Observational Study

Audiological characteristics and exploratory treatment of a rare condition of acute-otitis-media-associated sudden sensorineural hearing loss

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Abstract

BACKGROUND
Acute otitis media (AOM) is a common disease that is more prevalent in children. Most studies concerning AOM-associated sudden sensorineural hearing loss are case reports and retrospective in nature, hence the etiology of AOM-associated sudden hearing loss has not been fully established.

AIM
To analyze audiological characteristics of AOM-associated sudden hearing loss and evaluate efficacy of combined tympanostomy tube placement (TTP) and intratympanic methylprednisolone.

METHODS
Eight adult patients who were diagnosed with AOM-associated sudden hearing loss and ineffectively treated by conventional medical therapy were enrolled in this study. Basic data were collected, and pure tone audiometry was performed to assess the audiological characteristics. Combination therapy with TTP and intratympanic methylprednisolone injection was given to the patients.

RESULTS
Mixed or sensorineural hearing loss was observed at high frequencies (2–4 kHz). All the cases in this study were cured after TTP and intratympanic methylprednisolone. After treatment, the average hearing threshold at affected frequencies was significantly lower than those in the pretreatment group ($P < 0.05$) and was similar to that in the healthy ears ($P > 0.05$).

CONCLUSION
AOM rarely induces sudden sensorineural hearing loss. Combination therapy
INTRODUCTION

Acute otitis media (AOM) is a common disease that is more prevalent in children, affecting > 80% of children before the age of 3 years[1]. Globally, there are > 709 million new cases reported every year[2,3]. AOM is mainly caused by acute viral infection of the upper respiratory tract, which alters eustachian tube function and exposes the middle ear to bacterial infiltration[4]. There may be a conductive hearing loss if the patient also has tympanic effusion, and the degree of hearing loss can vary from negligible to 60 dB[5,8]. In the clinic, antibiotics and early myringotomy are the only two treatment options currently available for AOM patients[9]. Sudden sensorineural hearing loss is a frightening symptom that affects about 5–27 per 100000 people annually, with around 66000 new cases per year in the United States[10]. Most of these cases received corticosteroids as initial therapy[11]. Furthermore, intratympanic steroid administration is suggested as salvage therapy when initial therapy fails[11,12]. However, AOM-associated sudden sensorineural hearing loss is a rare otological condition and the mechanism and treatment methods have not been defined.

Most studies concerning AOM-associated sudden sensorineural hearing loss are case reports and retrospective in nature[12-14], hence, the etiology of AOM-associated sudden hearing loss has not been fully established. One of the hypotheses is that effusion in the middle ear causes vibration limitation and hypoxia of two windows, which leads to bone conduction hearing loss[15]. Another hypothesis for the sudden deafness is that the toxins released by infection enter the inner ear through the round window membrane (RWM)[16]. Since absorbing the effusion in the middle ear does not completely restore sensorineural hearing loss, the latter hypothesis currently seems more acceptable. Even though AOM-associated sudden hearing loss is a rare otological disorder, if not treated on time, it might cause permanent hearing loss. Therefore, it is important that the disorder is diagnosed early and treated immediately. This study described the audiological features of patients with AOM-associated sudden hearing loss and evaluated the clinical efficacy of tympanostomy tube placement (TTP) and intratympanic methylprednisolone injection after failure of conventional medical treatment.
MATERIALS AND METHODS

Subjects
Patients with AOM-associated sudden hearing loss who visited the Department of Otolaryngology of Beijing Tsinghua Changgung Hospital between October 1, 2018 and June 1, 2020 were enrolled for this retrospective study. Written consent was signed by all the subjects, and this study was approved by the Human Research Ethics Committee of Beijing Tsinghua Changgung Hospital.

The patients were chosen based on following criteria: (1) Age 18–70 years; (2) AOM was diagnosed based on clinical symptoms, pneumatic otoscopy, pure-tone audiometry (PTA) and tympanometry; (3) Sudden hearing loss was diagnosed according to the Guidelines for Diagnosis and Management of Sudden Hearing Loss (2015), if PTA showed a decrease in hearing threshold ≥ 20 dB, for at least two consecutive frequencies from 0.25 to 4 kHz[17]; and (4) Conventional medical therapy was ineffective.

Exclusion criteria were as follows: (1) Current administration of oral or topical antibiotics for the affected ear; (2) Steroid treatment within 10 d before enrollment; (3) Previous perforation in the affected ear; (4) Allergic to cefuroxime axetil, cefdinir or moxifloxacin; and (5) Grommet (ventilation tube) in the affected ear.

