Introduction

Although vaccination with vector-based or mRNA-based SARS-CoV-2 vaccines is usually well tolerated, they are not free of side effects. Some of these side effects can be severe and concern the primary care physician, otorhinolaryngologist, and the neurologist. Persisting, unilateral tinnitus time-linked to the first dose and worsening after the second dose of an mRNA-based SARS-CoV-2 vaccine has not been reported. Study Design: Case report. Methods: Routine tests were applied to investigate the patient. Results: A 35-year-old male experienced sudden onset of right-sided tinnitus, diffuse headache, and ear and right-sided facial pressure 22 days after the first dose of an mRNA-based SARS-CoV-2 vaccine. Since symptoms worsened after the second dose, 28 days later, the patient started a self-medication with non-steroidal anti-inflammatory drugs, without benefit. After an otorhinolaryngologist suspected Meniere’s disease, prednisone was given for 5 days with significant improvement. After discontinuation of steroids, however, previous symptoms recurred with similar intensity as before. Cetirizin and loratadin were started resulting in complete resolution of headache and pressures but persistence of tinnitus. After exclusion of various differentials, a causal relation between clinical presentation and vaccination was suspected. Conclusions: SARS-CoV-2 vaccination can be followed by unilateral persisting tinnitus, headache, and ear and right-sided facial pressure. Since steroids and anti-histamines had a beneficial effect, an immunological pathophysiology is quite likely.

Keywords: COVID-19, headache, SARS-CoV-2, steroids, tinnitus, vaccination
Symptoms worsened again after discontinuation of prednisone. Clinical neurologic exam, blood tests, electroencephalography (EEG), and cerebral magnetic resonance imaging (MRI) were non-informative. Cerebrospinal fluid investigations were not carried out. Seven days after discontinuation of prednisone, cetirizin and loratadin were started and improved symptoms except for tinnitus. Ear respectively facial pressure and headache transitioned from constant to occasional. Facial and aural fullness and headache resolved completely 1 month later but tinnitus persisted [Table 1]. Montelukast and fluticasone for 2 weeks were ineffective. A second neurologist prescribed nortriptyline but tinnitus still persisted. Only acetazolamide provided some relief [Table 1].

### Discussion

The presented patient is interesting for primary care physicians, otolaryngologists, and neurologists for unilateral, persisting tinnitus time linked to a vaccination with an mRNA-based SARS-CoV-2 vaccine and for the beneficial effect of steroids. Side effects after SARS-CoV-2 vaccinations, particularly neurological, are increasingly recognized. They include Bell's palsy,[8] dizziness, headache, pain, muscle spasms, myalgia, paraesthesias, tremor, diplopia, tinnitus, dysphonia, seizures, stroke, intra-cerebral bleeding, Guillain-Barre syndrome (GBS), transverse myelitis, acute disseminated encephalomyelitis, multiple sclerosis, neuromyelitis optica, hypophysitis, venous sinus thrombosis, reversible cerebral vasoconstriction syndrome, small fiber neuropathy, Tolosa-Hunt syndrome, and reactivation of herpes zoster.[5-7] All physicians involved in the management of SARS-CoV-2 vaccinees should be aware of these side effects to react appropriately in due time.

Arguments for a causal relation between tinnitus and the SARS-CoV-2 vaccination are that complaints started time linked to the vaccination, that reversible tinnitus has been recently reported as a complication of the first Astra Zeneca dose,[9] and that cranial nerve neuritis and GBS have been reported as complications of a SARS-CoV-2 vaccination.[10,11] Arguments against a causal relation are that persistent tinnitus has not been reported earlier and the long latency of 22 days between vaccination and onset of complaints. However, the vaccine adverse event reporting system (VAERS) lists 387 patients having undergone SARS-CoV-2 vaccination, who complained about post-vaccination tinnitus as per the end of May 2021. This means that 2.23% of VAERS reports for side effects of SARS-CoV-2 vaccines mention tinnitus. Thus, a VAERS report for a SARS-CoV-2 vaccine is 4.46 times more likely to mention tinnitus than a VAERS report for a flu vaccine over the 2020–2021 timeframe. Since more arguments can be raised in favor than against, a causal relation between vaccination and tinnitus is quite likely.

