showed 63 dB in the right ear and 92 dB in the left ear. He underwent CT and MRI to evaluate his ears. CT showed extensive bilateral demineralization of the cochlear capsule, which is characteristic of diffuse cochlear otosclerosis (Fig. 1). Enhanced T1-weighted MRI showed bilateral enhancement of the soft tissue in the cochlear capsule, instead of the normal signal void from the bone. He was diagnosed with cochlear otosclerosis. Bilateral Schwartze's sign was noted at this time. He was treated with hydrocortisone at 200 mg/d (first to fourth days of admission) and 100 mg/d (fifth to eighth days), but there was no improvement in hearing on the right.

In May 2006, at the age of 51, the patient experienced sudden deterioration of hearing in the right ear, without vertigo. The audiogram showed 80 dB in the right ear and 112 dB in the left ear. MRI three-dimensional fluid-attenuated inversion recovery (3D-FLAIR) images, before enhancement, revealed bilateral faint high-signal areas in the cochleas and vestibules (Fig. 2a). MRI scans were performed with a 3-T MR (Trio, Siemens, Erlangen, Germany) using a receive-only eight-channel phased-array coil. 3D-FLAIR was obtained before and after the administration of a single dose of gadolinium. Contrast-enhanced 3D-FLAIR was initiated 7 min after the gadolinium was administered, so that the contrast of 3D-FLAIR was determined approximately 10 min after the administration of gadolinium. The MRI protocols and the film settings have been described in detail in a previous report [4]. Postcontrast 3D-FLAIR revealed bilateral enhancement of the cochleas, especially in the basal turn of the left cochlea (Fig. 2b). Enhanced T1-weighted MRI revealed bilateral enhancement of the soft tissue around the cochlea, similar to the MRI findings 3 years ago. However, high-signal areas on 3D-FLAIR after enhancement were not detected by T2- and T1-weighted MRI (Fig. 2c). He was treated with 30 mg/d of prednisolone, but there was no significant improvement in hearing. The steroid dosage was reduced to 20 mg/d of prednisolone, and he experienced continued hearing deterioration in the right ear.

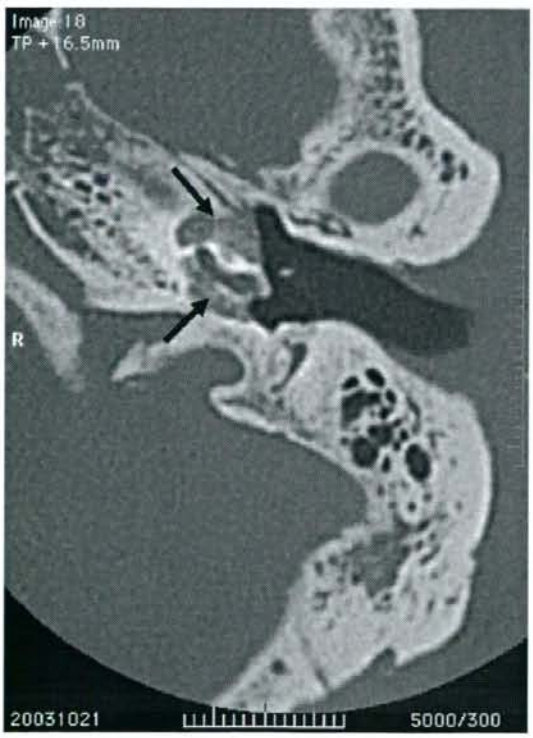

Fig. 1. Computed tomography. This image shows severe demineralization (arrows) around the left cochlea, which is characteristic of diffuse cochlear otosclerosis.

3. Discussion

In this case, postcontrast 3D-FLAIR revealed enhancement of the inner ear fluid, while conventional postcontrast MRI could only show enhancement of the decalcified area (or otosclerotic lesion) in otosclerosis. This enhancement suggested breakdown of the blood–labyrinth barrier. This is the first report to show breakdown of the blood–labyrinth barrier in a patient with cochlear otosclerosis, the identification of which has been made possible by the new method of 3D-FLAIR. These MRI findings may help to clarify the cause of hearing deterioration in a part of patients with cochlear otosclerosis.

The FLAIR sequence is a part of the routine protocol for MRI of the brain [5]. Subtle high-signal areas in the cerebrospinal fluid (CSF) can be an indicator of subarachnoid hemorrhage, meningitis, or acute infraction. The FLAIR sequence sometimes demonstrates hemorrhage or a high concentration of protein, which are difficult to detect by T1- and T2-weighted MRI. The two-dimensional (2D)-FLAIR sequence shows flow-related artifacts caused by the inflow of CSF from outside the slice volume, which sometimes obscures any pathology present. We have reported previously that CSF-related flow artifacts are significantly lower on 3D-FLAIR images than on 2D-FLAIR images [5]. The 3D-FLAIR sequence allows the detection on serial thin slices of conditions that mimic other pathologies of the inner ear, such as inner-ear hemorrhage and high concentrations of protein. We have recently reported high signals in the affected inner ears of patients with idiopathic sudden SNHL using 3D-FLAIR [4]. In that report, one of eight patients with sudden SNHL showed gadolinium enhancement in the affected cochlea on 3D-FLAIR, which suggested breakdown of the blood–labyrinth barrier. In this study, postcontrast 3D-FLAIR showed bilateral enhancement in the cochleas, especially in the basal turn of the left cochlea. The enhancement seen in both ears suggested breakdown of the blood–labyrinth barrier. Furthermore, the MRI findings suggested that the breakdown in the left ear was more severe than that in the right ear. We have recently

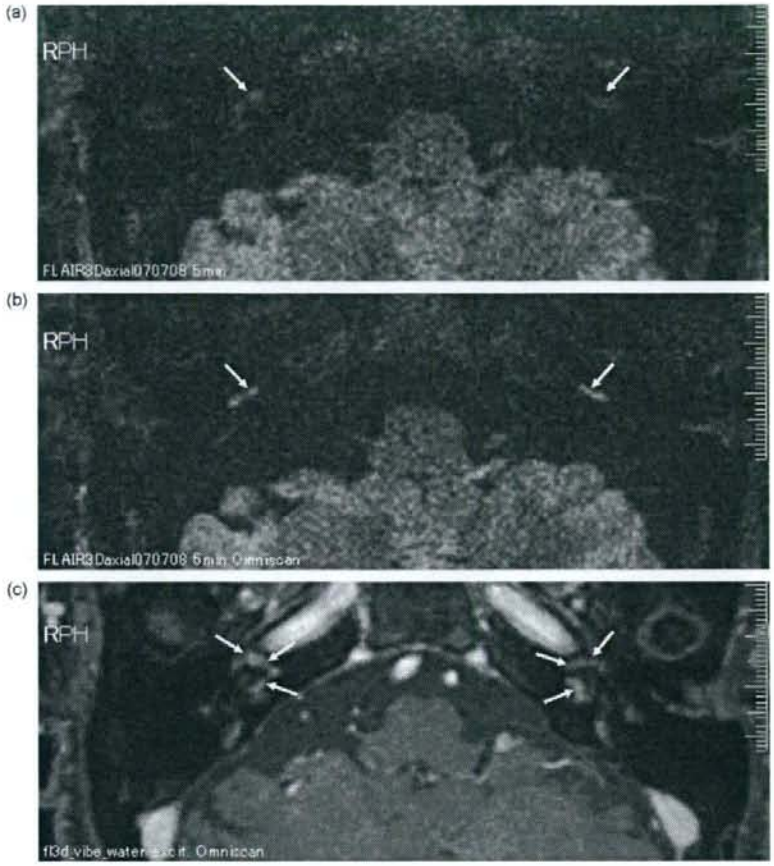

Fig. 2. Axial magnetic resonance imaging (MRI). (a) Three-dimensional fluid-attenuated inversion recovery (3D-FLAIR) images before enhancement. Bright signals are faintly visible bilaterally in the cochleas (arrows). (b) 3D-FLAIR after enhancement. Gadolinium enhancement is seen bilaterally in the cochleas (arrows), especially in the basal turn of the left cochlea. (c) Enhanced T1-weighted MRI. Bilateral enhancement of the soft tissue around the cochleas is seen (arrows). However, the high-signal areas visualized on 3D-FLAIR after enhancement were not detected.

reported that the cochlear fluid in normal subjects is enhanced on 3D-FLAIR imaging 4 h after gadolinium injection, but normal subjects show no enhancement on 3D-FLAIR 10 min after gadolinium injection [6]. From these results, it is clear that the positive findings in this 3D-FLAIR study are significant. We have demonstrated that 3D-FLAIR is a very useful tool in the detection of minute abnormalities in the inner ear that are not detected by conventional T1- or T2-weighted MRI.

The enhancement of the soft tissue around the cochlea which was detected by T1-weighted MRI is presumed to be owing to contrast pooling in the blood vessels of otosclerotic foci [3]. In contrast to this, the cochlea enhancement which was detected by 3D-FLAIR is presumed to be owing to the increased permeability of blood vessels [4].

