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Acute Vestibular Disorders Related to SARS-CoV-2 Infection: Literature Review and Case Series

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Abstract

Objectives: Coronavirus Disease (COVID-19) may be characterized by neurological symptoms among which the most common are alterations of smell and taste. Vestibular disorders have been reported, but instrumental audiovestibular evaluations have been seldom performed.

Methods: A structured search of the English literature published on PubMed was conducted. A description of consecutive cases presented at our tertiary referral center for audiovestibular disease is reported.

Results: Only 6 cases of vestibular neuritis simultaneous to COVID-19 instrumentally diagnosed have been reported to date. Moreover we presented two cases of patients with mild COVID-19 who had vestibular neuritis at the beginning of infection and in the subacute phase.

Conclusion: Further studies are needed in order to better characterize epidemiology, pathophysiology and prognosis of vestibular disorders related to SARS-CoV-2 infection.

Keywords: SARS-CoV-2; COVID-19; Audiovestibular disorders; Vertigo; Dizziness; Audiovestibular evaluation; Instrumental evaluations

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Introduction

The Coronavirus Disease (COVID-19) pandemic still represents a major global challenge for both physicians and patients. The spectrum of symptoms and organ involvements - in the acute, subacute phase and in post-COVID-19 syndrome - are still evolving and not fully known. Infected patients may be asymptomatic or they may present mild to severe multi-organ complications [1]. Among neurological manifestations of COVID-19 infection, an altered sense of smell or taste was early recognized as one of the most characteristic symptoms. Data from a multicenter European study reported olfactory and gustatory dysfunction among 85.6% and 88.0% of patients, respectively [2]. Recently, there has been a growing evidence of otoneurological symptoms such as tinnitus, hearing loss and balance disorders [3]. Several authors, however, remarked on the need of studies with follow-up assessments using standard objective tests [4].

Herein we reviewed the international literature of COVID-19-related vestibular disorders including only detailed cases with clinical confirmed diagnosis. Additionally, we reported two cases of objective vertigo with nausea and vomiting, experienced during COVID-19 infection and in post-COVID-19 period, referred to our hospital.

Methods

A structured search of the English literature published on PubMed, from December 01st, 2019 to January 22nd, 2022, was performed by searching the terms "vestibular neuritis" and "COVID-19". Only inherent reports with SARS-CoV-2-positive patients, as confirmed by molecular nasopharyngeal swab and with detailed clinical and diagnostic data were considered. Survey-based studies and papers clearly not related to the object were excluded.

A description of two consecutive cases of COVID-19-induced vestibular impairment evaluated at the Audiology and Phoniatrics Unit of Treviso Hospital between January 01st, 2021 and January 22nd, 2022 is reported. The study was conducted in accordance with the principles of the Helsinki Declaration. Patients gave their written consent for clinical case publication. Data were examined

in accordance with Italian privacy and sensitive data laws, and the in-house regulations of our Institution.

Results

Literature review

The review process is shown in Figure 1. After applying the above mentioned criteria, 15 papers were retrieved and 6 were included: 1 retrospective [5] study and 5 case reports [6-10].

Four patients were excluded from the article by Malayala et al. [6] due to repetition of previously published cases [7], and to the presence of unconfirmed cases of SARS-CoV-2 infection. We found 5 case reports which overall described 6 patients who were given the diagnosis of VN related to COVID-19. Five patients were female and one patient was a young male (age ranging from 13 to 63). They all were given the diagnosis of mild or moderate COVID-19 according to the international guidelines [1]. Table 1 summarizes characteristics of included patients.

All the patients experienced typical symptoms of VN: Rotatory vertigo and unsteady gait with associated nausea and vomit. Diagnosis was obtained through physical examination, instrumental tests and exclusion of other possible disorders (Table 2).

In three cases [6,8,9] the VN symptoms emerged at onset of COVID-19. In the other three patients the vestibular symptoms occurred after 13 days of COVID-19 [6], after 32 days [10] and after 2 months [7] from the beginning of infection. Notably two cases described by Vanaparthy et al. [7] and Aasfara et al. [10] also presented unilateral facial palsy. All patients were treated with corticosteroids and/or vestibular rehabilitation. In the cases who performed a follow-up [6,8-10], a resolution of symptoms was noticed after one month.

