ciation between 3D-FLAIR findings and clinical signs, especially those pertaining to vertigo. 3D-FLAIR MRI may be a key to resolving these problems. Therefore, it is possible that 3D-FLAIR MRI will provide made-to-order treatments for patients with sudden SNHL in the future. Further study is necessary to clarify the relationship between MRI findings and the efficiency of several treatments to develop more effective therapies.

CONCLUSIONS

High signals in the affected ear indicate a poor hearing prognosis in patients with sudden SNHL. 3D-FLAIR findings may be one of the prognostic factors in sudden SNHL. We believe that this method contributes to the definition of a prognosis for patients with sudden SNHL.

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ORIGINAL ARTICLE

Communication between cochlear perilymph and cerebrospinal fluid through the cochlear modiolus visualized after intratympanic administration of Gd-DTPA

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Abstract
Purpose. Intratympanic injection of gadolinium diethylenetriaminepentaacetic acid (Gd-DTPA) has been reported as a procedure to visualize endolymphatic hydrops of Meniere's disease. We frequently noted that cerebrospinal fluid (CSF) in the internal auditory canal (IAC) was also enhanced after this procedure. The purpose of this study was to evaluate how frequently this occurs and to investigate the specific features of patients who lack this communication.
Materials and methods. A total of 25 patients with clinically suspected endolymphatic hydrops underwent the procedure. After 24 h, three-dimensional fluid-attenuated inversion recovery (3D-FLAIR) and 3D constructive interference in steady state (3D-CISS) were performed. The presence of contrast enhancement in the CSF space of the fundus of the IAC was evaluated.
Results. The contrast ratio between CSF of the IAC fundus and cerebellar white matter on the injected side was 1.49 ± 0.65, and that of the noninjected side was 0.32 ± 0.16 ($P < 0.01$). Enhancement of the CSF space in the IAC fundus was seen in all but two subjects: one had enlarged endolymphatic duct and sac syndrome (EEDS), and the other had cochlear nerve agenesis. In these two patients, the cochlear modiolus seemed to be normal.
Conclusion. Intratympanic Gd-DTPA administration can reveal permeability of the modiolus and might facilitate evaluation of functional abnormalities of the modiolus not detected by conventional imaging tests.

Key words Magnetic resonance imaging · 3D imaging · Anatomy · Modiolus

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Introduction

It has been reported that there is communication between labyrinthine perilymph and the cerebrospinal fluid (CSF) space.[1–4] Physiologically, this communication is important as the origin of perilymph. Perilymph is thought to be derived from both CSF and the vascular supply.[5] Pathologically, this communication is important as a potential route for spreading infection, dissemination, and subarachnoid hemorrhage.[6] In addition, an extremely wide communication might result in a perilymph gusher during a round window operation[7] or cochlear implantation.[8]

Potential communication channels between CSF and perilymph are thought to be the cochlear aqueduct, pores in the cochlear modiolus, and the perineural space in the singular canal. In human adults, the cochlear aqueduct is anatomically totally occluded in 7% of the population and filled with loose connective tissue in 59%; its central lumen is patent in only 34% of the population.[9] A recent histological study revealed that the cochlear modiolus is highly porous.[2] The porous structure in the surface of the modiolus allows communication between perilymph and the perivascular and perineural space in the modiolus. The singular canal contains a nerve branch from the inferior vestibular

nerve, and the perineural space of this canal might communicate with the posterior ampulla and posterior part of the internal auditory canal through the perineural space.

Recently, it was reported that perilymphatic fluid can be enhanced on magnetic resonance imaging (MRI) after intratympanic injection of gadolinium diethylenetriaminepentaacetic acid bis(methylamide) (Gd-DTPA-BMA).[10] Consequently, endolymphatic hydrops can be visualized in patients with Meniere's disease. An enlarged endolymphatic space in patients with Meniere's disease has been successfully recognized as an area with low signal intensity partly surrounded by high-signal perilymphatic fluid on three-dimensional fluid-attenuated inversion recovery (3D-FLAIR) performed after intratympanic injection of Gd-DTPA at 3 tesla.[10] In addition, we noted that the CSF space in the fundus of the internal auditory canal (IAC) was also clearly enhanced in most of the patients, suggesting the possibility of communication between perilymph and the CSF space.

The purpose of this study was to evaluate how frequently communication between cochlear perilymph and CSF is visualized after intratympanic injection of Gd-DTPA and to determine which of the three potential channels is most dominant. Another purpose was to determine the specific features of patients who lack this communication.

Materials and methods

Patients

A total of 25 patients (17 with clinically diagnosed Meniere's disease, 2 with sudden sensorineural hearing loss, 1 with enlarged endolymphatic duct and sac syndrome (EEDS), and 5 with delayed endolymphatic hydrops; age 24–78 years, mean ± SD 48.8 ± 14.8 years; 13 men, 12 women) underwent intratympanic administration of Gd-DTPA-BMA (Omniscan; Daiichi Pharmaceutical, Tokyo, Japan). Two patients underwent intratympanic injection on both sides; thus, 27 ears were further evaluated.

These patients were scheduled for intratympanic injection therapy with gentamicin (for the patients with severe vertigo) or a steroid (for the sudden sensorineural hearing-loss patients). Intratympanic injection of Gd-DTPA was performed to evaluate the status of the endolymphatic space and to simulate drug distribution. Written informed consent was obtained from all patients, and the study was approved by the medical ethics committee of our university hospital.

Intratympanic gadolinium injection

The detailed methods for intratympanic gadolinium injection have been reported previously.[10] In that study, a delay of 24 h between the intratympanic gadolinium injection and MRI was found to be optimal to allow the gadolinium to distribute widely in the perilymphatic space of the labyrinth.