Schwartze's sign, which indicates proliferation or dilatation of the blood vessels in the promontory, is occasionally observed in cochlear otosclerosis. This sign has been reported to be associated with increased blood flow to the promontory [7]. In patients with cochlear otosclerosis, temporal bone histopathology shows significant dilatation of blood vessels, including the spiral modiolar vein and the vein of the cochlear aqueduct [8]. The inner ear artery (the labyrinthine artery), usually a branch of the anterior inferior cerebellar artery, nourishes the inner ear. The middle ear is usually supplied by the carotid arterial system. Despite their close anatomical relationship, there is no functional anastomosis of blood vessels between the middle and inner ear [9]. Vascular shunts between the cochlea and the surrounding bone, which have been described histologically in cochlear otosclerosis, are considered unique [8,10]. Histopathological studies of temporal bone in cochlear otosclerosis have suggested that venous congestion occurs inside the cochlea.

It is well known that one of the effects of steroids is to suppress the increased permeability of blood vessels. It is possible that the effect of steroids in this case was associated

with the suppression of permeability of the inner-ear blood vessels. This report is important in suggesting that a part of progressive SNHL in cochlear otosclerosis is associated with increased permeability of blood vessels. Further studies are needed to clarify the relationship between the MRI findings and hearing loss in cochlear otosclerosis. We believe that our study will help further understanding of the pathophysiology of cochlear otosclerosis.

Acknowledgements

This study was supported by research grants from the Ministry of Health, Labour and Welfare and from the Ministry of Education, Culture, Sports, Science and Technology of Japan.

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The Journal of Laryngology & Otology (2008), 122, 887–892.

doi:10.1017/S0022215107000941

Main Article

Vestibular aqueduct in sudden sensorineural hearing loss

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Abstract

Objective: To evaluate the vestibular aqueduct in patients with sudden sensorineural hearing loss.

Methods: We evaluated 19 patients (12 men and seven women; age range, 22 – 79 years) with unilateral sudden sensorineural hearing loss, using computed tomography and magnetic resonance imaging. All these patients had unilateral sudden sensorineural hearing loss. We also evaluated 47 control subjects (22 men and 25 women; age range, 22–79 years).

Results: In sensorineural hearing loss affected ears, the width of the vestibular aqueduct at the midpoint and at the operculum was significantly greater than that in contralateral ears or in control ears. The width of the vestibular aqueduct at the midpoint and the operculum did not correlate with the audiometric threshold or the audiogram configuration. Contrast enhancement of the ipsilateral endolymphatic sac was observed in 17 of 19 patients with sudden sensorineural hearing loss (89 per cent). Eleven of these 17 patients also showed enhancement on the contralateral side, but no patient showed enhancement only on the contralateral side. In sensorineural hearing loss affected ears, the width of the vestibular aqueduct did not differ significantly between those patients with and without enhancement.

Conclusions: The vestibular aqueducts of sudden sensorineural hearing loss affected ears are wider than those of controls. Precise imaging and evaluation of the inner ear is essential when investigating the pathological conditions responsible for sudden sensorineural hearing loss.

Key words: Sudden Hearing Loss; Endolymphatic Duct; Endolymphatic Sac; Computed Tomography; Magnetic Resonance Imaging

Introduction

The aetiology of sudden sensorineural hearing loss (SNHL) includes various pathophysiological processes. Many investigators have studied the aetiology of SNHL and identified such causal factors as: perilymphatic fistula, viral infections,[1] autoimmune disorders,[1] asymptomatic mumps infection,[2] inner-ear haemorrhage,[3] inner-ear anomaly[4] and disordered blood flow.[5]

Temporal bone[6] and computed tomography (CT) studies[7] have demonstrated that the width of the vestibular aqueduct is smaller in Ménière's disease patients than in normal controls. However, the width of the vestibular aqueduct in patients with sudden SNHL has not been reported. This study was conducted to evaluate the width of the vestibular aqueduct in patients with sudden SNHL. We have previously reported that, in patients with sudden SNHL, the frequency of contrast enhancement of the endolymphatic sac was significantly greater than that in control subjects.[8] In the present study, we attempted to investigate the relationship between the width of the vestibular aqueduct and the presence of endolymphatic sac enhancement, in patients with sudden SNHL, in association with the prognosis for the patient's hearing.

Patients and methods

A total of 19 patients (12 men and seven women; age range, 22–79 years; overall mean age ± standard deviation (SD) = 53.0 ± 14.7 years) and 47 control subjects without SNHL were evaluated prospectively. All the patients attended our university hospital between April 2005 and April 2006. All patients had unilateral sudden SNHL. The criteria for sudden SNHL in this study were: patients being able to describe the day of onset of sudden SNHL for which no cause was known; no hearing loss being observed before the onset of sudden SNHL; and hearing loss occurring in less than three days. We excluded patients with fluctuating hearing loss or progressive hearing loss. All patients were examined using both unenhanced and enhanced magnetic resonance imaging (MRI) and CT. All 47 control subjects suffered from unilateral chronic otitis media and were evaluated with CT.

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Accepted for publication: 24 July 2007. First published online 26 November 2007.

Audiological findings

Throughout the study, the same audiometer (Model AA-79S, Rion, Tokyo, Japan) was used to evaluate hearing levels in a sound-insulated chamber. Serial audiograms were compared with tympanograms and speech discrimination scores, when available. The average hearing level was expressed as the average score at three frequencies (500, 1000 and 2000 Hz). If the patients did not respond to the maximum sound level produced by the audiometer, we defined the threshold as 5 dB added to the maximum level.

The outcome of sudden SNHL was evaluated using the criteria of the Ministry of Health and Welfare of Japan.[9] By these criteria, the average hearing level is calculated as the average of the hearing levels measured at 250, 500, 1000, 2000 and 4000 Hz. Recovery was ranked as follows:[8] no change = improvement in hearing of less than 10 dB on average; slight improvement = improvement in hearing of 10 dB or more but less than 30 dB on average; marked improvement = improvement in hearing of 30 dB or more on average; and complete recovery = all five frequencies of the final audiogram were 20 dB or less, or improvement to the same degree of hearing as observed in the contralateral ear. The prognosis score was assigned as follows: zero = no change; one = slight improvement; and two = marked improvement or complete recovery.

Magnetic resonance imaging

From April 2005 to November 2005, MRI scans were performed using a 1.5-Tesla MR system (Visart, Toshiba, Tokyo, Japan) with bilateral, quadrature surface, phased-array coils over both ears. The MRI protocols have been described in detail in previous reports.[8,10,11] The film settings were the same as those previously reported.[8] From December 2005, MRI scans were performed with a 3-Tesla MR system (Trio, Siemens, Erlangen, Germany) using a receive-only, eight-channel, phased-array coil. The MRI protocols and the film settings have been described in detail in a previous report.[12]

Endolymphatic sac enhancement

Two observers, who were blinded to patients' medical histories, reviewed all images independently with regard to contrast enhancement in the vicinity of the intraosseous or extraosseous endolymphatic sac. Contrast enhancement was judged to be present when comparison of the pre- and post-contrast-enhanced T1-weighted images showed the appearance of a distinct linear or band-like area of increased signal intensity more than 2 mm in length, after administration of the contrast material. The image interpretation has been described in detail in a previous report.[8] 'Enhancement' of the sac does not mean a glittering sac, but the appearance of increased signal intensity after administration of the contrast material. Contrast enhancement in the vicinity of the endolymphatic sac was recorded as present or absent. If there was any disagreement between the observers, a consensus was reached by discussion. The relationship between enhancement and the period from the onset of hearing loss to the MRI examination was also evaluated. The relationship between enhancement and the patient's outcome with regard to hearing was also assessed.

Computed tomography

All CT images were obtained using a CT system with four detector rows (Aquillion, Toshiba) by 0.5 mm collimation, with a 512 × 512 matrix. The film settings have been described in detail in a previous report.[13]

Vestibular aqueduct measurement

The width of the aqueduct was measured at two points: at the operculum (i.e. a line perpendicular to the posterior surface of the petrous pyramid and extending to the most lateral or postlateral pixel in the medial wall of the operculum) and at the midpoint (i.e. the halfway point between the operculum and the posterior wall of the crus commune or vestibule), according to the method of Madden *et al.* (Figure 1).[14]

Two observers, who were blinded to the patients' medical histories, reviewed all images independently with regard to the width of the vestibular aqueduct. The width of the vestibular aqueduct was recorded as the average of the observers' measurements. If there was a large difference between these observations, a consensus was reached by discussion.

Statistical analysis

The width of the vestibular aqueduct at the midpoint and operculum was assessed, comparing: patients with sudden SNHL and control subjects; patients' affected and non-affected ears; and ears affected with otitis media and contralateral ears, in control

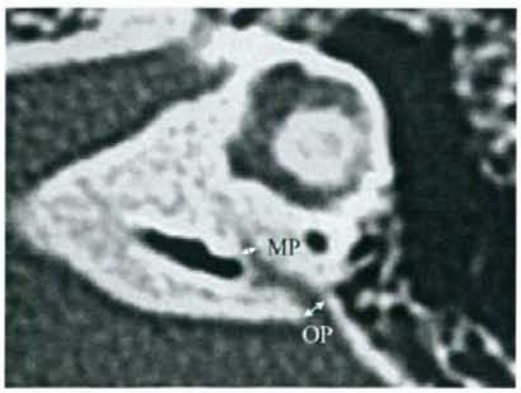

FIG. 1

Axial computed tomographic scan showing measurement of the vestibular aqueduct width. MP = midpoint; OP = operculum

subjects. The relationship between the width of the vestibular aqueduct and the audiometric threshold (in each of the initial and final audiograms) or the audiogram configuration was evaluated. The relationship between contrast enhancement of the endolymphatic sac and the width of the vestibular aqueduct in patients with SNHL was also evaluated.

