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Self-reported smell and taste alteration as the sole clinical manifestation of SARS-CoV-2 infection

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Chemosensory dysfunction has increasingly been reported in patients with coronavirus disease 2019 (COVID-19). Here, we document a case of a patient with taste and smell alterations as the only clinical manifestations of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. In March 2020, a 36-year-old woman presented with self-reported hypogeusia/ageusia and hyposmia/anosmia in the absence of any respiratory symptom. The patient, who had no clinical and radiographic signs of sinusitis and was otherwise healthy, eventually had a positive test result for SARS-CoV-2. She did not develop any COVID-19–related symptoms throughout her 6-month follow up. Her self-reported chemosensory dysfunction lasted for 12 weeks. To the best of our knowledge, this is the first report that has accurately documented taste and smell alteration as the sole manifestation of COVID-19 in an otherwise healthy individual. Overall, analysis of current evidence supports the inclusion of gustatory and olfactory alterations as cardinal symptoms of COVID-19. Dentists' awareness of the diagnostic criteria for case definition of COVID-19 can facilitate early detection of the disease. (Oral Surg Oral Med Oral Pathol Oral Radiol 2021;131:e95–e99)

Early detection of individuals infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is key to reducing the spread of coronavirus disease 2019 (COVID-19) and is particularly challenging in asymptomatic or paucisymptomatic patients. Commonly reported clinical manifestations of COVID-19 include fever, cough, myalgia or fatigue, pneumonia, and complicated dyspnea.¹ Although the most prevalent signs/symptoms in patients with COVID-19 (i.e., cough, fever, and fatigue, according to a recent meta-analysis²) have been used as cardinal clinical diagnostic criteria since the beginning of the outbreak, new olfactory and taste disorder(s) were not initially linked to SARS-CoV-2 infection and were not used for case identification and testing prioritization by the Centers for Disease Control and Prevention (CDC) or the World Health Organization (WHO) until August 2020.³

The first systematic assessments of the evidence available up to March 2020 failed to identify associations between anosmia/ageusia and COVID-19.^{4,5} For example, none of the studies included in an early systematic review reported olfactory or gustative dysfunction.⁴ When looking specifically at the evidence for anosmia in COVID-19 up to March 23, 2020, researchers found it to be “limited and inconclusive”.⁵ In sharp contrast, a most recent meta-analysis of smell and taste alterations reported not only that approximately half of

patients with COVID-19 had these symptoms but also, that 15% of patients had olfactory and gustatory abnormalities as their initial clinical manifestations.⁶

In agreement with the growing body of evidence, sudden onset of anosmia, ageusia, or dysgeusia has now been recognized as a major clinical characteristic of the disease and has been included in the list of key clinical criteria for case definition of COVID-19 by the European Centre for Disease Prevention and Control as well as other public health surveillance organizations across the world, such as the CDC, the WHO,³ and Public Health England.⁷ However, it is not known whether concurrent olfactory and gustatory alterations may indeed represent the only clinical signs of SARS-CoV-2 infection in otherwise healthy patients.

Here, we aimed to document a case of a patient with taste and smell alterations as the only clinical manifestations of SARS-CoV-2 infection. Furthermore, we surveyed current high-level evidence on this topic.

CASE DESCRIPTION

A 36-year-old Caucasian woman presented for observation to the Oral and Maxillofacial Surgery Unit, Azienda Ospedaliero-Universitaria University of Campania “Luigi Vanvitelli”, Italy, on March 7, 2020, complaining of a reduction of her ability to taste food in the last 7 days. She reported a score of 4 on a 10-cm visual analog scale (VAS), where 0 indicated lack of sensation and 10 was optimal. When questioned further, she also admitted a diminishing ability to smell odors (VAS score 7/10). Intraoral examination did not reveal the presence of any mucosal alteration such as atrophy, ulceration, or tongue coating. Extraorally, no preauricular, submandibular, or cervical lymphadenopathy was detected. The patient's medical history revealed no concomitant disease, systemic signs and symptoms, or use of medications. Despite not showing signs of nasal

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Received for publication Sep 5, 2020; returned for revision Oct 15, 2020; accepted for publication Nov 25, 2020.