Case report 1

A 31-year-old woman referred to our department. According to her history, in August 2020 she complained of cough, fever, rhinitis, headache, fatigue, muscular pain, and loss of smell and taste. The patient underwent nasopharyngeal swab and tested positive for SARS-CoV-2 infection, as confirmed with Real-Time PCR test. After three days since symptoms onset, she had sudden objective 24-h-lasting vertigo, with nausea and vomiting. She did not have any associated cochlear symptoms (e.g., tinnitus, hearing loss or ear fullness) or central nervous system symptoms (e.g., diplopia or loss of consciousness). According to her general practitioner's advice, she took symptom-relief medications and rested. During the following days her vertigo and dizziness progressively improved. One month later, she tested negative for SARS-CoV-2 infection (PCR test on repeated nasopharyngeal swab). During the following months she complained of recurrent episodes of dizziness, therefore she underwent clinical evaluations in our department. At physical examination no relevant clinical signs were present: No postural sway, external auditory canals and tympanic membranes were normal, spontaneous nystagmus was absent, and bed-side examination (Rose position, Dix-Hallpike and Pagnini-McClure maneuvers) were negative. Bithermal caloric test was performed at 50°C for warm air and 24°C for cold air, 60 sec of stimulation per year under direct visualization of tympanic membrane. It showed a left side hyporeflexia (40% left hypofunction with 15% right side directional preponderance). Dizziness handicap inventory resulted in 30/100 (mild handicap). All other instrumental tests were negative: ocular motility tests were normal, pure-tone audiometry and ABR revealed bilateral normal hearing, and Distorted Product Otoacoustic Emissions (DPOAE) were present.

The patient had not suffered from any pre-existent audiovestibular disorder before infection. According to the symptoms described during SARS-CoV-2 infection and reported findings, a diagnosis of COVID-19-related Vestibular Neuritis (VN) in compensatory phase at the moment of our evaluation was hypothesized, therefore vestibular rehabilitation exercises were prescribed. One month later, on a telephone follow-up interview, the patient stated that her dizziness episodes had resolved.

Case report 2

A 44-year-old man was evaluated at our unit complaining of sudden onset, 4 h before, of objective rotatory vertigo, nausea and vomiting. No headache, diplopia, paresthesia, loss of consciousness were reported. No subjective hearing changes and/or tinnitus were

Table 1: Clinical characteristics of the patients from literature review on vestibular disorders and COVID-19, including the present cases report.

1st Author (year)	Sex, age	Comorbidity and any AV past history	COVID-19 symptoms	COVID-19 classification	COVID-19 duration	Days from COVID-19 positivity to AV symptoms	AV Symptoms	Other relevant symptoms
Mat [8]	F, 13	NR	NR	Mild Illness	NR	0	Rotatory vertigo, vomiting	NR
Vanaparthy [7]	F, 63	Aplastic anemia, mitral valve prolapse, celiac disease. Motion sickness	GS, facial spasm, anosmia, disgeusia, skin rash, raynaud's phenomenon	Mild Illness	2 months	65	Rotatory vertigo, vomiting, unsteady gait	Facial palsy, anosmia and dysgeusia.
Malayala [6]	F, 31	NR	GS	Mild Illness	NR	13	Rotatory vertigo, unsteady gait	NR
Case 1								
Malayala [6]	F, 29	NR	NR	Moderate Illness	NR	0	Rotatory vertigo, vomiting	NR
Case 2								
Giannantoni [8]	M, 13	NR	Fatigue	Mild Illness	NR	0	Rotatory vertigo, vomiting, unsteady gait	NR
Aasfara [10]	F, 36	Pregnancy (37 weeks)	NR	Mild Illness	NR	42	Rotatory vertigo, vomiting, right ear hipoacusia	Facial palsy
Present case 1	F, 31	None	GS anosmia, dysgeusia	Mild Illness	1 month	2	Rotatory vertigo, vomiting, unsteady gait	Anosmia and dysgeusia
Present case 2	M, 44	None	Anosmia and dysgeusia	Mild Illness	9 days	32	Rotatory vertigo, vomiting, unsteady gait	Anosmia and dysgeusia

AV: Audiovestibular; COVID-19: Coronavirus Disease-19; F: Female; GS: General Symptoms Including Cough, Fever, Rhinitis, Headache, Fatigue, Muscular Pain; NR: Not Reported

Table 2: Evaluation, diagnosis treatment and outcome of the patients from literature review on vestibular disorders and COVID-19, including the present cases report.

