

Clinical case: Tongue hypoesthesia in Adults after Administration of the mRNA COVID-19 Vaccine in the United States

Yuliya Modna*, Dev Shah, Tyler Young and Alexandra Frazier

Trinity Medical Sciences University, Saint Vincent and the Grenadines, Baltimore, USA

*Corresponding author: Yuliya Modna, Email: ymodna@tmsu.edu.vc

Received: 17 June 2022; Accepted: 05 July 2022; Published: 08 July 2022

Abstract

Three COVID-19 vaccines are available in the United States under Emergency Use Authorization. Not all of the side effects of these vaccines are still known. The potential association between COVID-19 vaccines and serious neurological adverse events has not been confirmed or excluded yet. We present a case report of a 58-year-old man who developed persistent tongue hypoesthesia following the administration of the mRNA COVID-19 vaccine (Moderna), a unique side effect that was not mentioned before in any published case report or journal articles from the United States to the best of our knowledge. The patient in this clinical case had tongue hypoesthesia after administration of the first dose of Moderna vaccine, and the second dose caused the hypoesthesia to grow in size on his tongue. The hypoesthesia decreased to the original area of hypoesthesia three weeks after the administration of the second dose of the Moderna vaccine. The patient reported that over the course of the year the circle of numbness has grown and shrunk back down to the 7.4 cm² circle, but has never gotten smaller than the original circle of numbness. The hypoesthesia still remains on the patient's tongue. While the adverse effect of tongue paresthesia following the COVID-19 vaccine in the USA is a rare side-effect, it is interesting to observe, considering its long-lasting effects. Several pathogenic mechanisms, like molecular mimicry, direct neurotoxicity, and aberrant immune reactions, have been recognized to explain the neurological complication associated with vaccines. Large prospective studies are required to prove or disprove the association between such adverse effects and the COVID-19 vaccine. If such association is established, then discovering the related potential mechanism will be important for the prevention and management of the condition.

Keywords: SARS-CoV-2; COVID-19; Vaccine; Tongue hypoesthesia; Adverse event

Abbreviations

Emergency Use Authorization (EUA); Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2); U.S. Food and Drug Administration (FDA); United States of America (USA); Vaccine Adverse Event Reporting System (VAERS).

Background

Three COVID-19 vaccines are available in the United States under Emergency Use Authorization (EUA). Among them, Pfizer-BioNTech (Comirnaty) and Moderna (Spikevax) are mRNA vaccines while Johnson & Johnson's (Janssen) is a virus vector vaccine. mRNA vaccines deliver antigen-encoding mRNA molecules to the cytosol of the host's target cells. Host cells use this genetic material to make severe acute

respiratory syndrome coronavirus 2 (SARS-CoV-2) alarm protein which is recognized by the immune system to trigger a response to fight off SARS-CoV-2 in the future [1]. In another type of vaccine, a virus vector is used to deliver SARS-CoV-2 genetic material to the host cells for the production of alarm protein thereby activating the immune response to prevent future COVID-19 infection [2]. These vaccines were authorized by the U.S. Food and Drug Administration (FDA) for emergency use on the "best available evidence," rather than waiting for comprehensive analysis of all data, which may take years. Therefore, not all of the side effects of these vaccines are still known. Data available to date clearly demonstrate that the benefits of these vaccines still outweigh potential adverse effects. However, some serious adverse events of COVID-19 vaccines have been reported in a minority of cases. Neurological adverse events following COVID-19 vaccination are generally mild and transient and can be associated with autoimmune disorders. The World Health Organization listed Guillain-Barré syndrome, seizures, anaphylaxis, syncope, encephalitis, thrombocytopenia, vasculitis, and Bell's palsy as serious neurologic adverse events. In Mexico among 704 003 subjects who received first doses of the Pfizer-BioNTech mRNA COVID-19 vaccine, 6536 adverse events following immunization were recorded. Among those, 4258 (65%) had at least one neurologic manifestation, but 99.6% of them are mild and transient and were presented in forms of headache (62.2%), transient sensory symptoms (3.5%), and weakness (1%). In this study, there were only 17 serious adverse events, seizures (7), functional syndromes (4), Guillain-Barré syndrome (3), and transverse myelitis (2) [3].

