Clinical features of ears with otosclerosis and endolymphatic hydrops

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Abstract

Objective: Endolymphatic hydrops (EH) has been reported in ears with otosclerosis. The objective of this study was to investigate the clinical features of ears with otosclerosis and EH on magnetic resonance imaging (MRI) and identify predictors for the presence of EH.

Study Design: Retrospective study.

Setting: University hospital.

Materials and Methods: Forty-six ears from 37 patients with otosclerosis were included in the present study.

Interventions: The subjects were divided into three groups, those with no, mild, or significant EH, based on 3-T MRI with intravenous injection of gadolinium. Hearing levels and the extent of otosclerotic lesions graded based on the computed tomography (CT) findings were compared among the groups. Moreover, to examine the vascular activity of the disease, intraoperative measurements of blood flow were also evaluated.

Main Outcome Measures: Imaging, hearing levels, and blood flow values.

Results: The overall rate of EH was 58.7% (27 of 46 ears); cochlear EH (52.2%) was more frequent than vestibular EH (26.1%). Average thresholds in ears with significant EH were significantly higher at several frequencies, both on air and bone conduction, than those with no or mild EH. Significant EH was more frequently observed in ears with advanced stages on CT than in those without advanced stages. The values of blood flow in the area anterior to the oval window were higher in some ears with EH than in ears without EH.

Conclusion: EH was frequently present in ears with otosclerosis, especially those with severe hearing loss or advanced disease on CT.

Key words: otosclerosis, endolymphatic hydrops, MRI, blood flow

Introduction

Otosclerosis is a multifactorial temporal bone disorder the pathologic hallmarks of which include bony resorption, new bone deposition, and vascular proliferation (1). The most common clinical presentation of otosclerosis is slowly progressive conductive or mixed hearing loss. Sensorineural hearing loss (SNHL) may also occur depending on the evolution and degree of disease activity (2). Vestibular symptoms or SNHL could be observed in more advanced cases of the disease (3).

Endolymphatic hydrops (EH) represents a pathologic anatomic finding in which the structures bounding the endolymphatic space are distended by an enlargement of endolymphatic volume (4,5). EH associated with otosclerosis has been reported (6,7) and may be caused by the otosclerotic process (8,9). The massive amount of active otosclerosis has been suggested as a causative factor in the development of EH (6), but the pathological mechanism still remains to be elucidated. EH can now be seen on 3T magnetic resonance imaging (MRI) (10-12), and MRI evaluation showed that ears diagnosed as having otosclerosis had EH (13). Another report showed that the presence of EH, especially in the vestibule, was a possible high-risk factor for complications following stapes surgery (14), because the inserted piston might traumatize the enlarged membranous labyrinth because of EH. The presence of EH in the cochlea might also be a cause of unsatisfactory improvement in the hearing threshold following stapes surgery.

Among subjects clinically diagnosed as having otosclerosis, those with documented medical histories of inner ear disturbances, such as acute SNHL or rotatory vertigo, showed significant EH in the affected ears (14). Clinical symptoms of acute SNHL or rotatory vertigo might be the main predictors of the presence of EH, and surgeons could avert stapes surgeries for such ears to avoid complications. An important point is that subjects with no clinical symptoms related to inner ear

disturbances have been found to have significant EH (14).

The primary pathologic process begins with an inflammatory stage marked by increased vascularity, and otosclerotic foci could invade the inner ear structures and disrupt the vascular supply, which might affect the volume or flow of endolymph (9, 15,16). A previous study showed that intraoperative measurement of blood flow by laser-Doppler flowmetry could yield useful information to evaluate the progress of vascular activity (17).

The aim of this retrospective study was to investigate the clinical features of ears with otosclerosis and EH on MRI, and to identify predictors of EH in ears that are candidates for stapes surgeries in order to avoid possible complications following the procedures. Moreover, whether there is a relationship between the two entities was examined.

