

CLINICAL NOTE



Tinnitus following COVID-19 vaccination: report of three cases

Daniela Parrino^a , Andrea Frosolini^a , Chiara Gallo^a, Romolo Daniele De Siat^b , Giacomo Spinato^c  and Cosimo de Filippis^a 

^aDepartment of Neuroscience DNS, Audiology and Phoniatrics Unit, University of Padova, Treviso, Italy; ^bDepartment of Oto-Rhino-Laryngology and Head and Neck Surgery, Cliniques Universitaires Saint-Luc, Université Catholique de Louvain, Brussels, Belgium; ^cDepartment of Neurosciences DNS, Section of Otolaryngology and Regional Centre for Head and Neck Cancer, University of Padova, Treviso, Italy

ABSTRACT

Objective: To ensure the safety and quality of vaccines, especially the newest RNA-vaccines against COVID-19, is one of the World Health Organization's current highest priorities.

Design: Case description.

Study sample: We report three cases of sudden unilateral tinnitus following BNT162b2 mRNA-vaccine injection, which rapidly resolved in 2 out of 3 cases.

Results: The mechanism responsible for its development remains unclear. A hypersensitivity reaction with an abnormal autoimmune response or a vasculitic event may be implicated.

Conclusions: Large-scale and well-designed studies are needed to improve surveillance of the COVID-19 vaccine and better define possible adverse reactions involving the cochleo-vestibular system and/or immunisation anxiety-related reactions.

ARTICLE HISTORY

Received 24 March 2021

Revised 9 May 2021

Accepted 14 May 2021

KEYWORDS

COVID-19; BNT162b2; vaccine; tinnitus; side effects

Introduction

The rapid worldwide spread of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) began in December 2019. Since then, the development of a vaccine capable of protecting against the infection became the main objective of the international scientific community. A shared effort, combined with important investments, have led to the extremely rapid production of several vaccines, including new types of RNA-vaccine. The BNT162b2 mRNA vaccine (e.g. *Pfizer*) against CORONA VIRUS Disease 2019 COVID-19 was one of the first approved for mass vaccination campaigns in Europe (Polack et al. 2020). During the phase 2/3 trial on safety and efficacy of the BNT162b2 vaccine, local adverse reactions reported were pain, swelling and redness at injection site; among systemic events fatigue, headache, fever, chills, vomiting, diarrhoea, muscle and/or joint pain were noted (Polack et al. 2020). In early February 2021, side effects such as peripheral facial palsy, facial swelling, and swelling of the lips or tongue, also associated with anaphylaxis, were described after COVID-19 vaccination (Cirillo 2021). More recently (11th March 2021), the first safety update report from the United Kingdom Medicines and Healthcare products Regulatory Agency (MHRA) published adverse effects recorded from *Pfizer* vaccine recipients between January 1st and February 28th, listing 196 tinnitus reports among 33,207 vaccines administered. Sudden hearing loss was also mentioned in 11 cases (Buntz 2021).

Since the beginning of January the *Pfizer* vaccine has been administered to all medical staff at our hospital, immunising 5333 healthcare workers by 24th March 2021; about 7013 doses were administered during the first two months of the vaccine campaign (Fabiani et al. 2021). The reported adverse reactions in

our Health Care institution were moderately consistent with those reported by Polack et al. (2020).

Herein we describe three consecutive cases of tinnitus following BNT162b2 mRNA-vaccine injection, who presented at our tertiary referral centre for audio-vestibular disorders (Audiology Unit, Treviso Hospital) between 1st January and 28th February 2021. Otoscopy examination, Pure Tone audiometry (PTa) and Psychoacoustic Measures of Tinnitus by pitch and loudness matching were performed (Feldmann 1981). The Italian Version of the Tinnitus Handicap Inventory (THI) (Monzani et al. 2008) together with the Visual-Analogue Scale (VAS) (Figueiredo, Azevedo, and Oliveira Pde 2009) were administered to assess the tinnitus disturbance and its related psychological distress. All patients gave their written permission for clinical case publication. The suspected adverse reaction was reported in the dedicated pharmacosurveillance form. Data were examined in accordance with Italian privacy and sensitive data laws, and the in-house regulations of our institution.

Case reports

Case 1

A 37-year-old woman was referred to our department complaining of sudden onset of right tinnitus 7 hours after her first dose of COVID-19 vaccine. She reported short-term dizziness, but she did not notice hearing loss. Local pain at injection site was reported as another vaccine side effect. Her previous medical history was relevant for glaucoma and undifferentiated connective tissue disease. She denied any previous audio-vestibular disorder except for an episode of transient tinnitus related to unremembered side acute otitis media 20 years previously. She was not

Table 1. Clinical characteristics and audiological findings of the reported cases.

