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ENT symptoms in acute COVID-19: a narrative review

Sintomi ORL durante la fase acuta della COVID-19: una revisione narrativa

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SUMMARY

Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is characterised by a wide spectrum of disease severity ranging from asymptomatic or oligosymptomatic cases to severe and life-threatening forms. As this new coronavirus is a respiratory virus, it is not surprising that many symptoms caused by SARS-CoV-2 infection are related to the involvement of the upper respiratory tract. In addition the most pathognomonic of symptoms, i.e. the alteration of smell, nasal obstruction, sore throat and cough have been consistently described as early symptoms of the disease. However, for other ENT symptoms, such as oral lesions and audio-vestibular changes, a causal relation is far from proven. The rapid and extensive spread of COVID-19 makes it difficult to demonstrate a causative link between several ENT symptoms and SARS-CoV-2 infection and it is reasonable to assume that at least in some cases this link is actually coincidental in some cases. Moreover, following the phenomenon of the race to publish, there has been an uncontrolled release of poor-quality articles showing the most disparate associations mainly based on a temporal association between SARS-CoV-2 infection and symptoms of various types including those of the ENT area. In this narrative review of the literature, we will critically describe the ENT symptoms of COVID-19.

KEY WORDS: coronavirus, COVID-19, ear nose throat, manifestation, otolaryngologic, SARS-CoV-2, symptoms

RIASSUNTO

La malattia da coronavirus 2019 (COVID-19) causata dal coronavirus 2 della sindrome respiratoria acuta grave (SARS-CoV-2) può essere caratterizzata da un ampio spettro di gravità che va da casi asintomatici o pauci-sintomatici a forme gravi e letali. Poiché il nuovo coronavirus è un virus respiratorio, non sorprende che molti sintomi causati dall'infezione da SARS-CoV-2 siano legati al coinvolgimento delle prime vie respiratorie. Oltre al più patognomonico dei sintomi, ovvero l'alterazione del senso dell'olfatto, ostruzione nasale, mal di gola e tosse sono stati costantemente descritti come primi sintomi della malattia. Tuttavia, per altri sintomi ORL, come lesioni del cavo orale e alterazioni audio-vestibolari, una relazione causale è tutt'altro che dimostrata. L'estrema diffusione della COVID-19 rende spesso difficile dimostrare un nesso causale tra diversi sintomi ORL e l'infezione da SARS-CoV-2 ed è ragionevole presumere che almeno in alcuni casi questo legame sia effettivamente casuale. Inoltre, a seguito di un fenomeno di vera e propria corsa alla pubblicazione, c'è stato un rilascio incontrollato di articoli di scarsa qualità che mostravano le associazioni più disparate basate principalmente su un'associazione temporale tra infezione da SARS-CoV-2 e sintomi di vario tipo, compresi quelli dell'area ORL. In questa revisione narrativa della letteratura descriveremo in modo critico i sintomi ORL della COVID-19.

PAROLE CHIAVE: *coronavirus, COVID-19, orecchio naso gola, manifestazioni, otorinolaringoiatrico, SARS-CoV-2, sintomi*

Introduction

Since December 2019, a pandemic of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has spread globally [1,2]. A wide spectrum of disease severity has been reported ranging from asymptomatic or oligosymptomatic cases to severe and life-threatening forms of interstitial pneumonia, which can develop into acute respiratory distress syndrome and death.

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As the new coronavirus is a respiratory virus which spreads primarily through droplets generated when an infected person coughs or sneezes, it is not surprising that a wide range of symptoms caused by SARS-CoV-2 infection are related to the involvement of the upper respiratory tract. Consequentially, ENT symptoms are among the most common in COVID-19. In our original investigation, upper respiratory tract symptoms accounted for 69% of overall symptoms in patients with mild-to-moderate COVID-19 and were comprised of nasal obstruction, rhinorrhoea, sneezing, ear fullness, sore throat, tearing, neck swelling, hoarseness and dizziness [3]. However, following the phenomenon of the race to publish about coronavirus, there has been an uncontrolled release of poor-quality articles showing the most disparate associations between SARS-CoV-2 infection and symptoms of various types including those of the ENT area [4,5].