Gd-DTPA-BMA was diluted eightfold with saline (v/v 1:7). The diluted Gd-DTPA-BMA was injected intratympanically through the tympanic membrane using a 23-gauge needle and a 1-ml syringe after the patient was placed in the supine position with his or her head turned approximately 30° away from the sagittal line toward the healthy ear.

MR imaging

All scans were performed on a 3-T MRI scanner (MAGNETOM Trio; Siemens Medical Solutions, Erlangen, Germany) using a receive-only 12-channel phased-array coil. T1-weighted 3D fast low-angle shot (3D-FLASH) and 3D-FLAIR images were acquired 24 h after intratympanic injection of diluted Gd-DTPA-BMA.

In addition, T2-weighted 3D constructive interference in the steady state (3D-CISS) imaging was performed to obtain reference images of the labyrinthine fluid-space anatomy.

The parameters for T1-weighted 3D-FLASH were as follows: repetition time (TR) 4.3 ms, echo time (TE) 1.97 ms, flip angle 10° with radiofrequency (RF) spoiling, matrix size 256 × 256, 96 axial 0.8 mm thick slices with a 16-cm square field of view (FOV). The number of excitations was 2. The total scan time was 2 min 51 s.

The parameters for 3D-CISS were as follows: TR 11.42 ms, TE 5.71 ms, flip angle 50°, matrix size 320 × 320, 48 axial 0.8 mm thick slices with a 16-cm square FOV. The number of excitations was 1, and the scan time was 3 min 42 s.

The parameters for 3D-FLAIR were as follows: TR 9000 ms, effective TE 458 ms, inversion time 2500 ms, variable flip-angle echo train with an average flip angle of 120°, echo-train length 119, matrix size 214 × 256, 48 axial 0.8 mm thick slices with a 15 × 18 cm FOV, acceleration factor of 2 using the GRAPPA parallel imaging technique.[11] The voxel size was 0.7 × 0.7 × 0.8 mm. The number of excitations was 2, and the total scan time was 5 min 26 s. 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 150–220, without

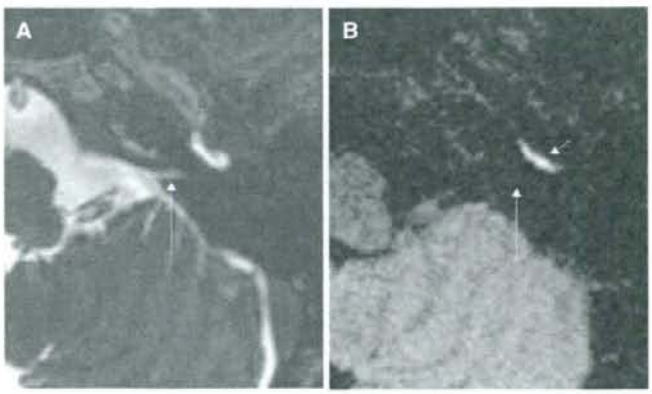

Fig. 1. A 66-year-old woman had Meniere's disease. **a** The cochlear aqueduct is apparent on a three-dimensional constructive interference in steady state (3D-CISS) image (*arrow*). **b** No enhancement of the cochlear aqueduct is seen on a three-dimensional fluid-attenuated inversion recovery (3D-FLAIR) image (*long arrow*). Note that the basal turn of the cochlea is strongly enhanced (*short arrow*)

severe blurring and while maintaining contrast similar to that of 3D-FLAIR obtained with a conventional turbo spin echo sequence, even with a long effective echo time.

Image evaluation

Qualitative evaluation

Two radiologists reviewed the images independently. If a discrepancy existed between the two, consensus was reached through discussion. Enhancement in the fundus of the IAC was evaluated on a negative or positive basis. Enhancement in the cochlear aqueduct, modiolus, and singular canal was also evaluated by referring to the anatomical position of these structures on 3D-CISS.

Contrast enhancement of CSF space in the fundus of the IAC was considered positive if both of the following conditions were fulfilled: (1) No mass other than the cranial nerves existed in the CSF space of the IAC fundus on 3D-CISS. (2) The intensity of the CSF space in the fundus of the IAC was the same or higher than that of the cranial nerves on 3D-FLAIR images.

Contrast enhancement of the cochlear aqueduct, modiolus, and singular canal was considered positive if the intensity of the cochlear aqueduct, modiolus, and singular canal was the same or higher than that of the cranial nerves on 3D-FLAIR images. The positions of the cochlear aqueduct, modiolus, and singular canal were defined by referring to 3D-CISS images.

Quantitative evaluation

The contrast ratio (CR) between the CSF space of the IAC fundus and cerebellar white matter was measured by drawing a region of interest (ROI) on 3D-FLAIR and referring to 3D-CISS images to delineate precisely the CSF space in the IAC. The CR value was defined as the signal of the CSF space in the fundus of the ipsilateral IAC divided by that of the cerebellar white matter on the same side. CR values of the injected side and noninjected side were compared using Student's *t*-test in the 23 patients who had received a unilateral injection.

Results

No side effects related to the intratympanic injection were seen. On T1-weighted 3D-FLASH, contrast enhancement in the labyrinth was quite faint in all patients; therefore, 3D-FLASH images were not used for further evaluation. No enhancement was seen in the cochlear aqueduct (Fig. 1) or the singular canal (Fig. 2) in any of the subjects, even on 3D-FLAIR images. Evaluation of the enhancement in the modiolus was difficult in all subjects owing to the strong enhancement in the surrounding fluid space.

