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Significance of Endolymphatic Hydrops in Ears With Unilateral Sensorineural Hearing Loss

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Objective: The purpose of this study was to investigate the existence of endolymphatic hydrops (EH) in affected and unaffected ears in patients with unilateral sensorineural hearing loss (SNHL) using contrast-enhanced magnetic resonance imaging (MRI), and to evaluate the significance of EH in various otological diseases.
Study Design: Retrospective study.
Setting: University hospital.
Methods: One hundred eighty-two ears from 91 patients with unilateral SNHL were studied. The endolymphatic space was evaluated using 3-Tesla MRI with gadodiamide hydrate. Imaging data about the degree of EH in the cochlea and vestibule were analyzed and compared between ears with various otological diseases.
Results: All affected ears with delayed endolymphatic hydrops had EH. In affected ears with definite Menière's disease, cochlear EH was observed in all ears and vestibular EH in 93% of ears, and these rates were significantly higher in the affected than in the unaffected ears. EH was also observed in the cochlea and vestibule in 66% and 41%, respectively, of the affected ears with idiopathic sudden SNHL; however, these percentages did not differ significantly from those in the unaffected ears (52% and 38%, respectively).
Conclusion: MRI showed that a high percentage of ears affected by Menière's disease or delayed endolymphatic hydrops had EH. Further studies should evaluate the implications of EH in ears, especially in those with sudden SNHL, in terms of secondary or pre-existing EH. **Key Words:** Endolymphatic hydrops—MRI—Sensorineural hearing loss—Unilateral.

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Endolymphatic hydrops (EH) is recognized as an essential pathological finding of Menière's disease (MD); however, their relationship is controversial. Merchant et al. (1) examined human temporal bones and reported that all MD patients showed idiopathic EH and that patients with secondary EH had similar symptoms to MD. These findings suggest that EH is not a pathological marker exclusive to MD. In another study of temporal bones, Foster and Breeze (2) stated that EH alone was insufficient to cause MD and that vascular risk factors should be studied as possible cofactors.

The presence of EH visualized by magnetic resonance imaging (MRI) has been recently reported in patients with inner ear disease (3–11). This development in the evaluation of EH in vivo is expected to improve the diagnosis of suspected MD (12). In unilateral MD, EH is often also observed in the asymptomatic contralateral ear (6,8,9,11), which suggests that the symptoms of MD might appear after the formation of EH. Gulya and Schuknecht (13,14) classified EH by distinguishing symptomatic and asymptomatic forms, and classified each form further into embryopathic, acquired, and idiopathic types. They concluded that MD can be redefined as idiopathic, symptomatic EH.

In the present study, we have used contrast-enhanced MRI to determine the existence of EH in affected and unaffected ears in patients with unilateral sensorineural hearing loss (SNHL), including MD. We speculate that comparison of affected and unaffected ears in patients with unilateral SNHL might be helpful for evaluating the significance of EH in various otological diseases.

METHODS

We reviewed the imaging and charts of 91 consecutive patients (43 men and 48 women; age range, 19–76 yr; mean age, 51.2 ± 13.6 yr) who had been diagnosed with unilateral SNHL and who underwent MRI evaluation in our hospital. In this study, unilateral SNHL was defined as follows: 1) ≥ 15 dB binaural difference in the average of hearing thresholds; 2) the

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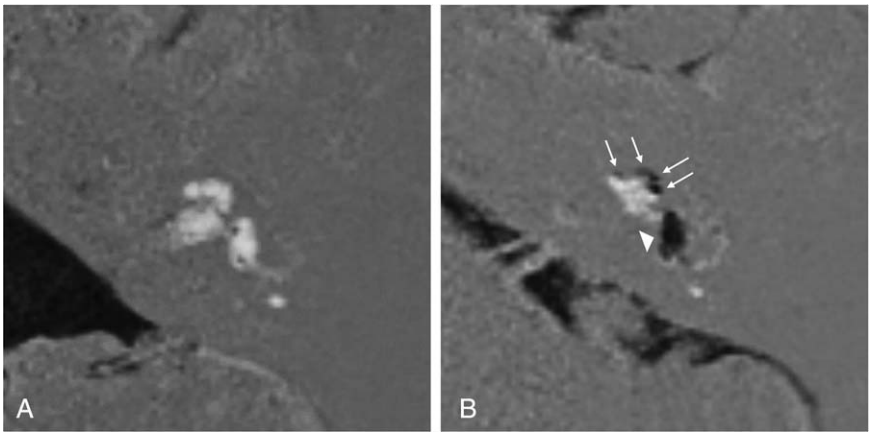