The average prognosis scores were compared for patients with and without enhancement. The relationship between the width of the vestibular aqueduct and the prognosis with regard to hearing was assessed.

These statistical analyses were performed using chi-square testing, Mann–Whitney *U* testing and Pearson correlation coefficients.

Results

The results for contrast enhancement of the endolymphatic sac and for the width of the vestibular aqueduct are presented in Table I, together with data on hearing outcomes and on the length of time from the onset of hearing loss to the MRI examination.

The width of the vestibular aqueduct at the midpoint and operculum in the SNHL-affected ears was significantly greater than that in the contralateral ears (midpoint, $p < 0.05$; operculum, $p < 0.05$) and that in the ears of control subjects (midpoint, $p < 0.05$; operculum, $p < 0.0005$) (Table II and Figure 2). The width of the vestibular aqueduct at the midpoint and the operculum did not differ significantly, comparing contralateral ears in sudden SNHL and control ears (Table II and Figure 2). In control subjects, the width of the vestibular aqueduct at the midpoint and operculum was not significantly different, comparing the chronic otitis media affected ears and the contralateral ears (Table II).

TABLE II

VESTIBULAR AQUEDUCT WIDTH AT MIDPOINT AND OPERCULUM

Ear	VA width (average ± SD; mm)	
	MP	OP
Affected, in sudden SNHL	0.6 ± 0.2	1.0 ± 0.3
Unaffected, in sudden SNHL	0.5 ± 0.2	0.8 ± 0.3
Affected, in control	0.5 ± 0.1	0.7 ± 0.2
Unaffected, in control	0.6 ± 0.2	0.8 ± 0.2

VA = vestibular aqueduct; SD = standard deviation; MP = midpoint; OP = operculum; SNHL = sensorineural hearing loss

The average hearing level (in both initial and final audiograms) showed no correlation with the vestibular aqueduct width. Audiometric configurations in this study were flat in 13 ears (68 per cent) and up-sloping in five ears (26 per cent). A down-sloping configuration was found in one ear (5 per cent). We then analysed the audiogram configuration for each patient and found no correlation with the vestibular aqueduct width. Four out of 19 patients had vertigo. No relationship between the presence of vertigo and the width of the vestibular aqueduct was found.

The MRI scans for nine patients (cases one to nine in Table I) were performed using a 1.5-Tesla MR system, and the MRI scans for 10 patients (cases 10–19) were performed using a 3-Tesla MR system. In patients with sudden SNHL, the frequency of

TABLE I

CLINICAL AND IMAGING RESULTS FOR PATIENTS WITH SUDDEN SENSORINEURAL HEARING LOSS

Case	Age (yr), gender	Side	Initial/final hearing level* (dBA)	Audiogram configuration	Vertigo?	MP width (mm)	OP width (mm)	ES enhancement†	Time from onset to MRI (days)
1	57, M	R	105/47	Flat	No	0.7	1.3	2	12
2	53, F	L	80/67	Flat	No	0.5	0.8	2	28
3	25, M	L	46/0	Flat	No	0.7	0.9	2	2
4	55, M	R	113/103	Flat	No	0.9	1.4	2	6
5	25, F	R	85/52	Flat	No	0.3	0.6	2	8
6	22, M	L	80/17	Up-sloping	Yes	0.8	1.3	1	13
7	56, M	R	78/30	Flat	No	0.5	1.4	2	48
8	62, M	L	80/72	Up-sloping	No	0.6	1.1	1	3
9	52, F	L	68/13	Flat	No	0.6	1.1	2	8
10	57, M	R	87/15	Up-sloping	No	0.8	1.2	0	2
11	51, M	R	100/75	Flat	No	0.6	1.2	1	8
12	59, M	R	97/28	Up-sloping	No	0.5	0.9	0	6
13	64, M	R	95/80	Flat	Yes	0.4	0.5	2	18
14	79, F	R	83/67	Down-sloping	Yes	0.6	0.8	2	8
15	56, M	R	77/57	Flat	No	0.6	0.8	1	13
16	51, F	L	93/25	Flat	No	0.7	1	1	4
17	62, M	L	78/78	Up-sloping	No	0.5	0.7	2	20
18	50, F	R	115/108	Flat	No	0.8	1.3	2	2
19	70, F	L	102/90	Flat	Yes	0.8	0.9	2	14

*Hearing level was expressed as the average score at three frequencies (500, 1000 and 2000 Hz), for the initial and final audiogram.
†0 = no enhancement; 1 = ipsilateral enhancement; 2 = bilateral enhancement. Yr = years; MP = vestibular aqueduct at midpoint; OP = vestibular aqueduct at operculum; ES = endolymphatic sac; MRI = magnetic resonance imaging; M = male; F = female; R = right; L = left

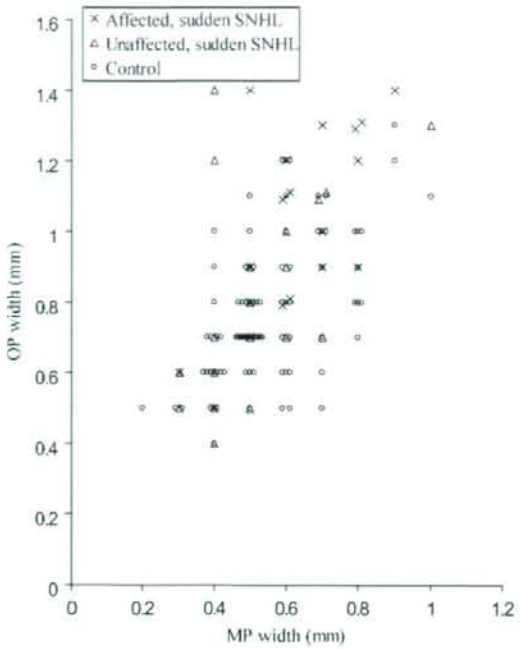

FIG. 2

Scatter plot of vestibular aqueduct widths at the operculum versus those at the midpoint, in affected and unaffected ears of patients with sudden sensorineural hearing loss and in control subjects. MP = midpoint; OP = operculum; SNHL = sensorineural hearing loss

enhancement of the endolymphatic sac did not differ significantly, comparing those patients examined with 1.5-Tesla MRI and those examined with 3-Tesla MRI.

Enhancement of the endolymphatic sac was judged to be present on the affected side in 17 patients (89 per cent). In 11 of these 17 patients, the enhancement was also judged to be present on the contralateral side. However, no enhancement was observed on the contralateral side only.

The frequency of enhancement of the endolymphatic sac was significantly greater in the SNHL-affected ears than in the contralateral ears ($p < 0.05$). In patients with sudden SNHL, the period between the onset of hearing loss and MRI scanning did not differ significantly between those patients who showed enhancement (average $\pm$ SD, 12.6 ± 11.4 days) and those who did not (4.0 ± 2.8 days).

In patients with sudden SNHL, the width of the vestibular aqueduct at the midpoint and operculum in the SNHL-affected ear did not differ significantly, comparing patients with enhancement of the endolymphatic sac (midpoint, 0.6 ± 0.2 mm; operculum, 1.0 ± 0.3 mm) and those without enhancement (midpoint, 0.7 ± 0.2 mm; operculum, 1.1 ± 0.2 mm). Furthermore, no difference in prognosis scores was noted between sudden SNHL patients with and without enhancement.

Discussion

The major finding of this study was that the width of the vestibular aqueduct in the ear affected with sudden SNHL was significantly greater than that in the contralateral ear or in the ears of control subjects. It has been reported that the width of the vestibular aqueduct is smaller in patients with Ménière's disease than in control subjects.[6,7] Evaluation of the vestibular aqueduct is important to our understanding of the pathophysiological mechanisms involved in sudden SNHL, considering that the vestibular aqueduct size in patients with sudden SNHL differs from that in patients with Ménière's disease.

Enlarged vestibular aqueduct is the most common congenital abnormality in the inner ear on radiological assessment. Enlarged vestibular aqueducts have been associated with a range of congenital disorders, such as the CHARGE association was defined as a non-random association of anomalies (Coloboma, Heart defect, Atresia choanae, Retarded growth and development, Genital hypoplasia, Ear anomalies/deafness). association,[15] Alagille syndrome,[16] Pendred syndrome[17] and the branchio-oto-renal syndrome.[18] The criteria to determine an enlarged vestibular aqueduct are vague. However, a vestibular aqueduct diameter larger than 1.5 mm at the midpoint or an opercular measurement of greater than 2 mm are generally considered to be the defining characteristics.[19,20] In the present study, all patients with sudden SNHL showed a vestibular aqueduct diameter of less than 1.5 mm at the midpoint or an opercular measurement of less than 2 mm. Thus, we found that none of the patients in this study showed evidence of an enlarged vestibular aqueduct.

