Characterization, treatment modalities, and self-perceived improvement of post-COVID-19 phantosmia: a case series of eleven patients*

Abstract

Background: Loss of smell & taste is one of the early and sensitive symptoms of COVID-19 that usually improves over time. Post-COVID-19 phantosmia, a smell distorted sensation without the presence of odorants, has deleterious and long-lasting effects on the patient’s quality of life. We aimed to present our experience with phantosmia.

Case presentations: We report a description of a series of eleven cases (age of 29 ± 9 years, and 54.5% females) of post-COVID-19 phantosmia without any other comorbidity, and the effects of combined treatment modalities (olfactory training, nasal irrigation with budesonide and oral prednisolone) on self-perceived improvement in phantosmia.

Conclusions: We postulate that the combined 10 days oral prednisolone, smell training, and nasal irrigation for three months improved post-COVID-19 phantosmia assessed as post vs. pre self-perceived improvement, although this was not aimed at as a treatment since it was not compared to untreated controls.

Key words: phantosmia, olfactory dysfunction, olfactory training, post-COVID-19 olfactory dysfunction, steroid therapy, self-perceived improvement

Introduction

Olfactory dysfunction (OD) is not only the most common neurological symptoms of patients with COVID-19, but it comes as the earliest and may be the only clinical manifestation [1]. Management-wise, the post-COVID-19 olfactory dysfunction lacks proper guidance. Empirically, the persisting post-viral anosmia was managed by medication and/or olfactory training. Phantosmia, presence of smell in absence of stimulus, is one of the qualitative smells changes that depend on patient’s history for diagnosis, and there are no tests to verify for it. It occurs mostly as a post-traumatic comorbidity. While topical and/or systemic corticosteroids along with olfactory training were used to manage post-COVID-19 olfactory dysfunction, investigations on persisting (after symptoms resolution and PCR-negative infection) post-COVID-19 phantosmia and its treatment are rare [2-6]. While olfactory training is an effective treatment for olfactory dysfunction, the antiinflammatory topical or systemic steroid treatments, by modulating the function of olfactory receptor neurons, are required to be initiated in the acute phase of the infection to be effective [7].

Phantosmia commonly happens after head trauma and viral infections. Olfactory dysfunction, mainly loss of smell, is one of the crucial symptoms of COVID-19. Phantosmia, as a subtype of olfactory dysfunction, is rarely reported as a symptom of COVID-19. While anosmia was tackled in a good number of previous reports, characterization and management of phantosmia was reported in a limited number of studies [8-10]. However, loss of smell & taste is a more frequent early symptom of COVID-19, ranging from 75 - 88% of cases. They tend to recover within a few months, where the taste loss recovers faster than smell

Abdullah N. Alrasheedi

ORL-H & N Surgery Department, College of Medicine, Jouf University, Sakaka, Saudi Arabia

Rhinology Online, Vol 5: 44 - 48, 2022
http://doi.org/10.4193/RHINOL/22.003

*Received for publication: February 15, 2022
Accepted: March 22, 2022
Published: March 31, 2022
loss (6,7,11-17). However, some individuals reported other olfactory dysfunction (namely phantosmia) later after 2-4 months at a rate of 20-40% cases (12,16,17). The present case series describes post-COVID-19 phantosmia, and effectiveness of a combined treatment modality among patients with PCR-confirmed COVID-19 infection. We evaluated the effect of oral and nasal steroid, and olfactory training on olfactory dysfunction, using self-perceived improvement score. Among patients, we narrated two impressive stories about how post-COVID-19 phantosmia has affected the patients’ quality of life. The first is for a young couple who visited the ENT clinic with a matrimonial problem due to post-COVID-19 phantosmia of the wife that almost resulted in their separation. The second was for a twelve-years-old boy with post-COVID-19 phantosmia. It resulted in significant weight loss, as he could not tolerate eating except a few unhealthy and innutritious fast-foods, while all home cooking smells were unbearably repugnant for him and induce retching and vomiting.