1st Author (year)	Evaluation	Vestibular signs	Diagnosis	Pharmacological therapy	Vestibular rehabilitation	Follow-up and outcome
Mat [8]	VNG; vHIT; ENT and neurological evaluation; audiometry	Right spontaneous Ny; left deviation (Fukuda test)	Left COVID-19-induced vestibular neuritis	NR	Yes	1 month, symptom resolution
Vanaparthy [7]	VNG, ENT and neurological evaluation	Right spontaneous Ny	Left COVID-19-induced vestibular neuritis	60mg oral prednisone, 10 days tapered	Yes	NR
Malayala [6]	MRI brain; ENT and neurological evaluation; audiometry	NR	COVID-19-induced vestibular neuritis	60mg oral prednisone, 10 days tapered	NR	1 month, symptom resolution
Case 1						
Malayala [6]	CT chest; CT cerebral; MRI brain; ENT and neurological evaluation; audiometry	NR	COVID-19-induced vestibular neuritis	Intravenous steroids (DNS)	Yes	NR
Case 2						
Giannantonio [9]	MRI brain; ENT evaluation; audiometry	Right spontaneous Ny, positive HIT	Left COVID-19-induced vestibular neuritis	20mg intravenous prednisone, 10 days tapered	NR	1 month, symptom resolution
Aasfara [10]	MRI brain, VNG with Caloric test, ENT evaluation, audiometry, electromyography, lumbar puncture	Left spontaneous Ny, Hyporeflexia	Right COVID-19-induced cochlear-vestibulopathy and facial palsy	Intravenous steroids (DNS)	Yes	1 month, symptom resolution
Present case 1	VNG with Caloric test, ENT evaluation, audiometry	Hyporeflexia	Left COVID-19-induced vestibular neuritis	NA	Yes	1 month, symptom resolution
Present case 2	VNG with Caloric test, ENT evaluation, brain CT, audiometry	Left spontaneous Ny, positive HIT	Right COVID-19-induced vestibular neuritis	50mg oral prednisone, 10 days tapered	Yes	1 month, symptom resolution

COVID-19: Coronavirus Disease 19; CT: Computed Tomography; DNS: Drug Not Specified; ENT: Ear Nose and Throat; HIT: Head Impulse Test; MRI: Magnetic Resonance Imaging; NA: Not Applicable; NR: Not Reported; Ny: Nystagmus; vHIT: video Head Impulse Test; VNG: Videonystagmography

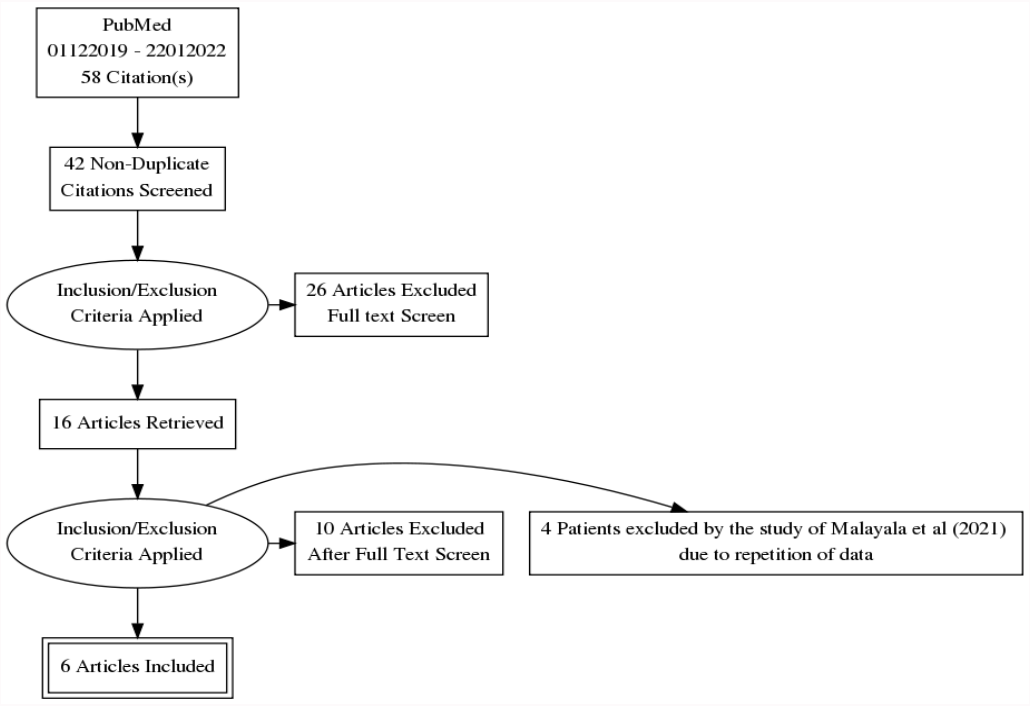

Figure 1: Flow-chart of literature research, from identification to inclusion of articles and patients.