Materials and methods

Subjects

The clinical charts of 46 ears (37 patients, 16 males and 21 females, aged 23-78 years, mean age 51.9 years) diagnosed as having otosclerosis in our hospital and who underwent MRI evaluation of EH, from February 2012 to February 2017, were reviewed. MRI is not a standard diagnostic procedure for the evaluation of otosclerosis, and MRI examination was not routinely performed for all cases with otosclerosis during that time. Of the 46 ears, 30 underwent stapes surgery for otosclerosis, while the remaining 16 ears were not scheduled to undergo surgery because of the patients' wishes or the risk of complications following the procedures. All patients underwent pure-tone audiometry (PTA) (AA-78, Rion, Tokyo, Japan), computed tomography (CT) (Asteion and Aquilion, Toshiba, Tokyo, Japan), and MRI

(MagnetomVerio; Siemens, Erlangen, Germany) examinations. Moreover, 23 ears of 22 patients underwent intraoperative measurements of blood flow.

Hearing levels on PTA

The pure-tone averages for air conduction (AC) and bone conduction (BC) at 0.25, 0.5, 1, 2, and 4 kHz were calculated for each ear, and the mean hearing thresholds at these frequencies were evaluated.

Stages of the disease based on CT grading of severity

According to the CT grading system for otosclerosis reported previously (18,19), the severity of the disease in each ear was graded as follows: grade 0, no sign of focal hypodensity; grade 1, solely fenestral; grade 2, patchy localized cochlear disease (with or without fenestral involvement) to either the basal cochlear turn (grade 2A), or the middle/apical turns (grade 2B), or both the basal turn and the middle/apical turns (grade 2C); and grade 3, diffuse confluent cochlear involvement (with or without fenestral involvement).

Evaluation of EH on MRI

MRI was performed 4 h after intravenous injection of a standard dose (0.2 mL/kg body weight, i.e. 0.1 mmol/kg body weight) of gadodiamide hydrate (Gd) (Omniscan; Daiichi-Sankyo Co. Ltd., Tokyo, Japan). All scans were performed using an MRI scanner (Magnetom Verio; Siemens) equipped with a receive-only, 32-channel, phased-array coil. Hydrops (hybrid of reversed image of positive endolymph signal and native image of positive perilymph signal) was used to detect EH (11). The details of the parameters of the sequences have been described elsewhere (13). At least two radiologists who were blind to the corresponding clinical information classified the degree of EH in the vestibule and cochlea into three grades (none, mild, and

significant) according to the criteria described previously (20). Example images of cochlear or vestibular EH are shown in Figure 1.

Blood flow measurements

Intraoperative measurements of blood flow were performed with a laser-Doppler flowmeter (LDF, model ALF 21, Advance, Tokyo, Japan), as described elsewhere (17). The tip of the probe was attached manually to the anterior portion of the oval window (AOW) directed to the fissula ante fenestram (defined as the blood flow in the AOW), which was selected as the most frequently involved lesion of the disease. After the blood flow had stabilized, 5-second mean values were obtained. Measurement of blood flow was not a routine procedure during the surgery, and the ears that underwent this evaluation were confined to those operated by the last author to perform stable measurements.

Data were analyzed using SPSS 25 for Windows. Statistical analysis was performed using the Chi-squared test, Fisher's exact test, the independent-samples *t*-test, the Kruskal-Wallis test, and the Cochran-Armitage trend test. A p value of 0.05 was threshold for significance.

All study protocols were approved by the ethics review committee of Nagoya University Hospital (2017-0492).

Results

Table 1 summarizes the presence of EH. The overall rate of EH was 58.7% (27 of 46 ears). Mild or significant EH in the cochlea was observed in 17/46 (37.0%) or 7/46 (15.2%), respectively, while mild or significant EH in the vestibule was observed in 6/46 (13.0%) or 6/46 (13.0%), respectively. Nine ears had EH in both the cochlea and the vestibule. The rate of EH was significantly higher in the cochlea than in the

vestibule (p=0.01).

Table 2 shows the averages of AC or BC thresholds at five frequencies in ears with no, mild, and significant EH in the cochlea or the vestibule. Average thresholds in ears with significant EH were significantly higher at 500 and 1000 Hz on AC (p=0.026 and 0.016, respectively) or 1000, 2000, and 4000 Hz on BC (p=0.004, 0.002, and 0.017, respectively) than in those with no or mild EH.

