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Paranasal sinuses computed tomography findings in anosmia of COVID-19

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ABSTRACT

Objective: Olfactory dysfunction in coronavirus disease-2019 (COVID-19) is poorly understood. Thus, mechanistic data are needed to elucidate the pathophysiological drivers of anosmia of COVID-19.
Methods: We performed the current study in patients who presented with anosmia and COVID-19 as documented by the polymerase chain reaction (PCR) assay between April 1st and May 15st, 2020. We assessed for the conductive causes of anosmia with computed tomography (CT) of paranasal sinuses.
Results: 49 patients who presented with anosmia and positive PCR assay for COVID-19 were included. The average age was 45 ± 12.2 years. Complete anosmia was present in 85.7% of patients and 91.8% of patients reported sudden onset of olfactory dysfunction. Taste disturbance was common (75.5%). There were no significant pathological changes in the paranasal sinuses on CT scans. Olfactory cleft and ethmoid sinuses appeared normal while in other sinuses, partial opacification was detected only in some cases.
Conclusion: We did not find significant mucosal changes or olfactory cleft abnormality on CT imaging in patients with anosmia of COVID-19. Conductive causes of anosmia (i.e., mucosal disease) do not seem play a significant role in anosmia of COVID-19.

1. Introduction

COVID-19, first detected in Wuhan, China in December 2019, fast spread across the globe, causing a pandemic affecting many countries around the world. The main manifestations of COVID-19 include fever, dry cough and dyspnea. Additionally, other manifestations such as constitutive, gastrointestinal or neurologic symptoms have also been reported, such as fatigue, headache, nausea, vomiting and myalgia [1]. Following several reports of anosmia as a common symptom in COVID-19, the American Academy of Otolaryngology-Head and Neck Surgery and the British Association of Otorhinolaryngology added anosmia and dysgeusia to the list of manifestations mandating screening for COVID-19 [2]. Olfactory dysfunction (loss of smell) includes anosmia (complete loss), hyposmia (partial loss), phantosmia (sensing odors without external stimulant) and parosmia (a change in the usual feeling of odor). Anosmia is the cardinal olfactory symptom in COVID-19. Interestingly, despite SARS-COV-2 and SARS-COV having similarities in genetic sequence, pathogenesis and cellular entry, anosmia has not been reported as a common symptom during the SARS-COV epidemic [3]. Conductive, sensorineural and mixed etiologies constitute the pathogenesis of post -viral anosmia. Sinonasal disease may lead to nasal obstruction, preventing the entry of odorants to the olfactory cleft, thus leading to conductive loss of olfaction. Treatment and outcomes of smell disorder due to conductive loss (mucosal thickening) are different from sensorineural loss. Basic clinical data including detailed history and physical examination are paramount in assessment of anosmia. The physical examination should include a complete ear, nose and throat (ENT) examination, including nasal endoscopy. Nonetheless nasal endoscopy for evaluation of patients with COVID-19 is not recommended due to the risk of virus transmission to health care workers. Therefore, vast majority of studies in anosmia of COVID-19 are based on the symptoms rather than complete ENT examination. This study seeks to assess anosmia and other nasal symptoms in patients with COVID-19. Since the paranasal sinus CT scan is the technique of choice for studying sinonasal structures [4], we considered it as an alternative to nasal endoscopy to determine the causes of anosmia and to evaluate mucosal thickening and edema in the nasal vault or olfactory cleft.

2. Methods

This prospective single center cross-sectional study was performed at Masih- Daneshvari hospital a tertiary, referral center in Tehran, Iran.

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The study was approved by the Institutional Review Board of Chronic Respiratory Disease Research Center of Shahid Beheshti University of Medical Sciences, Tehran, Iran. Consecutive patients with anosmia and COVID-19, confirmed by real time PCR assay performed on samples from pharyngeal swabs, who attended the inpatient or outpatient departments of the hospital between April 1st and May 15st 2020 were included. Olfactory function, sinonasal symptoms and altered taste were evaluated subjectively by filling out questionnaires. Subjects less than 18 years of age, pregnant woman and patients with previous history of smell disorder, neurologic problem, nasal surgery and endonasal neurosurgery were excluded. Screening CT scan of paranasal sinus in coronal view (64 -channel, Siemens) was performed for evaluation of conductive causes of anosmia. Lund–Mackay CT scoring system was used to assess the disease of each sinus and osteomeatal complex, which included 0 normal, 1 partial opacity, and 2 total opacities for the sinuses. Mucosal swelling of the olfactory cleft and/or inflammatory signs of the ethmoid sinuses are considered as criteria for obstructive olfactory loss. Data were analyzed by SPSS and reported in percentage, mean and standard deviation (SD).