Intervention
All patients underwent myringotomy under local anesthesia, a ventilation tube was placed, and intratympanic injection of methylprednisolone (approximate 0.4 mL, 40 mg/mL) was given once every 3–4 d. The surgical procedures were performed by an experienced physician. The injection was given at most four times and PTA was performed 2 d after the last treatment or when hearing improvement was reported by the subjects.

Audiometric evaluation
Pure-tone test: It was conducted by using audiometry (TDH-39P Telephonics headset; Clinical Audiometer AC40, Interacoustics Company, Assens, Denmark, and the B-71 bone vibrator) in a sound-insulated cabin. The frequency-specific threshold was determined as the lowest sound intensity that the patient could hear at the specific frequency. The air conduction thresholds at 0.25, 0.5, 1, 2 and 4 kHz were determined.

Measurement of bone conduction thresholds: A B-71 bone vibrator was placed on the mastoid protrusion of the temporal bone of the subjects. The BC threshold values were determined at 0.25, 0.5, 1, 2 and 4 kHz.

Air–bone gap: The air–bone gap (ABG) was calculated as the difference between the pure-tone bone conduction and air conduction thresholds.

Average hearing at affected frequencies: When the bone conduction threshold was ≥ 20 dB over two or more consecutive frequencies, these frequencies were determined as affected frequencies. An average hearing at the affected frequencies was determined as the average hearing threshold at the corresponding frequencies.

Evaluation of efficacy
An improvement of ≥ 15 dB of the average hearing threshold at the affected frequencies after treatment was identified as effective, whereas an improvement of < 15 dB was identified as ineffective. A cure was defined as restoring the average hearing threshold at the affected frequencies to the normal hearing levels or the contralateral hearing levels after treatment.

Statistical analysis
The data were evaluated by using SPSS version 26.0 (Chicago, IL, United States). The data were expressed as mean ± SD. The changes in the hearing threshold values before and after treatment were analyzed by nonparametric test, and the difference was considered statistically significant if \( P < 0.05 \).
RESULTS

**Demographics**
Eight patients who met the inclusion criteria were included in the study (Table 1), with an average age of 51.1 ± 13.60 years. All of them were affected in one ear with different degrees of bone conduction hearing loss.

**Audiological characteristics pretreatment**
The bone conduction and air conduction threshold values of the affected ears and healthy ears at different frequencies are listed in Table 2. Table 2 shows that the hearing threshold values of the affected ears were significantly higher than those of the contralateral healthy ears over 0.5, 1, 2 and 4 kHz for bone conduction \((P < 0.05)\) and at all frequencies for air conduction. The audiogram data clearly showed that conductive hearing loss was observed at low frequencies, and mixed or sensorineural hearing loss was seen at high frequencies (Figure 1). Bone conduction hearing was impaired at 2 kHz in all patients, i.e., an incidence rate of 100%. The average hearing threshold of the affected frequencies was 37.19 ± 9.49 dB.

The frequency ranges of 0.25–1 kHz and 2–4 kHz were defined as low and high frequencies, respectively. The bone conduction threshold values at low frequencies were close to normal, and hearing loss was observed at high frequencies, with significant difference \((P < 0.05)\) (Table 3). The average ABG was greater in the low frequency group, but the difference between the two groups was not statistically significant (Table 3).

**Audiological characteristics and efficacy after treatment**
The average interval from disease onset to the start of treatment was 8.63 ± 10.60 d (range, 3–30 d). All eight patients received TTP and intratympanic methylprednisolone injection (the average number of injections was 2), and were cured after treatment. The average hearing threshold value at the affected frequencies post-treatment was significantly lower than the pre-treatment value \((P < 0.05)\), whereas it was not significantly different from that of the healthy ears \((P > 0.05)\) (Table 4). The audiological changes observed after the treatment were shown in a post-treatment audiogram (Figure 2). The average ABG was significantly improved \((P < 0.05)\) (Table 5). These results indicated that the combination of TTP and intratympanic methylprednisolone injection was a good salvage treatment regimen for patients suffering from AOM associated sudden hearing loss after failure of the conventional treatment.

