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ORIGINAL ARTICLE

Magnetic resonance imaging of the inner ear after both intratympanic and intravenous gadolinium injections

TATSUO IIDA[1], MASAAKI TERANISHI[1], TADAO YOSHIDA[1], HIRONAO OTAKE[1], MICHIHIKO SONE[1], MASAHIRO KATO[1], MARIKO SHIMONO[1], MASAHIRO YAMAZAKI[2], SHINJI NAGANAWA[2] & TSUTOMU NAKASHIMA[1]

[1]*Department of Otorhinolaryngology and* [2]*Department of Radiology, Nagoya University, Nagoya, Japan*

Abstract

Conclusion: Using magnetic resonance imaging (MRI), endolymphatic hydrops could be visualized on both sides after intratympanic (IT) injection of gadolinium contrast agents (Gd) in one symptomatic ear and subsequent intravenous (IV) Gd injection. The MRI revealed a difference of intracochlear Gd distribution between the IT injection side and the contralateral IV side. *Objectives:* Although the IT method allows greater enhancement of the perilymph, many patients feel reluctance in receiving the IT injection in asymptomatic ears. We attempted to evaluate endolymphatic space size on both sides without the IT injection in asymptomatic ears. *Methods:* In 10 patients with Meniere's disease, MRI was performed 24 h after the IT Gd injection in one symptomatic ear and 4 h after the IV Gd injection. The signal intensity of Gd in the basal and apical turns of the cochlea was evaluated. *Results:* The signal intensity in the scala tympani of the basal turn of the cochlea was 1.70 ± 0.60 on the IT + IV side and 0.42 ± 0.10 on the contralateral (IV) side. Gd was distributed uniformly in the scala tympani in the cochlea on the IV side, whereas it was strongly localized in the basal turn on the IT + IV side.

Keywords: *Meniere's disease, gadolinium contrast agents, signal intensity, asymptomatic endolymphatic hydrops*

Introduction

Visualization of endolymphatic hydrops (EH) has become possible with three-dimensional fluid-attenuated inversion recovery (3D-FLAIR) 3 Tesla magnetic resonance imaging (MRI) after the intratympanic (IT) injection of gadolinium contrast agents (Gd) [1]. In many hospitals, MRI is performed 24 h after the IT injection of Gd, diluted eightfold with saline [2–4]. The IT method usually provides a sufficient Gd concentration in the perilymph except for approximately 10% of cases with anatomic barriers to the round window such as adhesions, bone dust blockage or thickened round window [5,6].

Recently, visualization of EH after intravenous (IV) Gd injection was reported [7,8]. Although the images of EH after the IV injection of Gd are generally not as good as those after its IT injection, the IV method has potentially wider clinical application [4]. The Gd contrast enhancement of the perilymph was higher at 4 h than at 10 min after IV injection [9]. Both the IT and IV methods have merits. The IT method allows greater enhancement of the perilymph. To evaluate the size of the endolymphatic space on both sides, the IT injection on both sides usually provides good images of the endolymphatic space bilaterally [10]. However, many patients with unilateral Meniere's disease feel reluctance in receiving the IT injection in asymptomatic ears. EH may exist even in asymptomatic ears [4,11]. We attempted to visualize the endolymphatic space on both sides by administering the IT injection only in symptomatic ears and subsequent IV injection.

Correspondence: Tsutomu Nakashima MD, Department of Otorhinolaryngology, Nagoya University Graduate School of Medicine, 65, Tsurumai-cho, Showa-ku Nagoya 466-8850, Japan. E-mail: tsutomun@med.nagoya-u.ac.jp

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Material and methods

Patients

Ten patients with Meniere's disease (six men and four women; aged 35–68 years, mean age 48.3 years) gave their informed consent to participate in the study. Nine patients had definite unilateral Meniere's disease and one patient had bilateral Meniere's disease, according to the 1995 criteria of the American Academy of Otolaryngology–Head and Neck Surgery.

MRI

Gadopentetate dimeglumine (Magnevist®) was diluted eightfold with saline (1:7 v/v) and injected intratympanically using a 23-gauge needle and a 1 ml syringe, as described previously [1]. The Gd was injected into the symptomatic ear with definite Meniere's disease. In one patient with bilateral Meniere's disease, the Gd was injected on the side with more pronounced symptoms. Thus, the IT Gd injection was performed unilaterally in all patients. The next day, a standard dose (0.2 ml/kg body weight, i.e. 0.1 mmol/kg body weight) of gadodiamide hydrate (Omniscan®) was injected intravenously. MRI was performed 24 h after the IT injection and 4 h after the IV injection.

