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## Journal Pre-proofs

COVID-19 and Anosmia in Tehran, Iran

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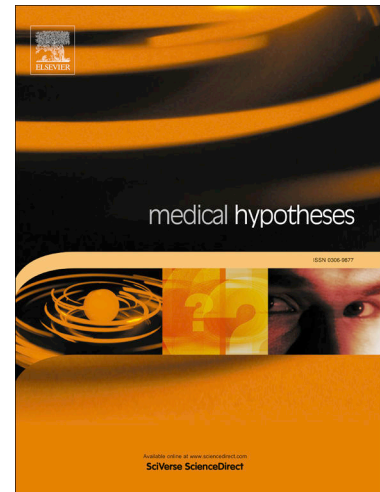
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Summary

Patients with acute olfactory disorders typically present to the otolaryngologist with both acute hyposmia and less often with anosmia. With the onset of COVID-19 we have noticed an increase in the number of patients who have presented with new onset of complete smell loss to the senior author's practice in Tehran, Iran. This anosmia and the frequency with which patients present is highly unusual. Coronaviruses have been known to cause common cold symptoms. COVID-19 infections have been described as causing more severe respiratory infections and the symptoms reported by authors from Wuhan, China have not specifically included anosmia. We describe patients who have presented during a two-week period of the COVID-19 pandemic with complete loss of sense of smell. Most had either no symptoms or mild respiratory symptoms. Many had a normal otolaryngologic exam. A relationship between COVID-19 and anosmia should be considered during the pandemic. We hypothesize that the mechanism of injury is similar to that of other coronavirus infections that cause central and peripheral neurologic deficits.

#### Key words

Anosmia, smell, COVID-19, adult, virus, respiratory, pandemic, hyposmia, central nervous system, olfactory bulb, coronavirus, ageusia

#### Introduction

In the head and neck area, coronaviruses have traditionally caused illnesses that are mild and along the spectrum of symptoms expected with the common cold.<sup>1</sup> The coronavirus was first cultivated by Tyrell and Bynoe in patients with the common cold in 1966.<sup>2</sup> The alpha coronaviruses typically cause asymptomatic or mildly symptomatic infections.<sup>3</sup> However, the beta coronaviruses (the group which includes SARS-CoV-2), cause severe respiratory disease and fatalities.<sup>3</sup> In the case of SARS-CoV-2, the coronavirus related disease has been named COVID-19. Symptoms at the onset of COVID-19 infection in hospitalized patients in China include fever, cough, fatigue,<sup>4</sup> myalgia, sputum production, dyspnea, oppression in the chest, diarrhea, headache, anorexia, chest pain, sore throat, dizziness, palpitations and vomiting.<sup>5</sup>

Although coronaviruses are known to cause the common cold and olfactory loss is known to be associated with the common cold,<sup>6</sup> the initial reports from China did not include anosmia as one of the possible presenting symptoms of COVID-19. A short communication from Italy reported a possible association between COVID-19 and anosmia.<sup>7</sup> A 2004 study from Japan evaluated 24 patients who presented over a four-year period with sudden onset of smell loss and had a normal exam of the nose. Ten of those patients were evaluated with viral analysis. Only one patient tested positive for human coronavirus 229E.<sup>1</sup> Of the ten patients the most common cause of post viral olfactory loss was human rhinovirus, followed by Epstein Barr virus. One patient out of the ten had anosmia and one had dysosmia. The remainder had hyposmia.<sup>1</sup>

In terms of prevalence of smell disorders, up to 10.6 percent of the population self-report a problem with smell or taste during a 12 month period.<sup>8</sup> The olfactory sensory neurons are bipolar and are directly exposed to the environment, which can result in damage from toxic, infectious, chemical or inflammatory agents.<sup>9</sup> Coronaviruses are known to cause respiratory, neurologic, gastrointestinal and hepatic diseases of varying severity in humans and animals.<sup>10</sup> Beta coronaviruses are known to cause encephalomyelitis in pigs and encephalitis and chronic demyelination in the mouse and rat.<sup>11</sup>

With the recent pandemic of COVID-19, patients reporting anosmia of recent and sudden onset have been more frequent in the senior author's office in Tehran, Iran. We present these cases as the history of these patients is atypical and the anosmia with which they present is unusual and the frequency with which we have seen anosmia over a two-week period is unusual. Early screening of patients with reports of acute anosmia and testing for COVID-19 may help identify patients who are infected who otherwise would be missed.