Case presentations
We present eleven cases of post-COVID-19 phantosmia. Phantosmia was defined as a hallucination of smell. Olfactory dysfunction in terms of anosmia was the presenting complaint among ten patients. The patient population belonged to Northern Saudi Arabia, where they were consecutively admitted and followed up at the ENT Clinic, Prince Moteb General Hospital, Sakaka, Saudi Arabia during the period from March 2020 to June 2021. Only patients with PCR-conformed COVID-19 were enrolled after signing a written informed consent. All the included patients were not vaccinated against COVID-19 at the time of infection. The patients with history of any comorbidity like head trauma, diabetes, COVID-related hospitalization, chronic nasal polyposis, history of cacosmia and chronic steroid use were excluded. The patients were examined, and different treatment modalities were initiated and evaluated for improvement over time, and were followed up for different duration; an appointment every four weeks on average. Local nasal examination was carried out to rule out any coexisting chronic sinusitis, chronic nasal polyposis or superadded local infection. Self-perceived improvement was assessed by using visual analogue scale that rates the improvement on a scale from 0 to 10. The improvement, after three months, was presented as percentage improvement of the score compared with baseline score.

Intervention
Although was not aimed at as a treatment, the cohort of 11 cases were prescribed oral prednisolone burst (1 mg/kg twice daily for ten days) followed by nasal irrigation with budesonide in normal saline, and smell training for three consecutive months. The patients were instructed to add two mL vial of liquid Budesonide in 240 mL of normal saline (0.9%) in the sinus rinse bottle. They must tilt their head forward, put the bottle in a nostril aiming towards the top of head and squeeze the bottle slowly. They were instructed using a video to flush out the nose. The patient must repeat the process twice daily for three months (90 days). A synchronized smell training regimen was used for three months. Daily zinc supplementation (20 mg PO daily) was also prescribed. After three months of the combined regimen, self-perception of improvement score was compared with baseline score. They were provided with the facility of electronic video calling, if unable to reach the clinic. We presented the data as frequencies (n and %), and median ± interquartile range (IQR).

Results
The age range of the patients was 12 to 47 years (29 ± 9 years) and 54.5% were females (n = 6). Five patients had presented with taste loss (45.5%), while ten patients had anosmia as a presenting complaint (90.9%). Phantosmia among our patients started after a median duration of 90 days from infection. Median ± IQR for self-perceived improvement in olfactory dysfunction at the start of the combined treatment was 0 ± 5. After the combined administration for 100 days (10 days of oral steroids

| Table 1. Description of demographics, clinical characteristics, and treatment modalities of patients with post-COVID-19 phantosmia (n = 11). |
|---|---|---|
| Age in years | Median ± IQR | 28 ± 8 |
| Gender (Male) | n (%) | 5 (45.5%) |
| Loss of taste | n (%) | 5 (45.5%) |
| Anosmia | n (%) | 10 (90.9%) |
| Start of phantosmia after start of infection | Median ± IQR | 90 ± 90 |
| Duration of follow up in days till the start of combined treatment | Median ± IQR | 392 ± 244 |
| Self-perception of improvement on a scale of one to ten before combined treatment | Median ± IQR | 0 ± 5 |
| Self-perception of improvement on a scale of one to ten after combined treatment | Median ± IQR | 5 ± 3 |

Data shown are frequencies; n (%), and median ± interquartile range (IQR).
and 90 days of nasal irrigation, smell training, and zinc supplementation), median ± IQR of the self-perceived improvement after the intervention was 5 ± 3 (Tables 1 and 2).

**Discussion**

The persistent olfactory dysfunction is caused by direct damage to the olfactory epithelium sensory neurons, and abnormal signal intensity of the olfactory bulb, along with neuro-inflammation by the retrograde persistent neuro-invasion of SARS-CoV-2 that involves proinflammatory cytokines, e.g., TNF-α [7,18-21]. Phantosmia is one of the rare phenomena among olfactory dysfunctions. The causes and prevalence of phantosmia are still not fully understood [6,15]. Classified as central or peripheral phantosmia, peripheral phantosmia is primarily due to damage to olfactory receptors or neurons, usually occurring after a viral infection, while central phantosmia is due to damage to olfactory pathway [13,22,23]. Available treatments include pharmacological treatment and surgical resection, depending on the cause of phantosmia. Endoscopic surgical resection of the olfactory cleft is the mainstay of treatment in trauma cases to the olfactory pathway [11]. Chemosensory dysfunctions in women are less frequent, but longer lasting [24]. Such a notion was not observed in the present small cohort of patients.