All scans were performed on a 3 T MRI scanner (Magnetom Verio; Siemens AG, Erlangen, Germany) using a receive-only, 32-channel, phased-array coil. 3D-FLAIR, 3D-real inversion recovery (3D-real IR), heavily T2-weighted 3D-FLAIR, and heavily T2-weighted SPACE MRI were performed in all patients.

The parameters for 3D-FLAIR were as follows: repetition time (TR), 9000 ms; effective echo time (TE), 130 ms; inversion time (TI), 2500 ms; 180° flip angle (constant throughout echo train) for the conventional turbo-spin-echo refocusing echo train; echo train length, 23; matrix size, 384 × 384; 12 axial, 2 mm thick slices covering the labyrinth with a 160 × 160 mm field of view (FOV); generalized autocalibrating partially parallel acquisition (GRAPPA) acceleration factor, 2; voxel size, 0.4 × 0.4 × 2 mm; number of excitations (NEX), 1; scan time, 15 min 2 s; readout bandwidth, 213 Hz/pixel; and echo spacing, 13 ms.

The parameters for 3D-real IR were as follows: TR, 6000 ms; effective TE, 181 ms; TI, 1650 ms; 180° flip angle (constant throughout echo train) for the conventional turbo-spin-echo refocusing echo train; echo train length, 27; matrix size, 384 × 384; 30 axial, 0.8 mm thick slices covering the labyrinth with a 160 × 160 mm FOV; GRAPPA acceleration factor, 2; voxel size, 0.4 × 0.4 × 0.8 mm; NEX, 1; scan time, 14 min 32 s; readout bandwidth, 213 Hz/pixel; echo spacing, 13 ms; and reconstruction mode 'real.'

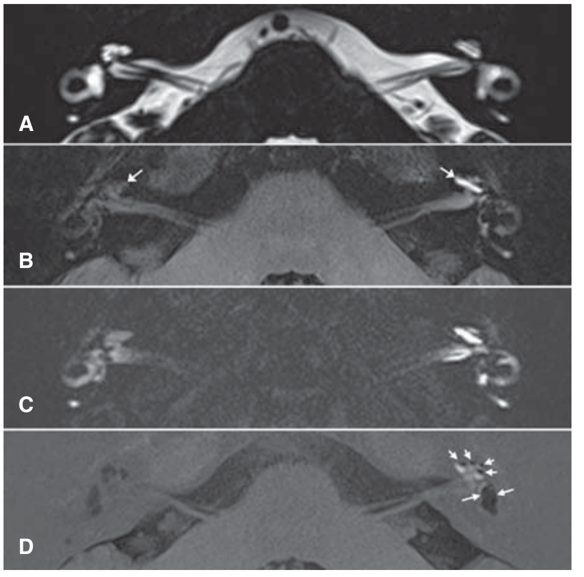

Figure 1. A representative MRI study (patient no. 4 in Table I). (A) Heavily T2-weighted SPACE MRI demonstrates the regular anatomy of the fluid-filled space containing the perilymph and the endolymph. (B) 3D-FLAIR MRI. Gadolinium (Gd) contrast enhancement is obviously stronger in the left ear (IT + IV side) than in the right ear (IV side). The arrows indicate the scala tympani of the basal turn of the cochlea. (C) Heavily T2-weighted 3D-FLAIR MRI (FLAIR constant). The enhancement of the right ear is clearer than that in (B). (D) 3D-real IR MRI. Endolymphatic hydrops (EH) of the left ear (IT + IV side). The short arrows indicate significant EH in the cochlea and the long arrows indicate significant EH in the vestibule. On 3D-real IR MRI, Gd contrast enhancement is not obvious in the right ear (IV side). IT, intratympanic injection; IV, intravenous injection.

The parameters for heavily T2-weighted 3D-FLAIR were as follows: TR, 9000 ms; effective TE, 544 ms; TI, 2250 ms; variable flip-angle echo train with average flip angle, 120°; echo train length, 173; matrix size, 384 × 322; 104 axial, 1 mm thick slices covering the labyrinth with a 180 × 150 mm FOV; GRAPPA acceleration factor, 2; voxel size, 0.5 × 0.5 × 1 mm; NEX, 4; scan time, 14 min 26 s; readout bandwidth, 434 Hz/pixel; and echo spacing, 5.6 ms.