We have already reported how smell and taste alterations are among the most frequent symptoms at the onset of the disease affecting around two-third of patients with mild-moderate disease [6], as they are among the most persistent symptoms [7,8], and they are predominant in long-COVID syndrome [9,10], as they can be an indication of infection in the context of patients in home isolation [11], since the self-reported alterations of the olfactory function underestimate the real prevalence and persistence that emerges through psychophysical tests [12,13]. As this topic will be the subject of a separate discussion in this special issue, in this review we will limit the description to non-chemosensory ENT symptoms of SARS-CoV-2 infection.

Upper airway-related general symptoms

The correct definition of the ENT symptomatology in COVID-19 is hampered by two main factors. On one hand, many of the clinical studies aimed at describing the clinical features of COVID-19 are focused on the more severe signs and symptoms of involvement of the lower airways, while completely or partially ignoring upper airway involvement. On the other hand, the extreme spread of COVID-19 makes it difficult to demonstrate a causal link between atypical ENT symptoms and SARS-CoV-2 infection and it is reasonable to assume that at least in some cases this link is actually coincidental.

Many studies have consistently described cough and nasal obstruction as the most common non-chemosensory ENT symptoms of COVID-19. Due to the retrospective design of many studies, the prevalence of ENT symptoms such as cough, sore throat, runny nose and nasal obstruction in the different studies is highly variable with rates ranging from 3 to 90% [14].

In a consecutive series of 202 home-isolated patients with PCR-confirmed SARS-CoV-2 infection, using a validated structured questionnaire, we observed the following prevalence of non-chemosensory ENT symptoms: cough 60%, blocked nose 31%, sore throat 31% and sinonasal pain 17% [6].

A recent meta-analysis reported a pooled prevalence of cough and nasal obstruction of 53 and 26%, respectively, followed by sore throat (18%) and rhinorrhoea (13%). While symptoms like fever, cough, fatigue, vomiting/diarrhoea, and dyspnoea were most common among hospitalised patients, nasal obstruction, sore throat and rhinorrhea were conversely most prevalent in patients with mild-to-moderate COVID-19 [15].

Outstandingly, ENT symptoms are among the first to manifest, and thus their prompt identification can dramatically prevent the spread of the infection [6,16]. Furthermore, olfactory loss and nasal obstruction are often dissociated symptoms and, if they coexist, the evolution of one is independent of the other [7].

Oral manifestations of COVID-19

Although the detection of SARS-CoV-2 in saliva reveals the presence of the virus in the oral cavity, the impact of SARS-CoV-2 on oral diseases is still poorly studied [17]. Numerous studies have described different types of lesions affecting the oral cavity in COVID-19 patients. While for many of these a coincidental relationship is rather probable, while for others lesions a direct or indirect link with COVID-19 seems established [18].

Oral cavity findings, including lingual papillitis, glossitis, aphthous stomatitis, xerostomia and mucositis were observed up to 26% of patients with COVID-19 [19]. Aragoneses et al. [18], in a very comprehensive review and meta-analysis, classified oral manifestations in COVID-19 according to the putative aetiology. Aphthous lesions and oral ulcers are among the most consistently observed manifestations for which a direct aetiological role of SARS-CoV-2 is likely [19,20]. These lesions can affect any sub-site of the oral cavity, although the tongue is more frequently involved. A variable prevalence of oral manifestations including oral ulceration, cheilitis and glossitis were observed in the context of multi-organ involvement, i.e. multisystem inflammatory syndrome and Kawasaki-like disease in children with COVID-19 [21-23]. Furthermore, a substantial group of oral lesions are attributable to iatrogenic lesions, such as intubation injuries, drug reactions and opportunistic infections during SARS-CoV-2 infection [24,25].

In addition, periodontal disease may increase during COVID-19 [26] and on the other hand, a poor periodontal state can

favour a vicious circle with an increase in the indexes of inflammation, aspiration of bacteria and consequent increased risk of pneumonia. Although it is difficult to state which of the various oral lesions associated with COVID-19 are the most prevalent, it seems that a higher frequency can be found in older, hospitalised patients with severe infection [27]. The hypothesis that the oral manifestations are secondary lesions resulting from the deterioration of systemic health or treatments for COVID-19 is most probably correct. The pharmacological agents against COVID-19 are related to several adverse reactions, including oral lesions [28].

