

Vocal Fold Paralysis Following COVID-19 Vaccination: Query of VAERS Database

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Summary: Objective. Vocal fold paresis or paralysis (VFP) may severely affect quality of life due to dysphonia and respiratory distress. As an increasing percentage of the United States population receives the COVID-19 vaccination, the objective of this study is to determine the correlation of COVID-19 postvaccination recurrent laryngeal neuropathy and resulting VFP.

Methods. The Vaccine Adverse Event Reporting System database was queried for patients exhibiting symptoms of VFP following COVID-19 vaccination. Patient demographics and clinical information including presenting symptoms, time of symptom onset, time of diagnosis and laterality.

Results. Twenty patients were found to have laryngoscopy confirmed VFP following COVID-19 vaccination. Vaccinations for Pfizer-BioNTech, Moderna, and Janssen were reported. Of those reported, 13 patients were female (65.0%) and seven were male (35.0%), with a mean age of 61.8 years. The most common presenting symptom was a hoarse voice (30.0%). A majority of these cases were unilateral in nature (64.0%). Mean time from vaccination to symptom onset was 12.1 days and mean time from vaccination to diagnosis was 37.6 days.

Conclusion. For patients presenting with voice or swallowing complaints after receiving the COVID-19 vaccine, prompt evaluation by an otolaryngologist should occur. However, the potential VFP side effect of vaccination is very rarely cited in the literature and largely outweighed by the benefits of vaccination. Further research is needed to delineate the exact pathophysiology of this complication and determine whether a causal relationship exists.

Key Words: COVID-19—Vaccination—Vocal fold paresis—Vocal fold paralysis—Vocal fold hypomobility—Vocal fold immobility—Postvaccination vagal neuropathy.

INTRODUCTION

Neurogenic hypomobility, known as vocal fold paresis (VFP), or immobility, known as vocal fold paralysis results from vocal fold denervation secondary to injury to one or both of the recurrent laryngeal nerves. Patients with VFP can present clinically with dysphonia or dysphagia, or are asymptomatic. Postviral vagal neuropathy has also been described as an etiology of unilateral or bilateral vocal fold paresis which occurs following an upper respiratory infection. Several cases of VFP have been described as consequence of viral infections such as Herpes Zoster, Herpes Simplex, West Nile, and Epstein Barr.¹⁻⁵ Vocal cord paralysis or paresis can also occur as a rare complication in the setting of COVID-19 infection and may be due to the neurotoxic effects of SARS-CoV-2.⁶⁻⁹ Though rare, vaccination induced VFP following has also been reported in the literature.¹⁰

Currently, COVID-19 vaccines serve as the only effective and safe form of disease prevention. As an increasing percentage of the United States population receives the COVID-19 vaccination, it is important for physicians to be aware of the potential adverse events and possible

neurological sequela. There are no reports to date of recurrent laryngeal nerve palsy manifesting as VFP following COVID-19 vaccination. As such, the objective of this study is to determine the possibility of COVID-19 postvaccination recurrent laryngeal neuropathy resulting in VFP.

METHODS AND MATERIALS

The United States Vaccine Adverse Event Reporting System (VAERS) database was queried for this study. VAERS is a public database that is co-managed by the Centers for Disease Control and Prevention and the United States Food and Drug Administration. Established in 1990, VAERS is a national early warning system designed to detect possible safety problems in United States licensed vaccines. Healthcare providers, vaccine manufacturers, and the public can submit reports to VAERS through an online form.

A VAERS search was performed for all patients diagnosed with vocal cord paresis or paralysis following vaccination with the COVID-19 vaccine from one of three manufacturers: Pfizer BioNTech, Moderna, or Janssen. Exclusion criteria were the presence of other neurological deficits, intubation, anaphylaxis or allergic reaction that may alter the voice, and recent head and neck surgery. Patients with isolated voice changes, without an established diagnosis of vocal fold paresis or paralysis or patient with reported paresis/paralysis without confirmation with laryngoscopy were noted but not included in analysis.

We collected data on the patient demographics, past medical history, the manufacturer of the vaccine, dose number,

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laterality of vocal fold paralysis, lag time between vaccination and onset of vocal fold dysfunction symptoms and time to diagnosis, and a free text description of the adverse event. Data were exported and compiled in Microsoft Excel (Microsoft Corp, Redmond, Washington, USA).

