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WILEY
The Relationship Between Endolymphatic Hydrops in the Vestibule and Low-Frequency Air-Bone Gaps

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Objectives/Hypothesis: To investigate the relationship between endolymphatic hydrops and hearing level, focusing on significant vestibular endolymphatic hydrops adjacent to the stapes footplate and low-frequency air-bone gaps.

Study Design: Retrospective study.

Methods: The study included 1,548 ears from 775 patients who underwent magnetic resonance imaging examination in our university hospital to investigate possible endolymphatic hydrops between January 2012 and December 2015. Ears were evaluated by magnetic resonance imaging performed 4 hours after intravenous injection of a standard dose of gadodiamide hydrate and/or 24 hours after intratympanic injection of gadopentetate dimeglumine diluted eightfold. Comparison of hearing thresholds on pure-tone audiometry was performed between ears having endolymphatic hydrops adjacent to the stapes footplate and those having nonadjacent endolymphatic hydrops.

Results: Forty-one ears (22 men and 19 women, mean age 48.4 years) showed significant cochlear and vestibular endolymphatic hydrops adjacent to the stapes footplate, and 79 ears (30 men and 49 women, mean age 45.0 years) showed significant nonadjacent cochlear and vestibular endolymphatic hydrops. The average air-bone gap at 250 Hz was significantly higher in the group of ears with adjacent hydrops than in those with nonadjacent hydrops.

Conclusions: The appearance of low-frequency air-bone gaps suggests deterioration of endolymphatic hydrops, particularly in ears with Ménière’s disease, and could be a useful indicator for evaluating and treating patients with endolymphatic hydrops.

Key Words: Endolymphatic hydrops, Ménière’s disease, air-bone gaps, magnetic resonance imaging.

Level of Evidence: 4.

INTRODUCTION

Ménière’s disease (MD) is a disorder of the inner ear that causes vertigo attacks, fluctuating hearing loss, tinnitus, and aural fullness. A characteristic pathological finding in MD is endolymphatic hydrops (EH), in which excessive endolymph accumulates in the inner ear, and which typically results in sensorineural hearing loss. Occasionally, audiograms of patients with MD show unexplained conductive components, or air-bone gaps (ABGs), predominantly at low frequencies, even though no middle ear pathology can be demonstrated. Two main theories have been proposed to explain the mechanisms of formation of low-frequency ABGs (LFABGs). One hypothesis is that increased perilymphatic pressure caused by EH might decrease the mobility of the stapes, the other is that decreased stapedial mobility caused by saccular dilatation might apply a direct force to the stapes footplate.

Visualization of EH has become possible using 3T contrast-enhanced magnetic resonance imaging (MRI). This MRI examination can evaluate the degree of EH present in the vestibule, which might influence the mobility of the stapes footplate. The purpose of this study was to investigate the relationship between EH and hearing level, focusing on the degree of vestibular EH and LFABGs, and to elucidate their pathogenic mechanisms.

MATERIALS AND METHODS

The study included 1,548 ears from 775 patients (306 men and 469 women; age range, 11–90 years), who underwent MRI examination in our university hospital to investigate the existence of EH between January 2012 and December 2015. Pure-tone audiometry was performed using an AA-79 diagnostic audiometer (Rion, Tokyo, Japan) in a soundproof compartment. Air-conduction and bone-conduction audiometric measurement thresholds were calculated for each ear at 250, 500, 1,000, 2,000, and 4,000 kHz.

Ears were evaluated by MRI performed 4 hours after intravenous injection of a standard dose (0.2 mL/kg body weight [i.e., 0.1 mmol/kg body weight]) of gadodiamide hydrate (Omniscan; GE Healthcare, Chicago, IL) and/or 24 hours after intratympanic injection of gadopentetate dimeglumine (Magnevist; Bayer Healthcare, Leverkusen, Germany) diluted eightfold with saline (1:7 v/v), as described previously. All scans were