Purcell *et al.*[21] reported significant differences in the shape of the inner ear in patients with congenital SNHL, even in cases with grossly normal CT scans, when compared in detail with those of patients without SNHL. These authors suggested that hearing loss in SNHL patients with a 'radiologically normal' cochlea may be related to dysfunction of both the membranous and bony labyrinths. However, they did not evaluate the vestibular aqueduct quantitatively.

- **This study sought to evaluate the vestibular aqueduct in patients with sudden sensorineural hearing loss**
- **Nineteen patients with sudden SNHL were evaluated using computed tomography and magnetic resonance imaging**
- **The width of the vestibular aqueduct in SNHL-affected ears at the midpoint and operculum was significantly greater than that in contralateral, unaffected ears or in control ears**
- **It is possible that sudden SNHL patients with a wider vestibular aqueduct are born with a 'fragile' inner ear**
- **Clarifying the pathophysiological mechanism responsible for endolymphatic sac enhancement may aid the understanding of sudden deafness**

Our previous study demonstrated that the endolymphatic sac was enhanced in 75 per cent of sudden SNHL-affected ears, in 53 per cent of contralateral ears in patients with sudden SNHL and in 18 per cent of control ears.[8] In the present study, the endolymphatic sac was enhanced in 89 per cent of sudden SNHL ears and in 63 per cent of the contralateral ears of patients with sudden SNHL. The frequency of endolymphatic sac enhancement in patients with sudden SNHL did not differ significantly between the previous and the present study (chi-square test). Enhancement of the endolymphatic sac suggests inflammation of the endolymphatic sac tissue or venous enlargement in the region of the sac. Based on the results of this study, we speculate that many patients with sudden SNHL may experience pathophysiological changes in the region of the endolymphatic sac. We have previously reported that the endolymphatic sac was enhanced in 63 per cent of affected ears in patients with acute low-tone SNHL without vertigo.[22] In contrast, the endolymphatic sac was enhanced in 20 per cent of affected ears in patients with Ménière's disease.[8]

It is known that the endolymphatic sac and duct are poorly developed in patients with Ménière's disease. The endolymphatic sac is believed to intervene in the absorption of the endolymphatic fluid, and damage to the endolymphatic sac results in endolymphatic hydrops.[22] It is possible that the narrow vestibular aqueduct in patients with Ménière's disease is associated with an impediment of the absorption of endolymphatic fluid. In contrast, the results of the present study show that the vestibular aqueduct in patients with sudden SNHL was wider than that in controls. A wider vestibular aqueduct might be associated with insufficient maturation of the inner ear, because an increased fluid-filled area of the inner ear may be related to insufficient maturation of the inner ear.[23] It is possible that sudden SNHL patients with a wider vestibular aqueduct are born with a 'fragile' inner ear,[4] or are apt to receive abnormal pressure transmission through the vestibular aqueduct.[24]

Clarifying the pathophysiological mechanism responsible for endolymphatic sac enhancement in patients with sudden deafness may be a key to understanding the cause of sudden deafness. Precise imaging and evaluation of the inner ear is essential to the investigation of the pathological conditions underlying sudden SNHL.

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Dr M Sugiura takes responsibility for the integrity of the content of the paper.
Competing interests: None declared

Magn Reson Med Sci, Vol. 7, No. 2, pp. 85-91, 2008

MAJOR PAPER

Imaging Endolymphatic Hydrops at 3 Tesla Using 3D-FLAIR with Intratympanic Gd-DTPA Administration

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(Received January 29, 2008; Accepted March 26, 2008)

Purpose: Visualization of endolymphatic hydrops by 3-dimensional fluid-attenuated inversion recovery-FLAIR using conventional turbo-spin-echo (3D-FLAIR-CONV) after intratympanic injection of Gd-DTPA has been reported in patients with Ménière's disease. Compared to 3D-FLAIR-CONV used in previous studies, the addition of a variable flip-angle technique (3D-FLAIR-VFL) enables very long echo trains and, therefore, shorter scan times. We evaluated whether 3D-FLAIR-VFL could replace 3D-FLAIR-CONV in detecting endolymphatic hydrops after intratympanic Gd-DTPA administration.

Methods: Eleven patients were included in this study. Twenty-four hours after Gd-DTPA injection, we performed 3D-FLAIR-CONV and 3D-FLAIR-VFL imaging at 3T. We compared the contrast-to-noise ratio (CNR) between cochlear fluid and the cerebellum between the 2 FLAIR sequences. We subjectively scored the size of the endolymphatic space in the cochlea and vestibule for each patient and correlated the scores with the clinical diagnoses.

Results: The CNR of 3D-FLAIR-CONV was significantly higher than that of 3D-FLAIR-VFL. Scores for the size of endolymphatic space in the vestibule were identical between the 2 sequences; however, those in the cochlea disagreed in 3 cases. 3D-FLAIR-CONV correlated better with the clinical diagnoses.

Conclusions: Currently, we may not be able to replace 3D-FLAIR-CONV with 3D-FLAIR-VFL, at least not with the scanning parameters used in the present study.

Keywords: ***3D imaging, advanced imaging techniques, magnetic resonance imaging, temporal bone disease***

Introduction

Visualization of endolymphatic hydrops by magnetic resonance (MR) imaging after intratympanic injection of gadolinium-diethylene-triamine pentaacetic acid (Gd-DTPA) has recently been reported in patients with Ménière's disease. In these patients, on 3-dimensional fluid-attenuated inversion recovery (3D-FLAIR) obtained with a conventional turbo spin-echo sequence after intratympanic injection of Gd-DTPA at 3T, the enlarged endolymphatic space without Gd-DTPA distribution has been recognized as an area of low signal intensity partly surrounded by high-signal perilymphatic fluid with Gd-DTPA distribution.[1] Although the in-plane resolution was relatively high at 0.42 mm × 0.42 mm, the scan time was rather long, 15 min, even when applying a parallel imaging technique and utilizing slices 2-mm thick.

On the other hand, 3D-FLAIR covering the entire labyrinth can be obtained in 5 to 6 min with a near isotropic resolution of 0.67 mm × 0.67 mm × 0.8 mm by using a variable flip-angle turbo-spin-echo (3D-FLAIR-VFL) technique.[2] This voxel volume is almost identical to that of the conventional turbo-spin-echo 3D-FLAIR (3D-FLAIR-CONV) used in previous studies.[1,3] The shorter scan time of 3D-FLAIR-VFL enables its routine use in clinical settings. Thus, 3D-FLAIR-VFL has been used to evaluate various inner ear disorders.[4-10] The pre-contrast 3D-FLAIR-VFL scan was used to detect subtle changes in labyrinthine fluid composition, and the post-contrast 3D-FLAIR-VFL scan

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(following intravenous Gd-DTPA administration) was used to detect disruption of the blood labyrinthine barrier.[4,8]

We evaluated whether 3D-FLAIR-VFL could replace 3D-FLAIR-CONV for detecting endolymphatic hydrops after intratympanic Gd-DTPA administration.

Materials and Methods

Patients

Eleven patients (5 men, 6 women, aged 24–74; eight with clinically diagnosed Ménière's disease, one with sudden sensorineural hearing loss, one with fluctuating sensorineural hearing loss, and one with delayed endolymphatic contralateral-type hydrops) underwent intratympatic administration of gadolinium-diethylene-triamine pentaacetic acid-bis (methylamide) (Gd-DTPA-BMA; Omniscan, Daiichi-Sankyo Pharmaceutical Co. Ltd., Tokyo, Japan). These patients were scheduled for intratympanic injection therapy with gentamicin or, for the patient with sudden sensorineural hearing loss, a steroid. Written informed consent was obtained from all patients. This study was approved by the institutional review board of our university hospital.

Intratympanic gadolinium injection

The detailed methods for intratympanic gadolinium injection have been reported.[1] In that study, a delay of 24 hours between the intratympanic gadolinium injection and MR imaging was found to be optimal to allow the gadolinium to distribute widely in the perilymphatic space of the labyrinth.

Gd-DTPA-BMA was diluted 8-fold with saline (v/v 1:7) and injected intratympanically using a 23-G needle and a 1-mL syringe after the patient was placed in the supine position with head turned approximately 30° away from the sagittal line toward the healthy ear. The diluted Gd-DTPA-BMA was injected until a backflow of fluid into the external ear was observed through a microscope, resulting in an injected volume of 0.4 to 0.5 mL per patient. After the injection, the patient remained in the supine position for 60 min with head turned approximately 60° away from the sagittal line toward the healthy ear. Gentamicin or steroid was not injected at the same time.

MR imaging

All scans were performed on a 3T MR imaging scanner (MAGNETOM Trio, Siemens Medical Solutions; Erlangen, Germany) using a receive-only, 12-channel, phased-array coil. T_1-weighted 3D-FLASH (fast low-angle shot) and 3D-FLAIR-CONV images were acquired 24 hours after intratympanic injection of diluted Gd-DTPA-BMA.

In addition, T_2-weighted 3D-CISS (constructive interference in the steady state) imaging was performed to obtain reference images of the labyrinthine fluid-space anatomy.

The parameters for 3D-FLASH were: repetition time (TR), 4.3 ms; echo time (TE), 1.97 ms; flip angle, 10 degrees with radiofrequency (RF) spoiling; matrix size, 256 × 256; 96 axial 0.8-mm-thick slices covering the posterior fossa with a 16-cm^2 field of view (FOV); and number of excitations (NEX), 2. Total scan time was 2 min 51 s.