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2212-4403/\$-see front matter

<https://doi.org/10.1016/j.oooo.2020.11.016>

congestion, she was initially prescribed posteroanterior occipitontal radiographic investigation to rule out sinus pathology, which eventually showed no abnormalities. At follow-up on March 11, the patient reported complete loss of taste and smell (ageusia and anosmia) and was referred to the neurology unit to rule out space-occupying lesions or other neurologic disturbances. Because anosmia and ageusia had occasionally been linked to SARS-CoV-2 infection at that time, the presence of other signs and symptoms suggestive of COVID-19 were investigated. The patient's body temperature taken orally with an electronic digital thermometer was 36.7°C, and her history was negative for headache, fatigue, and muscle pain. She eventually underwent SARS-CoV-2 testing (oropharyngeal swab and polymerase chain reaction), which returned a positive result on March 21. The patient underwent self-isolation at home and hence did not undergo any further diagnostic tests.

She was followed up by telephone surveys and, in the following weeks, did not report any respiratory or other symptoms except anosmia and ageusia. These self-reported alterations began to gradually improve in May and had resolved by May 25. No VAS testing was possible due to the telephone interviews. As of August 29, 2020, the patient had no new self-reported alterations of taste and smell. After providing thorough information regarding the publication of this case, informed consent was gathered.

DISCUSSION

To the best of our knowledge, this is the first report of a case of COVID-19 with no comorbidities and no medication history and without any symptoms except concomitant loss of smell and taste. A previous study described a patient with anosmia and ageusia as the only indicators of COVID-19⁸; however, that patient presented to the hospital with the chief complaint of headache, which is a well-known neurologic manifestation of COVID-19.⁹⁻¹² Furthermore, the 60-year-old woman in the previous study had a history of vertigo, seasonal allergies, and trigeminal neuralgia. In contrast, our patient had no systemic diseases or allergies. In another report from Norway, a married couple in their 60s reported anosmia (wife) and ageusia (husband); however, there was no concurrent alteration of smell and taste.¹³ Finally, another peculiarity of our case was the unusually long duration of the symptoms, which lasted for approximately 12 weeks.

We found retrospective studies where patients who had positive test results for SARS-CoV-2 appeared to have experienced chemosensory dysfunction in the absence of typical COVID-19 symptomatology.^{14,15} For example, Villareal et al.¹⁴ described taste and smell disorder as the only symptom in 3 cases (1.3% of the cohort). Other reports exist in which an altered sense of

smell or taste is described as the only symptom in a small number of patients;¹⁶⁻¹⁸ however, there was no indication whether these manifestations occurred concurrently (both smell and taste, as opposed to either smell or taste) or were associated with comorbidities or other systemic conditions. Also, one study¹⁸ included non-laboratory-confirmed cases, and participants were not required to have documented SARS-CoV-2 infection. These data suggest that the true prevalence of chemosensory dysfunction as the sole presenting symptom of COVID-19 could indeed be underreported. However, because of the nature of these studies, it is not possible to figure out whether these patients reported any comorbidity, history of medications, or the presence of sinus pathology. In addition, none of the studies published so far documented a follow-up of 6 months or longer. Hence, we believe that our patient is the first well-documented case of a COVID-19 with no concomitant disease presenting exclusively with smell and taste changes and is the one with the longest follow-up.

Given the potential usefulness of smell and taste assessment in the diagnosis of asymptomatic patients, we undertook a review of high-level evidence on this topic. The data extracted from published systematic reviews are reported in [Table I](#). The range of prevalence of olfactory and gustatory alterations, when reported individually, was 3.2%-100% and 0-92.6%, respectively. In the systematic reviews analyzing smell and/or taste together, the range was 5.6%-94%. The heterogeneity of these findings may be partially due to differences in the geographic distribution of this association.³ Interestingly, when the prevalence was pooled for the total number of cases examined, olfactory and gustatory alterations were found in approximately half of patients with COVID-19. In one systematic review,²⁹ 81.6% (8823) and 74.8% (8088) of 10 818 patients with COVID-19 presented with ageusia and anosmia, respectively. Studies⁶ also demonstrate that the same signs/symptoms are the initial manifestation in a sizable number of patients. In light of the data reported here, and given the high risk of work-related contagion,³⁹ it is imperative for dentists and oral health care providers to recognize ageusia as a potential clinical manifestation of COVID-19.

