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### COVID-19 mRNA Vaccine Linked to Dysgeusia and Hyposmia: A Case Report

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## Abstract

Commonly reported adverse effects of vaccine administration include localized erythema, pain, lymphadenopathy, myalgias, fatigue, nausea, vomiting, fever, and in extreme cases, anaphylaxis. Myocarditis, pericarditis, and thrombosis have been reported as rare side-effects of COVID vaccine administration.<sup>3</sup> Here, we present the case of a 74 year old male, who reported the onset of persistent dysgeusia and hyposmia shortly after receiving the Moderna COVID mRNA vaccine.

## Case Presentation

The patient is a 74 year old male never-smoker with past medical history of ESRD on hemodialysis, peripheral neuropathy, hypertension, hyperlipidemia, paroxysmal atrial fibrillation, cardiomyopathy, chronic diastolic heart failure, and CVA, who visited his PCP in June 2021, at which time he reported dysgeusia and hyposmia since receiving his first Moderna COVID mRNA vaccine in March 2021. He had numerous negative COVID PCR tests throughout the year.

He reported similar episodes of dysgeusia prior to the COVID pandemic. He described this as a hypersensitivity to sweet and salty foods. He recalled improvement in his symptoms after dialysis sessions, so it was presumed that his symptoms were secondary to complications of his end-stage renal disease. He became particularly concerned with his symptoms in early 2021 when his symptoms no longer improved with dialysis.

His nephrologist prescribed him multi-vitamin supplements, treated for thrush, and had the patient focus on improving his oral hygiene, but none of these improved his dysgeusia and hyposmia. He was referred to ENT early in 2022 and was treated for acid reflux, but again, there was no improvement. He saw his neurologist periodically over the next two years, who attributed his symptoms to ESRD. A1c, TSH, Zn, and B12 levels were all normal and Sjogren’s workup was also negative.

In April of 2023, his PCP presented the idea of treating the patient’s symptoms with a stellate ganglion block (SGB). Although this procedure had been around for quite some time, its use in the treatment of long-COVID symptoms was still experimental and offered only by a few institutions. The Cleveland Clinic was one such institution; however, the patient did not wish to travel across state lines for treatment.

## Discussion

mRNA vaccines are generally considered to be an effective and safe option for vaccination.<sup>8</sup> mRNA cannot integrate into host DNA, and are eventually degraded by host cells.<sup>8</sup> In the US, Pfizer/BioNTech and Moderna manufacture COVID mRNA vaccines that contain mRNA that codes for the spike protein that the COVID virus uses to facilitate entry into host cells.<sup>8,9</sup> The host’s immune system mounts an immune response to the viral proteins - producing antibodies, activating T cells, and generating memory cells that can combat future infections with the virus more quickly and effectively, thereby decreasing the severity and/or duration of symptoms.

While gustatory and olfactory dysfunction were prominent features of natural COVID infection early in the pandemic, numerous variants of the virus have emerged and these features do not appear to be as prominent as they once were.<sup>2,5</sup> Recently, there have been extremely rare reports of patients developing dysgeusia/ageusia and hyposmia/anosmia after receiving COVID vaccines.<sup>6</sup> Numerous vaccine manufacturers have been implicated in this phenomenon.<sup>6</sup>

There are many known causes of dysgeusia and anosmia, including normal aging, allergies, infections, sinusitis, trauma, dry mouth, medications, cancer treatments

(e.g. radiation), tobacco use, poor oral hygiene, thyroid disease, CNS lesions, and complications of ESRD (e.g. uremia).<sup>13</sup> These symptoms can lead to secondary anorexia, malnutrition, weight loss, weakness, fatigue, and depression - significantly decreasing quality of life.<sup>4</sup>