The parameters for 3D-CISS were: TR, 11.42 ms; TE, 5.71 ms; flip angle, 50 degrees; matrix size, 320 × 320; 48 axial 0.8-mm-thick slices; FOV, 16 cm^2; and NEX, 1. Scan time was 3 min 42 s.

The parameters for 3D-FLAIR-CONV were: TR, 9000 ms; TE, 128 ms; flip angle, 180 degrees (constant) for the turbo-spin-echo refocusing echo train; echo-train length, 23; matrix size, 384 × 384; 12 axial 2-mm-thick slices covering the labyrinth; FOV, 16 cm^2, acquired using the generalized autocalibrating partially parallel acquisition (GRAPPA) technique with an acceleration factor of 2;[11] and NEX, 1. The scan time was 15 min.

The parameters for 3D-FLAIR-VFL were: TR, 9000 ms; effective TE, 638 ms; variable flip-angle echo train with an average flip angle, 151 degrees; echo-train length, 171; matrix size, 384 × 384; 48 axial 0.8-mm-thick slices covering the labyrinth; FOV, 25.6 cm^2; acceleration factor, 2 using the GRAPPA technique;[11] voxel size, 0.67 mm × 0.67 mm × 0.8 mm; and NEX, 2. The total scan time was 5 min 26 s. The readout bandwidth was 592 Hz/pixel, and the echo spacing was 3.64 ms. Nonselective inversion pulses and slab-selective excitation pulses were used. The features of this variable flip-angle sequence have been reported elsewhere.[12–14] This sequence allows the use of very long echo-train lengths, in the range of 150 to 220, without severe blurring and while maintaining contrast similar to that of 3D-FLAIR-CONV, even with a long effective echo time. To achieve short echo spacing, field of view was larger than with other sequences.

Image evaluation

Qualitative evaluation

The size of the endolymphatic space in the vestibule was scored subjectively: a score of 3 indicated that the entire vestibule was occupied by endolymph; 2, more than half was occupied by endolymph; 1, from 30 to 50% was occupied by endo-

lymph; and 0, less than 30% was occupied by endolymph.

The size of endolymphatic space in the cochlear basal turn was scored subjectively: 3: the cochlear duct was larger than the perilymphatic space of the scala vestibule; 2: Reissner's membrane was bulging toward the scala vestibuli, though smaller than the perilymphatic space of the scala vestibule; 1: no bulging of Reissner's membrane; and 0: bulging of Reissner's membrane toward the scala media or no visualization of endolymphatic space. Two radiologists independently scored the size of the endolymphatic space. 3D-FLAIR-CONV and 3D-FLAIR-VFL were evaluated separately with an interval of 7 days. If a discrepancy existed between the two, consensus was obtained after discussion.

The probability of endolymphatic hydrops was scored tentatively from clinical records: 3, high; 2, moderate; 1, slight; and 0, low. This probability was scored subjectively based on the ratio of the summating potential to the action potential (SP/AP) on an electrocochleogram,[15,16] the vestibular evoked myogenic potential (VEMP),[17] audiogram frequency and fluctuation patterns, and clinical history. A positive VEMP response is considered to be a normal sign of vestibular function, especially for the saccule.[16] An SP/AP ratio larger than 36% is considered to be positive for cochlear endolymphatic hydrops.[16] However, because concrete diagnosis of endolymphatic hydrops is not possible, this probability score is not a perfect standard of reference.

Quantitative evaluation

The contrast-to-noise ratio (CNR) between the basal turn of the cochlea and the cerebellum was measured by drawing a circular region of interest (ROI) in the basal turn of the cochlea, in the cerebellum, and in air. The ROI diameter of the cochlea was 2 mm, and the ROI diameters of the cerebellum and air were 6 mm. The CNR value was defined as the difference in signal between the cochlea and cerebellum divided by the standard deviation of the air signal. CNR per scan time was defined as the CNR value divided by the square root of the scan time. CNR and CNR per scan time values were compared using student's t-test.

Results

No side effects related to the intratympanic injection were observed.

Table summarizes patients and evaluation results. On T_1-weighted 3D-FLASH, contrast enhancement in the labyrinth was quite faint in all patients; therefore, 3D-FLASH images were not used for further evaluation.

Image evaluation

Qualitative analysis

The scores for the size of the endolymphatic space in the vestibule were identical between the 2 sequences (Fig. 1). On the other hand, the scores for the size of the endolymphatic space in the cochlea disagreed in 3 cases (Fig. 2). In these 3 cases, 3D-FLAIR-VFL showed a score of 0 for the patients with a positive probability score.

Quantitative analysis

The CNR between the basal turn of the cochlea and the cerebellum was significantly higher with 3D-FLAIR-CONV (34.1 +/− 21.5) than with 3D-FLAIR-VFL (21.1 +/− 18.2) ($P<0.01$); however, CNR per scan time was not significantly different.

Discussion

Intratympanically injected Gd-DTPA is thought to be absorbed through round window membrane into labyrinthine space.[1] Gd-DTPA distributes mainly in the perilymph space, allowing separate visualization of the endo- and perilymph space.[1] A variable flip-angle turbo-spin-echo (VFL) sequence enabled the acquisition of images with a very long echo train (> 100) and very long effective echo time (> 300 ms) while keeping T_2-contrast and blurring at levels similar to that using a conventional turbo-spin-echo sequence with an echo train length of 15 to 30.[12,13]

A VFL sequence using a non-selective excitation pulse can image the whole brain with 1-mm isotropic resolution in a scan time of several minutes.[13] However, the 3D-FLAIR-VFL protocol employed in the present study used a slab-selective excitation pulse to reduce the imaged volume and scan time while obtaining sub-millimeter isotropic voxels.

This slab-selective 3D-FLAIR-VFL protocol can obtain images with a voxel volume comparable to that of 3D-FLAIR-CONV in a far shorter scan time. Scan time of 15 min by 3D-FLAIR-CONV is too long to include in routine practice in most hospitals. However, the CNR of cochlear fluid was significantly lower on 3D-FLAIR-VFL, and the in-plane acquisition spatial resolution was also lower. The effective in-plane resolution may be lower still as a result of blurring induced by the very long echo train, even though the variable flip-angle technique reduces blurring compared to a constant flip-angle echo train of the same length.

It might have been possible to compare reformatted 2-mm-thick 3D-FLAIR-VFL images made from 0.8-mm-thick data and 2-mm-thick 3D-FLAIR-

Table. Summary of patient's clinical and imaging results

age, gender	clinical diagnosis	side	hearing level	vertigo	SP/AP (%)	VEMP	contrast-to-noise ratio		size of endolymphatic space in cochlea			size of endolymphatic space in vestibule		
							3D-FLAIR-CONV	3D-FLAIR-VFL	3D-FLAIR-CONV	3D-FLAIR-VFL	probability of endolymphatic hydrops from clinical records	3D-FLAIR-CONV	3D-FLAIR-VFL	probability of endolymphatic hydrops from clinical records
46, M	Ménière's disease	left	60	yes	48%	noise	20	8.8	3	3	3	3	3	3
24, F	sudden deafness	right	68	yes	not recordable	bilateral response	25.3	11.3	0	0	0	0	0	0
55, F	Ménière's disease	left	58	yes	100%	noise	38.3	14.2	3	3	3	3	3	3
38, M	Ménière's disease	left	30	yes	38%	noise	9.7	7.8	3	3	3	3	3	3
69, M	Ménière's disease	left	32	yes	58%	noise	77.6	35.8	3	3	3	2	2	3
50, F	fluctuating hearing loss	right	13	no	19%	bilateral response	25.5	16	2	0	2	1	1	1
74, F	Ménière's disease	left	65	yes	60%	noise	38.3	21.7	3	3	3	2	2	3
44, F	vestibular Ménière's disease	left	10	yes	39%	bilateral response	29.2	17.1	2	0	2	1	1	1
38, M	vestibular Ménière's disease	left	8	yes	24%	bilateral response	20.3	10.2	0	0	1	0	0	1
47, F	Ménière's disease	left	22	yes	22%	bilateral response	20.1	18.8	2	0	2	2	2	1
38, M	delayed endolymphatic hydrops contralateral type	left	65	yes	77%	noise level	70.7	70.5	3	3	3	3	3	3

SP/AP = summating potential/action potential on electrocochleography
VEMP = vestibular evoked myogenic potential
3D-FLAIR-CONV = 3-dimensional fluid-attenuated inversion recovery (FLAIR) using conventional turbo-spin-echo
3D-FLAIR-VFL = 3-dimensional fluid-attenuated inversion recovery (FLAIR) using variable flip-angle technique