Enhancement of the CSF space in the fundus of the IAC was seen in all but two subjects: One had EEDS, and the other had cochlear nerve agenesis (Figs. 3–5). In these two patients, the cochlear modiolus was slightly small, although its shape was normally developed.

The mean CR value of the injected side was 1.49 ± 0.65, and that of the noninjected side was 0.32 ± 0.16 ($P < 0.01$).

Discussion

In previous MRI studies,[15–17] the size of the cochlear modiolus was measured and was reported to be smaller in patients with EEDS[17] and in those with sudden sensorineural hearing loss.[15]

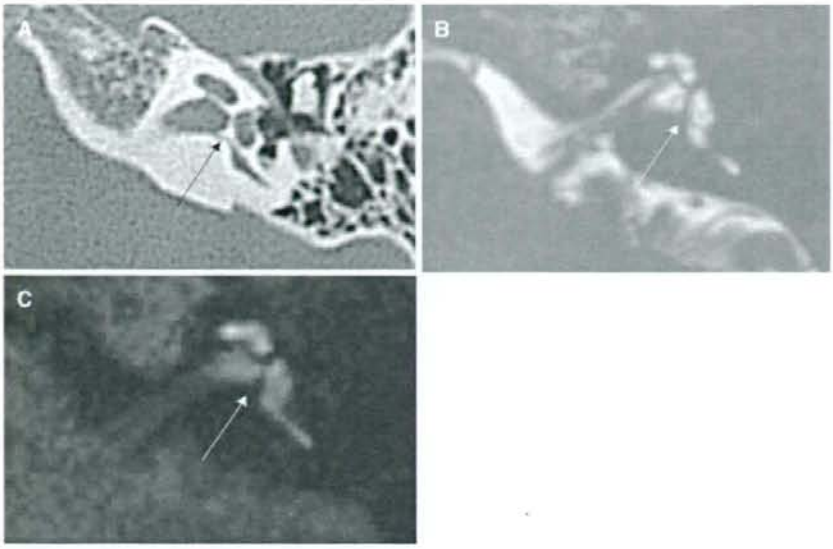

Fig. 2. A 43-year-old woman had Meniere's disease. The singular canal is visualized on computed tomography (CT) (**A**, *arrow*) and 3D-CISS (**B**, *arrow*). **C** No enhancement is seen on 3D-FLAIR (*arrow*), whereas the vestibule is enhanced

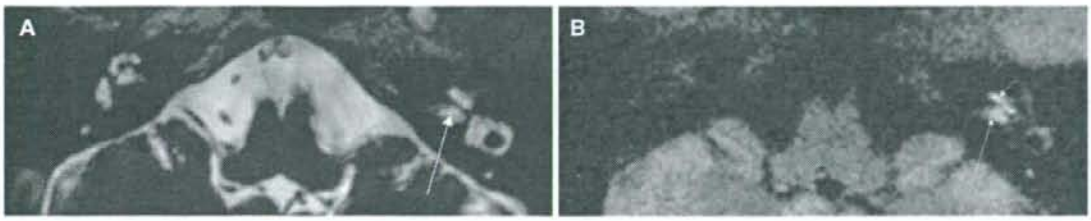

Fig. 3. A 65-year-old woman had Meniere's disease. **A** The cerebrospinal fluid (CSF) space in the fundus of the internal auditory canal (IAC) is apparent on 3D-CISS (*arrow*). **B** On 3D-FLAIR, prominent enhancement of both the CSF space (*arrow*) and the cochlear space (*short arrow*) can be seen

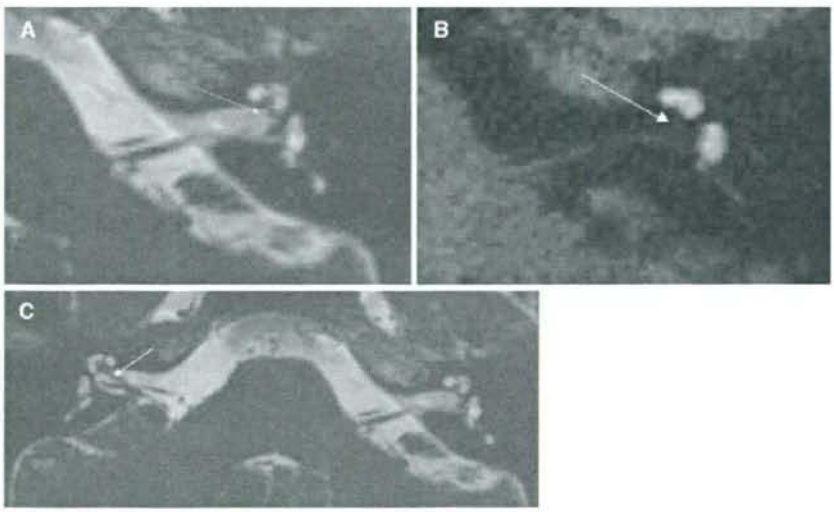

Fig. 4. A 24-year-old man with left-side congenital deafness had been complaining of vertigo and tinnitus for 1 year. Delayed endolymphatic hydrops was suspected. **A** On 3D-CISS, agenesis of the left cochlear nerve is apparent (*arrow*). **B** No enhancement of CSF in the IAC fundus is seen on 3D-FLAIR (*arrow*). **C** Note that the cochlear nerve on the right side is seen to be normally developed on 3D-CISS (*arrow*)