reported. At physical examination, external auditory canals and tympanic membranes were bilaterally normal, Romberg's and Unterberger's tests showed a slightly right-side postural sway. Head impulse test was right-positive, a third-grade left beating spontaneous nystagmus was present, and Dix-Hallpike maneuver was negative. A neurologic examination showed no abnormalities, a CT scan of the brain was negative for acute ischemic-hemorrhagic events; blood tests were within normal limits.

The patient had not suffered from any audiovestibular disorder previously. Recent medical history was relevant for mild COVID-19 disease one month before. The infection that was confirmed by a positive PCR nasopharyngeal swab for SARS-CoV-2 lasted 2 weeks and was characterized by anosmia and dysgeusia.

A right side VN of probable viral origin was then diagnosed. At discharge a counseling, including reassurance on benignity of symptoms, was performed, oral steroid therapy was prescribed (50

mg prednisolone daily for 5 days and subsequent tapering of the drug for 5 days) followed by vestibular rehabilitation exercises after therapy.

A follow-up appointment was set for one month after. At the second evaluation, the patient denied any rotatory vertigo. Romberg's and Unterberger's tests were normal, spontaneous and positional nystagmuses were absent. Bithermal caloric test was performed, as previously described, and the exams showed right side hyporeflexia (29% right hypofunction with 21% left side directional preponderance). Ocular motility was within normal limits, pure tone-audiometry, tympanometry DPOAE and ABR revealed normal hearing functions, dizziness handicap inventory resulted in 6/100 (no handicap).

Discussion

VN is an inflammatory inner ear disorder that involves the vestibular portion of the 8th cranial nerve [11]. Current findings about etiology mainly support the role of viruses (first infection and viral reactivation) and dysregulated immunological responses. VN is usually a benign and self-limiting condition, but in some cases can lead to residual imbalance. Diagnosis is typically based on clinical history and symptoms, ear nose and throat evaluation including vestibular test, videonystagmography with caloric test, and audiometry [12]. Application of the HINTS protocol (Head Impulse, Nystagmus, test of Skew) in the emergency room is essential to rule out a cerebellar stroke, with a sensitivity of 96.7% and a specificity of 94.8% [13]. The presence of unidirectional nystagmus, a positive head impulse test in the opposite side than the fast phase of nystagmus and the absence of vertical eye misalignment and other neurologic symptoms can be highly diagnosed of acute peripheral vestibulopathy [14]. In doubtful cases, a neurological evaluation - eventually including neuro-radiological images - is required in order to exclude any central causes of vertigo. In recent years, a growing interest was put in cervical and ocular Vestibular Evoked Myogenic Potentials (cVEMPS and oVEMPS) and in the video Head Impulse Test (vHIT) as useful tools for the diagnostic work-up of VN. In particular vHIT, by analyzing the distribution of semicircular canals involvement, allows identification of selective vestibular structures alterations [12]. Definition of the site of vestibular damage and distinction between upper and/or lower branch of vestibular nerve involvement may correlate with the underlying cause of acute peripheral vestibular deficit, but does not change the initial treatment. The management of VN typically includes symptomatic relief medications, such as antiemetic drugs. Corticosteroids are prescribed with the aim of reducing vestibular inflammation. Vestibular rehabilitation has the role of enhancing the mechanism of central balance compensation that usually occurs within 2 to 8 months [15].

The incidence of vestibular disorders in COVID-19 patients is still unknown and varies across different studies. Data based upon an Italian multicenter study questionnaire administration [16] showed that 18.4% of patients reported equilibrium disorders after COVID-19 diagnosis (dizziness in 94.1% and acute vertigo episodes in 5.9%). A recent investigation about possible residual vestibular impairment in 48 recovered patients found dizziness in 8.3% of subjects, spinning vertigo in 2%, dynamic and static imbalance in 2% and 6.3% respectively [4]. These symptoms were mostly transitory and there was no evidence of clinically relevant persistent vestibular damage. Preliminary meta-analysis showed a pooled prevalence of 7.2% for rotatory vertigo, but the authors reported a possible overestimation because it was not always clear whether the included studies report a new onset vertigo or change in preexisting symptom [3].