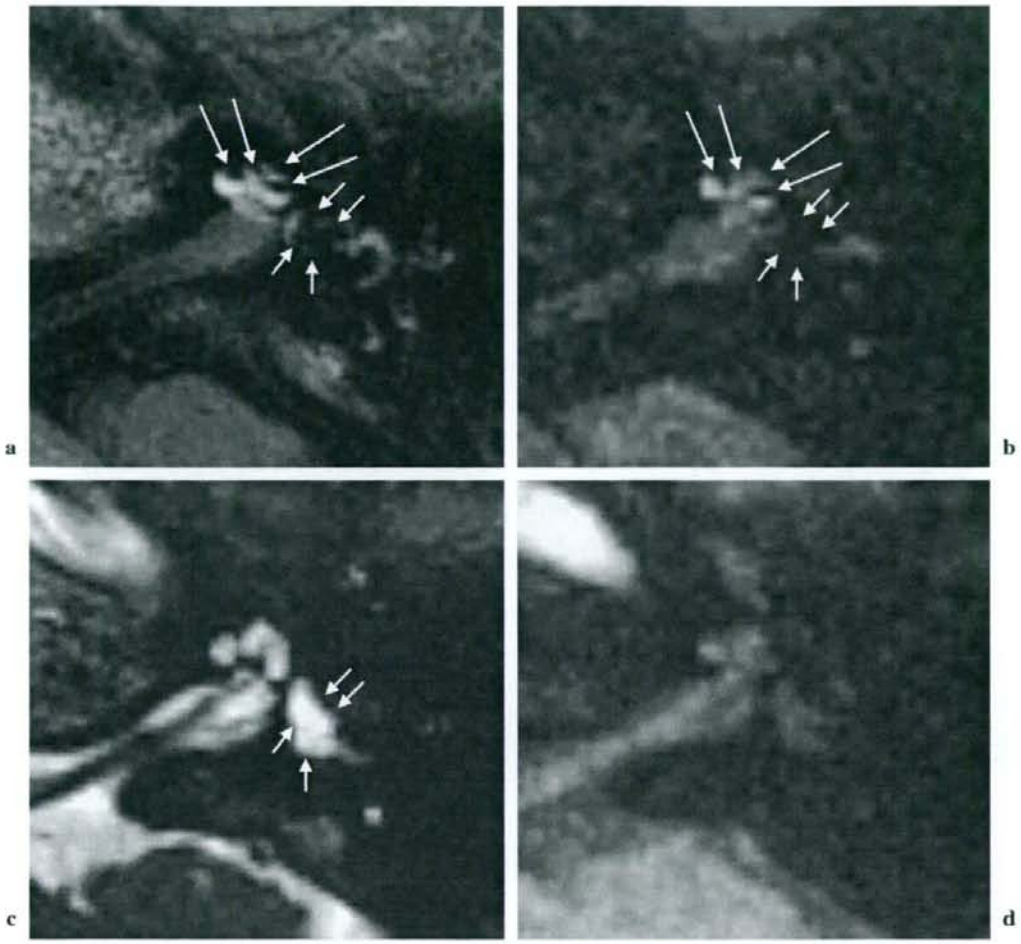

Fig. 1. A 46-year-old man with Ménière's disease. On both 3-dimensional fluid-attenuated inversion recovery using conventional turbo-spin-echo (3D-FLAIR-CONV) (**a**) and using variable flip-angle technique (3D-FLAIR-VFL) (**b**), the size of the endolymphatic space in the cochlea (arrows) and vestibule (short arrows) were scored as 3, although endolymphatic space in the cochlea is more clearly depicted on 3D-FLAIR-CONV. Almost no Gd-DPTA is seen in the vestibule in this case, whereas the vestibule is filled with lymphatic fluid on 3D- constructive interference in the steady state (CISS) (short arrows, **c**). On T_1-weighted 3D-fast low-angle shot (FLASH) (**d**), signal enhancement of perilymphatic fluid is quite faint; thus the discrimination between perilymph and endolymph is impossible.

CONV. However, increasing the reconstruction slice thickness of 3D-FLAIR-VFL would have resulted in the further degradation of the performance by 3D-FLAIR-VFL because the newly reconstructed voxel size of 3D-FLAIR-VFL was far larger than that of 3D-FLAIR-CONV.

The performance of 3D-FLAIR-VFL in detecting endolymphatic hydrops in the vestibule was comparable to that of 3D-FLAIR-CONV. In the cochlea, however, the 3D-FLAIR-CONV protocol was better, probably because of its higher in-plane resolution and higher CNR, as stated in the previous paragraph. The diameter of the cochlear duct (cochlear endolymphatic space) is smaller than the dimensions of the endolymphatic space in the vestibule, and the cochlear duct is in contact with surrounding bone tissue. Therefore, the recognition of endolymphatic hydrops in the cochlea might be more difficult than in the vestibule.

In the present study, we tried to reduce the scan time by a factor of 3 using 3D-FLAIR-VFL, which resulted in some image degradation. However, a

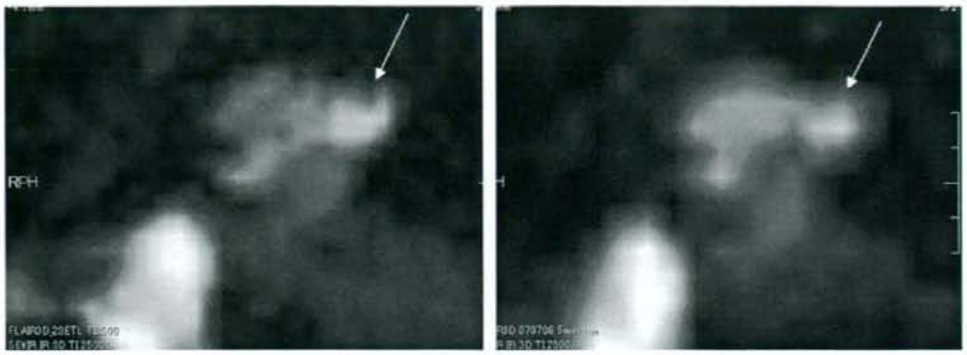

Fig. 2. A 50-year-old woman with fluctuating sensorineural hearing loss in the right ear. On 3-dimensional fluid-attenuated inversion recovery using conventional turbo-spin-echo (3D-FLAIR-CONV) (**a**), the size of endolymphatic space in the cochlea (arrow) was scored as 2; on 3D-FLAIR using variable flip-angle technique (VFL) (**b**), however, it was scored as 0 (arrow). This is probably due to the lower in-plane resolution and more blurring of 3D-FLAIR-VFL compared with 3D-FLAIR-CONV. The probability of endolymphatic hydrops from clinical records in cochlea was scored as 2.

factor-of-2 reduction, for example, might have been more practical. Further study is needed to determine a practical degree of scan time reduction.

The application of further technical developments also might improve the performance of 3D-FLAIR-VFL. For example, a T_2-selective inversion recovery scheme may provide a more time-efficient scan,[18] and the introduction of a 32-channel head array coil would improve the signal-to-noise ratio and thereby allow higher parallel imaging factors.[19]

In the present study, we reviewed the images only in the axial orientation. However, 3D-FLAIR-VFL had a higher spatial resolution in the z-direction than did 3D-FLAIR-CONV. The results might have been influenced if we had reviewed coronal or sagittal reformatted images, in addition to the original axial images.

One limitation of this study was the lack of a concrete standard of reference. We arrived at a tentative probability score for endolymphatic hydrops based not only on patient symptoms and history, but also on the results of objective tests such as the electrocochleogram and VEMP. However, it is difficult to evaluate the feasibility of using this score. In some cases, the results of the electorocochleogram and/or VEMP disagreed with clinical symptoms and disease history. The guidelines for Ménière's disease from the American Academy of Otolaryngology–Head and Neck Surgery (AAO-HNS) Committee of Hearing and Equilibrium define Ménière's disease mostly in terms of its symptoms,[20,21] describing the probability of the disease as *possible*, *probable*, *definite*, and *certain*. Certain Ménière's disease is defined as definite with histopathologic confirmation; objective diagnosis with histological confirmation is currently virtually impossible. To make the diagnosis of certain Ménière's disease in the future, MR imaging may be a desirable replacement for histological confirmation.

It would be very interesting if changes in 3D-FLAIR image findings were found to correlate with therapy-induced changes in the symptoms of endolymphatic hydrops. An individual longitudinal study might be useful to confirm the feasibility of this method in detecting and evaluating endolymphatic hydrops *in vivo*.

To compare the performance of 3D-FLAIR-VFL and 3D-FLAIR-CONV directly, a phantom simulating the actual dimensions of labyrinthine anatomy as well as the Gd-DTPA concentrations of labyrinthine endolymph and perilymph would also be helpful.

Conclusions

3D-FLAIR-VFL can obtain images with a voxel volume comparable to that of 3D-FLAIR-CONV and detect endolymphatic hydrops of the vestibule at a similar rate in a scan time that is nearly a factor of 3 shorter. However, the performance in detecting endolymphatic hydrops of the cochlea was lower with 3D-FLAIR-VFL. Thus, we currently may not be able to replace 3D-FLAIR-CONV with 3D-FLAIR-VFL, at least not with the scanning parameters used in the present study.

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The Laryngoscope
Lippincott Williams & Wilkins

Three-Dimensional Fluid-Attenuated Inversion Recovery Magnetic Resonance Imaging Findings and Prognosis in Sudden Sensorineural Hearing Loss

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Objectives/Hypothesis: Three-dimensional fluid-attenuated inversion recovery (3D-FLAIR) magnetic resonance imaging (MRI) has recently been developed to detect high concentrations of protein or hemorrhage. We have previously reported that 50% of patients with sudden sensorineural hearing loss (SNHL) show high signals in the affected inner ear on 3D-FLAIR MRI. However, the relationship between 3D-FLAIR findings and hearing prognosis is unclear. Our objective was to evaluate the relationship between the results of 3D-FLAIR MRI at 3 Tesla and prognosis in sudden SNHL.