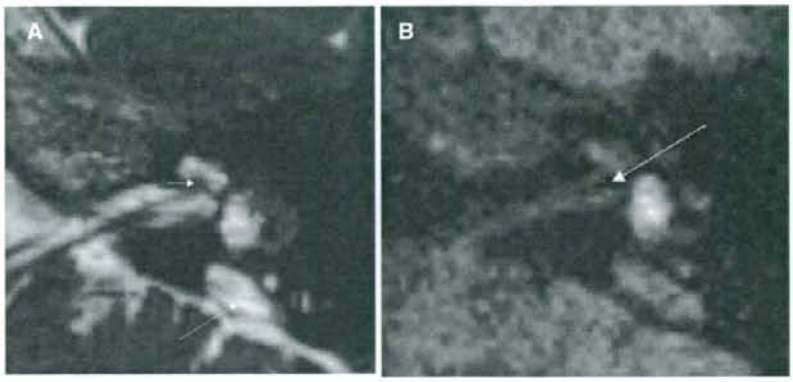

Fig. 5. A 27-year-old man had enlarged endolymphatic duct and sac syndrome (EEDS) and vertigo. **A** On 3D-CISS, an enlarged endolymphatic sac (*long arrow*) and slightly small but normally shaped modiolus (*short arrow*) can be seen. **B** On 3D-FLAIR after intratympanic injection of Gd-DTPA, no enhancement can be seen in the CSF of the IAC fundus (*arrow*)

The modiolus seemed to be slightly small in our patient who had agenesis of the cochlear nerve. The lack of a Rosenthal canal due to cochlear nerve agenesis might be why Gd-DTPA did not penetrate the modiolus, although the Rosenthal canal cannot be visualized with current clinical CT or MRI scanners, even in normal subjects.

In the patient with EEDS, the shape of the cochlear modiolus did not seem to be hypoplastic, although its size is slightly small. Most EEDS patients have a morphologically hypoplastic modiolus.[17,18] In this patient, the shape of the modiolus seemed to be normal; however, the lack of Gd penetration might indicate a microscopic abnormality of the modiolus.

To our knowledge, this is the first report to evaluate permeability of the cochlear modiolus by means of an imaging examination. We showed that communication between perilymph and CSF seems to occur mostly through the modiolus, not through the cochlear aqueduct or singular canal.

Enhancement of the cochlear modiolus was not visualized, which might be attributed to the fact that the strong enhancement of surrounding fluid space made recognition of faint enhancement in the modiolus difficult. The narrow part of the cochlear aqueduct and singular canal might be intrinsically too thin to be visualized on high-spatial-resolution T2-weighted images by clinical MRI. In this study, enhancement was not visualized on 3D-FLAIR images even in the larger part seen on T2-weighted images. To visualize very faint enhancement in the narrow part of the canal, 0.8 mm thick 3D-FLAIR might be too thick. However, such small channels could not be the significant or major communication route.

The patency and function of the cochlear aqueduct have been controversial.[9,19] The central lumen of the cochlear aqueduct is patent throughout in only 34% of adult subjects.[9] The mean diameter of the narrowest portion of the duct was 138 ± 58 μm. Such a narrow channel cannot support fluid flows large enough to explain stapedectomy gushers.[9] However, it has been reported that in newborn infants the cochlear aqueduct is short and patent.[19] A wide, patent cochlear aqueduct might cause endolymphatic hydrops in case of intracranial hypotension. It would be interesting to investigate whether the cochlear aqueduct is enhanced following intratympanic gadolinium injection in the case of a wide, patent cochlear aqueduct.

The clinical relevance of cochlear permeability assessment may be substantial for the following applications.

- Prediction of drug distribution after intrathecal or intratympanic administration
- Prediction of perilymph gusher before stapes surgery
- Evaluation of cochlear modiolar abnormality before cochlear implantation

Currently, we do not recommend intratympanic gadolinium administration for such candidates. Further study is necessary to establish the clinical indications for this examination.

The present study has some limitations. The patients included in the study had symptoms such as hearing loss or vertigo, and no healthy subjects were included. The lack of normal permeability data for the cochlear modiolus is one of the limitations of this study. Although no side effects were observed, intratympanic injection is an off-label use of gadolinium. It is difficult to apply this procedure to normal ears. Animal experiments are possible, although simulating the human normal modiolus might not be possible.

In the previous study using intravenously injected Gd-DTPA, prompt enhancement of the IAC fundus was observed in patients with meningitis without enhancement of the cochlea.[20] This enhancement of the IAC fundus was thought to come from increased permeability of the blood–nerve barrier, not from gadolinium in

perilymph. Further study is necessary to determine whether not only the perineural channel but also the intraneural channel contributes to modiolar permeability after intratympanic injection of Gd-DTPA.

Conclusion

The cochlear modiolus seems to be the main route of communication between perilymph in the labyrinth and CSF in the IAC. Intratympanic Gd-DTPA administration can reveal the permeability of the cochlear modiolus and might be useful for evaluating functional abnormalities of the modiolus not detected by conventional imaging tests.

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ORIGINAL ARTICLE

Imaging analysis in cases with inflammation-induced sensorineural hearing loss

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Abstract

Conclusion. 3D-FLAIR imaging is sensitive to inflammatory inner ear disturbances and may be a useful method in investigating the severity of inner ear disturbance in cases of inflammation-induced SNHL. *Objective.* To evaluate the usefulness of the three-dimensional fluid-attenuated inversion recovery (3D-FLAIR) magnetic resonance imaging (MRI) sequence in investigating different etiology of inner ear disturbances in cases with inflammation-induced acute sensorineural hearing loss (SNHL). *Patients and methods.* Five cases with inflammation-induced acute SNHL by different conditions are included in this study: acute meningitis, acute otitis media, and Wegener granulomatosis. Imaging analysis was performed using a three-dimensional fluid-attenuated inversion recovery (3D-FLAIR) magnetic resonance imaging (MRI) sequence, and correlation between clinical symptoms and FLAIR abnormalities was evaluated. *Results.* In the affected ears in all cases, 3D-FLAIR revealed high pre-contrast signal and increased signal in the cochlea after the administration of gadolinium. Enhancement was still observed in the inner ear after several months with continuing nystagmus in those cases induced by meningitis and severe otitis media. In a case with Wegener granulomatosis, increased signal in the post-contrast images was stronger on the side of the cochlea with the worse hearing level.

