Decrease and Recovery of Olfactory and Gustatory Function in a Case of SARS-CoV-2 Infection

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Keywords
Smell · Taste · COVID-19 · Recovery

Abstract
Self-reported chemosensory dysfunction in severe acute respiratory syndrome coronavirus 2 patients is common. We present a case of reversible smell loss in a young patient with mild coronavirus disease 2019 infection assessed with established testing methods over a period of 8 weeks.

Introduction
The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is responsible for the coronavirus disease 2019 (COVID-19) pandemic, keeping the world in suspense since its first outbreak in December 2019. A recent summary of the clinical characteristics of infected individuals suggested that the spectrum of presenting symptoms can vary greatly among different groups of disease severity [1]. One emerging symptom in young patients that has been reported by numerous professional societies is “smell loss” or anosmia. Various sources have suggested that young patients may experience smell and taste loss alone as a major, or even prodromal, symptom without difficulties in nasal breathing or general symptoms, such as fever or cough [2]. The interpretation of these symptoms is critical as young, asymptomatic, and unaware individuals represent a major source of viral transmission that can delicately interfere with worldwide efforts in combating this pandemic [3]. Reports of anosmia in COVID-19 rely on verbal patient complaints. Although patients with olfactory dysfunction (OD) generally report smell loss accurately, unnoticed anosmia or subjective complaints with normal test scores are found occasionally. Therefore, data on chemosensory function in COVID-19 patients are needed, as this disease spreads rapidly and symptoms require objectification. Here, we report the clinical and self-perceived course of OD combined with nasal airflow measurements in a young patient with mild COVID-19 infection who was monitored by established testing methods for smell and taste function.
Case Presentation

A 35-year-old male healthcare professional without any preexisting medical conditions, who had direct patient care responsibilities with COVID-19 patients (ear, nose, and throat examinations), reported a mild cough and sore throat starting on March 14. On March 17, he reported a sudden loss of smell after waking up in the morning, but no nasal congestion was noticed (Table 1). As he was a healthcare professional and represented a high-risk group, he voluntarily isolated at home and testing via nasopharyngeal swab was performed. The result obtained via real-time reverse transcription polymerase chain reaction was positive for SARS-CoV-2.

Seven days after symptom onset, on March 21, olfactory and gustatory testing were performed by means of validated test procedures using the 16-item Sniffin’ Sticks Identification test (Burghart GmbH, Wedel, Germany), the Candy Smell Test (for testing retro-nasal olfaction), and the Taste Strips Test (Burghart GmbH) for bilateral (whole-mouth) taste function according to the manufacturer’s instructions [4–6]. Uni- and bilateral nasal airflow was also measured based on a validated procedure using a peak nasal inspiratory flowmeter (Clement Clarke International Ltd., Essex, UK). All tests were sent by post to the patient and performed in a self-administered testing procedure based on video-assisted guidance.

From March 21 through March 28, self-rated olfactory and gustatory function were recorded on a daily basis using a visual analog scale ranging from 0 (“no smell/taste”) to 10 (“excellent smell/taste”). Similarly, uni- and bilateral nasal airflow were quantified daily using a visual analog scale ranging from 0 (“no airflow”) to 100 (“excellent airflow”). Every second day olfactory, gustatory, and retro-nasal olfactory testing were performed. Long-term chemosensory outcome was measured 8 weeks after symptom onset and 6 weeks after subjective recovery on May 12.

Ortho- and retro-nasal olfactory function objectively decreased, but no subjective complaints of nasal congestion were noted during the initial onset of anosmia. Follow-up testing revealed an increase in subjective and objective test scores during the next 7 days (Table 1). Long-term testing revealed full recovery of olfactory, gustatory, and retro-nasal olfactory function within the normative range.