Study Design and Methods: We used 3D-FLAIR at 3 Tesla with and without gadolinium enhancement to evaluate the pathologic conditions in the inner ears of 48 patients with sudden SNHL.

Results: Thirty-one of 48 patients with sudden SNHL showed high signals in the affected inner ear on precontrast 3D-FLAIR. Hearing improvement in patients with high signals in the affected inner ear on precontrast 3D-FLAIR (25 ± 19 dB) was significantly worse than that in patients with no signal (45 ± 27 dB; $P < .05$). Our analysis suggests that high signals in the affected inner ear on precontrast 3D-FLAIR MRI is a new prognostic factor for sudden SNHL.

Conclusions: 3D-FLAIR findings show that high signals in the cochlea on precontrast 3D-FLAIR are related to a poor hearing prognosis. These signals may reflect minor hemorrhage or an increased concentration of protein in the inner ear, which has passed through blood vessels with increased permeability or has originated in disrupted cells in the inner ear.

Key Words: Fluid-attenuated inversion recovery, sudden sensorineural hearing loss, magnetic resonance imaging, prognosis.

***Laryngoscope*, 118:1433–1437, 2008**

INTRODUCTION

The pathology of sudden sensorineural hearing loss (SNHL) remains unclear. The hypothesized pathologies include viral infection,[1] vascular compromise,[2] disruption of cochlear membranes,[2] inner ear anomaly,[3] and immunologic diseases.[1] However, no cause is found in most cases.

We have previously reported that four of eight patients with sudden SNHL showed high precontrast signals in the inner ear on three-dimensional fluid-attenuated inversion recovery (3D-FLAIR), and one of these four patients showed gadolinium (Gd) enhancement in the affected inner ear on 3D-FLAIR.[4] Furthermore, high signals in the affected inner ear are present in other inner ear diseases.[5–8] These signals may reflect minor hemorrhage or an increased concentration of protein in the inner ear, which has passed through blood vessels with increased permeability.[4] However, the relationship between 3D-FLAIR findings and clinical signs has not been clarified. We cannot make a prognosis for patients with sudden SNHL before treatment, although these patients wish to know the prognosis for sudden SNHL. In this study, we investigated the correlation between 3D-FLAIR findings and SNHL prognosis and between 3D-FLAIR findings and other clinical signs.

MATERIALS AND METHODS

Subjects

We evaluated 48 patients (24 men and 24 women; mean age ± standard deviation, 50.0 ± 16.4 yr) with unilateral sudden SNHL who visited Nagoya University Hospital between December 2005

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Editor's Note: This Manuscript was accepted for publication March 7, 2008.

This study was supported by research grants from the Ministry of Health, Labor, and Welfare and from the Ministry of Education, Culture, Sports, Science, and Technology of Japan.

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DOI: 10.1097/MLG.0b013e318172ef85

and July 2007. The criteria for sudden SNHL used in this study were that the patient could describe the day of onset of sudden SNHL, which had no obvious cause, and that no HL had been noted before the onset of SNHL. We excluded patients with fluctuating HL or progressive HL. All these patients were examined with T1- and T2-weighted magnetic resonance imaging (MRI) and 3D-FLAIR MRI before and after Gd enhancement. We also evaluated 11 patients at second and third examinations more than 3 months after onset using 3D-FLAIR MRI in a follow-up study. Eight patients, who had been reported in our previous study,[3] were included in this study. In all patients, hydrocortisone was administered intravenously 200 mg per day for 4 days and then 100 mg for 3 days with adenosine triphosphate (60 mg per day).

Audiologic Findings

Hearing levels were evaluated using an audiometer (Model AA-79S; Rion, Tokyo, Japan) in a sound-insulated chamber. The initial audiograms were obtained at the first visit, and the final audiograms were taken after 2 months had elapsed since the onset of deafness, except for patients who recovered completely within this period. Serial audiograms were compared with tympanograms and speech discrimination scores, when available. The average hearing level was expressed as the average score at three frequencies (500, 1,000, and 2,000 Hz). If the patient did not respond to the maximum sound level produced by the audiometer, we defined the threshold as 5 dB added to the maximum level.

The outcome of sudden SNHL was evaluated using the criteria of the Ministry of Health and Welfare in Japan.[9] The average hearing level on these criteria was calculated as the mean of the hearing levels measured at 250, 500, 1,000, 2,000, and 4,000 Hz. Recovery was ranked as follows:[10] no change (improvement in hearing of less than 10 dB on average); slight improvement (improvement in hearing of 10 dB or more but less than 30 dB on average); remarkable improvement (improvement in hearing of 30 dB or more on average); and complete recovery (all 5 frequencies on the final audiogram were 20 dB or less or improvement to the same degree of hearing as in the contralateral ear). The prognosis score was assigned as follows: 0 = no change; 1 = slight improvement; and 2 = remarkable improvement or complete recovery.

The periods between the onset of HL and the MRI study were compared between patients with and without high signals on 3D-FLAIR. The average prognosis scores were compared between patients with and without high signals on 3D-FLAIR. All statistical analyses were performed using the Mann-Whitney U test or the χ^2 test.

A multivariate regression analysis was used to identify the prognostic factors that were related to the final audiograms. The following factors were examined as explanatory variables: age, sex, presence of vertigo at the onset of sudden SNHL, the period from onset of sudden SNHL to first visit, precontrast high signals in the inner ear on 3D-FLAIR, and the initial audiogram. The data were analyzed by multivariate regression using the SPSS 8.0 statistical package (SPSS, Inc., Chicago, IL).

MRI

All scans were performed at 3 Tesla MRI (Trio; Siemens, Erlangen, Germany) using a receive-only eight-channel phased-array coil. Before and after the intravenous administration of a single dose of Gd–diethylenetriaminepentaacetic acid–bis methylamide (Gd–DTPA–BMA; Omniscan; Daiichi Pharmaceutical Co., Ltd., Tokyo, Japan) at 0.1 mmol/kg, T1-weighted 3D fast low-angle shot (FLASH) imaging and 3D-FLAIR imaging were performed. Heavily T2-weighted 3D constructive interference in the steady state imaging was performed only before the contrast material was administered to delineate the anatomy of the cerebrospinal fluid space. 3D-FLAIR and 3D-FLASH images were obtained before and after the administration of a single dose of Gd–DTPA–BMA. After the contrast was administered, 3D-FLASH was scanned first. Then, contrast-enhanced 3D-FLAIR was initiated 7 minutes after the Gd was administered so that the contrast 3D-FLAIR images were determined approximately 10 minutes after the administration of the Gd. These methods have been described in detail in previous reports.[4,10–12]

MRI Findings

The MRI findings for the inner ear in patients with sudden SNHL were evaluated using our own criteria. MRI findings were ranked as follows: none (no signal in the affected inner ear); faint (the signals in the affected inner ear were higher than those of the cerebrospinal fluid but lower than those of the cerebellar white matter); moderately high (the signals in the affected inner ear were as high as those of the cerebellar white matter); and very high (the signals in affected inner ear were higher than those in the cerebellar white matter).

RESULTS

The characteristics of 48 patients with sudden SNHL are summarized in Table I. Thirty-one of the 48 patients with sudden SNHL showed high signals in the affected inner ear on precontrast 3D-FLAIR. Sixteen of these 31 patients also showed Gd enhancement on 3D-FLAIR in the affected inner ear. The high-signal areas observed on 3D-FLAIR were not detected by T1- or heavily T2-weighted MRI in any of these patients. All patients had no signals in the unaffected inner ear. We could perform follow-up MRI study in 11 of 48 patients. In these patients, high signals in affected inner ears on precontrast or postcontrast 3D-FLAIR had disappeared after approximately 90 to 150 days from onset of sudden SNHL. Figure 1 shows a follow-up MRI finding of a patient with right sudden SNHL.

The average initial hearing level was 80 ± 17 dB in the group with high signals on precontrast 3D-FLAIR and 75 ± 19 dB in the group with no signals. There was no statistically significant difference in the initial hearing levels of the two groups (Mann-Whitney U test). However, hearing improvement in the high-signal group (25 ± 19 dB) was significantly worse than that in the no-signal group (45 ± 27 dB; $P < .01$; Mann-Whitney U test) (Fig. 2) (Table I).

A multivariate regression analysis of the audiologic assessment was made for all patients, which included age [a positive value of the β (normalized regression) coefficient indicates a better hearing prognosis in young patients], the presence of vertigo at the onset of sudden SNHL (a negative value of the β coefficient indicates that a lack of vertigo entails a better hearing prognosis than that of patients with vertigo), precontrast high signals in the inner ear on 3D-FLAIR (a positive value of the β coefficient indicates that a lack of high signals reflects a better hearing prognosis than the prognosis in the presence of high signals), the period from the onset of sudden SNHL to the first visit (a positive value of the β coefficient indicates a poorer hearing prognosis in patients who visited late), and initial audiogram (a positive value of the β coefficient indicates a poorer hearing prognosis in patients with a high level of initial HL). This analysis revealed that

TABLE I.
Patient Characteristics.