Keywords: *Inflammation, etiology, sensorineural hearing loss, inner ear disturbance, 3D-FLAIR*

Introduction

Inflammatory conditions that occur outside the inner ear, such as otitis media or meningitis, can induce inner ear disturbances with symptoms of sensorineural hearing loss (SNHL). Animal studies have investigated the mechanisms of inflammation-induced inner ear disturbances [1–5]; however, etiological investigations in clinical cases are limited.

Previous reports describe the usefulness of gadolinium enhancements in magnetic resonance imaging (MRI) for detecting inflammatory lesions of the inner ear [6–9]; this enhancement has been considered the result of breakdown of the blood–labyrinth barrier (BLB) [6,8,9]. The BLB maintains the composition of the inner ear fluid; its function is to protect the inner ear from toxic substances by selectively limiting the entry of substances into the inner ear [10]. The fluid-attenuated inversion recovery (FLAIR) MRI sequence has been recently applied to the inner ear [11–13]. FLAIR enables the demonstration of hemorrhage and high protein concentration in lesions; these conditions are difficult to detect using T1- and T2-weighted MRI [14]. FLAIR assessment can also be used to evaluate cerebrospinal fluid (CSF) changes in pathologic conditions that cause a breakdown in the blood–brain barrier [15].

In the present paper, we apply 3D-FLAIR MRI at three tesla to cases with inflammation-induced acute SNHL caused by different conditions, and evaluate the results with the aim of demonstrating its advantage in investigating etiologies in these inner ear disturbances.

Materials and methods

Patients

Five cases with inflammation-induced acute SNHL and by different conditions were included in this

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study: acute meningitis (1 case), acute otitis media (2 cases), and Wegener granulomatosis in the middle ear (2 cases).

MRI examination

MRI was performed using a three-tesla scanner (Trio, Siemens, Erlangen, Germany). 3D-FLAIR was performed before and after the intravenous administration of a single dose of gadolinium. To delineate the anatomy of the CSF space, we performed heavily T2-weighted 3D constructive interference imaging in the steady state prior to the administration of contrast material. High signal on 3D-FLAIR after contrast enhancement was scored depending by the degree of the enhancement as follows: weak = 1, moderate = 2, and strong = 3.

Results

The clinical observation and the MRI findings in the five cases are summarized in Tables I and II. 3D-FLAIR images in five cases showed high pre-contrast signal in the cochlea, the vestibule, and the semicircular canals in the inner ear, while the post-contrast images demonstrated enhancement in the inner ear of the affected ears. High post-contrast signals examined after treatment were decreased in all cases except one (Case 2), which were accompanied by improvement in symptoms of vertigo (Cases 1 and 4), and acute SNHL (Cases 3, 4, and 5). The post-contrast images were not available in one patient because of complete ossification of the cochlea (Case 1). Correlation between clinical symptoms and FLAIR abnormalities was observed in some cases. Representative cases from different condition were described below.

Acute meningitis (Case 1)

A 42-year-old man was hospitalized because of impaired consciousness, the cause of which was diagnosed as acute meningitis. He had had severe vertigo and profound SNHL on the left side. Six months later the patient again suffered acute meningitis and was referred to our department to investigate the possibility of otitis media-induced meningitis. The patient had chronic otitis media with a perforated tympanic membrane on the left side; however, he had had no experience of ear discharge for years. A computerized tomography (CT) examination demonstrated partial ossification in the cochlea on the left side, which was considered to be due to preceding meningitis. 3D-FLAIR revealed high signal intensity in the cochlea of the inner ear on the left side and strongly increased signal in this area after the administration of gadolinium (Figure 1A,B). Enhancement was also observed in the area of the cochlear aqueduct (Figure 1C) and in the fundus of the internal auditory canal. Otitis media was ruled out as a cause of meningitis in this case; however, during follow-up it was revealed that he had had fine spontaneous nystagmus with fast phase beating contralateral to the affected ear for one year.

Acute otitis media (Case 2)

A 35-year-old man who had been hospitalized at another hospital because of ear discharge and acute SNHL on his left side was referred to our department two months after the onset of the disease. The patient had nystagmus to the right and profound SNHL on the left side, and his disease was diagnosed as severe labyrinthitis caused by acute otitis media. 3D-FLAIR revealed high signal intensity in the cochlea, the vestibule, and the semicircular canals of inner ear on the left side and strongly increased signals in these areas after the administration of gadolinium (Figure 2A, B). This enhancement was also observed one year after onset; at that time he still had fine nystagmus with fast phase beating contralateral to the affected ear.

Wegener granulomatosis (Case 4)

A 69-year-old man was referred to our department with a history of bilateral acute SNHL for three months and facial palsy on his right side for two weeks. The patient's hearing level was worse in the right ear than the left, and he noticed vertigo. The patient had been treated for bilateral otitis media

Table I. Clinical observation in five cases.

	Age (years)/gender	Symptom of inner ear disturbance	Diagnosis (cause)
Case 1	42/M	Vertigo, acute SNHL	Bacterial meningitis
Case 2	35/M	Vertigo, acute SNHL	Acute otitis media
Case 3	79/M	Acute SNHL	Acute otitis media
Case 4	69M	Vertigo, acute SNHL	Wegener granulomatosis
Case 5	45/F	Acute SNHL	Wegener granulomatosis

SNHL, sensorineural hearing loss.

