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Persistent smell and taste disorders following COVID-19 vaccination: A report of three cases and review of the literature

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Abstract

Persistent smell and taste disorders following COVID-19 vaccination are rare adverse effects. Herein, we reported three cases in which patients developed smell and taste disorders 9 – 20 days after receiving their second dose of the AstraZeneca/Oxford COVID-19 vaccine in 2021. These symptoms persisted for 1 – 3 years. All patients underwent nasal endoscopy, imaging of the nasal and olfactory structures, as well as Sniffin' Odor along with flavor and taste identification tests. Case 1 was a 37-year-old male who presented in December 2022 with persistent dysgeusia for 18 months. Case 2 was a 40-year-old male who presented in February 2023 with persistent anosmia and parosmia for 20 months. Case 3 was a 48-year-old male who presented in August 2024 with persistent hyposmia for 3 years. These persistent disorders may be due to immune responses triggered by the vaccine, potentially affecting the olfactory neuroepithelium. Recognition and reporting of such adverse effects are important to acknowledge among physicians and for future studies and treatment trials targeting related disorders.

Keywords: COVID-19 vaccine; Anosmia; Ageusia; Parosmia; Dysgeusia

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1. Introduction

Several vaccines were rapidly developed and approved to combat COVID-19 in the early stages of the pandemic. The common and worldwide distributed vaccines included Pfizer-BioNTech, Moderna, AstraZeneca/Oxford, and Johnson and Johnson (J and J or Janssen). The Pfizer-BioNTech and Moderna vaccines are messenger RNA (mRNA) delivered to host cells to express the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike protein, which is used by the virus to gain entry into host cells. In contrast, the AstraZeneca/Oxford and Janssen vaccines are viral vectors encoding the SARS-CoV-2 spike protein. The expression or delivery of spike protein into the host cells by the vaccines will elicit an immune response, production of antibodies against the spike protein, activation of T-cells, and generation of memory cells to combat future SARS-CoV-2 infection, thereby preventing viral manifestations or decreasing their severity and duration.

Several studies have documented the significant contribution of COVID-19 vaccines in the reduction of morbidity and mortality.[1] However, as with other vaccines, adverse

effects have been reported. Common adverse effects such as fever, fatigue, muscle soreness, malaise, chills, arthritis, and headache occur more frequently than the otolaryngological ear, nose, and throat (ENT) effects, which include anosmia/hyposmia, ageusia/hypogeusia, parosmia, phantosmia, and dysgeusia. According to the COVID-19 vaccine analysis report released in the UK, there were 70 cases of anosmia, 58 parosmia, and six hyposmia out of the 100,809 recipients of the Pfizer-BioNTech vaccine;[2] 802 cases of anosmia, parosmia, and hyposmia among 25 million recipients of the AstraZeneca/Oxford vaccine; and 402 cases of parosmia were recorded among 842,270 recipients of the AstraZeneca vaccine.[3] Studies have suggested a higher incidence of ENT adverse effects with mRNA vaccines compared to viral vector vaccines (78.3% vs. 70.4%, p=0.064), while systemic adverse effects were more common with viral vector vaccines (87.2% vs. 61%, p=0.001).[4] Some studies reported a higher frequency of ENT adverse effects with the Oxford-Pfizer-BioNTech (BNT162b2) vaccine than with the Moderna COVID-19 vaccine (mRNA-1273) (Ageusia: 0.755% versus 0.608%, p=0.001; Dysgeusia: 0.681% versus 0.486, p=0.001).[5] Most of these reports estimated that the time elapsed from administration of the COVID-19 vaccine to the development of smell and taste disorders ranged from 1 to 20 days (mainly 1 – 9 days). They also reported favorable outcomes with complete resolution of manifestations within 4 – 8 weeks.[4,5] However, to date, there are six published case reports of long-term or persistent smell and taste disorders.[6-11]

Herein, we reported three Egyptian cases with post-COVID-19 vaccine olfactory and gustatory disorders. Vaccination was obligatory in their workplace. Smell and taste disorders developed within days following administration of the second dose of the AstraZeneca/Oxford vaccine in 2021. In some cases, these disorders persisted for years. Repeated nasal swabs and polymerase chain reaction (PCR) tests for SARS-CoV-2 were negative at symptom onset, excluding the possibility of COVID-19 infection. There was no history of comorbid medical, neurological, or other conditions that might cause smell and taste disorders, such as allergies, infections, sinusitis, trauma, dry mouth, medications, and specific treatments. Multiple ENT consultations were performed. Nasal endoscopy, computed tomography of the nasal cavities, anterior cranial fossa, and sinuses, and magnetic resonance imaging (MRI) of the brain, including olfactory bulbs and tracts, revealed no abnormalities. They presented to the ENT outpatient clinic because of persistent disorders lasting several years after the initial onset. Clinical evaluation at the presentation included neurological evaluation and objective testing of olfactory and gustatory function using Sniffin' Odor' identification test (SOIT), taste, and flavor identification tests, as previously described.[12,13]