Based on CT evaluation, 19 ears were grade 0, 19 were grade 1, 2 were grade 2a, 1 was grade 2b, and 5 were grade 3. Table 3 shows the presence of EH in each stage of the disease on CT. There was no linear trend between the presence of EH and the CT grade. On CT, significant EH was observed in 5 of 38 ears (13.2%) without advanced stages (0 or 1) and in 3 of 8 ears (37.5%) with advanced stages (2 or 3); thus, significant EH was more frequent in those with advanced stages.

Of the 16 ears that were not scheduled to undergo surgery, 12 had cochlear or vestibular EH. Of these 12 ears with EH, 7 had no previous episode of inner ear disturbance, but 2 had a clinical history of acute SNHL, and 3 had episodes of vertigo attacks in addition to acute SNHL.

Intraoperative measurement of blood flow was available for 23 ears, 12 ears with EH and 11 ears without EH. Figure 2 shows the average blood flow values in the AOW in ears with and without EH, which were 6.03 and 2.86 AU (ml/min/100 g), respectively. Blood flow in the AOW was significantly higher in ears with EH than in ears without EH (p=0.013). Only two ears with EH showed relatively higher blood flow values, which might have led to the significant difference in the values between ears with and without EH.

Discussion

The coexistence of otosclerosis and EH has been described in temporal bone studies (6,9), and massive amounts of active otosclerosis have been suggested as a causative factor in the development of EH (6). Paparella et al reported that 28% of temporal bones with otosclerosis had EH without symptoms of Ménière's disease (21). A previous study reported that cases with EH in the vestibule had long periods of dizziness following stapes surgeries, suggesting that the presence of EH in the vestibule on MRI might be a high-risk factor for postoperative complications (14). That is the main reason why we attempted to identify predictors of EH in ears with otosclerosis, in which EH was frequently present, as shown in the current study.

Ears with otosclerosis usually show conductive or mixed hearing loss. The presence of EH may induce elevations of hearing thresholds on both AC and BC. Average thresholds in ears with significant EH were significantly higher at several frequencies on both AC and BC than in ears with no or mild EH, which could be an indicator of significant EH.

A recent temporal bone study of otosclerosis showed a higher incidence of EH in ears with endosteal involvement of the disease (76%) than in those without such involvement (30%)(22). The CT grading system used in the present study has been introduced as a precise evaluation method for the location and appearance of otosclerosis (19). Significant EH was more frequently observed in ears with advanced stages on CT than in those without advanced stages, which could be another indicator of the presence of significant EH.

The primary pathologic process begins with an inflammatory stage marked by increased vascularity. Vascularity of otosclerotic foci might disrupt the vascular supply to the stria vascularis, which could play a significant role in controlling the volume of endolymph (15), or the vascular lesions of otosclerosis invading to the

endosteum might alter the chemical characteristics of endolymph and thus affect the flow of endolymph (9,16).

The most common site of involvement in otosclerosis is the AOW near the fissula ante fenestram, and the vascularity of the disease may be reflected in the blood flow of the AOW. Measurement of blood flow by laser-Doppler flowmetry could yield useful information to evaluate the progress of vascular activity (18). The present study showed high blood flow in the AOW in some ears with EH, which might suggest that vascularity plays an important role in the existence of EH in some ears with otosclerosis.

There are some limitations in the present study. The number of subjects enrolled in the study was small, and selection bias may be an issue. All of the ears were not surgically confirmed as having otosclerosis, because some ears had significant EH in the vestibule, which suggested a high risk for complications following stapes surgeries. Further investigations enrolling ears with more advanced otosclerosis, which would provide various degrees of hearing thresholds and grading on CT, might provide more information for predicting the presence of EH from their clinical features.

Conclusions

EH was frequently present in ears that were candidates for stapes surgeries, especially those with severe hearing loss or advanced disease on CT.