Characteristic	High Signals in the Cochlea Group	No Signal in the Cochlea Group	*P* Value
No. patients	31	17	
Age (yrs)	50.5 ± 17.7	49.3 ± 14.7	0.9
Sex (female/male)	17/14	6/11	0.19
Number of patients with vertigo	12	3	$P < 0.01$
Ear (right/left)	16/15	8/9	0.76
High signals in vestibule	10	1	$P < 0.01$
Gadolinium enhancement	16	0	$P < 0.01$
Initial audiogram (dB)	80 ± 17	75 ± 19	0.38
Final audiogram (dB)	55 ± 27	31 ± 21	$P < 0.01$
Period to initial visit	9 ± 8	5 ± 4	0.08
Period to MRI	15 ± 12	10 ± 8	0.08

High signal = high signal in the affected inner ear on precontrast three-dimensional fluid-attenuated inversion recovery (3D-FLAIR); High signals in vestibule = high signals in the vestibule on precontrast 3D-FLAIR; Gadolinium enhancement = gadolinium enhancement in the affected inner ear on postcontrast 3D-FLAIR; Period to initial visit = period from the onset of sudden sensorineural hearing loss to the initial visit; Period to MRI = period from the onset of sudden sensorineural hearing loss to magnetic resonance imaging.

the following factors were independently related to a worse hearing prognosis for patients with sudden SNHL: high signals in the affected inner ear on precontrast 3D-FLAIR, the period from the onset of sudden SNHL to the first visit, and the initial audiogram (Table II). The period between the MRI study and the onset of HL in patients with sudden SNHL did not differ significantly between patients with high signals (15 ± 12 d) and those with no signal (10 ± 8 d) (Mann-Whitney *U* test) (Table I).

Hearing improvement (24 ± 19 dB) in patients who showed Gd enhancement on 3D-FLAIR in the affected inner ear was not significantly different from that (36 ± 25 dB) in patients who did not (Mann-Whitney *U* test). On postcontrast 3D-FLAIR, three patients who had no signal on precontrast 3D-FLAIR showed Gd enhancement on 3D-FLAIR in the affected inner ear.

Ten patients showed high signals in both the cochlea and the vestibule on precontrast 3D-FLAIR in the affected ear, and 8 of these 10 patients suffered from vertigo at the onset of sudden SNHL. One patient showed high signals only in the vestibule, without high signals in the cochlea on precontrast 3D-FLAIR in the affected inner ear, and this patient suffered from vertigo at the onset of sudden SNHL. In this patient, 3D-FLAIR was performed 17 days after the onset of sudden SNHL. There was a relationship between the vertigo at the onset of sudden SNHL and high signals in the vestibule of the affected inner ear ($P < .05$; χ^2 test). Furthermore, the final hearing levels of patients with high signals in the vestibule were significantly worse than those of patients who did not have these high signals ($P < .05$; Mann-Whitney *U* test).

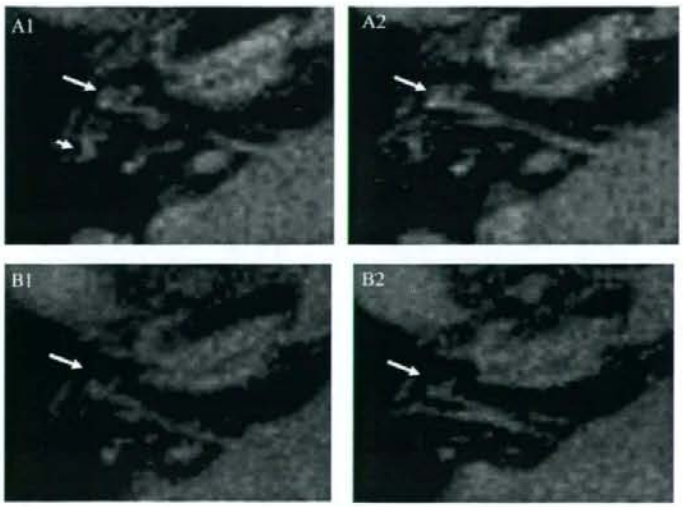

Fig. 1. Axial magnetic resonance image. Right inner ear of a 45-year-old man with vertigo and right sudden sensorineural hearing loss. (A1) First three-dimensional fluid-attenuated inversion recovery (3D-FLAIR) image before enhancement. Bright signals are very high in right cochlea (long arrow) and vestibule (short arrow). (A2) First 3D-FLAIR image after enhancement. Gadolinium enhancement is not observed in right cochlea (long arrow). (B1) Second 3D-FLAIR image before enhancement. No bright signal is visible in right cochlea or vestibule. (B2) Second 3D-FLAIR image after enhancement. No gadolinium enhancement is visible in right cochlea.

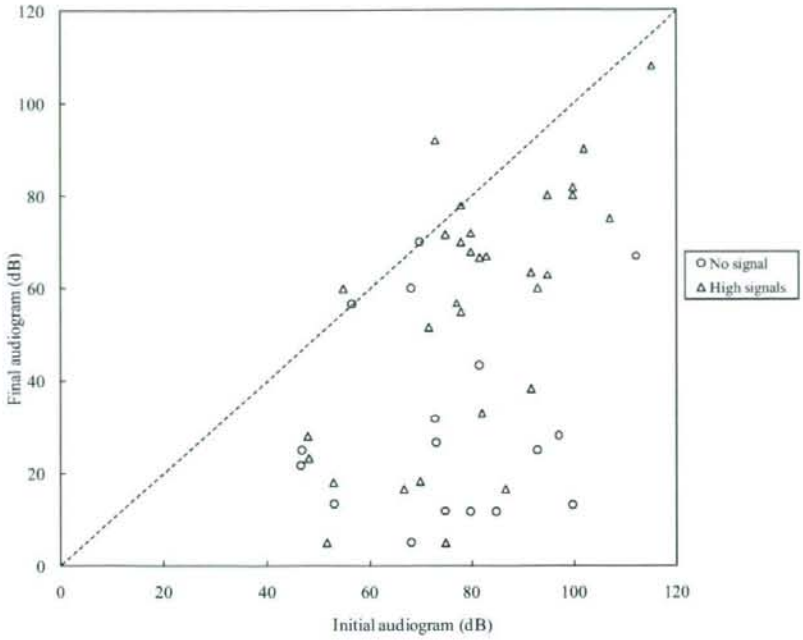

Fig. 2. Hearing improvement in patients with and without high signals in affected inner ear on precontrast three-dimensional fluid-attenuated inversion recovery (3D-FLAIR) magnetic resonance imaging. Spots near transverse dotted line show bad prognoses for sudden sensorineural hearing loss (SNHL). Conversely, spots near bottom line show good prognoses for sudden SNHL. High signals in cochlea in affected ear on precontrast 3D-FLAIR suggest poor hearing prognosis in sudden SNHL.

DISCUSSION

The major finding of this study is that 3D-FLAIR findings are closely related to hearing prognosis in sudden SNHL. This is the first report to demonstrate that high signals in the cochleae of affected ears on precontrast 3D-FLAIR suggest poor hearing prognoses in sudden SNHL. We have previously reported that four of eight patients with sudden SNHL showed high signals in the inner ear on precontrast 3D-FLAIR and that one of these four patients showed Gd enhancement in the affected inner ear on 3D-FLAIR.[4] However, in that study, our data were insufficient to evaluate the relationship between the 3D-FLAIR findings and hearing prognosis. It demonstrated that 3D-FLAIR is a very useful tool with which to predict the prognosis before treatment.

In this study, we have shown the possibility of identifying poor prognostic factors with 3D-FLAIR. The prognostic factors for sudden SNHL reported previously include age,[13] male sex,[14] the type of audiogram,[13] the level of HL,[14] tinnitus and vertigo,[14] the method of treatment,[13] and the time of treatment initiation.[13] However, the relationship between the hearing prognosis and the imaging findings is not clear. Precontrast high signals on 3D-FLAIR may reflect minor hemorrhage or an increased concentration of protein in the inner ear, which has passed through blood vessels with increased permeability or has originated in disrupted cells in the inner ear. We have shown that precontrast high signals on 3D-FLAIR are independently related to hearing prognosis. Therefore, precontrast high signals on 3D-FLAIR may be a new prognostic factor in sudden SNHL.

Sudden SNHL is caused by a variety of unknown pathophysiologic mechanisms. To develop more effective therapies, it is necessary to understand more precisely the pathology of sudden SNHL. We have also shown an asso-

TABLE II.
Multivariate Regression Model of Impact on Final Audiogram.

Independent Variables	Values	β (Standard Regression Coefficient)	Standard Error	t	*P* Value
Age		0.158	0.19	1.38	0.174
Sex	1 = male, 0 = female	−0.005	6.34	−0.04	0.964
Vertigo	1 = yes, 0 = no	0.091	7.3	0.74	0.464
Period to initial visit		0.312	0.5	2.58	$P < 0.05$
High signals in the cochlea	1 = yes, 0 = no	0.248	7.3	2.07	$P < 0.05$
Initial audiogram		0.416	0.2	3.36	$P < 0.01$

$R^2 = 0.502$, adjusted $R^2 = 0.429$.
Period to initial visit = period from the onset of sudden sensorineural hearing loss to the initial visit; high signals in the cochlea = high signals in the cochlea on precontrast 3D-FLAIR.