FIG. 1. Example images of endolymphatic hydrops (EH) in the cochlea and vestibule. These are the hybrid of reversed image of positive endolymph signal and native image of positive perilymph signal (HYDROPS) images acquired 4 hours after intravenous administration of single-dose gadolinium-based contrast material. The endolymphatic space is observed as the black area. *A,* No EH in the cochlea or the vestibule. *B,* Significant EH in both the cochlea (*arrows*) and vestibule (*arrowheads*).

average in the unaffected ear was ≤20 dB; and 3) the average in the affected ear was ≥30 dB. We used the average of the hearing thresholds at 0.5, 1, and 2 kHz, with no air-bone gap. Patients with a history of previous otologic surgery, conductive hearing loss, or acoustic tumors were excluded. The diagnoses included definite and probable MD, idiopathic sudden SNHL (SSNHL), and delayed endolymphatic hydrops (DEH).

The diagnosis of definite or probable MD was made according to the new international consensus diagnostic criteria for MD (15), which were approved at the Committee of the American Academy of Otolaryngology —Head and Neck Surgery (AAO—HNS) Annual Meeting in 2015 (16). According to the criteria, low-frequency SNHL caused by unilateral definite MD is defined as increases in pure-tone thresholds for bone-conducted sound that are higher in the affected ear than in the contralateral ear by ≥30 dB hearing level at each of two contiguous frequencies <2000 Hz. We used frequencies of 0.25, 0.5, and 1 kHz to establish the audiometric criteria for MD in our patients, who also met the vertigo criteria. The diagnosis of SSNHL was based on the criteria established by the Research Committee of the Ministry of Health, Labor and Welfare in Japan in 2012. By these criteria, SSNHL is defined as a sudden onset of ≥30 dB or more SNHL over three consecutive frequencies with unknown etiology (17). In the present study, ears with acute low-tone sensorineural hearing loss were not included in the SSNHL group.

Ipsilateral DEH was diagnosed according to the guidelines proposed by Kamei (18) as many years of monaural profound SNHL, development of recurrent vestibular symptoms resembling those of MD, and no perceived fluctuation in hearing loss related to episodic vertigo.

The ''other'' category included patients whose condition did not meet the new criteria for MD (15) but that met the criteria for probable or possible MD according to the AAO—HNS 1995 guidelines (19).

Three-dimensional fluid-attenuated inversion recovery MRI was performed using a 3-Tesla scanner (Trio or Verio, Siemens, Erlangen, Germany) 4 hours after intravenous administration of the gadolinium (Gd) contrast agent and/or 24 hours after intratympanic Gd injection. Eighty-one of the 91 patients received intravenous Gd injection only, 9 patients (7 with definite MD, 1 with probable MD, and 1 with DEH) received both intratympanic and intravenous Gd injections, and 1 patient with DEH received bilateral intratympanic Gd injections, as described previously (3,4,20,21). The contrast agent for intratympanic injection was eightfold-diluted gadopentetate dimeglumine (Magnevist; Bayer Co. Ltd., Osaka, Japan). The intravenous injection comprised a standard dose of 0.1 mmol/kg body weight (0.2 ml/kg body weight) of gadodiamide hydrate (Omniscan; GE Healthcare, Little Chalfont, UK). The hybrid of reversed image of positive endolymph signal and native image of positive perilymph signal (HYDROPS), the hybrid of reversed image of magnetic resonance cisternography and positive perilymph signal by heavily T2-weighted three-dimensional fluid-attenuated inversion recovery (HYDROPS2), and three-dimensional real inversion recovery sequences were used to evaluate the existence of EH (22,23). One radiologist who did not know the patients' clinical data classified the grade of EH in the cochlea and vestibule into three groups—none, mild, and significant—according to the criteria contributed previously (24,25). Example images of EH in the cochlea and the vestibule are shown in Figure 1.

The data were analyzed using SPSS software (version 24.0 for Windows; SPSS, IBM, Armonk, NY, U.S.A.). Differences in the grades of EH between the groups were assessed using the χ^2 test, and other variables were assessed using Student's *t* test, Mann–Whitney *U* test, and Kruskal–Wallis test. The level of significance was set at $p < 0.05$.

