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A New Mystery: Phantosmia after COVID-19 Infection

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Abstract: Coronavirus disease 2019 (COVID-19) has developed as a pandemic and has caused millions of deaths worldwide. Multiple studies have implicated anosmia and ageusia as symptoms associated with COVID-19. In this case report we present the cases who suffer from phantosmia after COVID-19 infection. As the prevalence of the virus increases, the symptomatology profile continues to be updated. More studies are needed to better understand this disease.

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Introduction

The 2019 coronavirus disease outbreak (COVID-19) originated in Wuhan, China, and quickly became a global pandemic. COVID-19, also known as coronavirus 2 of acute respiratory syndrome (SARS-CoV-2), infected 116,874,912 people worldwide by March 2021 and caused 2,597,381 deaths. The disease is mainly transmitted through the upper respiratory tract by inhalation of droplets. Patients with COVID-19 may experience cough, shortness of breath, fever, chills, myalgia, headache, new loss of taste or smell, nasal congestion and runny nose, vomiting and diarrhoea. These symptoms can range from mild to severe (Neto et al., 2021).

In May 2020, the Ear, Nose, and Throat Societies warned physicians about olfactory and gustatory disorders that occur before common symptoms develop. Odour and taste disturbances are not uncommon in viral upper respiratory tract infections. They are observed in more than 30% of patients (Dalton, 2004). Some studies have shown that COVID-19 may have an interest or tropism for certain olfactory sensors (Beltrán-Corbellini et al., 2020; Hopkins et al., 2020). The frequency of olfactory and gustatory disturbances ranged from 11 to 86% in COVID-19 positive patients (Lechien et al., 2020; Mao et al., 2020). It usually lasts for a period of 7 to 14 days, in most cases after two weeks (Klopfenstein et al., 2020; Yan et al., 2020). Parosmia is a disorder of the sense of smell. Phantosmia is a term for olfactory hallucinations or ghostly odours that occur in the absence of any odour. We presented two cases of phantosmia after recovery from COVID-19 infection.

Case 1

A 30-year-old female patient presented with one week of phantosmia and described a persistent cigarette tobacco odour. She did not smoke and there were no smokers in her family. She had an COVID-19 infection two months ago. She had no nasal obstruction or rhinitis, and no abnormalities were noted in her nasal or nasopharyngeal mucosa on medical examination. Complete blood count and biochemistry tests were normal. The patient underwent magnetic resonance imaging (MRI) of the brain, with and without contrast, to measure the volume of the olfactory bulb (OBV). Images were acquired with 1.5T MRI with a cranial coil (Philips Ingenia 1.5T, Eindhoven, The Netherlands). T2-weighted images in the coronal plane were obtained as a 1 mm notch at 5 mm slice thickness. The repetition time/time echo was 4833/100 (milliseconds/milliseconds), field of view was 220×183 mm and matrix was 356×209 mm. 22 coronal sections were acquired. Standard OBV measurements were obtained from coronal T2-weighted images. The volumes of the olfactory bulb were 64 mm^3 (left) and 65 mm^3 (right). These values were accepted as normal based on the limits in the study by Buschhüter et al. (2008). There is no abnormal signal intensity on T2 and FLAIR (fluid-attenuated inversion recovery) images at the primary olfactory cortex and visualized olfactory pathways.

Case 2

A 26-year-old female patient presented with one week of phantosmia and described a persistent odour of burnt plastic. She had an COVID-19 infection two months ago. Her otolaryngologic examination was normal except for septal deviation. She has a history of allergic rhinitis and urticaria. Routine laboratory tests were normal limits. SARS-CoV-2 IgM was 1.25 (reference range: 0–0.99) and SARS-CoV-2 IgG was 3.28 (reference range: 0–1.4). This patient underwent MRI like the other patient and was examined by the same radiologist. The volumes of the olfactory bulb were 70 mm^3 (left) and 68 mm^3 (right).

Oxymetazoline hydrochloride nasal spray for 5 days and daily saline nasal irrigation were recommended for both patients. The complaint of the first patient disappeared 4 weeks after admission to the hospital, but the resolution of the second patient's complaint took 12 weeks.