Salivary alterations

Xerostomia was reported by 50% of patients with a median dryness score of 5 (range: 3-8) and for 76.5% patients mentioning that it was their first-time experiencing xerostomia in their lifetime [29]. The hypothesis is that the xerostomia reported in patients with the COVID-19 occurs due to the neuro-invasive and neurotropism potential of SARS-CoV-2 [30]. In fact, angiotensin-converting enzyme 2 (ACE-2), reported to be the main site of entry of SARS-CoV-2 into the cell, was found to be present in the ductal elements of the salivary glands [31]. Overall, studies are still necessary to unveil the precise pathophysiological mechanism by which SARS-CoV-2 causes the reported xerostomia and taste disturbances [32].

Oropharynx

The oropharyngeal tissue is one of the main harbour sites of the infection, main site of taking the sample for testing and a main source of transmission of infection. However, it was reported that pharyngeal erythema and tonsil enlargement are not common manifestations of SARS-CoV-2 infection, and these signs are present in only about 5 and 1% of cases, respectively [33]. However, sore throat is referred by around one-third of patients [6].

Temporomandibular disorders

Indirectly caused by the coronavirus due to the stress related to the pandemic situation and the governmental choices of the various countries in its management, reports have noted an increased number of people experiencing teeth grinding and oral pain during the COVID-19 pandemic as a consequence of increased stress. On the other hand, stress, anxiety and depression due to COVID-19 lead to increased orofacial pain, TMD and bruxism [34].

Audio-vestibular symptoms

Adult human inner ear tissue has been shown to co-express the angiotensin-converting enzyme 2 receptor for SARS-CoV-2 virus, and the transmembrane protease serine 2 and FURIN cofactors required for virus entry [35]. However, data about possible audio-vestibular dysfunction secondary to SARS-CoV-2 infection are mainly based on case reports and small case series [36,37].

While generic dizziness was self-reported by 14% of patients with mild-to-moderate COVID-19 [6], more specific audio-vestibular symptoms, i.e. sensorineural hearing loss and vertigo, were indeed anecdotally described with authors theorising a direct correlation to SARS-CoV-2 infection mainly based on a temporal association [38].

A more recent study compared evolution of incidence of sudden sensorineural hearing loss and Meniere's disease from 2016 to 2020 and observed a decrease in the incidence of Meniere's disease, while the incidence of sudden sensorineural hearing loss remained unchanged from 2016 to 2020 indicating that audio-vestibular symptoms in COVID-19 patients are probably coincidental rather than causal [39]. However, one should consider that the restrictive measures implemented during the pandemic could have reduced exposure to triggers of audio-vestibular diseases and counterbalanced any increase related to SARS-CoV-2 infection.

Thus, based on the current literature, no definitive conclusions can be drawn about the possible clinical impact of SARS-CoV-2 on the inner ear and large case-control studies are necessary to clarify the effect of SARS-CoV-2 infection in the onset of audio-vestibular symptoms.

Regarding hearing disorders, it seems that SARS-CoV-2 infection may cause a worsening of symptoms in patients already suffering from tinnitus. This highlights the diverse response that both internal and external factors have on tinnitus levels. Some authors stated that clinical services should be mindful that tinnitus may be caused by contracting COVID-19 and pre-existing tinnitus may be exacerbated [40]. However, little evidence has been found regarding the onset of new tinnitus contextual to SARS-CoV-2 infection [41] and it is not clear if this could be a direct viral effect or the consequence of ototoxicity of drugs used during hospitalization of patients [42].

COVID-19 and acute otitis media

Concerning a hypothetical link between SARS-CoV-2 infection and otitis media, the literature includes small case series and case reports [43,44]. Although researchers have found the presence of virus in the middle ear of subjects who died from COVID-19, a direct role of SARS-CoV-2 in the aetiopathogenesis of otitis media has not been demonstrated [45].

It is reasonable to hypothesise that a viral infection of the upper airways such as that caused by SARS-CoV-2, in con-

Table I. Definitive, probable, possible and complication-related ENT symptoms of COVID-19.