RESULTS

Our preliminary search of the database found 30 patients with reported vocal cord paresis or paralysis after receiving the COVID-19 vaccine. However, five of these patients had concurrent neurological complications, adverse allergic reaction requiring intubation, or autoimmune disease with paresis as a known complication, and were hence excluded. Moreover, five additional patients without a reported laryngoscopy were also excluded. Ultimately, a total of 19 patients were included in our study. All but four of the cases were described as paralysis. However, we are unable to confirm paralysis vs paresis through the information provided through VAERS.

Half of patients presented due to voice complaints with the most common presenting symptom being hoarse voice in 6/19 (31.6%) patients. Symptoms that prompted evaluation are summarized in Table 1.

The mean age of this cohort was 62.3 years (SD = 12.9). Of the reported patients, seven were male (36.8%) and 12 female (63.2%). Laterality was reported in 17 patients, 15 of which were unilateral and two bilateral. Of the 15 unilateral cases, four involved the right vocal fold, seven the left vocal fold and four were unspecified. The demographics and additional clinical information are shown in Table 2.

The mean lag time between vaccination and symptom onset was 12.1 days (SD = 13.9) for all vaccines; 12.9 days (SD = 15.9) for Pfizer, 15.3 (SD = 11.2) days for Moderna, and 12 days (n = 1) for Janssen. Mean time for diagnosis, calculated as the time from vaccination until laryngoscopy, reported for 14 patients, was 37.6 days (SD = 16.8).

Thirteen of the 19 patients (68.4%) received the Pfizer-BioNTech vaccine, 5/19 (26.3%) received Moderna vaccine, and one (5.3%) received Janssen vaccine. There were 9/13 (69.2%) patients receiving Pfizer-BioNTech vaccine who developed symptoms after their second dose, only 1/13 (7.7%) after their first dose and 3/13 (23.1%) were not

TABLE 1.
Patient Reported Symptoms Prompting Evaluation

Presenting Symptom	n (%)
Dysphagia	1 (5.3%)
Weak voice	3 (15.8%)
Hoarse voice	6 (31.6%)
Sore throat	1 (5.3%)
Laryngitis	1 (5.3%)
Voice change	1 (5.3%)
Ear pain	1 (5.3%)
Not reported	5 (26.3%)

TABLE 2.
Patient Demographics and Clinical Information

Total Patients, n	19
Male, n (%)	7 (36.8%)
Female, n (%)	12 (63.2%)
Mean age at vaccination (SD)	62.3 (12.9)
VFP Laterality, n (%)	
Unilateral	15 (78.9%)
Bilateral	2 (10.5%)
Unspecified	2 (10.5%)
PMH, n (%)	
Diabetes	3 (15.8%)
HTN	4 (21.1%)
Hypothyroidism	3 (15.8%)
Depression & Anxiety	3 (15.8%)
Chron's Disease	1 (5.3%)
CKD on dialysis	2 (10.5%)
None reported	6 (31.6%)
VFP Onset	
Mean days to symptoms (SD)	12.1 (13.9)
VFP Diagnosis	
Mean days to diagnosis (SD)	37.6 (16.8)

Only 14/19 patients had a reported time for diagnosis.

reported. Three of the five (60.0%) patients receiving the Moderna vaccine developed symptoms after their first dose, 2/5 (40.0%) after their second dose.

We also found a total of 1,444 unique cases of reported dysphonia following COVID-19 vaccination. Seven hundred and twenty-three (50.1%) were associated with the Pfizer-BioNTech vaccine, 620 (42.9%) with the Moderna vaccine, and 101 (7.0%) with the Janssen vaccine. However, none of these patients were evaluated by an otolaryngologist and therefore no definitive diagnosis of VFP was established.

DISCUSSION

Postvaccination neuropathy has been controversially discussed in previous literature, with incidence of Guillain-Barre Syndrome first reported in 1976 during a national vaccination program against pandemic swine flu in the United States.¹¹ However, studies investigating the association between GBS and seasonal influenza vaccines after 1976 indicated the risk as very minimal with less than one case per million.¹² Reports of neuropathy have been linked to several other vaccines over the year, including hepatitis B, tetanus-diphtheria-pertussis series, Lyme, Pneumococcal, Polio, Rabies, and most recently the COVID-19 vaccine.¹³⁻²² These cases are very rarely cited and are largely outweighed by the benefits of vaccination.

While much of the existing literature regarding adverse reactions to vaccines describes peripheral neuropathy and other cranial neuropathies, there is a paucity of reports on vaccination induced vocal fold paresis. Talmor et al reported on twenty-two patients in the VAERS database found to have VFP following vaccination with influenza,

shingles, pneumococcus, and hepatitis B vaccine.¹⁰ Our study represents the first investigation of COVID-19 vaccination associated VFP. This study establishes a correlation, and not causation as there have been no clear casual links between vaccines, and more specifically the COVID-19 vaccine, and neuropathy.