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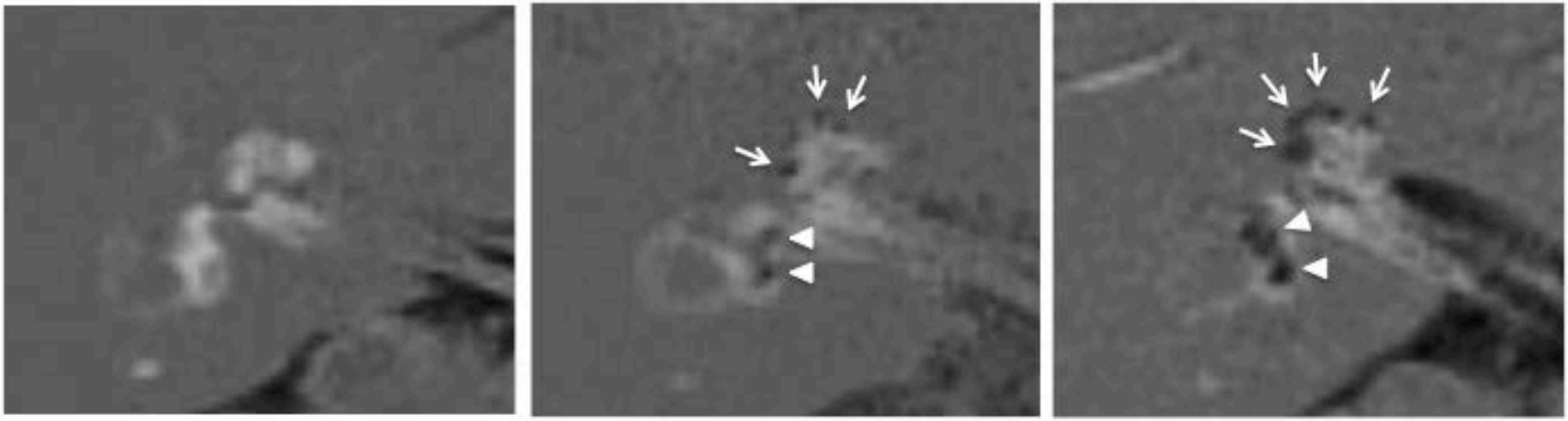
Figure legends

Figure 1: Example images from each grade of endolymphatic hydrops (EH) on MRI. HYDROPS (hybrid of reversed image of positive endolymph signal and native image of positive perilymph signal) was used to detect EH. The black areas represent the endolymphatic space in the labyrinth, and the white areas represent perilymphatic space. The presence of EH can be visualized as black areas surrounded by gadolinium-filled perilymph. No EH (A), mild EH (B), and significant EH (C) in the cochlea (arrows) or the vestibule EH (arrowhead).

Figure 2: Values of blood flow in areas anterior to the oval window (AOW) of ears with and without endolymphatic hydrops (EH) (A.U., arbitrary units). The average value is significantly higher in ears with EH than in those without EH.



A) B) C)