Definitive symptoms	Probable symptoms	Possible symptoms	COVID-19 complication-related symptoms
Cough [6,14,15,16]	Aphthous stomatitis [18,19,20]	Sudden hearing loss [36,37,38]	Intubation injuries [24]
Sore throat [6,14,15,16]	Cheilitis [21,22,23]	Vertigo [36,37]	Periodontal disease [26]
Nasal obstruction [6,7,14,15,16]	Glossitis [21,22,23]	Facial palsy [47,48,49]	Drug reactions [28]
Rhinorrhea [6,14,15,16]	Xerostomia [29,30,31]		Bruxism [34]
Hyposmia/Anosmia [6,7,8,9,10,11,12,13]	Dizzness [6]		Temporomandibular disorders [34]
Hypogeusia [6,7,8,9,10,11,12,13]	Tonsillitis [33]		Nasal swab complications [50,51,52,53]
Sinonasal pain [6,10]			Otitis media [43,44,45]

junction with Eustachian tube dysfunction, may be complicated with acute or effusive otitis media, similar to what is observed in rhinitis or nasopharyngitis caused by common respiratory viruses [46]. Thus, the concomitant occurrence of otitis media and COVID-19 should be considered a complication rather than a manifestation of COVID-19.

COVID-19 and facial palsy

Different clinical series on the prevalence of Bell's palsy (BP) in the pandemic are emerging in the literature. Even if some authors sustained a direct correlation between sars-CoV-2 infection and Bell's palsy in the first phase of the pandemic [47,48], the most recent epidemiological data have reduced the causal relationship [49] and there seems to be no association other than mere chance.

Complications of nasal swab

In addition to the more common symptoms treated above, it should be mentioned that indirectly the need to perform frequent nasal swabs for health surveillance during COVID pandemic implies a, albeit minimal, rate of complications, like nasal bleeding, foreign body retention (broken swab) [50,51] and cases of cerebrospinal fluid leak [52,53].

Conclusions

Consistent with the fact that SARS-CoV-2 is a respiratory virus, many symptoms observed during the acute phase reflect active upper airway infection. Importantly, upper airway symptoms, i.e. dry cough or coughing up mucus, blocked nose, rhinorrhoea, sinonasal pain and sore throat as well as chemosensory alterations are among the first to manifest, and thus their prompt identification can dramatically prevent the spread of infection (Tab. I). However, for other ENT symptoms, i.e. such as oral lesions, audio-vestibular changes and facial palsy, a causal relation has not been demonstrated (Tab. I). Due to the extensive spread of COVID-19, it is realistic to assume that in some cases the link between SARS-CoV-2 infection and atypical ENT symptoms can be coincidental. Furthermore, there has been an uncontrolled release of poor-quality articles showing the most disparate associations mainly based on a temporal association between SARS-CoV-2 infection and symptoms of various types including those of the ENT area. Finally, the evaluation of the incidence trends in ENT diseases during the COVID-19 pandemic in order to generate hypotheses on the direct role of SARS-CoV-2 in some ENT diseases is complicated by the fact that the restrictive measures implemented during the pandemic may have modulated the onset of ENT symptoms in the opposite direction.

Conflict of interest statement

The authors declare no conflict of interest.

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Authors' contributions

Both authors played a substantial role in conception, literature searching, drafting and revision of the manuscript.

Ethical consideration

Ethics approval was not required for this study because it was based on published studies.

References

1 Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. JAMA 2020:323:1239-1242. https://doi.org/10.1001/jama.2020.2648

2 Mannelli G, Ralli M, Bonali M, et al. Impact of COVID-19 pandemic on Italian Otolaryngology Units: a nationwide study. ACTA Otorhinolaryngologica Italica 2020;40:325-331. https://doi.org/10.14639/0392-100X-N0832

[3] Spinato G, Costantini G, Fabbris C, et al. The importance of early detection of ENT symptoms in mild-to-moderate COVID-19. Acta Otorhinolaryngol Ital 2021;41:101-107. https://doi.org/10.14639/0392-100X-N1038

[4] Moskovkin VM, Saprykina TV, Boichuk IV. Phenomenon of coronavirus publication race. In: Legach F, Archpriest EI, Sharov KS, editors. SARS-CoV-2 and coronacrisis: epidemiological challenges, social policies and administrative strategies, Singapore: Springer 2021, pp. 311-377. https://doi.org/10.1007/978-981-16-2605-0_20