Patient	Age, sex	Comorbidities	Type and vaccine dose	Other adverse reactions	Time from vaccination to tinnitus onset	PTA (dB)	THI	VAS	Therapy	Dosage and duration	Time from first visit to follow-up	Post-treatment PTA (dB)	Post-treatment THI	Post-treatment VAS
1	37, F	Glaucoma Undifferentiated connectivitis	BNT162b2 (1st dose)	Local pain	7 hours	14 right 10 left	90	9	Deflazacort	30 mg/day (5 days), 15 mg/day (5 days)	13 days	15 right 10 left	78	7
2	63, M	HP Gastritis Exertional asthma Depression	BNT162b2 (1st dose)	Local pain	20 hours	23 right 34 left	76	8	None	NA	7 days	26 right 30 left	36	5
3	30, M	Hashimoto thyroiditis	BNT162b2 (2nd dose)	Fever Nausea Local pain	6 days	10 right 10 left	78	7	Prednisone	50 mg/day (4 days), 25 mg/day (3 days), 12.5 mg/day (3 days)	16 days	10 right 10 left	6	1

PTA Pure Tone Average (hearing thresholds at 500, 1000, 2000 and 4000 Hz); THI: Tinnitus Handicap Inventory; VAS: Visual Analogue Scale; NA: Not Applicable.

taking any home medications and had no known allergies. She did not report any previous COVID-19 diagnosis. Otoscopy examination was normal bilaterally. Spontaneous nystagmus was absent as well as other focal neurological symptoms. PTA revealed bilateral normal hearing with slight asymmetry on the right ear. The Psychoacoustic Measures of Tinnitus resulted in a 20 dB pure tone at 10000 Hz. The THI score was 90/100. A 10-day course of oral corticosteroid therapy with tapering regimen was started. PTA performed after treatment showed no significant changes. The Psychoacoustic Measures of Tinnitus and THI score slightly improved (78/100), but the patient still complained of tinnitus and an accompanying bilateral ear fullness sensation. A second line therapy was started. A magnetic resonance imaging (MRI) of the internal auditory meatus or cerebellopontine angle ruled out any possible abnormality.

Case 2

A 63-year-old man presented with sudden onset of left tinnitus 20 hours after the first vaccine dose, associated to hyperacusis and dysacusis (increased sensitivity and altered perception of environmental sounds, respectively). He was already known at our department for bilateral symmetrical mild high frequencies sensorineural hearing loss (SNHL). He did not report other adverse effects except local pain. He suffered from chronic gastritis, extrinsic asthma and reactive depression for which he had undergone psychotherapy. He had not previously been diagnosed with COVID-19. Otoscopy examination was normal. PTA revealed a slight threshold worsening on his left ear in comparison with the latest available audiometry performed 6 months before. Psychoacoustic Measures of Tinnitus resulted with a white noise of 25 dB intensity, THI score was 76/100. Oral corticosteroid therapy was proposed, but the patient refused. Control evaluation after 7 days found a spontaneous improvement of PTA, Psychoacoustic Measures of Tinnitus and THI score (36/100). The patient is still on the waiting list for MRI.

Case 3

A 30-year-old man came to our attention complaining of sudden onset of left tinnitus, hyperacusis and dysacusis approximately one week after the 2nd vaccine dose. He also had fever and sickness as other injection side effects, treated with one dose of oral 1000 mg acetaminophen. He had never previously experienced audio-vestibular symptoms. He reported Hashimoto thyroiditis in his past medical history. He denied any home medical therapy or allergies. He had not previously been diagnosed with COVID-19. Otoscopy was normal. PTA showed bilateral normal hearing. THI score was 78/100. He underwent a 10-day course of oral prednisone with tapering regimen, resulting in significant improvement of the auditory phenomena and tinnitus perception (THI score after treatment: 6/100). The patient underwent MRI that excluded internal auditory meatus or cerebellopontine angle pathologies.

Table 1 summarises the patients' clinical characteristics and audiological findings.

Discussion

Vaccinations play a vital role in prevention and control of viral diseases, conferring immunity by exposure of the immune system to specific antigens. Like any other medication, vaccines can

cause adverse reactions. Nevertheless, unlike drugs, problems arising from vaccine administration are frequently less accepted by the general population. Although benefits of vaccination clearly outweigh the risks, fear of adverse reactions (real or perceived) may deter many people from adherence to the vaccination campaign (Yigit, Ozkaya-Parlakay, and Senel 2021).