Despite this information, the exact pathogenesis of the neurologic manifestations remains speculative. We present a case report of a 58-year-old man who developed persistent tongue hypoesthesia following the administration of the mRNA COVID-19 vaccine (Moderna), a unique side effect that was not mentioned before in any published case report or journal articles from the United States to the best of our knowledge.

Case Report

A 58-year-old Caucasian male with a past medical history of controlled hypertension since the age of 22 presented to the primary care facility in Nampa, Idaho, United States to receive the first dose of the COVID-19 vaccine. He was oriented to person place time and event. On physical exam, his blood pressure was 123/78. His current medications are 10 mg of lisinopril daily. He is currently allergic to Phenylpropanolamine, Doxycycline, Gluten, and Hymenoptera. He received the Moderna vaccine on April 4, 2021. Within 24 hours after receiving the first dose of the Moderna vaccine, his tongue became numb. Initially, the entire tongue felt numb, but then over the next month translated to become a 7.4 cm² circle of numbness in the central dorsal surface nearly midline of the tongue. After the second dose of the Moderna vaccine, on May 5, 2021, the 7.4 cm² circle of numbness in the center of his tongue grew to encompass the entire tongue again. The numbness then translated back to the same 7.4 cm² circle three weeks after the second dose.

He had no previous history of any symptoms related to neurological disorders or autoimmune diseases. We performed the clinical neurological examination which showed normal gait; no pronator drift; negative Romberg, Kernig's, Brudzinski's, and Babinski tests. Sensation to temperature, pain, touch, and vibration in all limbs were intact. Extensor and flexor muscle strength in all the limbs were found to be 5/5, and reflexes were 2+ and symmetric. All cranial nerve functions were found to be intact with the notable exception of sensory loss to touch and pinprick stimuli on the affected area of the tongue (7.4 cm² circle in the central dorsal surface). The taste sensation was found intact throughout the tongue, except for the decreased taste of sour substances. There were no areas of depapillation on the tongue surface.

During the follow-up visit on May 26, 2022, the patient reported that he continued to experience numbness in the same area of the tongue but described the persistent presence of taste sensation. The results of the repeated neurological examination were similar to the previous one. Thus, we found that over the course of the year the circle of numbness has grown and shrunk back down to the 7.4 cm² circle, but has never gotten smaller than the original circle of numbness.

Discussion

Some neurological complications have previously been reported in association with SARS-CoV-2 infection itself [4-8] but neuropathies after vaccination are a rare event. Some reported complications related to cranial nerve involvement after COVID-19 vaccines include facial palsy, olfactory dysfunction, abducent nerve palsy, otologic manifestations, and acute vision loss [9-13]. Development of left trigeminal neuritis presenting numbness to a greater degree over the mandibular (V3) division in a 52-year-old female after 3 hours of receiving 1st dose Pfizer-BioNTech vaccine that persisted even after 6 weeks has been reported from Singapore. MRI of the trigeminal nerve in this patient revealed an abnormal asymmetric thickening and robust perineural sheath enhancement of the V3 segment of the left trigeminal nerve [14]. With some similarity to this case, we presented a case that developed post-vaccination tongue hypoesthesia with no other causation that persisted for more than a year. We also used data collected by the Vaccine Adverse Event Reporting System (VAERS) to determine if there were other reported cases from the United States of America (USA) similar to the one discussed previously [15].

