

## Olfactory Dysfunction in COVID-19

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Since February 2020, the COVID-19 outbreak has spread rapidly in Northern Italy, determining an immediate rise in case numbers that have been accompanied by an unprecedented public health action. Due to the continuous admissions of patients with SARS-CoV-2 infection at San Gerardo Hospital in Monza, our ear, nose, and throat team visited a large number of patients with SARS-CoV-2 infection and noted a high frequency of presenting olfactory dysfunctions. In this cohort of patients, we observed the following: (1) anosmia or hyposmia usually occurred after fever but could also occur isolated (ie, without any systemic symptom); (2) most patients were young; and (3) there were no sex differences. The early outcome (from 1 to 3 weeks of follow-up) showed absence or only partial recovery. Due to the current health emergency, we reported our first clinical observations informally, as it was not possible to systematically collect and analyze the data. Awareness of this neglected association may be of great help in clinical practice, allowing one to promptly identify patients without respiratory symptoms who could nonetheless inadvertently spread the disease or subsequently worsen into a frank acute respiratory syndrome.

Anosmia or hyposmia could be explained by the neurotropism of SARS-CoV-2.<sup>1,2</sup> Given available evidence on the evolutionary related SARS-CoV, Li et al suggested that the neurologic damage may play a role in the development of acute respiratory failure as well as other neurologic symptoms of COVID-19, such as headache, nausea, and vomiting.<sup>1</sup> The brain dissemination may occur via circulation and/or a nasal transcribrial route. This latter pathway may explain the frequently observed smell alterations.

In fact, transient secondary olfactory dysfunction after upper respiratory tract infection is common, with reported incidences between 38%<sup>3</sup> and 50%.<sup>4</sup> The most common pathogens include viruses such those causing common cold and human influenza, rarely human coronavirus.<sup>5</sup> Considering the large number of patients with COVID-19 presenting anosmia or hyposmia, we presumed that the incidence of postinfectious olfactory dysfunctions could be higher and clinically more relevant in these patients. In light of this, anosmia or hyposmia should promptly trigger suspected COVID-19 for general practitioners during this current epidemic phase. Further studies

are needed to quantify this early clinical evidence and to disentangle the long-term evolution.

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## Acute Parotitis: A Possible Precocious Clinical Manifestation of SARS-CoV-2 Infection?

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Manifestations of coronavirus disease 2019 (COVID-19), resulting from primary infection by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), include fever, cough, dyspnea, myalgia, headache, and diarrhea. Rhinorrhea and sore throat are also reported<sup>1</sup> as olfactory impairment.

Transmission occurs through mucosal inoculation of infected droplets or direct contact from symptomatic or asymptomatic carriers.

Diagnosis is performed by reverse transcriptase real-time polymerase chain reaction (RT-PCR) of nasopharyngeal or oropharyngeal swabs (NPS). However, SARS-CoV-2 can be found at high viral loads in saliva specimens.<sup>2</sup> Given the high diagnostic concordance between nasopharyngeal and saliva specimens in detecting respiratory viruses, including coronaviruses, and considering that coronaviruses can be found in saliva specimens but not in nasopharyngeal aspirates,<sup>3</sup> To et al<sup>4</sup> tested SARS-CoV-2 in saliva samples from 12 patients: all but 1 were positive with a decreasing viral load trend.

A SARS-CoV-2 tropism for the epithelial salivary ducts cells was described in rhesus macaques.<sup>5</sup> This suggests the possibility of SARS-CoV-2 salivary infection, although its detection in saliva may be partially related to the contribution, in this milieu, of secretions from the nasopharynx or the lower airways.<sup>4</sup>

We describe a patient who was SARS-CoV-2 positive whose first clinical manifestation was an acute nonsuppurative parotitis.

In an Italian familiar cluster of infection under quarantine in Switzerland from March 9 (mother and 1 brother with asymptomatic COVID-19, another brother with mild symptoms, all with a positive RT-PCR NPS result), a previously healthy 26-year-old man developed left painful parotid swelling on the same day. Fever (maximum, 38 °C) and myalgia occurred (March 10-11). The patient slowly improved with complete recovery (March 13). Hyposmia and ageusia were self-reported (March 16).

Clinically, a discrete swelling of the left parotid gland was found without purulent discharge after parotid massage. Blood assays revealed a mild increase in reactive C-protein (8.9 mg/L), while the white blood cell count and formula were normal. Cytomegalovirus and paramyxovirus antibodies were negative, except for IgG-paramyxovirus (300 kAU/L). Ultrasonography showed an enlarged and diffuse hypoechoic parotid gland structure, with increased vascularization on color Doppler; no salivary duct enlargement or stones were identified. Traditional SARS-CoV-2 RT-PCR testing on NPS yielded negative results, while a rapid immunochromatographic test (PRIMA Lab SA) was weakly positive for SARS-CoV-2 IgG and negative for IgM (April 1).

Although we could not document SARS-CoV-2 RNA in the saliva, we believe that acute nonsuppurative parotitis should be considered a possible manifestation of the COVID-19 disease spectrum.

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