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performed using a 3T MRI scanner (Trio or Verio; Siemens, Erlangen, Germany). HYDROPS (hybrid of reversed image of positive endolymph signal and native image of positive perilymph signal) was used to identify EH. A radiologist who was blinded to the corresponding clinical information classified the degree of EH in the vestibule and cochlea into three grades (none, mild, and significant) according to the criteria described previously as listed in Table I. Degrees of EH were measured by tracing the images. The existence of vestibular EH adjacent to the stapes footplate was decided based on a radiologist’s suggestion. The criteria of EH with or without adjacency to the footplate depend on the presence or absence of a black area underneath the stapes footplate. Example images are shown in Figure 1. The left ear had significant vestibular EH nonadjacent to the stapes footplate (Fig. 1A). The left ear had significant vestibular EH adjacent to the stapes footplate (Fig. 1B). If ears had received multiple MRI evaluations, the first one was adopted in this study.

Ears with the following conditions were excluded from the present study: those with abnormal tympanic membranes, those with an abnormal inner ear as detected on MRI, a previous medical history of otitis media or intratympanic therapy, and unavailable audiometric measurement of air- and bone-conduction thresholds.

Statistical analyses were conducted using SPSS IBM Statistics version 24 (IBM Corp., Armonk, NY). The Mann-Whitney U test was used to compare ages, hearing thresholds, ABGs, and the duration of MD between ears having EH adjacent to the stapes footplate and those having nonadjacent EH. A \( \chi^2 \) test was performed to compare the sex distribution and the proportion of MD to non-MD appearance in the two groups. \( P < 0.05 \) were considered significant.

All study protocols were approved by the ethics review committee of Nagoya University School of Medicine, Nagoya, Japan (approval numbers 369, 587).

RESULTS

Mild or significant cochlear and/or vestibular EH was present in 1,103/1,548 ears (429 men and 674 women, mean age 51.2 years; 506 with mild cochlear EH, 473 with significant cochlear EH, 241 with mild vestibular EH, and 348 with significant vestibular EH). Most of the ears having EH adjacent to the stapes footplate showed significant cochlear and vestibular EH. To equalize the level of EH for comparing hearing level between the groups with or without adjacency, we selected ears with significant cochlear and vestibular EH from the both groups. Before applying the exclusion criteria described in the Materials and Methods section, 100 ears showed significant cochlear and vestibular EH adjacent to the stapes footplate, and 122 ears showed significant nonadjacent cochlear and vestibular EH. After the exclusion, 41 ears (22 men and 19 women, mean age 48.4 years) showed significant cochlear and vestibular EH adjacent to the stapes footplate, and 79 ears (30 men and 49 women, mean age 45.0 years) showed significant nonadjacent cochlear and vestibular EH.

| TABLE I. Grading of Endolymphatic Hydrops on Magnetic Resonance Imaging. |
|------------------------|-------------------------|-------------------------|
| Grading of Hydrops    | Vestibule (Area Ratio)* | Cochlea                 |
| None                  | \( \leq 1/3 \)           | No displacement of Reissner's membrane. |
| Mild                  | \( 1/3 < \), \( \leq 1/2 \) | Displacement of Reissner's membrane. |
| Significant           | \( 1/2 < \)              | The area of the endolymphatic space does not exceed the area of the scala vestibuli. |

*Ratio of the area of the endolymphatic space to that of the vestibular fluid space (sum of the endolymphatic space and perilymphatic space).

Fig. 1. Example images of left ears with significant vestibular endolymphatic hydrops (EH) nonadjacent to the stapes footplate (A) and with adjacent vestibular EH (B). HYDROPS (hybrid of reversed image of positive endolymph signal and native image of positive perilymph signal) was used to identify EH. The black areas represent the endolymphatic space in the labyrinth, and the white areas represent the perilymphatic space. The presence of significant nonadjacent vestibular EH (arrowhead) can be visualized as black areas surrounded by gadolinium-filled perilymph (A). The vestibule is occupied by black areas that represent more significant vestibular EH, and arrowheads show adjacency to the stapes footplate (B). Arrows show cochlear EH (A and B).

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Ears with significant cochlear and vestibular EH adjacent to the stapes footplate showed significantly more MD than those with nonadjacent EH (27/41 vs. 35/79, \(P < .05\)). The mean duration of MD in ears with significant cochlear and vestibular EH adjacent to the stapes footplate was significantly longer than in cases with nonadjacent EH (5.9 years vs. 1.8 years, \(P < .01\)).