As of March 14, 2022, there were a total of 532 cases of tongue paresthesia in the USA that occurred after a COVID-19 vaccine (Janssen, Moderna, or Pfizer-BioNTech) out of a total of 799,393 COVID-19 vaccines in the USA associated with adverse reactions since 2021 (0.067%). Out of the 532 cases of tongue paresthesia, 6.02% were associated with the Janssen vaccine (n=32), 40.60% with Moderna (n=216), and 53.38% with Pfizer-BioNTech (n=284) (Figure 1A). These numbers are consistent with the distribution of the total number of reported adverse effects following COVID-19 vaccines from the United States' VAERS database, with 8.46% of patients having received Janssen (n=67662), 45.42% with Moderna (n=363114), and 46.11% with Pfizer-BioNTech (n=368617) (Figure 1B). If we compare the number of reported tongue paresthesia cases of one of the three vaccines to the total number of patients who received that same vaccine, we see that tongue paresthesia is associated with 0.05% of all Janssen vaccinations, 0.06% with all Moderna vaccinations, and 0.08% with all Pfizer-BioNTech vaccinations. A Chi-square and post hoc analysis demonstrated there is a significant association between the presence of reported tongue paresthesia and the type of COVID-19 vaccine administered in the USA (χ^2 (2, N=799393) = 12.765, p

<0.005)), suggesting that the reported tongue paresthesia would not have occurred if the individuals did not receive the Moderna vaccine ($F(2,799392) = -26, p < 0.005$).

In addition to observing differences in the distribution of the three COVID-19 vaccines in the USA, we also investigated the difference in frequency of adverse reactions between men and women in the USA. Interestingly, 84.23% of the reported tongue paresthesia occurred in women (n=438) while only 15.77% (n=82) occurred in men ($t(2)=1.87, p=0.07$) (Figure 2A). Following a COVID-19 vaccine in the United States, 68.74% of the total reported adverse reactions occurred in women (n=529805) and 31.26% occurred in men (n=240888) (Figure 2B).

The reason for these differences could be due to the fact that vaccines inherently react differently in woman. Eighty percentage of all individuals affected by autoimmune disorders tends to be woman due to variation within the sex chromosomes (XX) and changing hormonal climate from puberty to menopause which influences the production inflammatory cytokines [16]. If such changes are triggered to develop of neurological symptoms in woman after the administration of COVID-19 vaccines needs to be confirmed. However, no history of autoimmune diseases in the patient and his family in our reported case suggests some other unidentified causes for this symptom. A behavioral difference in which women are more likely to report side effects of vaccines could be another reason for gender differences observed in reported case of tongue paresthesia [17].

In addition to differences in types of vaccine and gender in reporting adverse reactions following a COVID-19 vaccine in the USA, there is also an interesting trend in regards to age distribution. Of the total 532 reported incidents of tongue paresthesia following a COVID-19 vaccine in the USA, 482 cases also mentioned their age. 192 of these 482 had received the Moderna COVID-19 vaccine and 18.23% of them were between the ages of 30-39 years old (n=35), 21.35% were between the ages of 40-49 years old (n=41), and 19.27% were between the ages of 50-59 years-old (n=37) (Figure 3. Table 1). One possible explanation for this observation is that the age range of 30-59 encompasses a large majority of the working class in the United States, of which many were required by their jobs to receive a COVID-19 vaccination. Another reason for the increase in COVID-19 vaccines in this age group, therefore resulting in more adverse reactions, is that this demographic may be more likely to travel by air or train, for pleasure or work, resulting in them obtaining the COVID-19 vaccine more frequently than other age groups. Though some autoimmune neurological disorders like multiple sclerosis (MS) usually appears between ages 20 and 40, the development of post vaccination neurological symptoms in 30-59 years of age group with or without family history of autoimmune diseases needs further study to establish a relationship [18].