The parameters for heavily T2-weighted SPACE were as follows: TR, 4400 ms with driven equilibrium pulse (RESTORE); effective TE, 544 ms; variable flip-angle echo train with average flip angle, 120°; echo train length, 173; matrix size, 384 × 322; 104 axial, 1 mm thick slices; FOV, 180 × 150 mm; GRAPPA acceleration factor, 2; voxel size, 0.5 × 0.5 × 1 mm; NEX, 1.8; scan time, 3 min 15 s; readout bandwidth, 434 Hz/pixel; and echo spacing, 5.6 ms.

Evaluation of the endolymphatic space and Gd contrast enhancement

The degrees of EH in the vestibule and cochlea were classified into three levels, according to the criteria

Table I. Patients' characteristics and degrees of endolymphatic hydrops (EH).

Patient no.	Age (years)	Sex	Side	Hearing level (dB)	Vertigo	Tinnitus	Ear fullness	EH in the cochlea	EH in the vestibule
1	44	F	R	68	Yes	Yes	No	2	2
			l	15		No	No	0	2
2	60	M	r	10	Yes	No	No	0	0
			L	55		Yes	Yes	2	2
3	67	M	R	65	Yes	No	No	2	2
			l	35		No	No	2	2
4	47	M	r	13	Yes	No	No	0	1
			L	47		Yes	No	2	2
5	49	M	R	50	Yes	Yes	Yes	0	0
			l	13		No	No	1	0
6	68	F	r	27	Yes	No	No	0	0
			L	38		Yes	Yes	1	1
7	35	F	r	48	Yes	No	No	0	1
			L	48		No	No	1	1
8	42	M	r	10	Yes	No	No	1	0
			L	67		Yes	Yes	2	2
9	35	M	R	87	Yes	Yes	No	2	2
			l	12		Yes	No	1	2
10	36	F	r	12	Yes	No	No	0	0
			L	38		Yes	Yes	1	1

Patient no. 7 had definite Meniere's disease on both sides. The other nine patients had definite unilateral Meniere's disease. F, female; M, male. Side: intratympanic Gd injection was done in the ear shown with an upper-case letter; L, left; R, right. Hearing level is the average of three frequencies: 500 Hz, 1 kHz, and 2 kHz. EH: 0 = none, 1 = mild, 2 = significant.

described previously: none, mild, and significant [12]. On 3D-FLAIR MRI (Figure 1B), the regions of interest in the cochlear perilymph in the scala tympani of the apical turn (A) and basal turn (B) and in the cerebellum (C) were determined [9,13,14]. The signal intensity (SI) value for (C) was used as the control and the SI ratios (A) to (B) and (B) to (C) were calculated.

Statistical analysis

The data were analyzed using SPSS for Windows (version 18.0; SPSS Inc., Chicago, IL, USA). Student's t test and the Mann–Whitney test were performed, and $p < 0.05$ was considered statistically significant.

Ethics review

The Ethics Review Committee of Nagoya University School of Medicine approved the protocol of the study (approval no. 369-6). All patients gave their informed consent to their participation in the study. The written informed consent forms were attached to their electronic medical records.

Results

The patients' characteristics and their degrees of EH are listed in Table I. The degrees of EH could be evaluated on both sides in all cases without adverse effects. A representative MRI is shown in Figure 1. In the 10 symptomatic ears that received the IT injection, significant or mild EH was observed in both the cochlea and the vestibule in nine ears. In the 10 ears that did not receive the IT injection (IV side), significant or mild EH was observed in four cochleas and in five vestibules. The SI (B) to (C) ratio was 1.70 ± 0.60 on the IT + IV side and 0.42 ± 0.10 on the IV side. The distribution in each ear is shown in Figure 2. A significant increase in the Gd contrast enhancement was observed in the ears that received the IT injection compared with the ears with only IV Gd enhancement ($p < 0.001$).

The SI (A) to (B) ratio was 0.53 ± 0.16 on the IT + IV side and 0.70 ± 0.14 on the IV side. Figure 3

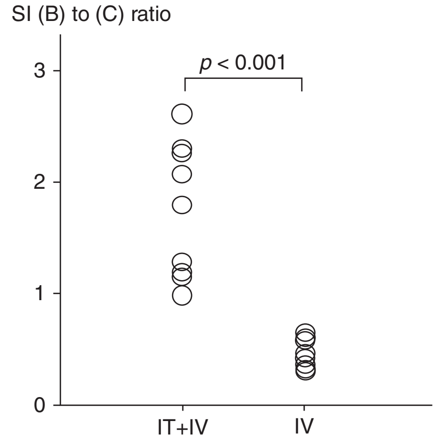

Figure 2. Signal intensity (B) to (C) ratio in the ears on the IT + IV side and the IV side. (B), cochlear perilymph of the basal turn; (C), cerebellum; IT, intratympanic injection; IV, intravenous injection; SI, signal intensity.

shows the SI ratio distributions for each ear. The SI (A) to (B) ratio for the ears that received the IT injection was smaller than that for the ears with only IV Gd enhancement ($p < 0.05$). Gd was more strongly localized in the basal turn in the ears that received the IT injection than in the ears with only IV Gd enhancement, in which the Gd was distributed more uniformly.

