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Loss of smell or taste as the only symptom of COVID-19

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BACKGROUND

Olfactory and taste disorders (OTDs) have recently been reported among patients with COVID-19, and it has been hypothesised that oral and nasal tissues may contain host cells of SARS-CoV-2. We report on two cases (spouses) with SARS-CoV-2 infection with self-reported OTDs, but otherwise no typical respiratory symptoms of COVID-19.

CASE PRESENTATION

A man in his nineties (index patient) had respiratory symptoms and dysgeusia, and was diagnosed with COVID-19. His daughter-in-law and son had no respiratory COVID-19 symptoms. However, they experienced complete loss of smell and taste, respectively, 7 and 10 days after their first close contact with the index patient. Both tested positive for SARS-CoV-2 RNA.

INTERPRETATION

Our case histories support recent reports hypothesising that anosmia and ageusia may be the only symptoms of SARS-CoV-2 infection, and that SARS-CoV-2 may infect oral and nasal tissues. Together, these findings may inform future research, diagnosis, prevention and treatment of COVID-19.

A married couple noticed that the wife lost her sense of smell and the husband his sense of taste a few days after being in close contact with a person with COVID-19. They had no other symptoms, but both were found to be infected with SARS-CoV-2.

A woman in her sixties was making waffles and was surprised to find that she was unable to smell their appetising aroma as they cooked. Her father-in-law had been hospitalised with COVID-19, and she had been in close contact with him 17 days previously. She had noticed via the media that loss of sense of smell (anosmia) could be a symptom. She was previously healthy and had never experienced disturbances of smell or taste or nasal and sinus symptoms, and she used no regular medication. She did not have fever, sore throat, cough or shortness of breath. Upon further thought, she concluded that the anosmia had been present for ten days. This, combined with close contact with a confirmed COVID-19 case and her status as a healthcare worker, resulted in her being tested. The test was positive for SARS-CoV-2-RNA. The patient experienced no symptoms other than total anosmia, and both her sense of taste and appetite were unchanged. Sixteen days after the disappearance of her sense of smell, the patient was able to detect the scent of a deodorant.

The patient's husband, also in his sixties, experienced complete loss of sense of taste (ageusia) for nine days. He had been in contact with his father ten and seven days before onset of symptoms, in addition to contact with his wife. He had no cough, sore throat or respiratory symptoms, and both his sense of smell and appetite were unchanged. He had previously undergone Billroth II surgery for gastric ulcers. With regard to regular medication, he used esomeprazole 40 mg daily for oesophagitis, rivaroxaban 20 mg daily for atrial fibrillation and vitamin B_{12} injections (1 mg) every 6 weeks as replacement therapy. He too had never previously had disturbances of smell or taste, or nasal/sinus symptoms. As he had been in close contact with two confirmed cases of COVID-19, and had total ageusia, he was tested for SARS-CoV-2-RNA. The result was positive. On the tenth day, he could detect the sweet and sour flavour of strawberries, and after 13 days the taste of a good meat and vegetable stew (umami).

Further questioning revealed that the father/father-in-law, who is in his nineties, had also experienced altered sense of taste (dysgeusia). Bread tasted like cardboard, and sweet food and drinks, which he normally enjoyed, tasted far too sweet. He also reported reduced appetite. These symptoms had manifested themselves after symptom onset and after he tested positive for SARS-CoV-2, but precisely when is uncertain. He also had shortness of breath, cough and fever.

The samples from all the patients were analysed for SARS-CoV-2 RNA (E gene) at the Department of Microbiology, Vestfold Hospital Trust, using in-house reverse transcription polymerase chain reaction in accordance with the recommended method (1). The samples were taken (with Transwab) from oropharynx and nasopharynx (father/father-in-law and daughter-in-law) or only nasopharynx (son) on days 5, 11 and 9 after symptom onset, respectively. These were positive with Ct values of 16.8, 20.7 and 30.5, respectively (increasing values with decreasing virus concentration). Based on data from local validation of the analysis, the Ct values indicate that the number of viral RNA copies per microlitre in the samples varied from approximately $2 \cdot 10^6$ in the father to 75 in the son.