All study protocols were approved by the ethics review committee of Nagoya University.

RESULTS

The diagnoses of the 91 patients were unilateral definite MD (n = 28), probable MD (n = 9), SSNHL (n = 29), DEH (n = 6), and other (n = 19). The average duration from the onset of disease to MRI examination was 89.9 ± 167.9 months (range, 1–1,200 mo). The average duration from audiometric documentation to MRI examination was 1.6 ± 1.4 months (range, 0–8 mo). The characteristics of patients are shown in Table 1. The average hearing thresholds at 0.5, 1, and 2 kHz in the affected ears differed significantly between definite MD and probable MD, probable MD and SSNHL, probable MD and DEH, definite MD and DEH, and DEH and other ($p < 0.05$).

TABLE 1. *Characteristics of patients*

Diagnosis	No	Age (Yr)	M:F	Duration (Mo)	Average Hearing Level (dB)	
					Affected Ear	Unaffected Ear
Definite MD	28	51	14:14	134	62	14
Probable MD	9	45	3:6	185	42	14
SSNHL	29	54	12:17	39	66	15
DEH	6	43	3:3	123	96	13
Other	19	52	11:8	48	56	14

DEH indicates delayed endolymphatic hydrops; F, female; M, male; MD, Menière's disease; No, number; SSNHL, idiopathic sudden sensorineural hearing loss.

The numbers of patients with mild or significant EH in the affected and unaffected ears are shown in Tables 2 and 3. Cochlear or vestibular EH was observed in 84 and 69%, respectively, of the 91 affected ears and in 48 and 43%, respectively, of the 91 unaffected ears. Both cochlear and vestibular EH were more frequent in the affected ears than in the unaffected ears (χ^2 test, $p < 0.01$).

Table 4 shows the percentages of affected and unaffected ears with mild or significant EH grouped according to the disease classification. In the affected ears with definite MD, cochlear EH was observed in all 28 ears and vestibular EH in 26 ears (93%). In the unaffected ears, cochlear or vestibular EH was detected in 11 (39%) and 12 (43%) ears, respectively. In the affected ears with SSNHL, cochlear EH was observed in 19 (66%) and vestibular EH in 12 (41%) ears. In the unaffected ears, cochlear or vestibular EH was detected in 15 (52%) and 11 (38%) ears, respectively.

Cochlear and vestibular EH was found in all of the affected ears with DEH but in 67 and 50%, respectively, of the unaffected ears. In ears with other conditions, cochlear or vestibular EH was observed in 79 and 63% of the affected ears, and 47 and 53% of unaffected ears, respectively. The percentage of ears with cochlear EH was significantly higher in the affected than in the unaffected ears (χ^2 test, $p < 0.05$).

In patients with definite MD, the percentages of cochlear and vestibular EH were significantly higher in the affected ears than in the unaffected ears (χ^2 test, $p < 0.01$). The percentage of EH in affected ears with definite MD was significantly higher than those in the affected ears with SSNHL (χ^2 test, $p < 0.01$). There was no significant difference in the percentage of ears with EH between the affected and unaffected ears with probable MD, SSNHL, and DEH. In the unaffected ears, the percentages of ears with EH did not differ between diseases.

DISCUSSION

In the present study, we used MRI to determine the existence of EH in the affected and unaffected ears in patients with unilateral SNHL to understand the significance of EH in various otological diseases. The definition of unilateral SNHL varies in different reports, and to our knowledge, there is no clear definition of this condition. In the present study, we defined unilateral SNHL as follows: 1) $\geq$15 dB binaural difference in the average of hearing thresholds; 2) the average in the unaffected ear was $\leq$20 dB; and 3) the average in the affected ear was $\geq$30 dB. We used the average of the hearing thresholds at 0.5, 1, and 2 kHz.

New diagnostic criteria for MD have been proposed recently (15). In our study, the affected ears with definite MD diagnosed according to the new criteria had mild or significant EH in at least the cochlea or vestibule, and EH was found in a significantly higher percentage of the affected ears than in the unaffected ears. The findings would indicate the significance of EH in the affected ears with MD diagnosed according to the new criteria. The percentage of unaffected ears with MD with EH varies between reports (8,9,11). These differences might reflect differences in the duration of the disease, hearing level, age, and the criteria used for the diagnosis. The ears

TABLE 2. *Numbers of EH in the affected ears*

Diagnosis	Cochlea (Significant/Mild/No)	Vestibule (Significant/Mild/No)
Definite MD	26/2/0	23/3/2
Probable MD	7/1/1	5/2/2
SSNHL	13/6/10	7/5/17
DEH	4/2/0	4/2/0
Other	11/4/4	8/4/7

DEH indicates delayed endolymphatic hydrops; EH, endolymphatic hydrops; MD, Menière's disease; SSNHL, idiopathic sudden sensorineural hearing loss.

