal PCR. She was kept admitted over the next 4 days for monitoring of symptoms. A repeat nasal PCR swab was obtained on June 4th 2020 which was resulted 2 days later as being positive for COVID-19. She did not have any further episodes during her hospital stay and was discharged on the day of the positive test result to quarantine at home. About 6 days post hospital discharge, the patient redeveloped the symptoms of nausea, vomiting, "buzzing noise" sensation and dizziness and had intermittent episodes of it over a duration of a month.

Case 6

A 57-year-old female residing in Switzerland had an exposure to COVID-19 at her workplace. 5-day post exposure she had tested negative to COVID-19 via nasal PCR. 7 days post exposure she developed sudden onset dizziness. The episodes were intermittent and recurred. She also developed accompanying nystagmus 3 days later. During the course of her illness as her symptoms progressively worsened in intensity, she also developed nausea and non-bloody non bilious vomiting.

She was evaluated by an Ear, Nose and Throat (ENT) physician and was diagnosed with vestibular neuritis. She was prescribed meclizine, ondansetron, and diazepam. Due to minimal improvement of symptoms her physician prescribed her a five-day course of steroid which brought about symptomatic relief.

DISCUSSION

These cases confirm the diagnosis of vestibular neuritis by excluding other possible differential diagnoses. Our cases had either known or suspected exposure to or confirmation of COVID-19. They lacked other neurologic signs and symptoms (dysarthria, dysphagia, weakness, sensory loss, or facial droop). There were no abnormalities in imaging studies thus excluding the possibility of an acute vascular event in the central nervous system [8]. Lack of abnormalities in blood tests and negative inflammatory markers excluded other differential diagnoses [9]. The history, presenting clinical signs and symptoms, exposure to or confirmation of Covid-19 confirmed the presumptive diagnosis of vestibular neuritis secondary to COVID-19.

An antigen test on an upper respiratory specimen obtained by nasopharyngeal or oropharyngeal swab is preferred for initial diagnostic testing. Nucleic Acid Amplification Tests (NAAT) such as RT-PCR that detect Viral Ribonucleic Acid (RNA) are considered as the gold standard test at present [10]. There are several factors that can lead to a false negative RT-PCR result in a COVID-19 infected patient. Multiple regions of the viral genome should be targeted to avoid target region and primer mismatches. Precision in sample collection affects the obtained sample. The exposure time to the virus and the viral load in the patient are also pertinent factors [11-13]. Antibody tests should not be utilized in diagnosing an acute COVID-19 infection as antibody development may take upto 2 weeks [14-18]. Total antibody testing could be more sensitive than IgM or IgG alone for early detection [14].

The severity of COVID-19 disease symptoms is attributed to the marked inflammatory response following the virus entry into the host cell. The effects of SARS-CoV-2 on the neuronal tissue could be due to a direct infection of the central nervous system or related to a vascular damage caused by vasculitis or vasculopathy, similarly to the mechanism described for Varicella Zoster Virus (VZV) and Human Immunodeficiency Virus (HIV). The other members of the coronavirus family have a history of invading the neurological system resulting in optic neuritis, encephalitis, encephalomyelitis [19, 20]. The invasion of SARS-COV2 within CNS is through binding to the Angiotensin Converting Enzyme (ACE) receptors once the viruses have gained entry into the CNS, they appear advancing by axonal transport [20]. Evidence about the virus shows that COVID-19 can affect the central nervous system resulting in neurological symptoms similar to other members in the coronavirus family [21]. The neurological symptoms of COVID-19 vary from dizziness, headache, and impaired consciousness to severe symptoms like encephalopathy, encephalomyelitis, ischemic stroke and intracerebral hemorrhage, anosmia, dysgeusia and neuromuscular diseases.

COVID-19 infection is also known to induce a hypercoagulable state that could also lead to a vascular compromise to the neuronal tissue [22]. Hearing alterations and balance disorders can be dependent on vascular damage because the inner ear structures are particularly susceptible to ischemia due to their characteristics of terminal vasculature and high-energy requirement. Despite the growing amount of scientific literature on COVID-19, studies that correlate audio vestibular symptoms to SARS-CoV-2 infection are still limited and further investigation is necessary for a better estimate of their incidence.

The treatment of vestibular neuritis includes symptomatic management with anticholinergic, anti-emetics, and antihistamines to reduce the severity of symptoms. Vitamin D and its potential role in improving outcomes in COVID-19 and respiratory viral illnesses has been postulated in literature [23]. Vestibular rehabilitation is proven to be efficacious to an extent. Corticosteroids are used in severe cases.

In our case series the symptoms of patients persisted for a few weeks in spite of conservative treatment. Some patients responded well to vestibular rehabilitation while in others early initiation of steroids was useful in alleviating the symptoms along with continuing conservative symptomatic treatment.

CONCLUSION

Once we published our case report on COVID-19 induced vestibular neuritis [5], multiple people from all around the globe reached out to us describing their symptoms and clinical presentations. The COVID-19 induced vestibular symptoms seem to be more common than once thought [24]. Though broader cross sectional and population based studies are required to further study these presentations, we noticed that COVID-19 induced vestibular neuritis seems to be common in otherwise healthy females and the symptoms are resolved with corticosteroids.

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