Smell and taste disorders are not rare in the general population and have a wide range of recognized causes, including cigarette smoking, nasal and sinus disease, oral or upper respiratory infection, head trauma, neurodegenerative disorders, brain neoplasms, and aging.³³ Medications, chemotherapy, and radiotherapy are also associated with chemosensory dysfunction.³⁴ It is not surprising, therefore, that changes of smell and/or taste were also found to be relatively common in patients with negative test results for SARS-CoV-2 infection.³⁵ In the case presented here, we ruled out smoking, trauma, medications, infections, and sinus disease on

Table 1. Systematic reviews assessing olfactory and gustatory alterations in COVID-19 patients.

Systematic review Reference	Study data collection (up to)					Scope and prevalence		
	Up to Mar	Apr	May	Jun	Jul	Range (%)	Pooled prevalence	Focus
Almqvist et al ⁹					26	39-88 (ST)	NR	N
Chi et al ⁶		8				5.6-94 (ST)	48.5%(ST)	ST
Samaranayake et al ¹⁹			30			5.1-85.6 (S) 5.6-88.8(T)	48.8% (S) 51.3%(T)	ST
Agyeman et al ²⁰		11				3.2-98.3 (S) 5.6-62.7(T)	41% (S) 38.2% (T)	ST
Di Carlo et al ¹⁰			29			NR	46.8 (S) 52.3% (T)	N
Chen et al ¹¹		20				5.1-85.6 (S) 5.6-88.8(T)	59.2% (S) 50.8% (T)	N
Abdullahi et al ¹²		17				5.1-85.6 (S) 5.6-82 (T)	35% (S) 33% (T)	N
Struyf et al ²¹		27				NR	18% (ST)	G
Borsetto et al ²²		4				11-84 (ST)	47% (ST)	ST
von Bartheld et al ²³			10			4.9-98 (S) 0-88.8 (T)	38.48%(S) 30.37% (T)	ST
Carrillo-Larco & Altez-Fernandez ²⁴		20				5.1-68 (S) 5.6-78.9 (T)	NR	ST
da Costa et al ²⁵		25				5.1-98.3 (S) 5.6-82 (T)	NR	ST
Hoang et al ²⁶		30				5.6-85.6(S) 5.1-88.8(T)	45.7%(S) 47%(T)	ST
Wang et al ²⁷			3			35.7-85.6(S) 33.3-88.8(T)	NR	G, N
Romoli et al ²⁸		24				48.2-85(S) 39.2-88(T)	NR	N
Passarelli et al ^{29*}		30				5.1-85.6(S) 5.6-88(T)	74.8%(S) 81.6%(T)	ST
Printza & Constantinidis ³⁰			3			5.1-100(S) 5.6-88.8(T)	NR	ST
Whittaker et al ^{31**}			NR			5-100(S) 6-25(T)	NR	N
Tong et al ³²		19				5.1-98.3(S) 5.5-92.6(T)	52.73%(S) 43.93%(T)	ST

Systematic reviews were sorted by date of publication on PubMed. S, smell; T, taste; ST, smell and taste; N, neurological; G, general symptoms; NR, not reported.

*, exact date not specified, assumed 30 April. **, date(s) of data collection not specified

the basis of information gathered from the patient’s medical history, clinical assessment, and radiographic investigations. Because of self-isolation, the patient could not undertake the neurologic assessment we prescribed, but given the transitory nature of her alteration and considering the positivity of her SARS-CoV-2 testing, it is unlikely that her disturbances were related to brain disease.

The possible mechanisms of chemosensory dysfunction in COVID-19 are still being elucidated. The high

incidence of smell loss without significant rhinorrhea or nasal congestion suggests that SARS-CoV-2 targets the chemical senses through mechanisms distinct from those used by endemic coronaviruses or other common cold-causing agents.³⁶ It has been proposed that the virus could bind to the olfactory and/or oral epithelium via the ACE2 receptor and induce cytolytic damage and inflammatory responses. In turn, this would lead to cellular and genetic changes that could ultimately alter taste and smell.³⁷ The same mechanism could also

directly affect the peripheral neuronal trajectory of the gustatory tract. Another study suggests that the rapid recovery of smell and taste functions in patients with COVID-19 could be attributed to a decrease in interleukin-6 levels.³⁸ Although intriguing, these reports are still very speculative and will need to be backed by further experimental and clinical evidence.

CONCLUSION

Smell and taste alterations not only are associated with COVID-19 but also can be the first or sole manifestations of the disease. As of August 29, 2020, our patient had not developed any COVID-19–related or other signs or symptoms. Hence, to the best of our knowledge, this is the first patient with COVID-19 presenting with prolonged ageusia and anosmia as the sole clinical manifestations of the disease during a 6-month follow-up.

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