TABLE 3. *Numbers of EH in the unaffected ears*

Diagnosis	Cochlea (Significant/Mild/No)	Vestibule (Significant/Mild/No)
Definite MD	3/8/17	7/5/16
Probable MD	0/5/4	1/2/6
SSNHL	8/7/14	4/7/18
DEH	2/2/2	2/1/3
Other	8/1/10	5/5/9

DEH indicates delayed endolymphatic hydrops; EH, endolymphatic hydrops; MD, Menière's disease; SSNHL, idiopathic sudden sensorineural hearing loss.

TABLE 4. *Percentages of EH in the affected and unaffected ears*

	Cochlea		Vestibule	
Diagnosis	Affected Ear (%)	Unaffected Ear (%)	Affected Ear (%)	Unaffected Ear (%)
Definite MD	100*] +	39	93**] ++	43
Probable MD	89	56	78	33
SSNHL	66	52	41	38
DEH	100	67	100	50
Other	79***	47	63	53

DEH indicates delayed endolymphatic hydrops; EH, endolymphatic hydrops; MD, Menière's disease; SSNHL, idiopathic sudden sensorineural hearing loss.

*, **, +, ++ $p < 0.01$; ***$p < 0.05$.

categorized as ''other'' in the present study did not meet the new criteria because of the duration of the episodes of vertigo and the level of their pure-tone thresholds; however, they were diagnosed as having probable or possible MD according to the 1995 AAO—HNS guidelines (19). The percentage of ears classified as ''other'' with EH in the cochlea differed significantly between the affected and unaffected ears.

In a human temporal bone study, EH was reported to be the main pathological finding in some patients with SSNHL (26). Chen et al. (5) reported the existence of EH in ears with SSNHL with vertigo and speculated that there is a relationship between EH and SSNHL. In the present study, cochlear and vestibular EH were observed in 66 and 41% of the affected ears with SSNHL, respectively. However, cochlear and vestibular EH were also detected in 52 and 38%, respectively, of the unaffected ears with SSNHL. The presence of EH in ears with SSNHL has been considered to be secondary EH. However, we identified EH in a non-negligible percentage of unaffected ears with SSNHL in this study. We speculate that the asymptomatic ear is also impaired, which results in the formation of secondary EH, or that pre-existing EH is present in both the affected and unaffected ears. In the latter situation, pre-existing EH might be a risk factor for the onset of SSNHL, even though other cofactors are required.

DEH is suggested to be a labyrinthine disorder of viral origin or to result from an autoimmune response in the inner ear (27,28). In the present study, ears with DEH were of the ipsilateral type, and the causes of the preceding SNHL were SSNHL in three ears, mumps deafness in one ear, and unknown in two ears. All affected ears with DEH had cochlear and vestibular EH. Cochlear and vestibular EH were also observed in 67 and 50% of the unaffected ears, respectively. It is not clear whether asymptomatic EH in the unaffected ear can become symptomatic.

Yoshida et al. (29) reported in an MRI study of 21 patients with nonotological diseases that EH was present in 38% of cochlea and only 7% of vestibule. They stated that EH in the vestibule might be a specific predictor of definite MD. The percentages of vestibular EH seem to be higher in the present subjects than those with nonotological diseases studied by Yoshida et al.

A limitation of this study is that we focused on the presence or absence of EH in ears with various types of otological diseases; however, if EH is causative, we do not yet know whether it is sufficient to cause symptoms by itself. Other risk factors, such as circulatory disorders, viral infection, diabetes, and autoimmune disorders, should be considered possible etiologies of unilateral hearing loss. In addition, time delays between disease onset and MRI evaluation may be a confounder of the percentages of EH. Further studies involving MRI are needed to identify possible cofactors for EH in various otological diseases.

CONCLUSIONS

EH was observed on MRI in a high percentage of affected ears with definite MD, or DEH. Further studies should evaluate the implications of EH, especially in ears with SSNHL, in terms of secondary or pre-existing EH.

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