Coincidence of COVID-19 Infection and Smell—Taste Perception Disorders

Erdem Atalay Cetinkaya, MD

Abstract: Many reports by physicians and patients during the 2019 to 2020 pandemic indicate that COVID-19 is associated with elevated levels of odor and taste perception disorders (anosmia, hyposmia, ageusia, and/or dysgeusia). Recent increase in olfactory dysfunction in patients referred to ear nose and throat clinics and COVID-19 infection at the same time encouraged us to examine anosmic/hyposmic patients to establish any association between these signs. It has been shown that the COVID-19 virus exploits the uses angiotensin-converting enzyme 2 receptor to obtain cell entry. This result increases the interest to examine the expression of angiotensin-converting enzyme 2 in neurological tissue, and to assess the possible contribution of damage. This mini review provides fundamental knowledge on coincidence of COVID-19 infection and smell—taste perception disorders from an objective perspective.

Key Words: Coronavirus infections, COVID-19, olfaction disorders

Previous studies documented olfactory dysfunction, also called postviral anosmia, following upper respiratory tract viral infections. Epithelial damage and the involvement of the central nervous system is identified as the possible causes but the exact pathogenesis remains unclear.[1,2] The association between the amount of anosmia, hyposmia, ageusia, and/or dysgeusia and COVID-19 patients was highly important. These signs' emergence may be sudden or slow. Results to date indicate the widespread prevalence of anosmia/hyposmia across the pandemic region, and a strong linear association between COVID-19 prevalence and olfactory impairment. Detailed neurological symptoms of the hospitalized COVID-19 patients are recorded in the analysis: 5% of patients had hyposmia, and of these patients, almost 3 quarter also had decreased sensation of taste.[3–6]

CLINICAL AND RESEARCH EFFECTS

On February 11, 2020, a taxonomic classification "severe acute respiratory syndrome coronavirus 2" (SARS-CoV-2) became the official way of referring to the 2019-nCoV and Wuhan coronavirus strain. The same day the WHO formally called the disease COVID-19 within a few hours. The SARS-CoV-2 genome is a coronavirus with 29.903 bp single-stranded RNA (ss-RNA). During April 2020, in parallel with the COVID-19 outbreak, the number of olfactory dysfunction patients in many reports has increased.[4–6] This prompted the development of an online questionnaire to determine the prevalence of this olfactory condition. The COVID-19 Anosmia Reporting Tool for Clinicians was designed by the American Academy of Otolaryngology-Head and Neck Surgery in an attempt to determine the significance of these symptoms in the diagnosis and development of COVID-19.[7] The association between the amount of anosmia, hyposmia, ageusia, and/or dysgeusia and COVID-19 patients was identified in all reports until April 2020. These signs' emergence may be sudden or slow. Results to date indicate the widespread prevalence of anosmia/hyposmia across the pandemic region, and a strong linear association between COVID-19 prevalence and olfactory impairment. Detailed neurological symptoms of the hospitalized COVID-19 patients are recorded in the analysis: 5% of patients had hyposmia and of these patients, almost 3 quarter also had a decreased sensation of taste. The onset of anosmia was abrupt in 76%, and continuously reduced sense of smell in 60% of patients until the time of completing the questionnaire. Of these patients, 83% also had decreased taste sensation in connection with anosmia. The latest high incidence of olfactory flu-related dysfunction (75%), higher incidence in women (71%), and high incidence of anosmia in family members (48.23%) indicate postviral olfactory dysfunction.[4,5,8]

Suzuki et al first detected rhinovirus, coronavirus, parainfluenza virus, and Epstein-Barr virus in the nasal secretion of patients with postviral olfactory disorders in 2007. Suzuki also reported that rhinoviruses can target olfactory impairment by means of mechanisms other than nasal obstruction, and that rhinoviruses may induce different olfactory dysfunction time courses.[9] Various animal studies have demonstrated that various viruses may cause damage to central olfactory routes and other brain regions.[10–12] Previous reports have not yet identified the neurological effects of COVID-19. Mao et al found that 36.4% of COVID-19 patients had a number of neurological symptoms including central nervous system, peripheral nervous system, and skeletal muscles. Detailed neurological symptoms of the hospitalized COVID-19 patients are recorded in the analysis: 5% of patients had hyposmia.[8] It has been shown that the COVID-19 virus, similar to SARS-CoV, uses angiotensin-converting enzyme 2 (ACE2) receptor to obtain cell entry. This result increases the interest to examine the expression of ACE2 in neurological tissue, and to assess the possible contribution of neurological tissue damage to COVID-19 morbidity and mortality. To identify cell types in the olfactory epithelium that express molecules that mediate COVID-19 infection, Brann et al preliminarily reported bulk and single cell RNA-Seq datasets. Two primary genes necessary for COVID-19 entry, ACE2 and transmembrane serine protease 2, were shown in both animal and human datasets that olfactory sensory neurons do not express.[13] For comparison, olfactory epithelial supporting cells and stem cells express none of these genes, as do cells in the epithelial nasal respiratory. Taken together, these results indicate possible mechanisms by which infection with COVID-19 may result in anosmia or other types of olfactory dysfunction.[13–15]