DISCUSSION

The pathogenesis of sensorineural hearing loss in patients with AOM has been investigated, and the leading proposed theory is that an inflammation induces increased permeability of RWM, which allows the entry of endotoxins and ionic disequilibrium in the cochlea[17]. The bacterial (e.g., Streptococcus pneumoniae) byproducts and inflammatory mediators associated with AOM have been proven to enhance the permeability of RWM and cause subsequent cochlear damage[16,18,19]. It was found that the resulting hearing loss predominantly affected the hearing threshold values at high frequencies, which supports the above-mentioned theory [20]. In this study, it was found that the audiological characteristics of the patients with AOM-associated sudden hearing loss were as follows: ABG at low frequencies and bone conduction hearing loss at high frequencies. These results were in accordance with a previous case report, in which a female patient who was diagnosed with AOM-associated bilateral sudden hearing loss presented with higher hearing threshold values for both bone and air conduction at 2 and 4 kHz frequencies[13]. Despite the similar results reported in several studies, the pathological explanation for the elevation in hearing thresholds at high frequencies following AOM with effusion has not been fully elucidated. It is noteworthy that the prognosis of low frequency hearing loss was demonstrated to be better than that of high frequency. Patients with low frequency hearing loss showed a significantly higher recovery rate (74.1%, 40/54) than those with high frequency hearing loss (45.6%, 26/57) \((P < 0.001)\)[21]. High-frequency hearing loss has also been associated with various symptoms such as deterioration in music perception[22]. In addition, a longitudinal cohort study showed that patients who had chronic suppurative otitis media and hearing loss after recurrent AOM are more likely to suffer from dizziness in adulthood[23], indicating that AOM-associated high frequency
Table 1 Demographics of the enrolled patients (n = 8, mean ± SD)

| Case No. | Side of the affected ear | Gender | Age (yr) | Hearing loss | Tinnitus | Curve type |
|---------|--------------------------|--------|----------|-------------|----------|------------|
|         | Left                     | Right  | Male     | Female      | Yes      | No         | No         | Light      | Middle    | Severe    | A | B | C |
| 1       | ✓                        | ✓      | 37       | ✓           | ✓        | ✓          | ✓          | ✓          |           |           |   |   |   |
| 2       | ✓                        | ✓      | 38       | ✓           | ✓        | ✓          | ✓          | ✓          |           |           |   |   |   |
| 3       | ✓                        | ✓      | 47       | ✓           | ✓        | ✓          | ✓          | ✓          |           |           |   |   |   |
| 4       | ✓                        | ✓      | 63       | ✓           | ✓        | ✓          | ✓          | ✓          |           |           |   |   |   |
| 5       | ✓                        | ✓      | 59       | ✓           | ✓        | ✓          | ✓          | ✓          |           |           |   |   |   |
| 6       | ✓                        | ✓      | 67       | ✓           | ✓        | ✓          | ✓          | ✓          |           |           |   |   |   |
| 7       | ✓                        | ✓      | 34       | ✓           | ✓        | ✓          | ✓          | ✓          |           |           |   |   |   |
| 8       | ✓                        | ✓      | 64       | ✓           | ✓        | ✓          | ✓          | ✓          |           |           |   |   |   |
| Total   | 6                        | 2      | 2        | 6           | 8        | 0          | 6          | 0          | 2          | 0        | 1 | 7 | 0 |

Table 2 Comparison of bone conduction and air conduction thresholds between the affected and contralateral healthy ears (dB HL, mean ± SD)

| Group             | No. | 0.25 kHz, BC   | 0.5 kHz, BC   | 1 kHz, BC   | 2 kHz, BC   | 4 kHz, BC   |
|-------------------|-----|----------------|----------------|-------------|-------------|-------------|
| Affected ears     | 8   | 9.38 ± 5.60    | 17.50 ± 9.63  | 18.75 ± 9.16| 33.12 ± 12.51| 39.38 ± 17.41|
| Healthy ears      | 8   | 8.13 ± 5.30    | 13.13 ± 5.30  | 11.25 ± 6.40| 17.50 ± 8.86 | 22.50 ± 11.34|
| Z                 | -0.220 | 0.200      | -1.282         | -1.973     | -0.570     | 0.031       |
| P value           | 0.826 | 0.200      | 0.200          | 0.010     | 0.031     | 0.031       |
| Group             | No. | 0.25 kHz, AC   | 0.5 kHz, AC   | 1 kHz, AC   | 2 kHz, AC   | 4 kHz, AC   |
| Affected ears     | 8   | 28.13 ± 11.63  | 31.88 ± 15.34 | 38.75 ± 18.27| 38.75 ± 16.42| 56.25 ± 22.16|
| Healthy ears      | 8   | 8.13 ± 5.30    | 13.13 ± 5.30  | 11.25 ± 6.40| 17.50 ± 8.86 | 22.50 ± 11.34|
| Z                 | 2.965 | 2.971      | 2.971          | 3.242     | 2.979     | 2.905       |
| P value           | 0.003 | 0.003      | 0.003          | 0.005     | 0.005     | 0.005       |

AC: Air conduction; BC: Bone conduction.