The retrospective study by Charpiot et al. [5] is a quantification of the number of hospital admissions for Acute Peripheral Vestibulopathy (APV) in 5 French Hospitals over the period February-May 2020 [3]. A comparison with 2018 and 2019 showed no significant increase in admission for APV, no significant difference among hospitals located in COVID-19 high- and low-risk zones and no significant increase in the severity of the APV cases [3]. In accordance, a retrospective review of acute cochleo-vestibular disorders after and before pandemic conducted at our department found no significant changes regarding incidence of APV.

Our review retrieved only 5 case reports, in which overall 6 different patients with COVID-19 related acute vestibular impairment were included. Moreover we reported clinical and instrumental findings of two cases of vestibular impairment possibly associated with SARS-CoV-2 infection. Other main differential diagnoses of acute peripheral vestibulopathy have to be considered. A first episode of Ménière's disease [17] or vestibular migraine attack18 could have occurred [18,19]. Nevertheless, the literature review we have presented may support our clinical hypothesis. According to our review, in three cases VN was present at the onset of COVID-19 [6,8,9]. The mechanism by which SARS-CoV-2 can cause VN is unclear and speculative. Given its neurotrophic potential, a direct effect on the cochleo-vestibular nerve can be postulated, similarly to its pathogenesis in hypo/anosmia and optic neuritis. In this respect, the cellular receptor Angiotensin-Converting Enzyme 2 (*ACE2*), that mediates the intracellular entry of SARS-CoV-2, has been found in nasal tissues in murine and human model and in Eustachian tube, middle ear and cochlear tissues in murine model [20]. A relationship with vasculitis or vasculopathy has also been suggested [6]. Another possibility is that the physical and emotional stress that people with SARS-CoV-2 infection experienced could have played a role in the expression of vestibular symptoms - as occurred for headache patients [21] - or could have triggered the reactivation of possible latent viruses (e.g., HSV-1) [22]. This latter mechanism could be hypothesized especially in patients in which VN was not present at COVID-19 symptoms onset but later during the course of the disease [6,7,10]. Our second case, as well as the cases of Vanaparthy et al. [7], due to the temporal delay between PCR negativity and onset of vertigo, suggests the possibility of VN occurrence in the subacute phase of infection. To date, the post-COVID-19 syndrome is characterized by neurological symptoms such as headache, anxiety/depression, sleep and cognitive disturbances [23]. Finally, a SARS-CoV-2 neuro-invasive disease, leading to a COVID-19-related meningoencephalitis, may be implicated, as described for audiovestibular impairment in other neurotrophic viruses [24]. The latter situation does not certainly regard our patients, as oculomotor testing was accurate and ruled out any functional change in the central vestibular pathways.

The data we found in literature could be underestimated because many patients may not have undergone medical evaluation [25]. Therefore, many diagnoses of possible COVID-19-related VNs may have been missed and only disclosed in later assessments, as occurred in our first described case. In general, a decrease in the number of vertigo/dizziness outpatients during the pandemic outbreak has been observed, due to visit cancellations and government restrictive measures [26]. Therefore, to give support to patients in diagnosis and therapy, the role of telemedicine was enhanced and a specific guideline of virtual management of vestibular disorders was recently published

[27]. Preliminary data have shown the role and utility, during the pandemic, of telemedicine in the management of dizziness patients [28], but further studies are necessary to better define possibilities and limits of these methods.

Conclusion

According to the present review, only a few cases of instrumentally diagnosed COVID-19-related VN have been reported so far. Since hearing and balance disorders are rarely reported among patients with COVID-19, it would be appropriate to routinely test for SARS-CoV-2 infection patients with diagnosed VN. Moreover, prospective studies on a large series of COVID-19 patients should try to better define the epidemiology of cochlear-vestibular involvement and elucidate the SARS-CoV-2-related prognosis on peripheral and central audiovestibular functions. Among patients that can't be easily visited due to quarantine regimen, a telemedicine evaluation could be helpful, as performed in accordance with standards of recent guidelines. In cases with cochlear-vestibular involvement, a long-term follow-up of more than 6 months should be preferred.

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