3. Results

This study included 49 patients with anosmia and COVID-19 confirmed with positive PCR assay. The average age was 45.1 ± 12.2 (range 27–80) years. Relevant background medical issues and habitual history (cigarette and hookah smoking, alcohol and opium addiction) are summarized in Table 1. The most common underlying disease was diabetes mellitus. Complete loss of smell was detected in 42(85.7%) of patients and 45(91.8%) of patients had sudden loss of smell. The time between the onset of COVID-19 and perception of olfactory dysfunction by patients was variable because of a general lack of specific attention given to the symptoms. Taste disturbance was common (75.5%). Other sinonasal findings (rhinorrhea, sneezing, nasal obstruction, purulent discharge, facial fullness and pain, fever, halitosis, headache, ear pain, dental pain, fatigue, and cough) were variably reported and are summarized in Table 1. The most common symptoms accompanying anosmia were fever (83.7%), headache (71.4%), fatigue (63.3%) and cough (63.3%).

Despite a complete lack of olfaction, there were no significant changes in the paranasal sinuses on CT imaging. Involvement of sinuses on CT analysis was as follows: total Lund-Mackay score was 0 in 41 (83.7%) patients, 1 in 3 (6.1%) patients, 2 in 4 (8.2%) patients, and 4 in 1 (2%) patient. There were no abnormalities in cribriform plate, and no mucosal thickening of the olfactory cleft area was detected in any of the cases. A summary of findings on CT imaging is presented in Table 2.

Table 1
Demographic and clinical characteristics of patients with anosmia of COVID-19.

Criteria	Number(%)
Age(Y)	
Range	(27–80)
Mean	45.08 (12.2 SD)
Sex	
Male	27(44.9%)
Female	22(55.1%)
Underlying disease	
Hypothyroidism	5(10.2%)
Diabetes mellitus	13 (26.5%)
Hypertension	10(20.4%)
Asthma	6(12.2%)
Neurologic disease	0(%)
Habitual history	
Cigarette	4(8.2%)
Hookah	9(18.4%)
Alcohol	5(10.2%)
Opium	3(6.1%)
Ent symptom	
Anosmia	42(85.7%)
Hyposmia	7(14.3%)
Rhinorrhea	9(18.4%)
Sneezing	7(14.3%)
Nasal itching	0(%)
Nasal obstruction	16(32.7%)
Purulent discharge	8(16.3%)
Facial fullness	7(14.3%)
Facial pain	12(24.5%)
Fever	41(83.7%)
Halitosis	2(4.1%)
Headache	35(71.4%%)
Ear pain	4(8.2%)
Dental pain	1(2%)
Fatigue	31(63.3%)
Cough	31(63.3%)
Sore throat	22(44.9%)
Dyspnea	32(65.5%)
Fantosmia	16(32.7%)
Dysgeusia	37(75.5%)

Table 2
Lund-Mackay score of paranasal sinuses on CT scan in anosmia of COVID-19.

Site specific number(%)	Right			Left		
	0	1	2	0	1	2
OMC	49(100%)			49(100%)		
Ant ethmoid	49(100%)			49(100%)		
Post ethmoid	49(100%)			49(100%)		
Maxillary sinus	45(91.8%)	4(8.2%)		46(93.8%)	3(6.1%)	
Frontal	46 (93.8%)	3(6.1%)		47(95.9%)	2(4.1%)	
Sphenoid	47(95.9%)	2(4.1%)		48(97.9%)	1(2%)	
Other findings						
Olfactory cleft (Mucosal Swelling, Osteitis, Occupying lesion)				0(%)		
Septal deviation				24 (49%)		
Concha bullosa				27(55.1%)		

4. Discussion

Several clinical features have been reported since the onset of the COVID-19 pandemic, including anosmia [5–7]. Olfactory loss is a symptom that is associated with significantly impaired quality of life. Post-viral olfactory loss is a well-known entity [8–10], which has been explained with different mechanisms such as congestion, secretions, inflammatory changes in the nasal mucosa [10–12] and obstruction in the olfactory cleft or neurogenic invasion/olfactory bulb involvement [10,11]. Accordingly, olfactory disturbance consists of airflow blockage, sensory deficit arising from direct neuroepithelium injury; and neural deficits consist of damage to the olfactory bulb, olfactory tract, or the central olfactory pathway including the prefrontal lobe, septal nuclei, amygdala, and temporal lobe [4].