Discussion

The government's strategy to combat the outbreak of COVID-19 in Norway is based on each infected person infecting a maximum of one other person (2). It is therefore important to identify as many infected people as possible and to isolate them until they have been free of symptoms for one week (3). Modelling of the spread of the virus based on clinical data from China indicates that persons with few or no symptoms can be carriers of SARS-CoV-2 (4). It is therefore also meaningful to identify these persons. Criteria for testing for SARS-CoV-2 in Norway as of 1 April 2020 are acute respiratory infection with fever, cough or shortness of breath in selected groups, including healthcare personnel, who may also be considered for

testing if they have milder acute respiratory symptoms (5). Similarly, the criterion *acute respiratory illness* is used in the World Health Organization's case definition (6, 7). Persons with acute respiratory infection who are not encompassed by the criteria for testing are recommended to remain at home until they have been symptom-free for 24 hours (8). However, this advice does not include persons who have anosmia or ageusia as their only symptom. Our case studies indicate that such persons may constitute sources of infection that currently slip under the radar.

INTERNATIONAL EXPERIENCES

A research group in Milan recently published a cross-sectional study on the prevalence of disturbances of smell and taste in 59 SARS-CoV-2-positive hospitalised patients. The study showed that 34 % had this type of disturbance, 20 % before and 14 % after hospitalisation (9). The media have also reported clinical experiences indicating that anosmia and ageusia may be common symptoms in otherwise mild cases of COVID-19 (10, 11). Hendrik Streeck, a German professor of virology, recently stated in the Frankfurter Allgemeine Zeitung newspaper that at least two-thirds of all those infected (n > 100 who were not admitted to hospital) describe a loss of smell and taste (10).

Professor Claire Hopkins, president of the British Association of Otorhinolaryngology, emphasises that these symptoms have been observed in infected persons without other classic symptoms in the UK, USA, France and Northern Italy (11). She expresses concern that these individuals may be hidden carriers and spreaders of the virus, and recommends that persons with these symptoms should isolate themselves for at least seven days (11). Similarly, American otorhinolaryngologists have proposed that anosmia, hyposmia and dysgeusia in the absence of other explanatory conditions be placed on the list of symptoms that should give rise to suspicion of COVID-19, and that testing and isolation should be considered (12).

ACE2 RECEPTORS IN NASAL AND ORAL MUCOSA

Peng Zhou et al. identified and characterised the novel coronavirus (SARS-CoV-2) in the journal *Nature* on 3 February 2020 (13). The authors also confirmed that SARS-CoV-2 used the same receptor, angiotensin converting enzyme 2 (ACE2), as SARS-CoV to enter the cell. In a report that has not yet been peer-reviewed, it is claimed that the number and proportion of ACE2-expressing cells in nasal and oral tissue are comparable to the corresponding cells in lung tissue and in the colon (14, 15), and the authors wonder whether nasal and oral tissue may be the first to be infected by SARS-CoV-2 (14). These results are partly supported by another publication that showed that the ACE2 receptor was expressed on oral mucosa, especially on the epithelial cells of the tongue (16). In the latter, non-peer-reviewed report, it is claimed that olfactory epithelial support cells, stem cells, and nasal respiratory epithelium express two genes that are involved in the transport of SARS-CoV-2 into the cell, namely *ACE2* and *TMPRSS2*, and that these may be potential mechanisms whereby SARS-CoV-2 infection can lead to anosmia (17).

CONCLUSION

An increasing volume of empirical data and some publications point to disturbances of smell and taste as possible symptoms of COVID-19, independent of or alongside classic symptoms. Limited data indicate that SARS-CoV-2 can infect oral and nasal mucosa. Our case reports show that patients with SARS-CoV-2 infection may have loss of taste or smell as the only symptom. In sum, these provisional findings may influence future research, diagnosis, prevention and treatment of COVID-19. National and international health authorities should consider whether isolated disturbances of smell and/or taste are a sufficient basis for testing for COVID-19 and/or isolation to limit spread of the infection.

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