## Methods

This is a retrospective review of 8 patients who presented with sudden onset olfactory loss between March 11 and April 1, 2020. Five patients were tested for COVID-19. Because of restrictions on visits to clinics and hospitals during the epidemic, not all patients were examined in the office. Five of them were examined by free virtual consultation and telemedicine. Due to constraints on testing availability, not all patients had COVID-19 testing, particularly as some reported no other respiratory symptoms or only mild symptoms, thus precluding them from testing. All patients described complete anosmia affecting their taste, so there was no need to do smell testing due to limitations imposed by COVID-19 pandemic.

## Results

Patient 1 was a 39-year-old male radiologist who presented with the sudden onset of fever progressing to respiratory symptoms and no anosmia initially. COVID-19 was positive. He was self-isolated. He later required an ICU stay. He reported anosmia 4 days after the onset of fever.

Patient 2 was a 28-year-old female with a history of rhinoplasty 1 year prior who called the office during the COVID-19 pandemic to report sudden olfactory loss and a very mild upper respiratory illness. She described complete ageusia.

Patient 3 was a 38-year-old female who was post rhinoplasty 13 years prior. She called the office and reported a 10-day history of complete loss of sense of smell and taste. She described fever and malaise two days before anosmia. She was not tested for COVID-19.

Patient 4 was a 22-year-old female with a history of rhinoplasty 1.5 years ago who presented with new anosmia. She reported anosmia 3 days after the onset of fever. She was not tested for COVID-19.

Patient 5 was a 35-year-old female with the anosmia 2 days after the onset of dyspnea. She initially visited the pulmonary specialist for dyspnea and later consulted with otolaryngology for anosmia. She was COVID-19 positive.

Patient 6 was a 44-year-old female physician who presented with anosmia 3 days after onset of fever and malaise. Her COVID-19 test was positive.

Patient 7 was a 39-year-old man. He was a friend of patient 3 who presented with anosmia. He reported anosmia two days after fever and mild respiratory symptoms. He was COVID-19 positive.

Patient 8 was a 38-year-old female. She was spouse of patient number 7 who presented with mild fever and anosmia. She was also COVID-19 positive.

## Discussion

Viruses have been known to cause smell loss and presentation to the otolaryngologist has been previously described in a paper from Japan<sup>1</sup>. According to that experience from January 2001 to December 2004, a total of 24 patients presented with sudden onset of viral anosmia over a 4-year period. This presentation frequency is consistent with the frequency with which we saw acute viral olfactory disorders in our offices in the past. In contrast, our case series presents 8 patients during a two-week period of the COVID-19 pandemic. Five patients out of eight were tested for COVID-19. The other three have not been able to be tested given the limitations of testing during the pandemic. Additionally, the majority of patients had atypical histories-- they either had no symptoms or mild respiratory symptoms, and the smell loss is complete. In the previous study of acute viral olfactory change, the majority of patients had hyposmia. Only one had anosmia and the other had dysosmia.<sup>1</sup> In our case series all presented with anosmia and many had the sensation of loss of sense of taste. Lastly, in the previous study, only one patient in 10 had coronavirus 229E. In our case series, five out of the 8 were tested and were positive for COVID-19.

Given the COVID-19 pandemic and the current limitations during this time it is not possible to test every patient with a fever nor do the guidelines, in this rapidly evolving pandemic, typically include testing for those with anosmia. Also, with the use of telemedicine and video visits, it is not possible to perform nasal endoscopy on every patient. Many otolaryngologists have either closed offices or have limited office hours, or have been assigned to take care of acutely ill COVID-19 patients who need critical or ICU care—as is especially the case in Iran. Because the caseload of patients with routine otolaryngologic complaints is reduced during this time, the frequency with which anosmia is presenting is even more unusual.

Sudden and complete losses of sensory function in the head and neck area have been previously described for sudden hearing loss with a seasonal preponderance, suggesting an infectious etiology.<sup>12</sup> Seasonal variation of presentation of smell disorders has not been described. The authors conclude that this presentation of anosmia is most likely related to the COVID-19 pandemic.

Given the mammalian history of encephalitis, encephalomyelitis and chronic demyelination that is possible with coronaviruses,<sup>11</sup> serious consideration should be given to asking about the loss of sense of smell in any patient who is suspected of having COVID-19. Also, any patient with anosmia during the COVID-19 pandemic should be ruled out for this viral disease. Future studies could explore viral analysis in patients with acute smell loss during the pandemic of COVID-19.

## Conclusions

The mechanism of injury for anosmia patients in a COVID-19 pandemic may be similar to that of other central and peripheral neurologic disturbances previously described for coronaviruses. Further investigation of anosmia in patients who test positive for COVID-19 may help elucidate the mechanism of injury.

## Funding and Disclosures

None

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#### Supplemental Materials

None

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