Discussion

Our results suggest that otherwise asymptomatic patients infected with SARS-CoV-2 report their olfactory (dys-)function correctly; thus, self-perceived olfactory impairments may be a concomitant symptom of COVID-19 infection. We also found that these impairments are reversible, as both subjective and objective results improved during the first 2 weeks after symptom onset and fully recovered within the long-term follow-up period of 2 months. These findings support previous reports that
OD is common in mild to moderate COVID-19 cases and may serve as a potential marker in otherwise asymptomatic and healthy young patients [7–9]. The pathophysiology can only be speculated on, however, previous studies suggested that SARS-CoV-2 might impair olfactory function through targeting of olfactory epithelium (OE)-supporting cells (such as sustentacular or microvillar cells). These cells express both the angiotensin-converting enzyme 2 and the transmembrane protease, serine 2, which are both believed to be crucial for SARS-CoV-2 cell entry [10]. Therefore, the observed chemosensory dysfunction might be related primarily to the local peripheral inflammation. The suspected local inflammation within the OE might also explain OD without nasal congestion as the main symptom in SARS-CoV-2 patients. By way of contrast, the common (long-lasting) postinfectious smell loss is believed to be the result of a direct damage to olfactory receptor neurons within the OE. Regarding recovery rates, COVID-19-associated smell loss seems to resolve spontaneously within a short timeframe of a few weeks in the majority of cases [11]. Noteworthy, although recovery rates for patients with common postinfectious smell loss have been reported previously, these data refer only to those with long-lasting smell loss (i.e., months) [12, 13]. The percentage of patients in whom an acute non-COVID-associated postinfectious OD only persists for a short period of time is currently still unknown.

Furthermore, radiological studies of SARS-CoV-2 patients with OD also revealed alterations to the olfactory bulb, hence a central involvement cannot be ruled out at this point [14, 15]. Indeed, a recent study comparing olfactory function of patients with COVID-19-associated smell loss and common postinfectious OD revealed that results from odor identification and discrimination testing were significantly lower in those with COVID-19-associated smell loss compared to those with common postinfectious OD. Moreover, the authors found that odor identification test results (compared to discrimination and threshold test results) were most sensitive to discriminate between the above-mentioned entities. The authors hypothesized that this difference might be explained by an involvement of central structures related to the sense of smell [16]. The epidemiological characteristics of patients with COVID-19 and postinfectious OD have also been summarized previously [17]. The authors found a female predominance in both COVID-19 and postinfectious OD patients. Similarly, older age was also associated with both entities. Based on these findings, the authors hypothesized that the pathomechanisms might be similar. Nonetheless, they also mentioned that histological studies of the OE are necessary to further elucidate the role of SARS-CoV-2 in smell loss.

Regarding gustatory function, a validated test for sweet, salty, sour, and bitter taste in a self-administered testing procedure based on video-assisted guidance revealed an impaired sense of taste, which recovered within the same period compared to olfactory function. This finding was not surprising, since gustatory dysfunction has also been reported previously in patients with OD [16, 18, 19]. Interestingly, self-reported gustatory function was initially not impaired and showed no relevant changes within the follow-up period. This finding might be explained by the difficulty of patients to self-evaluate gustatory function, since true taste problems are often mistaken for flavor-related deficits [20]. Therefore, validated smell and taste tests are indispensable and should always be incorporated into routine clinical practice.

**Conclusion**

Care should be taken not to overlook the symptom of smell loss in otherwise asymptomatic COVID-19 patients, and awareness needs to be raised within the general population and among healthcare personnel worldwide about these potential markers of SARS-CoV-2 infection. Further studies are needed to evaluate chemosensory function and incidence of recovery in patients with SARS-CoV-2.

**Statement of Ethics**

This case report was conducted in accordance with the World Medical Association Declaration of Helsinki. Written informed consent to publish this case report was given by the patient.

**Conflict of Interest Statement**

The authors have no conflicts of interest to declare.

**Funding Sources**

No funding was obtained for this case report.

**Author Contributions**

D.T. Liu, B. Prem: data collection. D.T. Liu, G. Besser, B. Renner, C.A. Mueller: analysis of results. D.T. Liu, B. Prem, G. Besser, B. Renner, C.A. Mueller: writing of the manuscript. D.T. Liu, B. Prem, G. Besser, B. Renner, C.A. Mueller: critical review of all contents.
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