Discussion

Many studies have shown that acute anosmia and ageusia seem to be among the important symptoms and signs for the diagnosis of COVID-19 infection, especially in the early stage of the disease (Lee et al., 2020). Initially, mechanical obstruction due to overproduction of mucus during active infection was thought to be the cause of anosmia. But patients suffering from persistent anosmia with normal acoustic rhinometry after infection suggest a different pathophysiology leading to more permanent damage (Netland et al., 2008).

Viral damage to the olfactory epithelium causes acute onset anosmia or ageusia. Viruses such as influenza A, parainfluenza, herpes viruses, adenoviruses, polioviruses, rabies viruses, and Japanese encephalitis reach the central nervous system via the olfactory nerve (Netland et al., 2008). Studies from the 1960s have shown us that coronaviruses are neuroinvasive and neurotropic. In mouse models, SARS-CoV showed transneuronal access through the olfactory bulb in mice after intranasal inoculation (Netland et al., 2008). Recent studies demonstrated that ACE2 and TMPRSS2 are critical for SARS-CoV and SARS-CoV-2 entry into host cells (Dong et al., 2020). In addition, a recent study has shown that ACE2 and TMPRSS2 are found in nasal respiratory tissue, olfactory neuroepithelium, central nervous system and lymphoid tissues (Fodoulian et al., 2020). This information supports the occurrence of neurologic symptoms such as headache, nausea, and vomiting in some patients with COVID-19.

Phantom odour perception is an olfactory disorder in which people perceive an odour in the absence of a stimulus. While perceived odours vary from person to person, they are usually described as burnt bread, metallic or chemical odours.

Phantosmia has been documented in various conditions such as chronic rhinosinusitis, viral upper respiratory tract infections, intracranial hemorrhage, tumours, epilepsy, psychiatric disorders, Parkinson's disease, radiation therapy, and head trauma. In most cases, however, phantosmia has no identifiable origin and is diagnosed as idiopathic phantosmia (Morosanu et al., 2020). The cause of phantosmia is not fully understood.

The phantom sense of smell may be caused by a neuronal signal imbalance that causes non-sensory olfactory signals to achieve the central nervous system. The sense of smell may arise from the peripheral nervous system at the level of olfactory sensory neurons or may arise from the central brain. Also it may be due to damage to the olfactory nerve (Patel and Pinto, 2014). Many viruses can cause parosmia and phantosmia, either as part of the first deficit or when the nerves make abnormal connections as they try to heal. Based on this information, we can say that COVID-19 virus causes olfactory phantosmia with a mechanism similar to other viruses.

Diagnostic work-up should start a standard head and neck examination. Nasal endoscopy is indicated to examine the olfactory pathways in the nose. A dental examination should be included for the oral diseases that may produce a foul odour. At the same time, magnetic resonance imaging should be the modality of choice to rule out neoplasm, cerebrovascular or sinus disease and malignancies.

MRI is of great importance in demonstrating olfactory bulb abnormalities in patients with olfactory dysfunction after trauma and upper respiratory tract infection. Findings may indicate that olfactory deficiency both after trauma and after upper respiratory tract infection causes decreased sensory input in olfactory bulbs, leading to structural changes at the bulbus level and formation of parosmia. As correlational analyses show, olfactory bulb volumes decrease in parallel with olfactory function. Therefore, damage to peripheral olfactory structures was associated with the presence of olfactory dysfunction and reduced olfactory bulb volumes (Cummings et al., 1997). Therefore, we looked at the changes in olfactory bulb volume in our patients with MRI, but we could not find a significant change.

The treatment of phantosmia can be divided into medical treatment and surgical methods, and treatment is determined by the underlying cause, which is usually determined by the diagnostic workup.

Our article has several limitations. First, only two cases were presented in this study. Second, a formal quantitative chemosensory test was lacking. The olfactory problem is not precisely diagnosed neither by objective (olfactometry, rhinomanometry) nor by subjective examination (sniffing test). We performed only MRI examination for rolling out the other pathologies. We diagnosed phantosmia based on the patients' medical history. Phantosmia related with COVID-19 is an interesting topic that could be explored in further studies.

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