On the IV side, neither the cochlea nor the vestibule displayed EH in three ears (patient nos 2, 6, and 10 in Table I). The SI (B) to (C) ratio was 0.48 ± 0.14 in these three ears and 0.39 ± 0.08 in the other seven ears. The SI (A) to (B) ratio was 0.77 ± 0.17 in the three ears without EH and 0.68 ± 0.12 in the other seven ears. No significant difference was observed between the ears with and without EH.

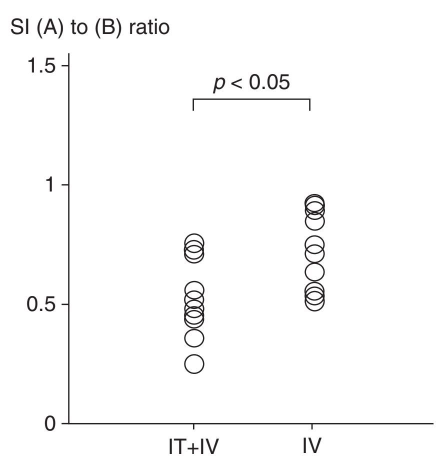

Figure 3. Signal intensity (SI) ratio of the apical turn (A) to the basal turn (B) in the cochlear perilymph in the ears of the IT + IV side and IV side. IT, intratympanic injection; IV, intravenous injection.

Discussion

This is the first investigation of the visualization of the endolymphatic space after the administration of IT + IV Gd. So far, more than 10 hospitals have reported the evaluation of EH with MRI after IT Gd injections [1–4,10,15,16]. To visualize the endolymphatic space bilaterally, bilateral IT injection is a useful method [10]. However, the IT injection into an asymptomatic ear with normal hearing was not approved by the Ethics Review Committee of our university. We attempted to evaluate endolymphatic space size on both sides without the IT injection in asymptomatic ears. We used two different Gd for the IT and IV route. The selection of Gd merely depended on the accessibility to the syringe at that moment in our hospital. Contrast enhancement of the inner ear after IT injection of these two kinds of Gd was not different significantly [17].

The visualization of EH after IV Gd injection is still new. Initially, a double dose of Gd was used to obtain a high SI in visualizing the endolymphatic space [7]. It is now possible to visualize EH after the IV administration of a standard dose using improved imaging techniques [18,19]. However, the quality of the image after an IV Gd injection is not as good as after an IT Gd injection. The IT + IV method provides images that allow the IV Gd and IT+ IV Gd contrast effects to be compared simultaneously.

Temporal bone histopathology and MRI revealed that EH is occasionally observed in the asymptomatic ear in patients with unilateral Meniere's disease [4,11,20]. We think that evaluating the endolymphatic space in the asymptomatic ear may be important, given the probability that in these patients, Meniere's disease will become bilateral in the future. MRI after IT Gd injection reveals the degree of permeability of the round window. Evaluating this permeability may be useful in predicting the efficacy of IT gentamicin or IT steroid therapies for inner ear diseases [5], although the relationship between the distribution of Gd in the inner ear and the efficacy of an IT therapy has not yet been determined [15,16]. Therefore, MRI with IT Gd in the symptomatic ear and IV Gd in the asymptomatic ear in patients with unilateral Meniere's disease provides important information, especially when IT gentamicin therapy is being considered.

In the present study, the SI (A) to (B) ratio in the ears that received the IT Gd injection was smaller than in the ears with only IV Gd enhancement. A similar tendency was reported in a previous study that compared the distribution of Gd in the cochleas of patients who received only IT Gd or only double-dose IV Gd [14]. The difference in the Gd distribution may reflect the flow of Gd from the basal turn toward the upper turn after the IT Gd injection [2]. A future study of the dynamic changes in the Gd distribution in the inner ear should provide a new perspective on the pathophysiology of inner ear diseases.

In conclusion, MRI after a unilateral IT Gd injection and subsequent IV Gd injection is an option when evaluating the size of the endolymphatic space in both ears and when evaluating the passage of Gd from the middle ear to the inner ear on the IT Gd side. Use of this method will improve the effectiveness of imaging and evaluation techniques for EH after IV Gd injection.

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Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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