Table II. 3D-flair MRI findings in five cases.

	High signal (at the initial visit)		High signal (post-treatment)
	Pre-contrast	Post-contrast	Post contrast
Case 1	Cochlea, CA	Cochlea (3), fundus (3), CA (3)	NA
Case 2	Cochlea, vestibule, Scc	Cochlea (3), vestibule (2), Scc (1)	Cochlea (3), vestibule (2), Scc (1)
Case 3	Cochlea	Cochlea (1)	None
Case 4	Cochlea, vestibule, Scc	Cochlea (3), vestibule (2), Scc (2)	Cochlea (2)
Case 5	Cochlea, Scc	Cochlea (1), Scc (1)	Cochlea (1)

CA, cochlear aqueduct; Scc, semicircular canal; Fundus, fundus of the internal auditory canal; NA, not available.

with effusion for one year. CT examination revealed widespread inflammation in the bilateral middle ear cavities; however, the inner ear appeared normal. 3D-FLAIR revealed high signal intensity in the cochlea, the vestibule, and the semicircular canals of the inner ear on both sides and increased signal in these areas after the administration of gadolinium, especially in the right ear (Figure 3A, B). Final diagnosis was Wegener granulomatosis, which was treated by chemotherapy with prednisolone and cyclophosphamide. 3D-FLAIR MRI performed after six times of the chemotherapy showed decreased post-contrast signals in the inner ear.

Discussion

3D-FLAIR images in five cases showed high pre-contrast signal in the cochlea, the vestibule, and the semicircular canals of the inner ear, while the post-contrast images demonstrated enhancement in the affected areas. This post-contrast enhancement is considered the result of a breakdown in the BLB [6,8,9,11]. The BLB supports inner ear homeostasis by maintaining constant composition of the inner ear fluid [10]; this inner ear system is concentrated in the cochlear lateral wall. Animal studies have shown breakdown of the BLB in the cochlear lateral wall following acute middle ear inflammation and an associated decrease in lateral blood flow [5,16]. Breakdown of the BLB also occurs in meningogenic suppurative labyrinthitis [17]. The findings of the 3D-FLAIR images in the present study support the explanation that etiologies similar to those in the animal studies might have occurred in the present cases.

The 3D-FLAIR images in Case 1 (acute meningitis) showed strongly increased signal in the cochlear aqueduct on the post-contrast images. This finding supports that of a previous study that the cochlear aqueduct could serve as potential pathway for the spread of infection from the meninges to the inner ear [18]. Contrast enhancement observed in

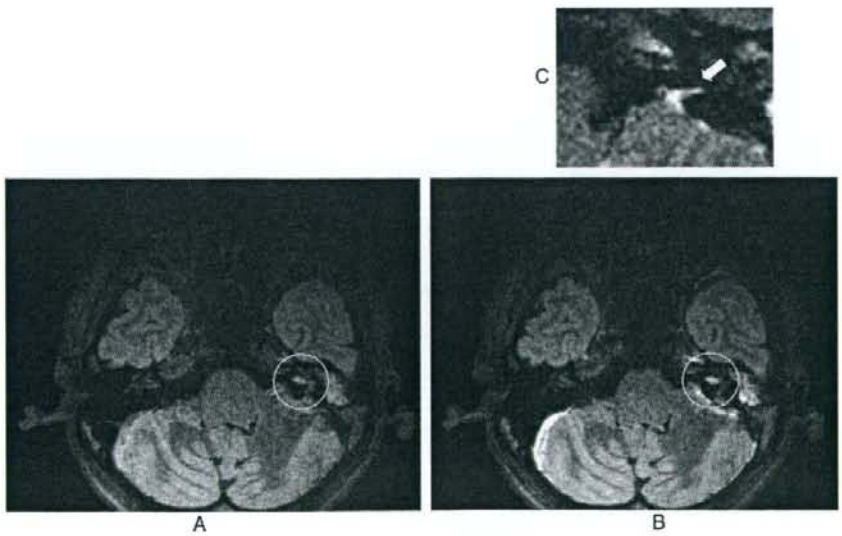

Figure 1. 3D-FLAIR images of Case 1. A, B. Pre-contrast (A) and post-contrast (B) inner ear lesions (circled). The inner ear is morphologically abnormal because of partial ossification. C. High-magnification image of enhancement in the cochlear aqueduct (arrow).

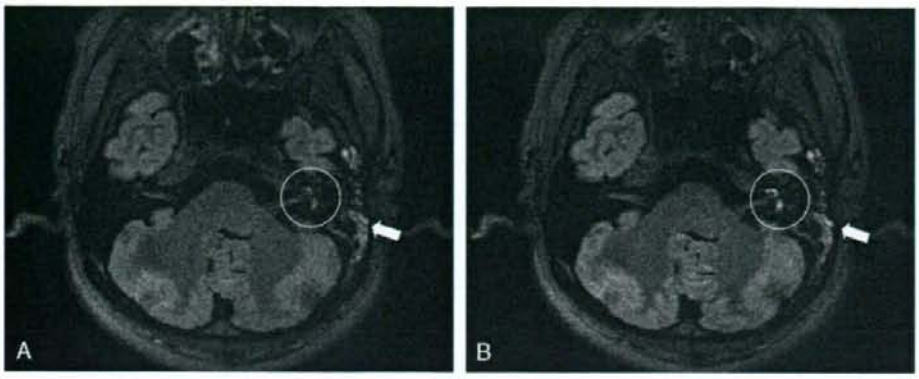

Figure 2. 3D-FLAIR images of Case 2. A, B. Pre-contrast (A) and post-contrast (B) middle ear inflammation (arrows) and inner ear lesions (circled).

the fundus of the internal auditory canal suggests a meningeal rather than otitis media origin as the cause of inner ear disturbance [15].