MRI scans and audiograms of an example case are shown in Figure 2. The right ear in this patient had significant vestibular EH adjacent to the stapes footplate (Fig. 2A). The audiogram showed LFABGs at 250 and 500 Hz in the right ear (Fig. 2B), which disappeared after administration of an intravenous drip of glycerol (Fig. 2C).

**DISCUSSION**

Recently, MRI has been used to evaluate the presence of EH\(^{12-17}\) and has demonstrated that all patients who have definite MD also have EH.\(^{15,14,17}\) In the present study, we investigated the relationship between EH and hearing levels, focusing on the degrees of vestibular EH and LFABGs. The results showed that ears with significant cochlear and vestibular EH adjacent to the stapes footplate had significant deterioration of the ABGs at 250 Hz. Two possible mechanisms that could cause this are that the dilated saccule adjacent to the stapes footplate,\(^2\) and/or increased perilymphatic pressure caused by EH\(^3,5\) could decrease stapedial mobility. Okuno and Sando investigated the localization, frequency, and severity of EH in 22 temporal bones of 16 individuals with MD, and reported that the dilated saccular membrane was attached to the stapes footplate in 17 of 22 temporal bones.\(^{18}\) This relationship between vestibular EH and the stapes footplate has been demonstrated here. Besides these two possible mechanisms, adjacency of EH to the stapes footplate might influence the improving threshold of bone sound conduction.

We found here that the average hearing thresholds on bone-conduction testing were significantly higher at all frequencies in the group of ears with EH adjacent to the stapes footplate. Moreover, ears with significant cochlear and vestibular EH adjacent to the stapes footplate had more MD with long duration than those of nonadjacent. According to the progression of MD, hearing level typically worsens. We consider that this relationship is one reason for the deterioration in hearing thresholds at all frequencies in the group of ears with adjacent EH.

The clinical diagnosis and symptoms of 41 adjacent ears was as follows: 27 cases of MD,\(^{10}\) two cases of delayed endolymphatic hydrops (DEH),\(^{11}\) six cases of fluctuating hearing loss, two cases of acute sensorineural hearing loss (SNHL), and four cases of other types with otological and symptoms (chronical hearing loss, vertigo, and ear fullness). Clinical diagnosis of 79 nonadjacent ears was as follows: 35 cases of MD,\(^{10}\) one case of DEH,\(^{11}\) five cases of fluctuating hearing loss, nine cases of acute sensorineural hearing loss, and 29 cases of others with otological and symptoms (including chronic hearing loss, vertigo, floating sensation, ear fullness, tinnitus, and hyperacusis).

Ears with significant cochlear and vestibular EH adjacent to the stapes footplate showed significantly

| TABLE II. Demographic and Hearing Data of Ears With or Without the Adjacency to the Stapes Footplate. |
|-------------------------------------------------|---------------------------------------------|---------------------------------------------|
| Ears With the Adjacency (n = 41) | Ears Without the Adjacency (n = 79) |
| Average | SD | Average | SD |
| Age, yr | 48.4 | 17.1 | 45.0 | 15.4 |
| Sex (male/female) | 22/19 | 30/49 |
| Air-conduction thresholds (dB HL) | | | | |
| 250 Hz* | 45.5 | 16.2 | 29.5 | 15.9 |
| 500 Hz* | 41.3 | 17.4 | 25.6 | 16.2 |
| 1,000 Hz* | 39.6 | 19.4 | 21.5 | 14.0 |
| 2,000 Hz* | 35.7 | 18.9 | 20.3 | 14.7 |
| 4,000 Hz* | 37.3 | 20.0 | 22.0 | 16.9 |
| Bone-conduction thresholds (dB HL) | | | | |
| 250 Hz* | 36.8 | 12.3 | 26.5 | 12.3 |
| 500 Hz* | 37.6 | 18.2 | 22.9 | 15.1 |
| 1,000 Hz* | 39.2 | 18.6 | 20.6 | 13.8 |
| 2,000 Hz* | 36.5 | 17.2 | 21.1 | 14.1 |
| 4,000 Hz* | 31.6 | 18.4 | 18.2 | 15.5 |
| Air-bone gaps (dB HL) | | | | |
| 250 Hz* | 8.7 | 8.1 | 3.0 | 7.9 |
| 500 Hz | 3.8 | 6.7 | 2.7 | 5.4 |
| 1,000 Hz | 0.5 | 7.7 | 0.9 | 6.5 |
| 2,000 Hz | -0.7 | 4.6 | -0.8 | 4.6 |
| 4,000 Hz | 5.7 | 5.8 | 3.8 | 5.4 |