[5] Safieddine M, Kassir R. COVID 19 and the race to publish: an ethical issue. Br J Surg 2020;107:e504. https://doi.org/10.1002/bjs.11966

[6] Spinato G, Fabbris C, Polesel J, et al. Alterations in smell or taste in mildly symptomatic outpatients with SARS-CoV-2 infection. JAMA 2020;323:2089-2090. https://doi.org/10.1001/jama.2020.6771

[7] Boscolo-Rizzo P, Borsetto D, Fabbris C, et al. Evolution of altered sense of smell or taste in patients with mildly symptomatic COVID-19. JAMA Otolaryngol Head Neck Surg 2020;146:729-732. https://doi.org/10.1001/jamaoto.2020.1379

[8] Boscolo-Rizzo P, Polesel J, Spinato G, et al. Predominance of an altered sense of smell or taste among long-lasting symptoms in patients with mildly symptomatic COVID-19. Rhinology 2020;58:524-525. https://doi.org/10.4193/Rhin20.263

[9] Boscolo-Rizzo P, Guida F, Polesel J, et al. Sequelae in adults at 12 months after mild-to-moderate coronavirus disease 2019 (COVID-19). Int Forum Allergy Rhinol 2021;11:1685-1688. https://doi.org/10.1002/alr.22832

[10] Boscolo-Rizzo P, Guida F, Polesel J, et al. Self-reported smell and taste recovery in coronavirus disease 2019 patients: a one-year prospective study. Eur Arch Otorhinolaryngol 2022;279:515-520 https://doi.org/10.1007/s00405-021-06839-w

[11] Boscolo-Rizzo P, Borsetto D, Spinato G, et al. New onset of loss of smell or taste in household contacts of home-isolated SARS-CoV-2-positive subjects. Eur Arch Otorhinolaryngol 2020;277:2637-2640. https://doi.org/10.1007/s00405-020-06066-9

[12] Boscolo-Rizzo P, Menegaldo A, Fabbris C, et al. Six-month psychophysical evaluation of olfactory dysfunction in patients with COVID-19. Chem Senses 2021 Jan 1;46:bjab006 https://doi.org/10.1093/chemse/bjab006

[13] Boscolo-Rizzo P, Hummel T, Hopkins C, et al. High prevalence of long-term olfactory, gustatory, and chemesthesis dysfunction in post-COVID-19 patients: a matched case-control study with one-year follow-up using a comprehensive psychophysical evaluation. Rhinology 2021;59:517-527. https://doi.org/10.4193/Rhin21.249

[14] Al-Swiahb JN, Motiwala MA. Upper respiratory tract and otolaryngological manifestations of coronavirus disease 2019 (COVID-19): a systemic review. SAGE Open Med 2021;9:20503121211016964. https://doi.org/10.1177/20503121211016965

[15] Mair M, Singhavi H, Pai A, et al. A meta-analysis of 67 studies with presenting symptoms and laboratory tests of COVID-19 patients. Laryngoscope 2021;131:1254-1265. https://doi.org/10.1002/lary.29207

[16] Jia X, Shao S, Ren H, et al. Sinonasal manifestations and dynamic profile of RT-PCR results for SARS-CoV-2 in COVID-19 patients. Ann Palliat Med 2021;10:4174-4183. https://doi.org/10.21037/apm-20-2493

[17] Naqvi AR, Schwartz J, Brandini DA, et al. COVID-19 and oral diseases: assessing manifestations of a new pathogen in oral infections. Int Rev Immunol 2021 Sep 16:1-15. https://doi.org/10.1080/08830185.2021.1967949. Epub ahead of print.

[18] Aragoneses J, Suárez A, Algar J, et al. Oral manifestations of COVID-19: updated systematic review with meta-analysis. Front Med (Lausanne) 2021;8:726753. https://doi.org/10.3389/fmed.2021.726753

[19] Nuno-Gonzalez A, Martin-Carrillo P, Magaletsky K, et al. Prevalence of mucocutaneous manifestations in 666 patients with COVID-19 in a field hospital in Spain: oral and palmoplantar findings. Br J Dermatol 2021;184:184-185.https://doi.org/10.1111/bjd.19564