We have applied 3D-FLAIR to cholesteatoma cases with labyrinthine fistula and usefulness of images of the inner ear has been reported for evaluation of labyrinthine fistula in patients with cholesteatoma [13]. Case 4 with Wegener granulomatosis revealed high signal intensity in the bilateral inner ears. Increased signal of the cochlea in the post-contrast images was stronger on the side with the worse hearing level. SNHL is a significant finding in Wegener granulomatosis, and its detection is important for appropriate patient management [19]. 3D-FLAIR assessment can be a useful method in evaluating the inner ear disturbances caused by Wegener granulomatosis.

Another important finding was the duration over which the high post-contrast signal was observed. Enhancement in inflammatory conditions usually resolves over several months [7]. Decreased signal in the 3D-FLAIR was found in case 3 with mild acute otitis media and cases 4 and 5 with Wegener granulomatosis following treatment with chemotherapy. Hearing improvement was observed in these cases, however, in Cases 1 and 2, in which the

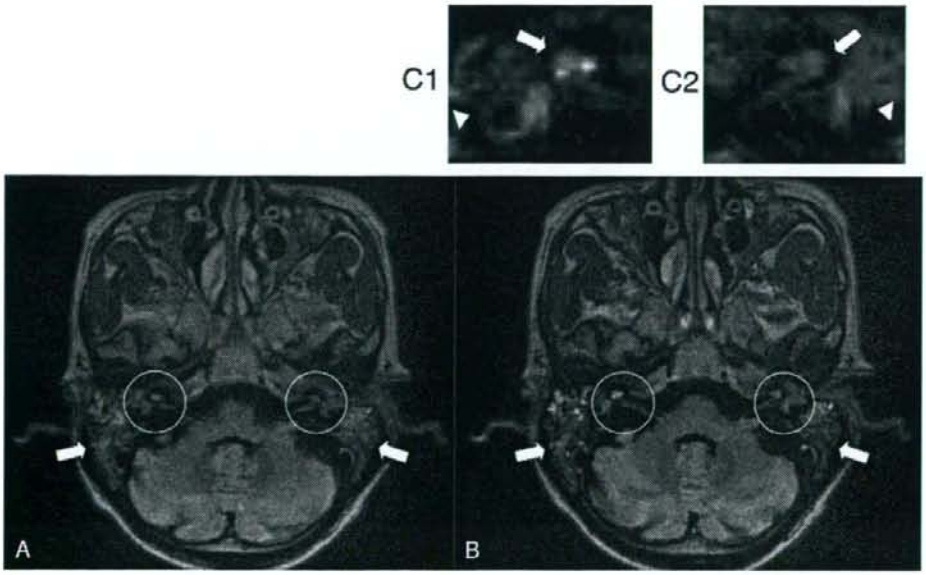

Figure 3. 3D-FLAIR images of Case 4. A, B. Pre-contrast (A) and post-contrast (B) bilateral middle ear inflammation (arrows) and inner ear lesions (circled). A stronger signal is observed in the inner ear on the side with the worse hearing level. C. Higher-magnification image of the lesions circled in B. The cochleas (arrows) and the semicircular canals (arrowheads) are indicated in the right (C1) and left (C2) ears.

patients had continuing nystagmus, high signal was observed in the inner ear over a period of several months. The severity of inner ear disturbances and clinical symptoms may correlate with 3D-FLAIR findings; breakdown of the BLB might last for a longer period in cases with aggressive disease.

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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突発性難聴に対する局所療法

Topical therapy for the treatment of sudden sensorineural hearing loss

診断の指針 / 治療の指針

中島 務
NAKASHIMA Tsutomu

1. 突発性難聴とは

突発性難聴の診断基準は，1973年厚生省特定疾患突発性難聴調査研究班により作成され35年経過しているが，突然の高度な感音難聴で原因不明であることが，その診断基準の中心となっている．この診断基準を用いて，今までに4回の全国疫学調査が行われた．突発性難聴は，2001年の全国調査で，年間発症数が3万5千人と推定され，日常診療で少なくない疾患である．

2. 問　診

問診で，突然聞こえが悪くなった状況を聞く．何月何日に聞こえが悪いことに気づいたと日にちを特定できるのが突発性難聴である．難聴を自覚した日を発症第1日目とするが，時に発症第2日目や3日目の聴力が，1日目より悪くなることがある．発症から1週間くらいまで聴力が低下するものまで，一応，突発性難聴に含めているが，1ヵ月かけて聴力が落ちていったものは，突発性難聴には含めない．

小児例では，難聴が起こっても，それを訴えない例がある．また，成人例でも時に発症に気づかない例もある．突発性難聴は，ほとんどの例で1側性であり，会話は，可能であるからである．耳鼻科の外来に，「電話の受話器をとったら電話が故障していると思った．反対側の耳できいたら聞こえたので，はじめて耳が悪くなっているのに気づいた」といって来院する例がある．このような症例では，電話がなければ発症に気づかなかったので，最後に電話で話したのはいつかなど詳しく問診をとって発症日を特定する．成人例で突発性難聴発症時に異常に気づかない例は，きわめて少ないが，発症を訴えない例が存在することを認識しておく必要がある．