Post-viral phantosmia may resolve with time as nature takes its course to regenerate the neuronal endings and pathways. Oral and nasal corticosteroids with and without olfactory training has shown promising results [25,26]. Oral and nasal corticosteroids significantly improved post-viral olfactory dysfunction (PVOD) particularly in combination with classic olfactory training. Mixing budesonide with normal saline irrigation and olfactory training was more effective than olfactory training alone; with a significant improvement of PVOD in 42.6% of the patients [25,19,26-28]. However, others did not detect superiority for steroid intranasal spray over olfactory training [29]. Intranasal application of vitamin A, and systemic supplementation with omega-3 and zinc showed some promise [29].

For patients in the present case series, on a median follow up time of 392 days, the median of the self-perceived improvement before treatment was only 0.0 ± 5.0 on the visual analogue scale. After the combined treatment for 100 days (10 days of oral steroids and 90 days of nasal irrigation, smell training and zinc supplementation), the self-perceived improvement showed improvement. Reportedly, the quality of life has changed dramatically in patients with phantosmia that involves safety issues, like smelling gas leaks and fire, to personal hygiene like bathing for body odor changes, and eating issues that become less pleasant and disgusting, leading to weight loss, and all the related socio-psychiatric issues [11,13,30]. Aberrant regeneration of the olfactory nerves, due to unresolved neuroinflammation may negatively impact olfactory recovery, inducing distorted olfactory signals and possible contribution of central misperception [31]. The paucity of existing studies on the treatment of post-COVID-19 phantosmia is a challenge, which needs collaborative robust studies to dissect the underlying causes, pathogenesis of phantosmia, and to establish a unifying guideline for its treatment.

**Conclusion**

In conclusion, post-COVID-19 phantosmia hampers the daily life activities of patients for long durations. The effects are physical, psychological, and social, including matrimonial. The suggested modality containing oral steroid burst treatment, nasal steroid irrigation in saline, and smell training was effective in improving

**Table 2. Detailed characteristics of each patient (n = 11).**

| Item                                         | 1   | 2   | 3   | 4   | 5   | 6   | 7   | 8   | 9   | 10  | 11  |
|----------------------------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Age in years                                 | 47  | 22  | 27  | 26  | 29  | 27  | 40  | 12  | 28  | 28  | 34  |
| Gender                                       | F   | F   | F   | F   | F   | M   | M   | M   | M   | F   | F   |
| Loss of taste                                | No  | No  | No  | No  | No  | Yes | Yes | Yes | Yes | No  | Yes |
| Loss of taste after the first symptom in days| NA  | NA  | NA  | NA  | NA  | 0   | 3   | 14  | 14  | NA  | 14  |
| Development of anosmia after first symptom in days | 3   | 2   | 3   | 4   | 10  | 3   | 3   | 0   | 14  | 8   | 2   |
| Recovery from anosmia in days                | 120 | 300 | 90  | 21  | 7   | 42  | 14  | NA  | 90  | 8   | 14  |
| Start of phantosmia after start of infection | 120 | 300 | 90  | 90  | 180 | 90  | 30  | 10  | 120 | 42  | 14  |
| Duration of follow up in days till the start of combined treatment | 485 | 471 | 446 | 403 | 403 | 392 | 338 | 273 | 202 | 134 | 69  |
| Self-perception of improvement on a scale of one to ten before combined treatment | 0   | 0   | 0   | 0   | 5   | 5   | 8   | 2   | 5   | 0   | 0   |
| Self-perception of improvement on a scale of one to ten after combined treatment | 5   | 6   | 4   | 2   | 5   | 5   | 8   | 8   | 5   | 3   | 7   |

F = female, M = male.