CONCLUSION

The COVID-19 virus movement into the brain through the cribriform plate close to the olfactory bulb may be a mechanism that would enable the virus to reach and influence the brain. In addition, findings such as anosmia or hyposmia in an uncomplicated early COVID-19 patient will require a comprehensive central nervous system involvement assessment. Because olfactory dysfunction may affect the quality of life in patients affected, more clinical studies need to determine the exact correlation, pathogenesis, prognosis, and any connection between the seriousness of the disease and olfactory dysfunction worldwide. In the absence of other respiratory disorders,

From the Department of Otorhinolaryngology and Head & Neck Surgery, University of Health Sciences, Antalya Training and Research Hospital, Antalya, Turkey.
Received April 3, 2020.
Accepted for publication April 3, 2020.
Address correspondence and reprint requests to Erdem Atalay Cetinkaya, SBÜ Antalya Eğitim Araştirma Hastanesi, KBB Kliniği Antalya 07100, Turkey; E-mail: drerdemcetinkaya@gmail.com
The authors report no conflicts of interest.

ISSN: 1049-2275
DOI: 10.1097/SCS.0000000000006601

such as allergic rhinitis, acute rhinosinusitis, or chronic rhinosinusitis; anosmia, hyposmia, and dysgeusia will alert doctors to the possibility of COVID-19 infection and warrant serious consideration for self-isolation and testing of these individuals.

REFERENCES

1. Yamagishi M, Fujiwara M, Nakamura H. Olfactory mucosal findings and clinical course in patients with olfactory disorders following upper respiratory viral infection. *Rhinology* 1994;32:113–118
2. Hummel T, Whitcroft KL, Andrews P, et al. Position paper on olfactory dysfunction. *Rhinol Suppl* 2017;54:1–30
3. Duncan HJ. Postviral olfactory loss. *Seiden A M ed, Taste and Smell Disorders*. New York: Thieme; 1997:72–78
4. Mao L, Wang M, Chen S, et al.Neurological Manifestations of Hospitalized Patients with COVID-19 in Wuhan, China: a retrospective case series study. Available at: https://www.medrxiv.org/content/10.1101/2020.02.22.20026500v1. Accessed April 1, 2020
5. World Health Organization Coronavirus disease (COVID-19) pandemic study. Available at: https://www.who.int/emergencies/diseases/novel-coronavirus-2019. Accessed April 1, 2020
6. Rabin R. Loss of sense of smell may be peculiar clue to coronavirus infection. Available at: https://www.nytimes.com/2020/03/22/health/coronavirus-symptoms-smelltaste.html. Accessed March 22, 2020
7. American Academy of Otolaryngology-Head and Neck Surgery. COVID-19 anosmia reporting tool for clinicians. Available at: https://www.entnet.org/content/reporting-tool-patients-anosmia-related-covid-19. Accessed March 26, 2020
8. Bagheri SHR, Asghari AM, Farhadi M, et al. Coincidence of COVID-19 epidemic and olfactory dysfunction outbreak. Available at: https://www.medrxiv.org/content/10.1101/2020.03.23.20041889v1.full.pdf+html. Accessed March 26, 2020
9. Suzuki M, Saito K, Min WP, et al. Identification of viruses in patients with postviral olfactory dysfunction. *Laryngoscope* 2007;117:272–277
10. Mohammed A, Magnusson O, Maehlen J, et al. Behavioural deficits and serotonin depletion in adult rats after transient infant nasal viral infection. *Neuroscience* 1990;35:355–363
11. Perlman S, Evans G, Afifi A. Effect of olfactory bulb ablation on spread of a neurotropic coronavirus into the mouse brain. *J Exp Med* 1990;172:1127–1132
12. Seiden AM. Postviral olfactory loss. *Otolaryngol Clin North Am* 2004;37:1159–1166
13. Brann D, Tsukahara T, Weinreb C, et al. Non-neural expression of SARS-CoV-2 entry genes in the olfactory epithelium suggests mechanisms underlying anosmia in COVID-19 patient. Available at: https://www.biorxiv.org/content/10.1101/2020.03.25.009084v2.full.pdf. Accessed March 26, 2020
14. Bertram S, Heurich A, Lavender H, et al. Influenza and SARS-coronavirus activating proteases TMPRSS2 and HAT are expressed at multiple sites in human respiratory and gastrointestinal tracts. *PLoS One* 2012;7:e35876
15. Netland J, Meyerholz DK, Moore S, et al. Severe acute respiratory syndrome coronavirus infection causes neuronal death in the absence of encephalitis in mice transgenic for human ACE2. *J Virol* 2008;82:7264–7275