[20] Fidan V, Koyuncu H, Akin O. Oral lesions in COVID-19 positive patients. Am J Otolaryngol 2021;42:102905. https://doi.org/10.1016/j.amjoto.2021.102905

[21] Cant A, Bhujel N, Harrison M. Oral ulceration as presenting feature of paediatric inflammatory multisystem syndrome associated with COVID-19. Br J Oral Maxillofac Surg 2020;58:1058-1059. https://doi.org/10.1016/j.bjoms.2020.06.037

[22] Verdoni L, Mazza A, Gervasoni A, et al. An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: an observational cohort study. Lancet 2020;395:1771-1778. https://doi.org/10.1016/S0140-6736(20)31103-X

[23] Young TK, Shaw KS, Shah JK, et al. Mucocutaneous manifestations of multisystem inflammatory syndrome in children during the COVID-19 pandemic. JAMA Dermatol 2021;157:207-212. https://doi.org/10.1001/jamadermatol.2020.4779

[24] Walsh A, Peesay T, Newark A, et al. Association of severe tongue edema with prone positioning in patients intubated for COVID-19. Laryngoscope 2022;132:287-289. https://doi.org/10.1002/lary.29773

[25] Rajendra Santosh AB, Muddana K, Bakki SR. Fungal infections of oral cavity: diagnosis, management, and association with COVID-19. SN Compr Clin Med 2021 Mar 27:1-12. https://doi.org/10.1007/s42399-021-00873-9. Epub ahead of print.

[26] Coke CJ, Davison B, Fields N, et al. SARS-CoV-2 infection and oral health: therapeutic opportunities and challenges. J Clin Med 2021;10:156. https://doi.org/10.3390/jcm10010156

[27] Samaranayake L, Fakhruddin KS, Bandara N. Oral manifestations of coronavirus disease 2019 (COVID-19): an overview. Dent Update 2021;48:418-422. https://doi.org/10.12968/denu.2021.48.5.418

[28] Godinho GV, Paz ALLM, de Araújo Gomes EPA, et al. Extensive hard palate hyperpigmentation associated with chloroquine use. Br J Clin Pharmacol 2020;86:2325-2327. https://doi.org/10.1111/bcp.14313

[29] Fantozzi PJ, Pampena E, Di Vanna D, et al. Xerostomia, gustatory and olfactory dysfunctions in patients with COVID-19. Am J Otolaryngol 2020;41:102721. https://doi.org/10.1016/j.amjoto.2020.102721

[30] Saniasiaya J. Xerostomia and COVID-19: unleashing Pandora's box. Ear Nose Throat J 2021;100:139S. https://doi.org/10.1177/0145561320960353

[31] Usami Y, Hirose K, Okumura M, et al. Brief communication: immunohistochemical detection of ACE2 in human salivary gland. Oral Sci Int 2020 Sep 28;10.1002/osi2.1085. https://doi.org/10.1002/osi2.1085. Epub ahead of print.

[32] Belchior Fontenele MN, Pedrosa da Silva M. Xerostomia and taste alterations in COVID-19. Ear Nose Throat J 2021;100:186S-187S. https://doi.org/10.1177/0145561320982686

[33] El-Anwar MW, Elzayat S, Fouad YA. ENT manifestation in COVID-19 patients. Auris Nasus Larynx 2020;47:559-564. https://doi.org/10.1016/j.anl.2020.06.003

[34] Emodi-Perlman A, Eli I, Smardz J, et al. Temporomandibular disorders and bruxism outbreak as a possible factor of orofacial pain worsening during the COVID-19 pandemic – concomitant research in two countries. J Clini Med 2020;9:3250. https://doi.org/10.3390/jcm9103250

[35] Jeong M, Ocwieja KE, Han D, et al. Direct SARS-CoV-2 infection of the human inner ear may underlie COVID-19-associated audiovestibular dysfunction. Commun Med 2021;1:1-14. https://doi.org/10.1038/s43856-021-00044-w

[36] Karimi-Galougahi M, Naeini AS, Raad N, et al. Vertigo and hearing loss during the COVID-19 pandemic – is there an

association? Act Otorhinolaryngol Ital 2020;40:463-465. https://doi.org/10.14639/0392-100X-N0820

[37] Malayala SV, Mohan G, Vasireddy D, et al. A case series of vestibular symptoms in positive or suspected COVID-19 patients. Infez Med 2021;29:117-122.