Inflammation, infection and chemical agents can impact the dendritic processes of the olfactory receptors in the cleft area via inflammatory cytokine release, thus inducing apoptosis in neurons [13]. Coronaviruses are one of the many viruses identified to cause post infection olfactory dysfunction [14,15]. During the COVID-19 pandemic, one of the symptoms attributable to the disease has been anosmia/ageusia, which occurs as an isolated symptom or in combination with other respiratory symptoms [16–18]. Detailed clinical history and imaging (e.g. CT scan and/or magnetic resonance imaging (MRI)) are necessary in assessment of anosmic patients to identify the underling etiology.

In this study, we evaluated the sinonasal symptoms and performed CT scan to assess for a conductive mechanism for anosmia of COVID-19. We did not detect significant mucosal thickening or opacification of sinuses and olfactory area. Thus, our study de-emphasizes the role of

conductive mechanism for anosmia of COVID-19 and implicates other non-conductive mechanisms such as sensory neural olfactory loss as the likely etiology. Anosmia caused by mucosal disease usually has a relatively rapid recovery, but in sensory neural loss the course of anosmia is uncertain and prolonged recovery may be expected. Thus, understanding the mechanism of anosmia is of utmost importance in prognostication and treatment of this symptom.

There has been limited research by imaging in anosmia of COVID-19. Olfactory bulb MRI in a patient presenting with isolated anosmia secondary to COVID-19 revealed normal olfactory bulb volume without abnormal signal intensity. Similar to the present study, no signal for mucosal congestion was detected [19]. In another study, FDG PET/CT scan was performed in a patient with COVID-19-associated anosmia to assess the metabolic activity of the olfactory processing pathways. Hypometabolism of the left orbit-frontal cortex was observed under neutral olfactory condition, suggesting impaired neural function as an underlying cause of anosmia [20].

Nasal epithelial cells exhibit high angiotensin converting 2 (ACE2) receptor expression, thus permitting a route for viral entry [21]. Despite this observation, nasal signs commonly seen in other upper respiratory infections are absent in patients with COVID-19 [2]. Similarly, in the present study, nasal obstruction was reported only in 32.7% and rhinorrhea in 18.4%. It is suggested the non-neuronal cells in olfactory epithelium and not the olfactory neurons are the direct targets of virus in COVID-19 [22]. Indeed, olfactory mucosa express key genes involved in virus entry such as ACE2 receptor and the priming enzyme TMPRSS2 [23] while neither olfactory sensory neurons nor olfactory bulb neurons express these genes. These findings suggest that infection of non-neural cell types in the olfactory epithelium leads to anosmia of COVID-19.

5. Conclusion

To the best of our knowledge, this is the largest study to-date utilizing CT of paranasal sinuses to assess anosmia of COVID-19, providing anatomical details in lieu of nasal endoscopy, which is not routinely performed due to high-risk of COVID-19 transmission. We did not find significant mucosal changes on CT imaging of the paranasal sinuses in patients with anosmia of COVID-19. Since there were no significant mucosal changes detected, utility of therapies such as steroids for treatment of anosmia in this group of patients is questionable. Additional imaging studies are needed to further elucidate the etiology of olfactory loss in COVID-19.

Authorship contributions

Ali Safavi Naeini: concept and design, data collection and analysis and interpretation, writing

Mahboobeh Karimi-Galougahi: concept and design, data collection and analysis and interpretation, writing

Nasim Raad: concept and design, data collection and analysis and interpretation, writing

Jahangir Ghorbani: concept and design, data collection and analysis and interpretation, writing

Ayeh Taraghi: concept and design, data collection and analysis and interpretation, writing

Sara Haseli: data collection and analysis and interpretation

Golfam Mehrparvar: data collection and analysis and interpretation, writing

Mehrdad Bakhshayeshkaram: data collection and analysis and interpretation

Ethics approval

Approved by the Institutional Review Board, Masih Daneshvari Hospital, Tehran, Iran.

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Declaration of competing interest

The authors report no competing interests.

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