In this study, we identified 19 cases of laryngoscopy confirmed VFP after COVID-19 vaccination in an analysis of the VAERS database. The scarcity of reports of recurrent laryngeal nerves involvement may likely be due to the difficulty in establishing a diagnosis. Our study found 1,444 cases of reported dysphonia following vaccination, however, these patients were not evaluated by an otolaryngologist and therefore no definitive diagnosis of VFP was established. This suggests that COVID-19 vaccine induced VFP may be under-reported in the VAERS database.

Our analysis revealed the majority of cases to be unilateral (78.9%) which is consistent with Talmor et al's finding of 50% unilateral cases of vaccine related paresis¹⁰ and with viral induced VFP, which has largely been reported as unilateral.²³ Our average time from vaccination to symptom onset was 12.1 days, which is longer than those previously described by Talmor et al in VFP patients (6.3 days) and Woo et al in extraocular palsies (9 days).^{10,24} However, 84.2% of our patients reported symptoms within 30 days of vaccination which is comparable to 90.0% of patients presenting with VFP⁶ and 77% patients presenting with Bell's palsy.²⁵ There was only one patient who received the Janssen COVID-19 vaccine, with a reported lag time of 12 days. Our average time from vaccination to diagnosis via laryngoscopy was 37.6 days. Interestingly, while 69.2% of patients receiving the Pfizer-BioNTech vaccine developed symptoms after their second dose, 60.0% of patients receiving Moderna developed symptoms after their first dose. However, there was a much smaller cohort of Moderna patients.

Due to the lack of available follow up on these patients, the long-term outcome of the paresis remains unknown. Presumed postimmunization cranial nerve palsies typically resolve spontaneously within 6 months.²⁶ Long-term outcomes for postimmunization VFP have not been reported and further investigation is required to determine if these cases of paresis resolve or are permanent.

Although the pathophysiology behind possible postimmunization paresis remains unknown, we suspect it is similar to that of other cranial nerve palsies following vaccination, which have been described more commonly in the literature.^{26,27} Nerve damage could be due to an immune-mediated, viral-like inflammatory reaction to the vaccine that caused insult to the recurrent laryngeal nerve.

The Centers for Disease Control and Prevention reports that 182 million people have been fully vaccinated in the United States, thus this adverse complication is exceedingly rare. The incidence rate of VFP in vaccinated patients is even rarer than the 19/100,000 reported for Bell's palsy in vaccinated patients. Both of which are significantly lower than the incidence of Bell's palsy in patients with COVID-

19 infection, reported as 82/100,000 patients.²⁸ Recent studies continue to cite the effectiveness of the COVID-19 vaccine against severe disease, with 92% of recent hospitalizations occurring in patients who are not fully vaccinated.²⁹ Therefore, we continue to advocate for the vaccine as a safe and effective form of disease prevention, especially considering the severe laryngeal complications, and vocal fold paresis, that can occur from the disease itself. This potential, side effect pales in comparison to the severity of infections with COVID-19. Nevertheless, for patients presenting with voice or swallowing complaints after receiving the COVID-19 vaccination, we recommend further investigation with laryngoscopy.

This study has several key limitations. The VAERS database is a compilation of reports filed by providers, manufacturers, patients and families. Therefore, we are reliant on public reports that may include incomplete, inaccurate, coincidental, and unverified information. There is no documentation as to how many of these reports are self-reported as opposed to reported by a Licensed Independent Practitioner, nor if there is oversight for legitimacy. As such, the data can be inconsistently described, particularly with use of important descriptive terminology such as paralysis or paresis. Additionally, the reports document when laryngoscopy was performed along with the final diagnosis, however we are unable to review the images and verify their findings. Furthermore, we cannot confirm that there was not a preexisting paresis that was not recognized until after the vaccination. Only the presence of normal laryngoscopy findings prior to the vaccine, followed by documented changes postvaccination are we able to definitively identify when the paralysis or paresis occurred. Nevertheless, this is the most complete information available, and despite these limitations, this study brings to light important considerations for patients presenting to an otolaryngologist with voice complaints.

CONCLUSION

Our investigation of the VAERS database found 19 unique cases of VFP possibly related to COVID-19 vaccination. For patients presenting with voice or swallowing complaints after receiving the COVID-19 vaccine, prompt evaluation by an otolaryngologist should occur. However, it is important to note that the potential VFP side effect of vaccination is very rarely cited in the literature, and no causation has been established. Furthermore, the risks are largely outweighed by the benefits of vaccination.

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