3. 随伴症状

突発性難聴では，9割の症例が耳鳴りを訴える．また約3割の症例でめまいが併発する．この他，耳がふさがったような耳閉感を訴える例が半数程度ある．難聴は，ほとんどの例で内耳性であり，内耳性難聴の特徴である補充現象(リクルートメント現象)を訴えることが多い．補充現象とは，大きな音を内耳でしぼることができないために，小さな音は聞こえないが，大きな音は，不快に響いてしまう現象である．そのため，患耳にわざわざ耳栓をしている例まである．難聴は多くの例で1側性であり，静かなところでの1対1の会話は，とくに問題はないが，ざわざわしたところでの会話が，なかなかできない．これは，ざわざわしたところで聞きたい音のみ聞く能力(カクテルパーティー効果)に，両耳を要するからである．

4. 鑑別診断

原因不明のものを，突発性難聴としているが，原因が明らかな突然の感音難聴に，ムンプス難聴，外リンパ瘻，聴神経腫瘍や頭部外傷後の急性感音難聴などがあげられる．また，最近画像診断の進歩により前下小脳動脈梗塞や内耳出血と診断されるケースが増加してきている．前下小脳動脈梗塞では，時に症状が難聴，耳鳴，めまいなど，一見突発性難聴と同様で，その他の神経症状がない場合があり，注意を要する．MRIで内耳出血が認められた場合，これを突発性難聴として含めるか，内耳出血として分類していくかは，今後の課題である．現在の診断技術では，前下小脳動脈の枝である内耳動脈に梗塞が起こっても，これを診断することができない．

突発性難聴は，原因不明という項目を含んでいるので，診断技術の進歩により，突発性難聴という診断名が減少していくことが期待されている．しかしながら，現段階では，突然に起きる高度の感音難聴のほとんどが，原因不明である．

5. 一般的な治療

突発性難聴では，発症後，聴力は，ほぼ1ヵ月で固

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定し，2ヵ月たてば完全に固定するといってよい．したがって，治療は，発症後，1ヵ月間が勝負ということになる．耳鳴を苦にする症例も多いが，聴力の経過がよい症例では，耳鳴も軽快していく．

薬物療法として全国調査の結果から，ステロイドが85％の症例に用いられている．このほか，循環障害の改善を目的にプロスタグランディンが33％の症例に，循環・代謝改善を目的にATPが87％の症例に用いられている．治療効果が乏しい症例では，高気圧酸素療法や星状神経節ブロックを行っている施設もある．

6. なぜ局所治療か

内耳血流量は，心拍出量に比べてきわめて小さい．モルモットで心拍出量の1万分の1程度，ウサギで10万分の1程度であり，人では，百万分の1程度といわれている．このように，全身の血流量と比較するとおどろくほど少ない．したがって，全身投与ではなく，局所的に薬剤を内耳に投与し，内耳への薬剤移行量を格段に上げようとするものである．一般的な治療としてステロイドの全身投与が行われているが，糖尿病患者では，ステロイドが使いにくいことも局所療法が注目されている理由である．

突発性難聴に対する局所療法の文献的報告は，ほとんどが21世紀になってから出てきている．緑内障など眼科の疾患に目薬が広く用いられているが，内耳疾患においてもようやく局所療法が広まりつつある．

7. 局所療法の一般的な方法

ステロイド(デキサメタゾンかメチルプレドニゾロン)を1mL注射器と長針を用いて鼓膜経由に鼓室内に注入する．注入できる量は，だいたい0.5mL程度までである．鼓室内の薬剤は，薄い蝸牛窓(正円窓)を通って内耳に入っていくが，できるだけ内耳に入りやすくするために，注入後，30分間，注入した耳を上にして臥位を保つ．このような内耳への薬剤投与法は，保存的治療に抵抗するメニエール病に対するゲンタマイシン鼓室内注入療法と同様である．

図1は，8倍に薄めたガドリニウム造影剤を鼓室内に注入し，1日たって撮ったMRIである．注入側内耳全体(正確には内耳の外リンパ腔)に薬剤がよく分布しているのがわかる．注意すべきは，蝸牛窓の透過性が，まったくないか相当悪い人が1割程度いることである．

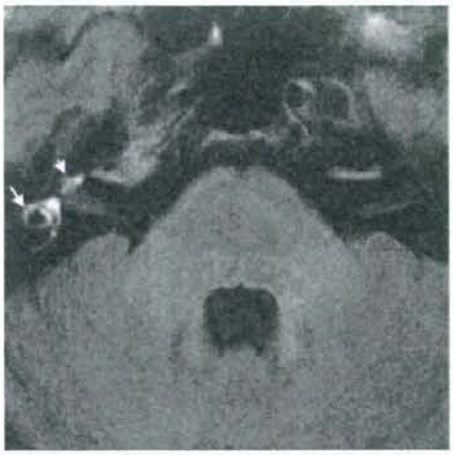

図1 ガドリニウム造影剤を8倍に薄めて右鼓室内に投与し，1日後に撮ったMRI所見(3D-FLAIR)
長い矢印は，外側半規管，短い矢印は蝸牛を示している．右側内耳の外リンパ腔全体に投与したガドリニウムが入っている．

8. 内耳局所療法の将来

内耳局所療法は，内耳血流量の観点からも，もっと検討されなければならない．マイクロウイックといって小さなろうそくの芯のようなものを鼓膜に開けた穴経由に蝸牛窓近くまで挿入し，その芯に薬をしみこませて内耳に薬剤を連続的に投与する方法も一部で行われている．また，特殊な薬剤をしみこませたゲルを内視鏡下に蝸牛窓の近くに置く方法も臨床試験されている．まだ，動物実験の段階であるが，感音難聴に対する遺伝子治療も，内耳への局所療法をどのように行っていくかという問題でもある．内耳手術で，現在もっとも普及しているのは人工内耳手術であるが，将来的には，より広い観点での内耳局所治療法の開発が求められている．