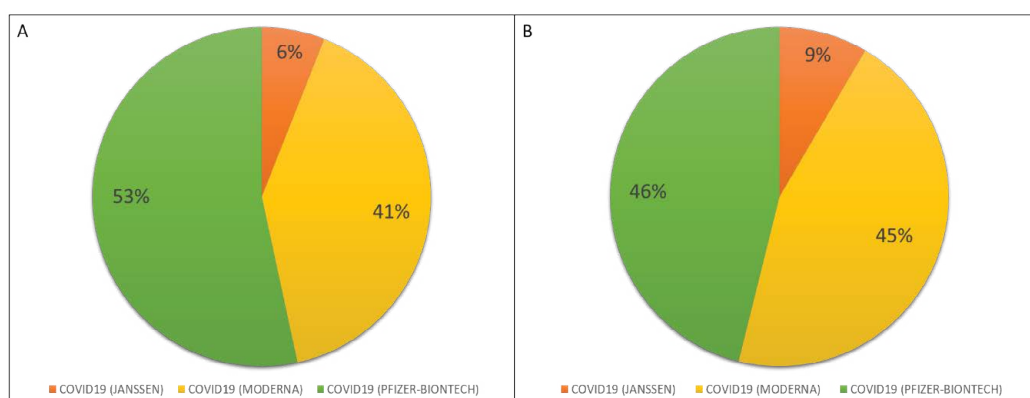


Figure 1: Percentage of Reported Adverse Reactions Following Janssen, Moderna, and Pfizer-BioNTech COVID-19 Vaccinations in the USA. A. Adverse Reaction of Tongue Paresthesia in the USA Since 2021 Grouped by COVID-19 Vaccine. B. Total Adverse Reactions Following COVID-19 Vaccine in the USA Since 2021.

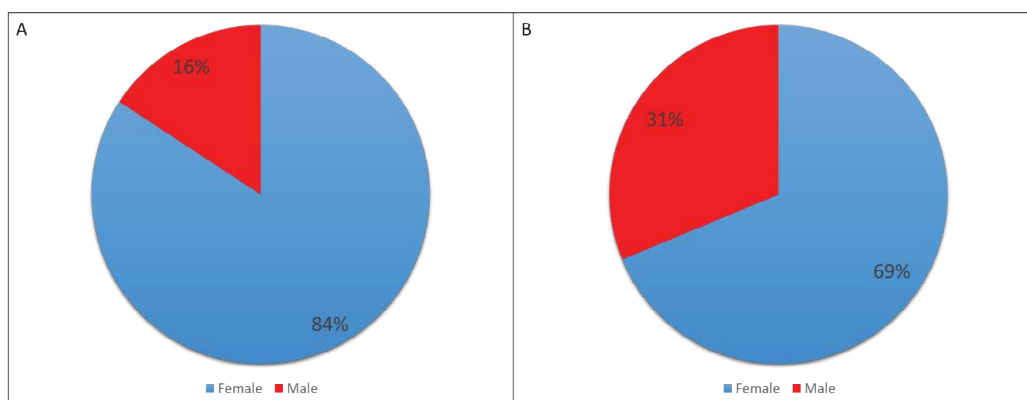


Figure 2: Percentage of Reported Adverse Reactions Following Janssen, Moderna, and Pfizer-BioNTech COVID-19 Vaccinations in the USA, Grouped by Sex. A. Adverse Reaction of Tongue Paresthesia Following A COVID-19 Vaccine in the USA Grouped by Sex. B. Total Adverse Reactions Following A COVID-19 Vaccine in the USA Grouped by Sex.