Figure 1

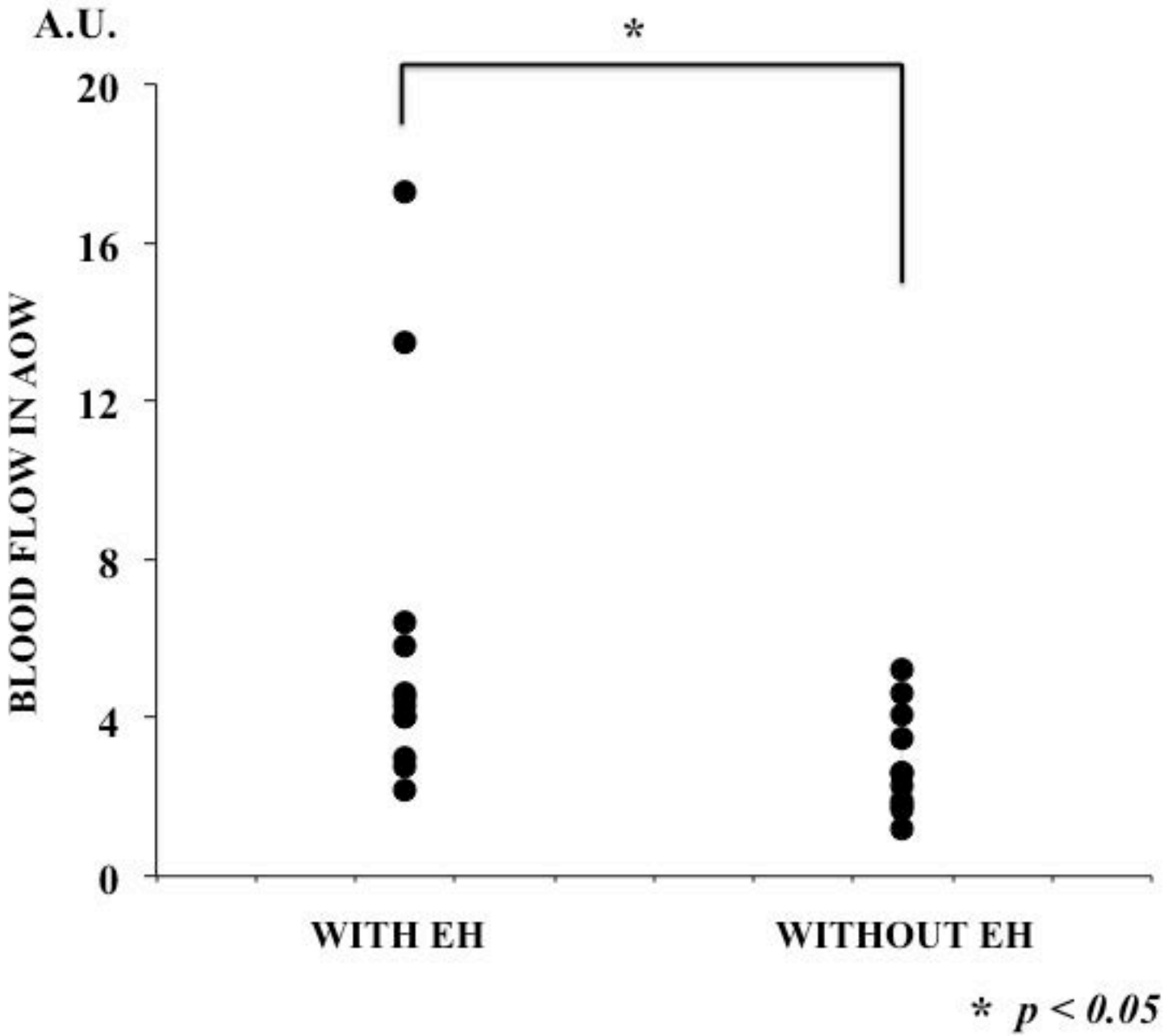


Figure 2

TABLE 1.
The presence of endolymphatic hydrops (EH)

	No	Mild	Significant
Cochlear EH	**22**	**17**	**7**
Vestibular EH	**34**	**6**	**6**

TABLE 2.

Average air conduction (AC) and bone conduction (BC) thresholds at five frequencies of ears with no, mild, and significant endolymphatic hydrops (EH)

EH		250Hz	500Hz	1000Hz	2000Hz	4000Hz
No	**AC**	**61.8±2.9**	**61.3±2.9***	**60.0±4.1****	**58.7±4.8**	**51.3±4.9**
(n=19)	**BC**	**14.5±1.8**	**22.6±1.5**	**34.7±2.3$^{\#}$**	**44.2±2.3$^{\#\#}$**	**27.6±3.0$^{\#\#\#}$**
Mild	**AC**	**65.5±3.3**	**62.9±3.0***	**53.4±3.0****	**51.8±4.5**	**47.6±5.4**
(n=19)	**BC**	**12.4±2.5**	**20.3±3.2**	**27.6±3.2$^{\#}$**	**35.8±3.4$^{\#\#}$**	**24.7±4.7$^{\#\#\#}$**
Significant	**AC**	**71.9±6.3**	**82.5±8.1***	**80.6±8.9****	**75.0±8.6**	**75.6±11.3**
(n=8)	**BC**	**26.9±6.3**	**35.6±7.1**	**50.0±7.3$^{\#}$**	**59.4±5.5$^{\#\#}$**	**48.1±6.9$^{\#\#\#}$**

(average ±standard error**)** *,**, ### *p<0.05*, #, ## *p<0.01*

TABLE 3.

Relationship between the presence of endolymphatic hydrops (EH) and the stages of the disease on computed tomography (CT)

Stage on CT	No EH	Mild EH	Significant EH
0	6	10	3
1	11	6	2
2a	1	-	1
2b	-	1	-
2c	-	-	-
3	1	2	2