The pathophysiology of tinnitus remains speculative. Conceivable are that the mRNA entered the cochlea via hematogenic spread, thrombosis of a cochlear vein occurred, there was isolated neuritis of the cochlear nerve, there was focal encephalitis, or thrombosis of cerebral veins had occurred. It is also conceivable that immunologic reactions against the virus secondarily affected cochlear structures or the cochlear nerve. Unfortunately, the patient had not undergone magnetic resonance venography and the D-dimer had not been measured in the serum. Missing are also CSF investigations and a cerebral MRI with contrast medium. Missing are cytokine levels and other immunological parameters.

| Symptoms and measures                                      | Date    | Consequence                                      |
|-----------------------------------------------------------|---------|--------------------------------------------------|
| 1. Dose of mRNA-based SARS-CoV-2 vaccine                  | 9.1.21  | No immediate reaction                            |
|                                                           | 31.1.21 | Right-sided tinnitus, diffuse                    |
|                                                           |         | Headache, right-sided aural fullness             |
|                                                           |         | Right-sided facial pressure                      |
| 2. Dose of mRNA-based SARS-CoV-2 vaccine                  | 6.2.21  | Tinnitus, headache, facial/ear pressure increase, takes pseudoephedrine, oxymetazoline, paracetamol, ibuprofen (no benefit) |
| PCP diagnoses external otitis and gives neomycin + amoxicillin ear drops | 17.2.21 | No benefit                                      |
| ENT diagnoses Meniere’s disease and gives prednisone 40 mg/d for 5 days | 27.2.21 | Headache improves, but tachycardia and paraesthesias, tingling of right face |
| Chest XR + ECG + cCCT at ER                                | 27.2.21 | Normal                                           |
| Off prednisone                                            | 3.3.21  | Headache, pressures recur                        |
| 1. Neurologist orders cerebral MRI, blood work             | 3.3.21  | Normal                                           |
| EEG                                                       | 10.3.21 | Normal                                           |
| Starts cetirizin, loratadin                               | 10.3.21 | Symptoms improve, except tinnitus               |
| Pressures, headache                                       | mid March | Transition to occasional                        |
| 2. Neurologist gives nortriptyline                         | 2.4.21  | Ineffective                                      |
| Hearing test                                              | 7.4.21  | Normal                                           |
| Headache, pressures                                       | mid April | Resolve Completely                              |
| PCP gives montelukast, fluticasone for 2 w                 | 23.4.21 | No benefit                                       |
| PCP gives prednisone (50 mg/d)                             | 26.4.21 | No benefit                                       |
| Neurologist stops nortriptyline, starts acetazolamide     | 4.5.21  | Drops volume of tinnitus                        |
| Immunologist orders blood work                             | 10.5.21 | Non-informative                                  |
In conclusion, SARS-CoV-2 vaccination can be followed by unilateral persisting tinnitus, diffuse headache, and unilateral ear respectively facial pressure. Since steroids and anti-histamines had a beneficial effect, an immunological cause of the tinnitus is quite likely. These findings are novel and should be considered by those managing SARS-CoV-2 vaccines.

**Author contribution**
JF: design, literature search, discussion, first draft, and critical comments; RE: literature search, discussion, critical comments, and final approval.

**Informed consent**
Obtained.

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Nil.

**Conflicts of interest**
There are no conflicts of interest.

**References**
1. Anand P, Stahel VP. Review the safety of Covid-19 mRNA vaccines: A review. Patient Saf Surg 2021;15:20.
2. Finsterer J, Scorza FA. SARS-CoV-2 vaccines are not free of neurological side effects. Acta Neurol Scand 2021;144:109-10.
3. Waheed S, Bayas A, Hindi F, Rizvi Z, Espinosa PS. Neurological complications of COVID-19: Guillain-Barre syndrome following Pfizer COVID-19 vaccine. Cureus 2021;13:e13426.
4. Finsterer J. Exacerbating Guillain-Barre syndrome eight days after vector-based COVID-19 vaccination. Case Rep Infect Dis 2021;2021:3619131.
5. Goss AL, Samudralwar RD, Das RR, Nath A. ANA investigates: Neurological complications of COVID-19 vaccines. Ann Neurol 2021;89:856-7.
6. Bhopal SS, Olabi B, Bhopal R. Vaccines for COVID-19: Learning from ten phase II trials to inform clinical and public health vaccination programmes. Public Health 2021;193:57-60.
7. Finsterer J. Neurological side effects of SARS-CoV-2 vaccinations. Acta Neurol Scand 2022;145:5-9.
8. Tseng PT, Chen TY, Sun YS, Chen YW, Chen JJ. The reversible tinnitus and cochleopathy followed first-dose AstraZeneca COVID-19 vaccination. QJM 2021;114:663-4.
9. Leber HM, Sant’Ana L, Konichi da Silva NR, Raio MC, Mazzeo TJMM, Endo CM, et al. Acute thyroiditis and bilateral optic neuritis following SARS-CoV-2 vaccination with CoronaVac: A case report. Ocul Immunol Inflamm 2021;1-7. doi: 10.1080/09273948.2021.1961815.
10. 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.