The Journal of Laryngology & Otology

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Vocal fold paralysis following first dose of Oxford-AstraZeneca coronavirus disease 2019 vaccine

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Clinical Record

Mr G M Jama takes responsibility for the integrity of the content of the paper

Cite this article: Jama GM, Amin M, Hassaan A, Kaddour H. Vocal fold paralysis following first dose of Oxford-AstraZeneca coronavirus disease 2019 vaccine. *J Laryngol Otol* 2022;1–3. https://doi.org/10.1017/S0022215122000597

Accepted: 4 October 2021

Key words:
Vocal Cord Paralysis; Dysphonia; COVID-19; Immunization; Vaccines; Drug Side Effects

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Abstract

Background. In a bid to end the ongoing coronavirus disease 2019 pandemic, many countries, including the UK, have rolled out mass immunisation programmes. While considered generally safe and effective, vaccines against coronavirus disease 2019 have been reported to be associated with rare and potentially adverse reactions and side effects.

Case report. This paper reports an unusual case of a patient who developed a unilateral vocal fold paralysis shortly after receiving the first dose of the Oxford-AstraZeneca ChAdOx1 nCov-19 vaccine.

Conclusion. To our knowledge, this is the first reported case of vocal fold paralysis following administration of the Oxford-AstraZeneca vaccine. The authors support the position that currently approved coronavirus disease 2019 vaccines remain safe and effective; however, further surveillance and vigilance using real-world data are highly encouraged.

Introduction

The ongoing global pandemic has resulted in 168 040 871 confirmed cases of coronavirus disease 2019 (Covid-19) and has claimed the lives of 3 494 758 people worldwide, at the time of writing.[1] On 8 December 2020, the United Kingdom became the first country in the world to implement a national vaccination programme, following approval of the Pfizer-BioNTech messenger RNA (mRNA) vaccine (BNT162b2) by the Medicines and Healthcare products Regulatory Agency (MHRA). Since then, the roll-out has expanded to include two further vaccines – the Oxford-AstraZeneca adenovirus vector vaccine, ChAdOx1 nCov-19 (AZD1222), and the Moderna mRNA-1273 vaccine.[2]

Data from clinical trials and national surveillance programmes support the effectiveness of currently approved vaccines in preventing severe infection, hospitalisation and death as a result of Covid-19.[3] Furthermore, there is growing evidence to suggest a marked and sustained decline in the incidence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), corresponding to an increase in vaccine coverage in the general population.[4]

However, as with any new medicines, once vaccines have been approved for the use in people, there is a need to continuously and proactively collect and monitor data outside of the clinical trials setting, to improve our understanding of their safety profile.[5] Known reported side effects of Covid-19 vaccines include localised and systemic reactions that are typically moderate in frequency, mild in severity and relatively short-lived.[6] There have been a small number of reports of rare concurrent thrombocytopaenia and thromboembolic events observed in vaccinated individuals, although a definitive causal link remains to be proven.[7]

This article reports an unusual and, to our knowledge, not previously described case of a patient who developed new-onset dysphonia within days of receiving the first dose of the Oxford-AstraZeneca ChAdOx1 nCov-19 vaccine.

Case report

A 52-year-old man was referred to the otolaryngology clinic on the 2-week-wait suspected cancer referral pathway with a 4-week history of persistent dysphonia. He reported experiencing intermittent episodes of coughing and choking when attempting to swallow food and drink. He had no other associated 'red flag' symptoms related to his upper aerodigestive tract. There was no history of unintentional weight loss or systemic symptoms. He denied any preceding laryngeal trauma, upper respiratory tract infection or clinical features suggestive of underlying gastroesophageal reflux disease.

He reported that his otherwise unexplained symptoms had developed 3 days after receiving the first dose of the Oxford-AstraZeneca ChAdOx1 nCov-19 vaccine. Although he had initially experienced some mild injection site pain and swelling, he reported no other adverse reactions to the vaccine.

His past medical history included hypertension, type 2 diabetes mellitus, hypercholesterolaemia, atrial fibrillation, ischaemic heart disease, myocardial infarction and cardiac

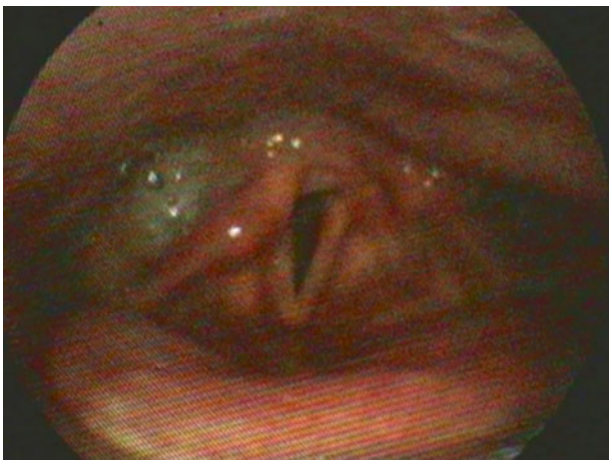

Fig. 1. Endoscopic view of the larynx with the vocal folds in the open (breathing) position, showing a paralysed right vocal fold and pooling of saliva in the right pyriform fossa.

pacemaker insertion. His regular medications included ramipril, eplerenone, metformin, gliclazide, linagliptin, atorvastatin, edoxaban and bisoprolol. He was a smoker with a 15 pack-year history.