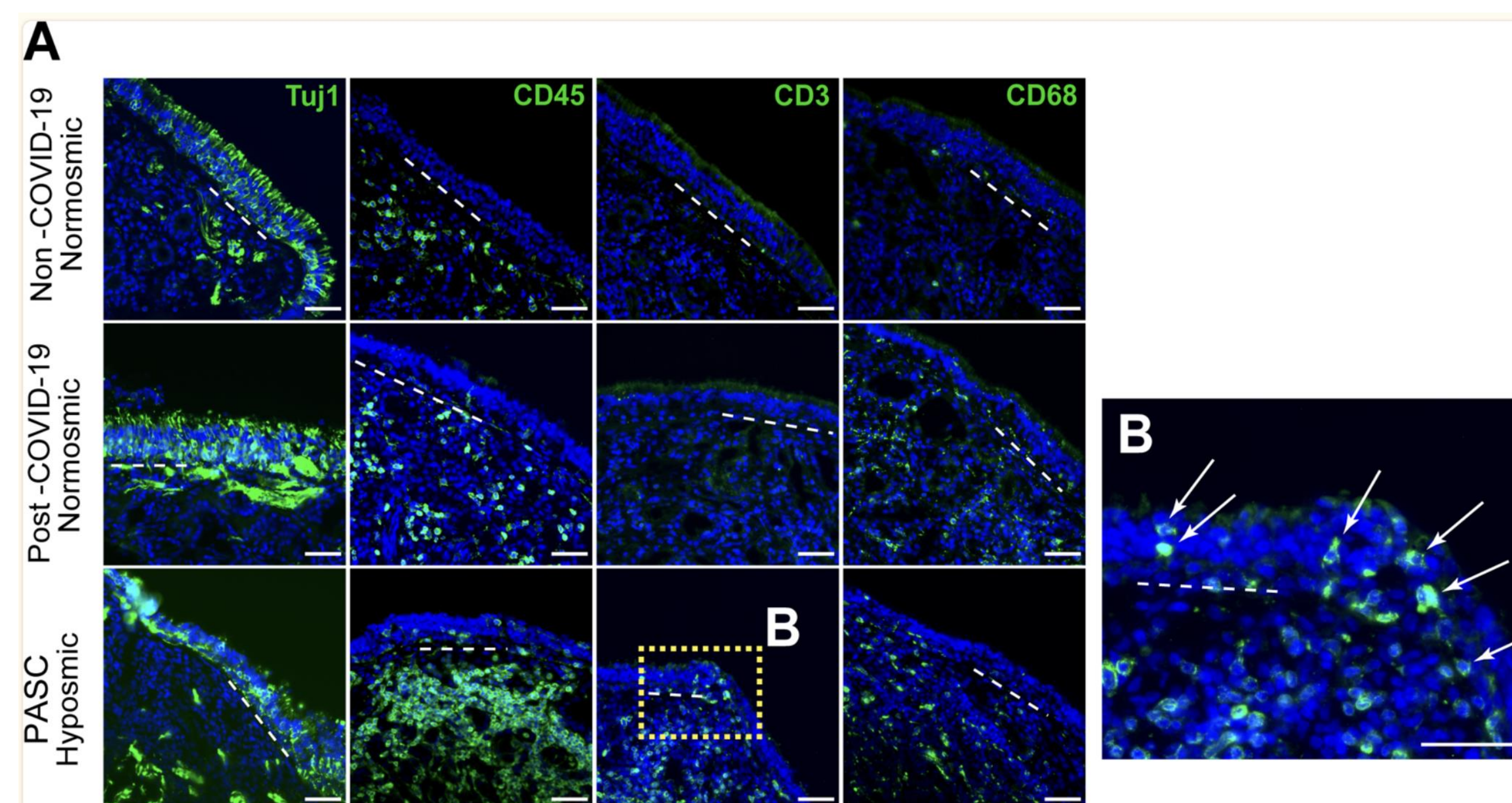
It is hypothesized that COVID infections cause dysgeusia/ageusia and hyposmia/anosmia by infecting structural and metabolic support cells of the nasal and respiratory epithelia, resulting in infiltration of immune cells, inflammation, tissue damage, altered neuronal signaling, and downregulation of chemoreceptor genes in the olfactory receptor neurons.<sup>2,5,10</sup> Researchers have discovered that persistent inflammation in olfactory epithelium may explain the persistent symptoms after a COVID infection.<sup>2</sup>

Researchers from the National Institute of Aging examined tissue biopsies of tongue and taste bud cells in patients with persistent ageusia (six weeks after a negative COVID nasal swab test). They discovered that the COVID virus was detectable in low levels in tongue and taste bud cells, despite undetectable levels by PCR. Furthermore, infected taste bud basal cells were deformed and had fewer taste receptor cells than normal.

Some researchers speculate that the spike protein may be responsible for the gustatory and olfactory dysfunction seen with long COVID and in extremely rare cases, COVID vaccination.<sup>6,9</sup> Interaction between the spike protein and host ACE2 receptors facilitates viral entry into cells, while also potentiating inflammation and autonomic dysregulation.<sup>1,5,10</sup> Studies have shown that patients expressing higher levels of ACE2 have been associated with a higher incidence of anosmia.<sup>1</sup>

In 2022, Dr. Liu, a pain management specialist in Alaska, published a case series in which he identified aberrant adaptation to autonomic dysregulation as the culprit for long COVID in two of his patients. He pioneered the use of SGBs to decrease regional sympathetic hyperactivity, allowing patients to “reboot” their autonomic nervous systems, leading to improvement of their long COVID symptoms.<sup>7</sup> Since then, numerous clinicians/researchers have also published case reports/series demonstrating similar results with use of SGBs to treat patients with long COVID.<sup>1,4</sup> Some institutions, such as the Cleveland Clinic, is now offering this as a treatment modality specifically for the treatment of long COVID.

## Photos



Shown are representative immunohistochemistry images of nasal biopsy tissue from normosmic non-COVID-19, normosmic post-COVID-19 or PASC (post-acute sequelae of COVID) hyposmic individuals. Tissue sections were immunostained for the TUJ1 neuronal marker, CD45 pan-immune cell marker, CD3 T cell marker and CD68 myeloid cell marker. PASC hyposmic tissue showed dense CD45+ immune cell infiltration including prominent CD3+ lymphocytic infiltration, which was absent in the normosmic groups; scattered CD68+ cells were present in all conditions. From Finlay et al.<sup>2</sup>

## Conclusions

The etiology of this patient’s symptoms may be multifactorial. The fact that the patient had dysgeusia and hyposmia prior to the COVID pandemic, improved with dialysis, tells us that his ESRD was at least partially responsible for his symptoms. At some point, his symptoms became persistent and did not improve with dialysis, suggesting that there may have been another factor contributing to his altered taste and diminished smell.

It is possible that he had a rare side-effect to COVID vaccine administration, as it has recently been reported in literature. Although the patient had numerous negative COVID tests in 2021, it is also possible that he had a COVID infection prior to that, where he had minimal symptoms and now suffered from long COVID. He was not the most reliable historian due to his memory impairment issues.

It would be interesting to see if SGBs would provide improvement for patients with COVID vaccine-related gustatory and olfactory dysfunction, since it has been rather successful in treating a subset of patients with long COVID. Perhaps biopsies and examination of the patients olfactory epithelia and taste bud cells may reveal more information about structural and functional changes to explain his symptoms.

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