Table 3 Comparison of average bone conduction thresholds and air-bone gap at low and high frequency

| Group                  | 0.25-1 kHz    | 2-4 kHz      | Z          | P value |
|------------------------|--------------|--------------|------------|---------|
| Average BC threshold   | 15.25 ± 6.52 | 36.25 ± 6.52 | -2.897     | 0.004   |
| Air-bone gap           | 16.25 ± 11.64| 11.56 ± 6.80 | -0.527     | 0.598   |

BC: Bone conduction.

hearing loss in childhood may influence the hearing and quality of life in the long term. Therefore, high-frequency audiometry should be considered for AOM patients to detect early changes in the auditory thresholds, and early intervention should be planned when plausible. To the best of our knowledge, this study is the largest case study that has investigated the audiological characteristics of patients with AOM-associated sudden deafness.

Currently, the front-line treatment choices for AOM, according to the guidelines and clinicians, are antibiotics and myringotomy, alone or in combination with ventilation tube placement. Song et al.[9] suggested that early myringotomy (with or without placing ventilation tubes) and antibiotics significantly improved clinical outcomes of eight patients with AOM. As for the sudden sensorineural hearing loss, it was recommended by the American Academy of Otolaryngology guidelines that systemic...
corticosteroids and/or hyperbaric oxygen therapy should be adopted as soon as the diagnosis was made, if needed an intratympanic steroid injection was recommended as a possible salvage therapy[11].

However, there is no standard treatment modality for patients with AOM-associated sudden deafness due to limited evidence and rarity of the disease. In the current study, antibiotics and intravenous methylprednisolone were administered in all eight patients; however, the treatment was ineffective. A combination treatment of TTP and intratympanic methylprednisolone injection was applied as a salvage and exploratory therapy. All the patients in this study showed improvement in BC threshold values at the affected frequencies and showed improvement in ABG. The results were in accordance with a previous study. Seven patients with sensorineural hearing loss associated with AOM were offered intratympanic steroids after oral antibiotics and oral prednisolone failed to improve hearing. Hearing improvement was achieved in 57% of patients (4/7) after intratympanic injections of methylprednisolone. A possible reason is that intratympanic methylprednisolone injection can provide a concentrated local steroid effect in nonresponders to antibiotics. The results clearly indicated that the combination therapy of TTP and intratympanic glucocorticoid injection was a good choice for treating patients with AOM-associated sudden deafness after failure of conventional medical treatment.

However, further well-designed studies are needed to verify the findings of the current study as there were some limitations to this study. Firstly, AOM-associated sudden hearing loss is a rare disease in adults, thus, the sample size of this study was too small. Secondly, a control group in which no further treatment was provided after failure of the first treatment was not accommodated in this study. Hence in the future,
Figure 2 Audiogram. Audiogram after treatment: Conductive hearing loss at low frequencies of the same patient disappeared and sensorineural hearing loss observed at high frequencies of 2–4kHz was restored to the hearing level of the healthy ear; the hearing threshold of the left ear was normal. O: Air conduction of right ear = bone conduction of right ear; ×: Air conduction of left ear = bone conduction of left ear; blue markers = left ear; red markers = right ear.

well-designed studies with a larger sample size are required to further corroborate findings of this study.

CONCLUSION
In summary, the current case study indicated that AOM may rarely induce sudden sensorineural hearing loss, and high frequencies (2–4 kHz) are often involved. Combination therapy with TTP and intratympanic methylprednisolone injection may be a good salvage treatment modality for patients with AOM-associated sudden hearing loss after failure of conventional treatment.

ARTICLE HIGHLIGHTS

Research background
Acute otitis media (AOM) is a common disease in children, affecting > 80% of children before the age of 3 years. AOM-associated sudden sensorineural hearing loss is a rare otological disorder, and the mechanism and treatment methods remain to be investigated.

Research motivation
If AOM-associated sudden hearing loss is not treated on time, it might cause permanent hearing loss. Therefore, early diagnosis and treatment of AOM-associated sudden hearing loss are important.