On examination, fibre-optic laryngoscopy revealed a paralysed right hemilarynx, with the right vocal fold in the paramedian position. The left vocal fold, although moving adequately, was not fully compensating for the contralateral vocal fold palsy, resulting in incomplete glottic closure and a phonatory gap (Figure 1). There were no overt mucosal lesions seen in the upper airway. The remainder of the physical examination was unremarkable. Specifically, there were no palpable cervical lymph nodes.

A computed tomography scan including the skull base, neck and thorax was organised. Particular attention was paid to the course of the right vagus and recurrent laryngeal nerves, which was found to be unremarkable. There was some evidence of bilateral mild to moderate pulmonary emphysema, particularly in the upper lobes, as well as features of mild bronchiectasis in the lower lobes of the lung. There were also a small number of right-sided paratracheal and hilar lymph nodes measuring 11 mm in maximum diameter.

He was referred to the speech and language therapy department to assist in his further assessment, and to offer therapy to optimise his vocal and swallowing function. He remains under follow up within our department to monitor his ongoing progress.

Discussion

Vocal fold paralysis is the restriction of vocal fold movement due to either a mechanical fixation or a neurological deficit. This can result from a number of aetiologies, including malignancy, trauma, iatrogenic injury, endotracheal intubation or central nervous system disease.[8] Iatrogenic injury as a result of surgery remains the most common cause of unilateral vocal fold paralysis.[9]

It has been postulated that some forms of vocal fold immobility are idiopathic and may be related to viral infections.[10] The pathophysiology of this process is considered to be analogous to viral-induced polyneuritis associated with Guillain–Barré syndrome, or cranial neuropathies such as Bell's palsy, trigeminal neuralgia or glossopharyngeal neuralgia.[11]

While most post-viral neuropathies have been linked to acute infections, some have been observed after vaccination using the influenza, shingles, pneumococcus and hepatitis B vaccines.[12] More recent reports have raised a possible temporal association between the administration of the Pfizer-BioNTech and the Oxford-AstraZeneca vaccines and the incidence of Guillain–Barré syndrome and Bell's palsy in vaccinated individuals.[13–16]

Biological mechanisms have been proposed that might explain the observed association between the use of mRNA vaccines, such as the Pfizer-BioNTech vaccine, and the imbalance in the incidence of Bell's palsy in the vaccine groups compared to placebo groups. These include the suggestion that mRNA vaccines are associated with a marked type I interferon response, which, in some individuals, may trigger and mediate a breakdown of tolerance to myelin sheath antigens, leading to autoimmune neuropathy.[17]

- In light of the ongoing global pandemic, the development of vaccines to protect against coronavirus disease 2019 (Covid-19) infection has become an important public health priority
- While considered generally safe and effective, currently approved vaccines have been reported to be associated with rare and potentially adverse reactions and side effects
- This paper reports an unusual and, to our knowledge, not previously described incident following Covid-19 vaccination
- Specifically, a 52-year-old man developed unilateral vocal fold paralysis days after receiving the Oxford-AstraZeneca ChAdOx1 nCov-19 vaccine

Unlike vaccines using mRNA technology, however, the Oxford-AstraZeneca vaccine consists of a replication-deficient (inactivated) chimpanzee adenovirus vector expressing the full-length SARS-CoV-2 spike (S) protein. Following intramuscular administration of the vaccine, the spike proteins are expressed locally, allowing the immune system to mount a neutralising cellular and humoral response.[18] A proposed mechanism linking the ChAdOx1 nCov-19 vaccine to the development of neuropathy has yet to be described, although it is possible that the underlying process may be mediated by an immune response comparable to the recently observed phenomenon of vaccine-induced immune thrombotic thrombocytopaenia.[19]

Conclusion

To the best of our knowledge, this is the first reported case of vocal fold paralysis following administration of the Oxford-AstraZeneca ChAdOx1 nCov-19 vaccine. Although the clinical presentation may be entirely incidental, and certainly no cause and effect can be concluded at this time, this report raises an important and timely issue around vaccine safety. As with the development of any new vaccine or medicine, the size of clinical trial cohorts invariably means that very rare side effects can only be identified and fully characterised once the product is used in large populations. The authors support the position that the Oxford-AstraZeneca ChAdOx1 nCov-19 vaccine remains safe and effective; however, further surveillance and vigilance using real-world data are highly encouraged.

Competing interests. None declared

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