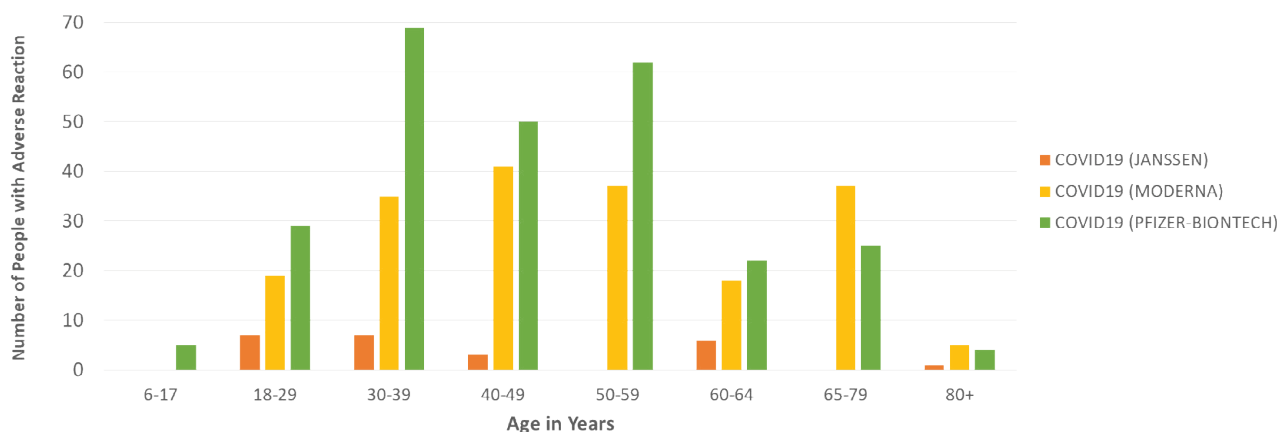


Figure 3: Adverse Reaction of Tongue Paresthesia Following a COVID-19 Vaccine in the USA, Grouped by Age and Vaccine Subtype.

Table 1: Distribution of Tongue Paresthesia Following A COVID-19 Vaccine by Age (in Years) in the USA.

	Age (years)							
	6-17	18-29	30-39	40-49	50-59	60-64	65-79	80+
COVID19 (Janssen)	0	7	7	3	0	6	0	1
COVID19 (Moderna)	0	19	35	41	37	18	37	5
COVID19 (Pfizer-Biontech)	5	29	69	50	62	22	25	4

Table 2: Distribution of Tongue Paresthesia Following A COVID-19 Vaccine by Age (in Years), Sex, and Vaccine Subtype in the USA.

	Age (years)							
	6-17	18-29	30-39	40-49	50-59	60-64	65-79	80+
COVID19 (Janssen) – FEMALE	0	6	7	6	2	0	5	0
COVID19 (Janssen) – MALE	0	1	1	1	1	0	1	0
COVID19 (Moderna) – FEMALE	0	15	31	30	31	17	32	3
COVID19 (Moderna) – MALE	0	4	4	10	6	1	5	2
COVID19 (Pfizer-Biontech) – FEMALE	2	27	59	37	53	20	22	4
COVID19 (Pfizer-Biontech) – MALE	3	2	10	12	8	2	2	0

While the adverse effect of tongue paresthesia following the COVID-19 vaccine in the USA is a rare side-effect, it is interesting to observe, considering its long-lasting effects. Several pathogenic mechanisms, like molecular mimicry, direct neurotoxicity, and aberrant immune reactions, have been recognized to explain the neurological

complication associated with vaccines [19]. Post-vaccination tongue hypoesthesia described above indicates the potential functional loss of lingual nerve or sensory receptors which has been gradually limited to a small area (7.4 cm²) after encompassing the entire tongue initially. Considering the ascribed mechanisms like molecular

mimicry, neurotoxicity, and aberrant immune reactions for the possible explanation of gradual reduction and persistent numbness in a specific area, in this case, seems unclear. The likely presence of neural and/or sensory receptor protein in some areas with higher affinity to cross-reacting host antibodies or more susceptible to direct neurotoxicity compared to other areas in the tongue could be interesting areas to explore. Along with this, the consideration of vascular cause for neurological manifestation should not be undermined.

Conclusion

The tongue hypoesthesia could be a possible neurological adverse effect of COVID-19 vaccines. Large prospective studies are required to prove or disprove the association between such adverse effects and the COVID-19 vaccine. If such association is established, then discovering the related potential mechanism will be important for the prevention and management of the condition.

Limitations

The limitations of this report are that it is only cases that were reported to VAERS, it was mostly women that reported the symptoms, and that symptoms could have been misinterpreted by the nurse or physician taking notes. This data only represents the United States.

Contributors List

Marcus Caine of Trinity Medical Sciences University.

Conflicts of Interest

The authors report no conflicts of interest.