\(\*P < .05\). Results of comparisons between age, sex, hearing thresholds, and air-bone gaps of ears with the adjacency and ears without the adjacency:

SD = standard deviation.

The demographic and hearing data for these patients are presented in Table II. There were no significant differences in age and sex distributions between the groups. The average hearing thresholds in the air- and bone-conduction testing were significantly higher at all frequencies in the group of ears with adjacent EH than in those with nonadjacent EH. Moreover, the average ABG at 250 Hz was significantly higher in the group of ears with adjacent EH than in those with nonadjacent EH.

The clinical diagnosis and symptoms of 41 adjacent ears was as follows: 27 cases of MD,\(^{10}\) two cases of delayed endolymphatic hydrops (DEH),\(^{11}\) six cases of fluctuating hearing loss, two cases of acute sensorineural hearing loss (SNHL), and four cases of other types with otological and symptoms (chronical hearing loss, vertigo, and ear fullness). Clinical diagnosis of 79 nonadjacent ears was as follows: 35 cases of MD,\(^{10}\) one case of DEH,\(^{11}\) five cases of fluctuating hearing loss, nine cases of acute sensorineural hearing loss, and 29 cases of others with otological and symptoms (including chronic hearing loss, vertigo, floating sensation, ear fullness, tinnitus, and hyperacusis).

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Lee et al. investigated the prevalence and clinical significance of spontaneous LFABGs in 337 patients with definite MD. They reported that the number of vertigo spells and hearing thresholds were significantly higher during the period of LFABG development, and suggested that LFABGs reflect the aggravation of EH in the cochlea and vestibule. Their results, together with those of the present study, suggest that the appearance of LFABGs, especially ABGs at 250 Hz, indicates deterioration of EH and could be a useful indicator for evaluating and treating patients with EH.

Enlarged vestibular aqueduct syndrome and superior canal dehiscence syndrome can also demonstrate LFABGs, which are thought to arise from the influence of the third mobile inner ear window. A recent MRI study showed that ears with such pathological third-window lesions also had EH, which might affect the patients’ auditory symptoms including LFABGs.

Evaluation of EH in the vestibule can be applied for middle ear surgery. Preoperative evaluation of the existence of EH in the vestibule is desirable in ears that are candidates for stapes surgery, to prevent unpredictable complications after surgery. Patients with significant vestibular EH adjacent to the stapes footplate have a high risk of postoperative complications, such as prolonged dizziness, following stapes surgery.

Sex differences in the incidence of MD have been reported; for example, the female:male ratios were 1.3:1 in Japan and 1.89:1 in the United States, and hormonal influences have been speculated to cause this difference. In the present study, ears with vestibular and/or cochlear EH were more frequently found in women than men overall; however, this tendency was not observed in ears with vestibular EH adjacent to the stapes footplate.

There are some limitations to the present study. Computed tomography examinations to rule out anomalies in middle and inner ears were not available for all ears. Moreover, multiple MRI evaluations were not conducted in ears showing fluctuating LFABGs. We are planning further studies to analyze the relationship between degrees of EH and LFABGs.

CONCLUSION

The average ABG at 250 Hz was significantly higher in the group of ears with EH adjacent to the stapes footplate than in those with nonadjacent EH. The appearance of LFABGs suggests deterioration of EH, which could be a useful indicator for evaluating and treating patients with EH. Such MRI evaluation might also provide clues to understanding EH-associated LFABGs.

BIBLIOGRAPHY