[38] Fancello V, Hatzopoulos S, Corazzi V, et al. SARS-CoV-2 (COVID-19) and audio-vestibular disorders. Int J Immunopathol Pharmacol 2021;35:20587384211027372. https://doi.org/10.1177/20587384211027373

[39] Chao C-H, Young Y-H. Evolution of incidence of audiovestibular disorders during the pandemic COVID-19 period. Eur Arch Otorhinolaryngol 2021 Aug 13;1-5. https://doi.org/10.1007/s00405-021-07037-4. Epub ahead of print.

[40] Beukes EW, Baguley DM, Jacquemin L, et al. Changes in tinnitus experiences during the COVID-19 pandemic. Front Public Health 2020 Nov 5;8:592878. https://doi.org/10.3389/fpubh.2020.592878

[41] Munro KJ, Uus K, Almufarrij I, et al. Persistent self-reported changes in hearing and tinnitus in post-hospitalisation COVID-19 cases. Int J Audiol 2020;59:889-890. https://doi.org/10.1080/14992027.2020.1798519

[42] Ciorba A, Virginia Corazzi V, Skarżyński PH, et al. Don't forget ototoxicity during the SARS-CoV-2 (COVID-19) pandemic! Int J Immunopathol Pharmacol 2020;34:2058738420941754. https://doi.org/10.1177/2058738420941754

[43] Ye W, Xianyang L. A novel coronavirus pneumonia case report from an ear, nose, and throat clinic. Laryngoscope 2020;130:1106-1107. https://doi.org/10.1002/lary.28655

[44] Raad N, Ghorbani J, Mikaniki N, et al. Otitis media in coronavirus disease 2019: a case series. J Laryngol Otol 2021;135:10-13. https://doi.org/10.1017/S0022215120002741

[45] Jeican II, Aluaș M, Lazăr M, et al. Evidence of SARS-CoV-2 virus in the middle ear of deceased COVID-19 patients. Diagnostics (Basel) 2021;11:1535. https://doi.org/10.3390/diagnostics11091535

[46] Fireman P. Otitis media and eustachian tube dysfunction: connection to allergic rhinitis. J All Clin Immunol 1997;99:s787-797. https://doi.org/10.1016/S0091-6749(97)70130-1

[47] Zammit M, Markey A, Webb C. A rise in facial nerve palsies during the coronavirus disease 2019 pandemic. J Laryngol Otol 2020 Oct 1:1-4. https://doi.org/10.1017/S0022215120002121. Epub ahead of print.

[48] Codeluppi L, Venturelli F, Rossi J, et al. Facial palsy during the COVID-19 pandemic. Brain Behav 2021;11:e01939. https://doi.org/10.1002/brb3.1939

[49] Martin-Villares C, Alba JR, Gonzalez-Gimeno MJ. Data from 235 cases of Bell's Palsy during COVID-19 pandemic: were there clusters of facial Palsy? NED 2021;55:495-496. https://doi.org/10.1159/000518671

[50] Koskinen A, Tolvi M, Jauhiainen M, et al. Complications of COVID-19 nasopharyngeal swab test. JAMA Otolaryngol Head Neck Surg 2021;147:672-674. https://doi.org/10.1001/jamaoto.2021.0715

[51] Fabbris C, Cestaro W, Menegaldo A, et al. Is oro/nasopharyngeal swab for SARS-CoV-2 detection a safe procedure? Complications observed among a case series of 4876 consecutive swabs. Am J Otolaryngol 2021;42:102758. https://doi.org/10.1016/j.amjoto.2020.102758

[52] Sullivan CB, Schwalje AT, Jensen M, et al. Cerebrospinal fluid leak after nasal swab testing for coronavirus disease 2019. JAMA Otolaryngol Head Neck Surg 2020;146:1179-1181. https://doi.org/10.1001/jamaoto.2020.3579

[53] Yılmaz M, Bahadır Z, Madendere B, et al. A brief report: cerebrospinal fluid rhinorrhea after repetitive nasal swab testing for coronavirus disease 2019 (COVID-19). Otolaryngol Case Rep 2021;20:100313. https://doi.org/10.1016/j.xocr.2021.100313