In conclusion, post-COVID-19 phantosmia hampers the daily life activities of patients for long durations. The effects are physical, psychological, and social, including matrimonial. The suggested modality containing oral steroid burst treatment, nasal steroid irrigation in saline, and smell training was effective in improving
post-COVID-19 phantosmia, although was not aimed at as a treatment since it was not compared to an untreated control group. Moreover, prednisolone was not previously characterized as a treatment. There is a need for research to determine the pathogenesis of phantosmia and a more efficient treatment for it.

Acknowledgments
No acknowledgements to be mentioned.

Funding
The reporting of this case series was not funded and was conducted as a part of my employment duties at Jouf University.

Ethics approval and consent to participate
Informed consents were collected from all participants.

Consent for publication
Written informed consents were collected from all participants, and the study and reporting details were explained to participants before they consented to join the study. All participants were informed of their right to withdraw at any time during the study's duration with no consequences, as participation was entirely voluntary.

Availability of data and materials
All data and study protocol are already included.

Conflict of interest
None declared.

References
1. Wei G, Gu J, Gu Z, Du C, Huang X, Xing H, et al. Olfactory dysfunction in patients with coronavirus disease 2019: A review. Front Neurol. 2020;12:783249.
2. Whitcroft KL, Hummel T. Olfactory dysfunction in COVID-19: Diagnosis and management. JAMA. 2020;323(24):2512-4.
3. Abdelalim AA, Mohamady AA, Elsayed RA, Elawady MA, Ghallab AF. Corticosteroid nasal spray for recovery of smell sensation in COVID-19 patients: A randomized controlled trial. Am J Otolaryngol. 2021;42(2):102884.
4. O’Byrne L, Webster KE, MacKeith S, Philpott C, Hopkins C, Burton MJ. Interventions for the treatment of persistent post-COVID-19 olfactory dysfunction. Cochrane Database Syst Rev. 2021;7(7):CD013876.
5. Kasiri H, Rouhani N, Salehifar E, Ghazaeian M, Fallah S. Mometasone furoate nasal spray in the treatment of patients with COVID-19 olfactory dysfunction: A randomized, double blind clinical trial. Int Immunopharmacol. 2021;98:107871.
6. Islek A, Balci MK. Phantosmia with COVID-19 related olfactory dysfunction: Report of nine case. Indian J Otolaryngol Head Neck Surg. 2021;71:1-3.
7. Seo MY, Lee SH. Treatment and prognosis of COVID-19 associated olfactory and gustatory dysfunctions. J Pers Med. 2021;11(10):1037.
8. Kooper D, Coerts, H., Mkdami, H. Self-reported olfactory and gustatory dysfunctions in patients with COVID-19 infection. Rhinology online. 2021;4(1):140-46.
9. Hopkins C, Surda P, Vaira LA, Leckien JR, Safarian M, Saussez S, et al. Six month follow-up of self-reported loss of smell during the COVID-19 pandemic. Rhinology. 2021;59(1):26-31.
10. Cook E, Kelly CE, Burges Watson DL, Hopkins C. Parosmia is prevalent and persistent amongst those with COVID-19 olfactory dysfunction. Rhinology. 2021;59(2):222-24.
11. Parma V, Ohla K, Veldhuizen MG, Niv MY, Kelly CE, Bakke AJ, et al. More than smell? COVID-19 is associated with severe impairment of smell, taste, and chemesthesis. Chem Senses. 2020;45(7):609-22.
12. Hänner A, Hummel T. Classic phantosmia. Dtsch Arztebl Int. 2020;117(41):e689.
13. Ferdenzi C, Bousquet C, Aguera PE, et al. Recovery from COVID-19-related olfactory disorders and quality of life: Insights from an observational online study. Chem Senses. 2021;46:eb0628.