2. Case presentation

2.1. Case 1

A 37-year-old male developed anosmia and ageusia 9 – 10 days after receiving the second dose of the AstraZeneca/Oxford vaccine (June 2021, administered in Egypt). No systemic manifestations were reported after vaccination. After 3 months, parosmia and dysgeusia (described as smoked or burned-out smell and taste) developed and resulted in weight loss, depression, and insomnia. Improvement in smell and taste were reported several months after onset, along with resolution of parosmia. Past medical history included a confirmed COVID-19 infection in May 2020, verified by a positive PCR test for SARS-CoV-2. Viral manifestations included fever, fatigue, cough, expectoration, and loss of smell and taste, all of which resolved completely within 30 days. Presentation in December 2022 was due to persistent severe dysgeusia for 18 months. Sniffin'odor, flavor, and taste identification tests revealed intact smell, flavor, and taste sensations.

2.2. Case 2

A 40-year-old male developed anosmia 20 days after receiving the second dose of the AstraZeneca/Oxford vaccine (June 2021, administered in Saudi Arabia). Parosmia (described as a rotten odor) developed 4 months later. No systemic manifestations were reported after vaccination. Initial treatment included local steroids and vitamin B complex. No history of prior COVID-19 infection was documented. Only minimal improvement in olfactory function was reported over the past 2 years. Presentation in February 2023 was due to persistent anosmia and severe parosmia for 20 months. The SOIT score showed anosmia with a result of 4 out of 16. Both flavor and taste sensations remained intact.

2.3. Case 3

A 48-year-old male developed anosmia 10 days after receiving the second dose of the AstraZeneca/Oxford vaccine (August 2021, administered in Kuwait). A history of myalgia and fatigue after vaccination was reported, which resolved completely within 1 week. Two previous episodes of COVID-19 infection were documented. The first episode occurred in February 2020 and was manifested by fever, flu-like symptoms, myalgia, cough, and loss of smell and taste. The second episode occurred in January 2021 and presented with fever, myalgia, fatigue, flu-like symptoms, and cough. Viral manifestations in both episodes resolved completely within 7 – 15 days. Presentation in August 2024

Table 1. Case reports of persistent smell and taste disorders following COVID-19 vaccination

References	Causative vaccine	Onset after vaccination	Manifestations	Persistent manifestations and duration	Previous COVID-19 infection and course
Zamzami *et al.*[6]	Second dose of the AstraZeneca/Oxford vaccine (August 2021)	7 days	- A 38-year-old male - Sudden onset of parosmia (unpleasant smoke-like odor) - No smell or taste loss - Treatment included oral and nasal steroids, omega-3 supplement	Parosmia for more than 4 months	- Yes - Smell and taste loss - Complete resolution within 10 – 12 days
Fantin *et al.*[7]	First dose of the AstraZeneca/Oxford vaccine	2 days	- A 76-year-old male - Hyposmia, dysgeusia, parosmia, left aural fullness, and tinnitus - Treatment included nasal steroids, multivitamins, and olfactory training - MRI showed mild atrophy of the olfactory bulbs	Hyposmia for more than 3 months	N/A
Ogata *et al.*[8]	Second dose of the Pfizer-BioNTech vaccine	1 day	- A 70-year-old Japanese man - Acute onset of weakness and paresthesia in all four limbs, impaired proprioception, sensory ataxia (acute inflammatory demyelinating polyneuropathy, more commonly known as GBS), tongue paresthesia, and dysgeusia (bitter taste sensation) - Normal smell, sweet, sour, and salt sensation - Seronegative for post-infective GBS antibodies - Partial improvement of dysgeusia and motor and sensory manifestations with corticosteroids, not IVIG. - The authors suggested that the improvement with steroids, rather than IVIG, might be due to that the mechanism of GBS after COVID-19 vaccination is related to immune-mediated inflammation rather than molecular mimicry	Dysgeusia for several months	No
Barter and Bagnato[9]	Johnson and Johnson (Janssen) vaccine	3 weeks	- A 39-year-old male - Phantosmia (burning or smoke odor): Initially daily for~1 h, then decreased in duration, frequency, and intensity over 11 months (1 to 2 times per week)	Phantosmia for more than 21 months	No
Shin and Tam.[10]	First dose of the Moderna vaccine (March 2021)	Several days	- A 74-year-old male - Hyposmia and dysgeusia - History of ESKD (on hemodialysis), peripheral neuropathy, hypertension, hyperlipidemia, atrial fibrillation, cardiomyopathy, heart failure, and cerebrovascular stroke. - Prior dysgeusia improved with dialysis (pre-pandemic) - Post-vaccine hyposmia and dysgeusia did not improve with dialysis - Normal blood glucose, zinc, vitamin B12, thyroid function, and Sjogren's disease workup	Hyposmia and dysgeusia for more than 2 years	No

(Cont'd...)