The World Health Organization updated guidelines defined 5 types of adverse events following immunisation: (i) vaccine product-related reaction; (ii) vaccine quality defect-related reaction; (iii) immunisation error-related reaction; (iv) immunisation anxiety-related reaction; and (v) coincidental event (WHO 2018).

Tinnitus following immunisation is uncommon. It has been reported after hepatitis B, rabies, measles and H1N1 vaccines, associated to SNHL (Okhovat et al. 2015). With regard to Pfizer vaccine against SARS-CoV-2, there was no mention of tinnitus in the article regarding its safety and efficacy (Polack et al. 2020). However, according to the most recent safety update report (21st April 2021) about pharmacosurveillance of the different vaccines against SARS-CoV-2 from the United Kingdom MHRA, there were 2258 reports of tinnitus out of 33 million doses administered (<https://www.tinnitus.org.uk/>). This means that less than 1 in 14,700 people is affected; following the definition of Guidelines for Clinical-Safety Information on Drugs, this side effect is classified as “very rare” (CIOMS 2021). Therefore, tinnitus onset may involve Pfizer vaccine as well as the other mRNA vaccine Moderna and the viral vector vaccine Vaxzevria by Astrazeneca, although infrequently (Buntz 2021). With reference to Janseen by Johnson & Johnson, a causal link between tinnitus and the vaccine has been hypothesised but yet to be established. During its phase 3 trial, 0.03% of vaccine recipients (6 out of 19,630) reported tinnitus after inoculation, but all of them presented underlying risk factors for presenting the symptom (hypertension, hypothyroidism, depression, prior history of tinnitus, allergic rhinitis and medicine use; Buntz 2021).

A clinical description of tinnitus after COVID-19 vaccine and the possible mechanisms responsible for its development is still lacking. This is the first descriptive report of three cases of sudden unilateral tinnitus following BNT162b2 vaccine injection, which rapidly resolved in 2 out of 3 cases. A hypersensitivity reaction may be implicated in the pathogenesis, causing an abnormal autoimmune response (mediated by circulating immune complexes or cytotoxic vestibule-cochlear autoantibodies) or a vasculitic event with subsequent localised damage to the cochlea (Ciorba et al. 2018). Patients' pre-existing history of atopy (case 2) and autoimmune disorders (cases 1 and 3) may have increased the likelihood of a dysregulated autoimmune response. On the other hand, an immunisation anxiety-related reaction can be postulated, as anxiety has also been related to the severity and persistency of tinnitus (Elarbed et al. 2021). Autoimmune inner ear disease also has to be considered in the differential diagnosis, although it typically differs in clinical presentation (Ciorba et al. 2018). Lastly, a coincidental event may have occurred. We prescribed an MRI to all patients to rule out any possible abnormality of the internal auditory meatus or cerebellopontine angle. As previously reported, no abnormalities were found.

In conclusion, given our reported experience, the recent report by MHRA and the preliminary data on tinnitus and SNHL caused by Sars-CoV-2 infection (Almufarrij and Munro 2021), large-scale well-designed studies are needed to improve surveillance of the COVID-19 vaccine, to clearly establish if

tinnitus is an adverse effect and better define possible adverse reactions involving the cochleo-vestibular system.

Acknowledgments

The authors thank: Alessandro Incognito, MD and all audiometrists of Audiology Unit, Treviso Hospital, for their contribution in assisting the patients. Mauro Ramigni, MD, Local Health Unit, ULSS 2 Marca Trevigiana, Treviso, for information with regard to COVID-19 vaccine doses administered. Ms. Alison Garside for correcting the English version of the paper.

Disclosure statement

No potential conflict of interest was reported by the author(s).