References

- Schlake T, Thess A, Fotin-Mleczek M, Kallen KJ. Developing mRNA-vaccine technologies. *RNA Biol.* 2012; 9:1319–1330.
- Voysey M, Clemens SAC, Madhi SA, Weckx L, Folegatti PM, Aley PK, et al. Single-dose administration and the influence of the timing of the booster dose on immunogenicity and efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine: a pooled analysis of four randomised trials. *Lancet.* 2021; 397:881–891.
- García-Grimshaw M, Ceballos-Liceaga SE, Hernández-Vanegas LE, Núñez I, Hernández-Valdivia N, Carrillo-García DA, et al. Neurologic adverse events among 704,003 first-dose recipients of the BNT162b2 mRNA COVID-19 vaccine in Mexico: A nationwide descriptive study. *Clin Immunol.* 2021; 229:108786.
- Duong L, Xu P, Liu A. Meningoencephalitis without Respiratory Failure in a Young Female Patient with COVID-19 Infection in Downtown Los Angeles, Early April 2020. *Brain Behav Immun.* 2020; 87:33.
- Gutiérrez-Ortiz C, Méndez A, Rodrigo-Rey S, Pedro-Murillo ES, Bermejo-Guerrero L, Gordo-Mañas R, et al. Miller Fisher Syndrome and polyneuritis cranialis in COVID-19. *Neurology.* 2020; 95:e601-e605.
- Filatov A, Sharma P, Hindi F, Espinosa PS. Neurological Complications of Coronavirus Disease (COVID-19): Encephalopathy *Cureus.* 2020; 12:e7352.
- Zhao H, Shen D, Zhou H, Liu J, Chen S. Guillain-Barré syndrome associated with SARS-CoV-2 infection: causality or coincidence?. *Lancet Neurol.* 2020; 19:383-384.
- Sedaghat Z, Karimi N. Guillain Barre syndrome associated with COVID-19 infection: A case report. *J Clin Neurosci.* 2020; 76:233-235.
- Shemer A, Pras E, Hecht I. Peripheral Facial Nerve Palsy Following BNT162b2 (COVID-19) Vaccination. *Isr Med Assoc J.* 2021; 23:143-144.
- Konstantinidis I, Tsakiropoulou E, Hähner A, de With K, Poulas K, Hummel T. Olfactory dysfunction after coronavirus disease 2019 (COVID-19) vaccination. *Int Forum Allergy Rhinol.* 2021; 11:1399-1401.
- Reyes-Capo DP, Stevens SM, Cavuoto KM. Acute abducens nerve palsy following COVID-19 vaccination. *J AAPOS.* 2021; 25:302-303.
- Wichova H, Miller ME, Derebery MJ. Otologic manifestations after COVID-19 vaccination: the house ear clinic experience. *Otol Neurotol.* 2021; 42:e1213–e1218.
- Santovito LS, Pinna G. Acute reduction of visual acuity and visual field after Pfizer-BioNTech COVID-19 vaccine 2nd dose: a case report. *Infamm Res.* 2021; 70:931–933.
- Narasimhalu K, Lee WC, Salkade PR, De Silva DA. Trigeminal and cervical radiculitis after tozinameran vaccination against COVID-19. *BMJ Case Rep.* 2021; 14:e242344.
- “Vaccine Adverse Event Reporting System,” 2022.
- Angum F, Khan T, Kaler J, Siddiqui L, Hussain A. The Prevalence of Autoimmune Disorders in Women: A Narrative Review. *Cureus.* 2020; 12:e8094.
- Klein SL, Marriott I, Fish EN. Sex-based differences in immune function and responses to vaccination. *Trans R Soc Trop Med Hyg.* 2015; 109:9-15.
- Ghezzi A. Clinical characteristics of multiple sclerosis with early onset. *Neurol Sci.* 2004; 25(supplement 4):S336–S339.
- Piyasirisilp S, Hemachudha T. Neurological adverse events associated with vaccination. *Curr Opin Neurol.* 2002; 15:333–338.