Table 1. ***(Continued)***

References	Causative vaccine	Onset after vaccination	Manifestations	Persistent manifestations and duration	Previous COVID-19 infection and course
Keir *et al.*[11]	Second dose of the Pfizer's vaccine	Several days	- A 57-year-old female - Constant phantosmia and hyposmia (smoke smell) - MRI showed edema of olfactory bulbs and tracts, clumping of olfactory nerve filia (suggestive of inflammation) - No history of parosmia or taste loss	Phantosmia and hyposmia	No

Abbreviations: ESKD: End-stage kidney disease; GBS: Guillain–Barré Syndrome; IVIG: Intravenous immunoglobulins; MRI: Magnetic resonance imaging.

was due to persistent hyposmia for 3 years. The SOIT score was 9 out of 16, indicating hyposmia. Both the flavor and taste sensations remained intact.

3. Discussion

In this study, three adult males were reported to have developed smell and taste disorders between 9 and 20 days after the second dose of the AstraZeneca vaccine was administered in 2021. Persistent disorders, including dysgeusia, anosmia, parosmia, and hyposmia, lasting 1 – 3 years were observed. A temporal relation between the vaccination and the development of the disorders, together with repeatedly negative nasal swabs and PCR tests for SARS-CoV-2 and the exclusion of alternative causes, further confirms that these disorders were adverse effects of the vaccine. To date, only six case reports have been published describing persistent smell and taste disorders, which lasted more than 3 months to over 3 years following COVID-19 vaccination. These disorders included parosmia, hyposmia, dysgeusia, and phantosmia[6-11] (Table 1).

The pathogenic mechanisms of post-COVID-19 vaccine smell and taste disorders have not yet been understood and remain speculative. Some mechanisms have been hypothesized: (1) It has been proposed that the vaccine may have similar effects to the attachment of SARS-CoV-2 to the olfactory epithelium and perivascular angiotensin-converting enzyme type 2 receptors, causing inflammation of the olfactory neuroepithelium. This has been supported by findings of olfactory edema, blocked olfactory clefts, and clumping of olfactory filia in some patients with post-vaccination anosmia.[7,14] However, this mechanism has not been considered applicable because most cases had normal MRI at the acute condition. (2) It has been suggested that the humoral immune response triggered by the spike protein induced by the mRNA vaccine may directly damage the olfactory neuroepithelium without replication of the virus.[15] It has been observed that most patients developed the disorders after the second dose of the vaccine. Studies have observed that inactivated viral and viral vector-based vaccines induced a stronger immune response after the second dose compared to the weak cellular immune responses against spike protein after the first dose of the vaccine, which has been considered compatible with an antibody-dependent enhancement mechanism.[15] (3) It has been suggested that the local expression of the spike protein after vaccination and its interaction with the α7 nicotinic acetylcholine receptors in macrophages may cause deregulation of the cholinergic pathway, release of proinflammatory cytokines, and activation of the inflammatory reflex. Signals could be produced and transmitted via neural pathways from the local injection site to the distant one.[16,17] (4) It has been suggested that these disorders may be due to demyelination of the chemosensory nerves. Demyelination of the central and peripheral nervous systems may be triggered by the vaccines.[8,18] (5) Reduction in olfactory bulb volume has been suggested as a cause of persistent post-COVID-19 vaccine anosmia/hyposmia.[7,19] In support of this, a reduction in the volume of the olfactory bulbs has been reported in patients with persistent post-COVID-19 olfactory disorders.[20] (6) Activation of COVID-19 infection by the vaccine in asymptomatic carriers has been recommended. However, this suggestion is not currently applicable because all reported cases demonstrated negative repeated PCR and repeated nasal swabs for SARS-CoV-2 at the onset of the conditions, which ruled out COVID-19 infection as a cause of smell and taste disorders.

4. Conclusion

Persistent smell and taste disorders may occur as complications following post-COVID-19 vaccination. Reports of COVID-19 vaccine-related smell and taste adverse effects should not be ignored and must be recognized by otolaryngologists and different medical specialties, including neurologists. These adverse effects should also be considered in future studies on vaccine

complications and in clinical trials targeting persistent post-COVID-19 vaccine disorders.

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Conflict of interests

The authors declare that they have no competing interests.

Author contributions

Conceptualization: All authors
Investigation: All authors
Writing – original draft: All authors
Writing – review & editing: All authors

Ethics approval and consent to participate

This study was done in accordance with the revised Helsinki Declaration (2013) and its amendments and approved by the local ethics committee of Assiut University Hospitals, Assiut, Egypt (ID: AUFM_COVID_00020).

Consent for publication

We declare that we have obtained written informed consent from all patients for releasing their data and the results of their evaluations in this paper.

Availability of data

Data supporting the findings of this study are available from the corresponding author upon reasonable request.

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