Research objectives
This study aimed to describe the audiological features of the patients with AOM-associated sudden hearing loss and evaluate the clinical efficacy of tympanostomy tube placement (TTP) and intratympanic methylprednisolone injection after failure of conventional medical therapy.

Research methods
Patients with AOM-associated sudden hearing loss who visited the Department of Otolaryngology of Beijing Tsinghua Changgung Hospital between October 1, 2018 and June 1, 2020 and were ineffectively treated by conventional medical therapy were enrolled in this study. Basic data were collected, and pure-tone audiometry was performed to assess the audiological characteristics. Combination therapy with TTP and intratympanic methylprednisolone injection was given to the patients.
Research results
Mixed or sensorineural hearing loss was observed at high frequencies (2–4 kHz). All the patients in this study were cured after TTP and intratympanic methylprednisolone. After treatment, the average hearing threshold at affected frequencies was significantly lower than those in the pretreatment group and was similar to those in the healthy ears.

Research conclusions
Our study indicated that AOM may rarely induce sudden sensorineural hearing loss, and high frequencies (2–4 kHz) are often involved. Combination therapy with TTP and intratympanic methylprednisolone injection may be a good salvage treatment modality for patients with AOM-associated sudden hearing loss after failure of conventional treatment.

Research perspectives
Our study may bring more chances for recovery of patients with AOM-associated sudden hearing loss after failure of conventional treatment. However, our findings remain to be verified by well-designed studies with a large sample size.

REFERENCES
1 Leung AKC, Wong AHC. Acute Otitis Media in Children. Recent Pat Inflamm Allergy Drug Discov 2017; 11: 32-40 [PMID: 28705758 DOI: 10.2174/1874609810666170712124332]
2 Cartel JL, Sechan Y, Bounin JP, Celierer P, Plichart R, Roux JF. Ivermectin for treatment of bancroftian filariasis in French Polynesia: efficacy in man, effect on transmission by vector Aedes polynesiensis. Trop Med Parasitol 1990; 41: 241-244 [PMID: 2255839 DOI: 10.1371/journal.pone.0036226]
3 Vergison A, Dagan R, Arguedas A, Bonhoeffer J, Cohen R, Dhoooge I, Hoberman A, Liese J, Marchisio P, Palmu AA, Ray GT, Sanders EA, Simões EA, Uhari M, van Eldere J, Pelton SI. Otitis media and its consequences: beyond the earache. Lancet Infect Dis 2010; 10: 195-203 [PMID: 20185908 DOI: 10.1016/S1473-3099(10)70012-8]
4 Marom T, Nokso-Koivisto J, Chomnatree T. Viral-bacterial interactions in acute otitis media. Curr Allergy Asthma Rep 2012; 12: 551-558 [PMID: 22968233 DOI: 10.1007/s11882-012-0303-2]
5 Pagrani M, Srivastava A, Mohan C. Adult onset acute otitis media - a preliminary report. J Evolut Med Dental Sciences-Jemds 2014; 3: 5094-5099 [DOI: 10.14260/jemds/2014/2559]
6 Park JH, Park SJ, Kim YH, Park MH. Sensorineural hearing loss: a complication of acute otitis media in adults. Eur Arch Otorhinolaryngol 2014; 271: 1879-1884 [PMID: 23990061 DOI: 10.1007/s00405-013-2675-x]
7 Kasemodell ALP, Castle LEM, Monsanto RDC, Tomaz A, Penido NO. Sensorineural hearing loss in the acute phase of a single episode of acute otitis media. Braz J Otorhinolaryngol 2020; 86: 767-773 [PMID: 31324458 DOI: 10.1016/j.bjorl.2019.06.001]
8 Margolis RH, Hunter LL. Audiologic evaluation of the otitis media patient. Otolaryngol Clin North Am 1991; 24: 877-899 [PMID: 1870880]
9 Song JE, Saphavee A, Cager GR, Saadia-Redleaf MI. Pseudo-sudden deafness. Ann Otol RhinoLaryngol 2012; 121: 96-99 [PMID: 22397217 DOI: 10.1177/000348941212100204]
10 Chandrasekhar SS, Tsai Do BS, Schwartz SR, Bontempo LJ, Faucett EA, Finestone SA, Hollingsworth DB, Kelley DM, Kmucha ST, Moonis G, Poling GL, Roberts JK, Stachler RJ, Zeitler DL, Valente M, Warren BE, Yaremchuk KL, Robertson PJ; American Academy of Otolaryngology-Head and Neck Surgery. Clinical practice guideline: sudden hearing loss. Otolaryngol Head Neck Surg 2012; 146: S1-35 [PMID: 22383545 DOI: 10.1177/1945998112436449]
11 Heywood RL, Ifeacho SN, Narula AA. Effect of intratympanic steroid administration on sensorineural hearing loss associated with acute otitis media. J Laryngol Otol 2016; 130: 532-535 [PMID: 27087111 DOI: 10.1177/00222151166001110]
12 Smith A, Gutteridge I, Elliott D, Cronin M. Acute otitis media associated bilateral sudden hearing loss: case report and literature review. J Laryngol Otol 2017; 131: S57-S61 [PMID: 28412992 DOI: 10.1017/S0022215117000779]
13 Steen M, Jecker P, Gouveris H, Mann W. [Treatment of sensorineural hearing loss in acute viral otitis media with intratympanic dexamethasone and hyaluronic acid in comparison with intravenous therapy]. Laryngorhinootologie 2006; 85: 32-37 [PMID: 16444653 DOI: 10.1055/s-2005-870274]
14 Bhutta MF, Lambie J, Hobson L, Williams D, Tyer HE, Nicholson G, Brown SDM, Brown H, Piccinelli C, Devaillly G, Ramsden J, Cheeseman MT. Transcript Analysis Reveals a Hypoxic
Inflammatory Environment in Human Chronic Otitis Media With Effusion. *Front Genet* 2019; 10: 1327 [PMID: 32153623 DOI: 10.3389/fgene.2019.01327]