ORCID

Daniela Parrino  <http://orcid.org/0000-0002-1841-4805>

Andrea Frosolini  <http://orcid.org/0000-0003-1347-4013>

Romolo Daniele De Siati  <http://orcid.org/0000-0003-4514-8095>

Giacomo Spinato  <http://orcid.org/0000-0001-5295-5077>

Cosimo de Filippis  <http://orcid.org/0000-0002-2491-7783>

References

- Almufarrij, I., and K. J. Munro. 2021. “One Year on: An Updated Systematic Review of SARS-CoV-2, COVID-19 and Audio-Vestibular Symptoms.” *International Journal of Audiology*. Mar 22:1–11. doi:10.1080/14992027.2021.1896793.
- British Tinnitus Association. <https://www.tinnitus.org.uk/coronavirus-vaccines-and-tinnitus/> Accessed 5 May 2021.
- Buntz, Brian. 2021. “Is JJS COVID-19 Vaccine Linked to Tinnitus?,” February 25. <https://www.drugdiscoverytrends.com/is-jjs-covid-19-vaccine-linked-to-tinnitus/>
- Buntz, Brian. 2021. “Tinnitus Reports Grow Amid COVID-19 Vaccinations,” March 11. <https://www.drugdiscoverytrends.com/tinnitus-reports-grow-amid-covid-19-vaccinations/>
- Ciorba, A., V. Corazzi, C. Bianchini, C. Aimoni, S. Pelucchi, P. H. Skarżyński, and S. Hatzopoulos. 2018. “Autoimmune Inner Ear Disease (AIED): A Diagnostic Challenge.” *International Journal of Immunopathology and Pharmacology*. 32: 2058738418808680. Mar-Decdoi: 10.1177/2058738418808680.
- Cirillo, N. 2021. “Reported Orofacial Adverse Effects of COVID-19 Vaccines: The Knowns and the Unknowns.” *Journal of Oral Pathology & Medicine* 50 (4): 424–427. doi:10.1111/jop.13165.
- Council for International Organizations of Medical Sciences (CIOMS). 2001. *Guidelines for Preparing Core Clinical-Safety Information on Drugs. Report of CIOMS Working Groups III and V* (2nd ed.). Geneva: CIOMS.
- Elarbed, A., K. Fackrell, D. M. Baguley, and D. J. Hoare. 2021. “Tinnitus and Stress in Adults: A Scoping Review.” *International Journal of Audiology* 60 (3): 171–182. doi:10.1080/14992027.2020.1827306.
- Fabiani, M., M. Ramigni, V. Gobetto, A. Mateo-Urdiales, P. Pezzotti, and C. Piovesan. 2021. “Effectiveness of the Comirnaty (BNT162b2, BioNTech/Pfizer) Vaccine in Preventing SARS-CoV-2 Infection among Healthcare Workers, Treviso Province, Veneto Region, Italy, 27 December 2020 to 24 March 2021.” *Eurosurveillance* 26 (17): 2100420. doi:10.2807/1560-7917.ES.2021.26.17.2100420.
- Feldmann, H. 1981. “Homolateral and Contralateral Masking of Tinnitus.” *Journal of Laryngology and Otology. Supplement* 4: 60–70.
- Figueiredo, R. R., A. A. Azevedo, and M. Oliveira Pde. 2009. “Correlation Analysis of the Visual-Analogue Scale and the Tinnitus Handicap Inventory in Tinnitus Patients.” *Brazilian Journal of Otorhinolaryngology* 75 (1): 76–79. doi:10.1016/s1808-8694(15)30835-1.
- Monzani, D., E. Genovese, A. Marrara, C. Gherpelli, L. Pingani, M. Forghieri, M. Rigatelli, T. Guadagnin, and E. Arslan. 2008. “Validity of the Italian Adaptation of the Tinnitus Handicap Inventory; Focus on Quality of Life and Psychological Distress in Tinnitus-Sufferers.” *ACTA Otorhinolaryngologica Italica* 28 (3): 126–134.

- Okhovat, S., R. Fox, J. Magill, and A. Narula. 2015. "Sudden Onset Unilateral Sensorineural Hearing Loss after Rabies Vaccination." *BMJ Case Rep* 2015: bcr2015211977. doi:[10.1136/bcr-2015-211977](https://doi.org/10.1136/bcr-2015-211977).
- Polack, F. P., S. J. Thomas, N. Kitchin, J. Absalon, A. Gurtman, S. Lockhart, L. Perez, et al. 2020. "Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine." *New England Journal of Medicine* 383 (27): 2603–2615. doi: [10.1056/NEJMoa2034577](https://doi.org/10.1056/NEJMoa2034577).
- World Health Organization (WHO). 2018. *Causality Assessment of an Adverse Event following Immunization (AEFI): User Manual for the Revised WHO Classification* (2nd ed.). Geneva: World Health Organization; Licence: CC BY-NC-SA 3.0 IGO.
- Yigit, M., A. Ozkaya-Parlakay, and E. Senel. 2021. "Evaluation of COVID-19 Vaccine Refusal in Parents." *The Pediatric Infectious Disease Journal* 40 (4): e134–e136. doi:[10.1097/INF.0000000000003042](https://doi.org/10.1097/INF.0000000000003042).