14. Yxdakis MS, Albers MW, Holbrook EH, Lyon DM, Shih RY, Frasnelli JA, et al. Post-viral effects of COVID-19 in the olfactory system and their implications. Lancet Neurol. 2021;20(9):753-61.
15. Koyama S, Ueha R, Kondo K. Loss of smell and taste in patients with suspected COVID-19: Analyses of patients’ reports on social media. J Med Internet Res. 2021;23(6):e26459.
16. Ohla K, Veldhuizen MG, Green T, Hannum ME, Bakke AJ, Moen S, et al. Increasing incidence of parosmia and phantosmia in patients recovering from COVID-19 smell loss. medRxiv. 2021;2021:1-23.
17. Keir G, Maria Ni, Kirsch CFE. Unique imaging findings of neurologic phantosmia following Pfizer-BioNTech COVID-19 vaccination: A case report. Top Magn Reson Imaging. 2021;30(3):133-7.
18. Torabi A, Mohammadbagheri E, Akbari Dilmaghani N, Bayat AH, Fathi M, Vakili K, et al. Proinflammatory cytokines in the olfactory mucosa result in COVID-19 induced anosmia. ACS Chem. Neurosci. 2020;11:1909-1913.
19. Vaira LA, Hopkins C, Sandison A, Manca A, Machouchas N, Turilll D, et al. Olfactory epithelium histopathological findings in long-term coronavirus disease 2019 related anosmia. J Laryngol Otol. 2020;134(12):1123-7.
20. de Melo GD, Lazarrini F, Levallois S, Hautefort C, Michel V, Larrous F, et al. COVID-19-related anosmia is associated with viral persistence and infiltration in human olfactory epithelium and brain infection in hamsters. Sci Transl Med. 2021;13(659):eaav8396.
21. Chiu A, Fischbein N, Wintermark M, Zaharchuk G, Yun PT, Zeineh M. COVID-19-induced anosmia associated with olfactory bulb atrophy. Neuroradiology. 2021;63(1):147-8.
22. Amanat M, Rezaei N, Roozbeh M, Shojaei M, Tafakhori A, Zoghi A, et al. Neuropsychological manifestations as the predictors of severity and mortality in hospitalized individuals with COVID-19: A multicenter prospective clinical study. BMC Neurol. 2021;21(11):116.
23. Sagar P, Kumar R, Fatima R, Bollu S, Mehmi N, Subagar AS, et al. Prospective analysis of the chronology of smell and taste dysfunction in COVID-19 positive ENT doctors. Indian J Otolaryngol Head Neck Surg. 2021;1-6.
24. Meini S, Suardi LR, Busoni M, Roberts AT, Fortini A. Olfactory and gustatory dysfunctions in 100 patients hospitalized for COVID-19: Sex differences and recovery time in real-life. Eur Arch Otorhinolaryngol. 2020;277(12):3519-23.
25. Swain SK, Pani SRIAM. Role of oral corticosteroid and olfactory training for treatment of post-COVID-19 olfactory dysfunction: Our experiences. Apollo Medicine. 2021;18(3):162.
26. Yuan F, Huang T, Wei Y, Wu D. Steroids and olfactory training for postviral olfactory dysfunction: A systematic review. Front Neuosci. 2021;15:708510.
27. Singh CV, Jain S, Parveen S. The outcome of fluctuasinal nasal spray on anosmia and triamcinolone oral paste in dysgeusia in COVID-19 patients. Am J Otolaryngol. 2021;42(3):102892.
28. Wu TJ, Yu AC, Lee JT. Management of post-COVID-19 olfactory dysfunction. Curr Treat...
29. Neta FI, Fernandes ACL, Vale AJM, Pinheiro FI, Cobucci RN, Azevedo EP, et al. Pathophysiology and possible treatments for olfactory-gustatory disorders in patients affected by COVID-19. Curr Res Pharmacol Drug Discov. 2021;2:100035.

30. Leopold DA, Schwob JE, Youngentob SL, Hornung DE, Wright HN, Mozell MM. Successful treatment of phantosmia with preservation of olfaction. Arch Otolaryngol Head Neck Surg. 1991;117(12):1402-6.

31. Di Stadio A, D’Ascanio L, La Mantia I, Ralli M, Brenner MJ. Parosmia after COVID-19: olfactory training, neuroinflammation and distortions of smell. Eur Rev Med Pharmacol Sci. 2022;26(1):1-3.