16 Schachern P, Tsuprun V, Cureoglu S, Ferrieri P, Briles D, Paparella M, Juhn S. The round window membrane in otitis media: effect of pneumococcal proteins. *Arch Otolaryngol Head Neck Surg* 2008; 134: 658-662 [PMID: 1859736 DOI: 10.1001/archotol.134.6.658]

17 Editorial Board of Chinese Journal of Otorhinolaryngology Head and Neck Surgery; Society of Otorhinolaryngology Head and Neck Surgery CMA. [Guideline of diagnosis and treatment of sudden deafness (2015)]. *Zhonghua ErBiYanHouTouJing WaiKe ZaZhi* 2015; 50: 443-447

18 Juhn SK, Jung MK, Hoffman MD, Drew BR, Preciado DA, Sausen NJ, Jung TT, Kim BH, Park SY, Lin J, Ondrey FG, Mains DR, Huang T. The role of inflammatory mediators in the pathogenesis of otitis media and sequelae. *Clin Exp Otorhinolaryngol* 2008; 1: 117-138 [PMID: 19434244 DOI: 10.3342/ceo.2008.1.3.117]

19 Joglekar S, Morita N, Cureoglu S, Schachern PA, Deroee AF, Tsuprun V, Paparella MM, Juhn SK. Cochlear pathology in human temporal bones with otitis media. *Acta Otolaryngol* 2010; 130: 472-476 [PMID: 19895333 DOI: 10.3109/00016480903311252]

20 Cordeiro FP, da Costa Monsanto R, Kasemodel ALP, de Almeida Gondra L, de Oliveira Penido N. Extended high-frequency hearing loss following the first episode of otitis media. *Laryngoscope* 2018; 128: 2879-2884 [PMID: 30194735 DOI: 10.1002/lary.27309]

21 Choo OS, Yang SM, Park HY, Lee JB, Jang JH, Choi SJ, Cheong YH. Differences in clinical characteristics and prognosis of sudden low- and high-frequency hearing loss. *Laryngoscope* 2017; 127: 1878-1884 [PMID: 28719039 DOI: 10.1002/lary.26382]

22 Moreno-Gómez FN, Vélez G, Rojas M, Martínez C, Olmedo R, Panussis F, Dagnino-Subiabre A, Delgado C, Delano PH. Music Training and Education Slow the Deterioration of Music Perception Produced by Presbycusis in the Elderly. *Front Aging Neurosci* 2017; 9: 149 [PMID: 28579956 DOI: 10.3389/fgagi.2017.00149]

23 Aarhus L, Tambs K, Hoffman HJ, Engdahl B. Childhood otitis media is associated with dizziness in adulthood: the HUNT cohort study. *Eur Arch Otorhinolaryngol* 2016; 273: 2047-2054 [PMID: 26335289 DOI: 10.1007/s00405-015-3764-9]
