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ORIGINAL REPORT

Changes in endolymphatic hydrops after sac surgery examined by Gd-enhanced MRI

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Abstract

Conclusion: Endolymphatic hydrops could be a reversible inner ear pathological condition. After sac surgery, hydrops was reduced and symptoms went into remission in some cases, although vertigo suppression was not always a result of the reduced hydrops. *Objective:* To examine the changes in endolymphatic hydrops detected by gadolinium (Gd) contrast-enhanced magnetic resonance imaging (MRI) before and 6 months after endolymphatic sac surgery in patients with unilateral Ménière's disease. *Methods:* Fluid-attenuated inversion recovery MRI was obtained 4 h after intravenous administration or 24 h after intratympanic administration of Gd contrast medium. An enlarged negative stain corresponding to the cochlear duct and endolymphatic space of the vestibule was assessed as hydrops. *Results:* Of seven patients with hydrops confirmed by MRI before surgery, both cochlear and vestibular hydrops became negative in two, cochlear hydrops became negative in one, both hydrops were present, but reduced, in one, and there was no change in three patients. The number of vertigo spells was reduced in all cases at 6–12 months after surgery. As for the three cases of negative hydrops, vertigo was completely suppressed. In two cases in which hearing level improved, hydrops became negative after surgery.

Keywords: *Ménière's disease, vertigo, hearing, magnetic resonance imaging, inner ear pathology*

Introduction

Endolymphatic hydrops is widely recognized as a pathologic change in the inner ear related to Ménière's disease (MD). Histopathologic examination initially revealed an enlarged endolymphatic space with no inflammatory change in patients with MD [1,2]. Subsequently, experimental hydrops in animals was developed, and these animals showed inner ear dysfunction [3,4]. Diuretic administration temporarily relieves the hearing impairment caused by MD, probably due to a reduction in hydrops [5]. These accumulated findings support the idea that endolymphatic hydrops is involved in the pathophysiology of MD. Gadolinium (Gd) contrast-enhanced inner ear MRI, introduced by Nakashima and colleagues to clinical practice [6], made it possible to prove that hydrops exists in living patients suffering from MD. We have also observed hydrops in more than 90% of patients with typical and active MD [7,8].

As a treatment option, endolymphatic sac surgery has had a long history since its introduction by Portmann in 1927 [9], but its efficacy has been debated since the 1980s [10]. Our recent modification to the surgery using high-dose steroid instillation into the sac added to a sac-mastoid shunt showed good results in terms of postoperative hearing, as well as vertigo control [11].

In the present study, we examined hydrops by Gd-enhanced MRI before and 6 months after sac

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Table I. Summary of clinical profiles and MRI findings.

				Hearing*		Vertigo attack†		Cochlear hydrops		Vestibular hydrops	
Case no.	Age (years)	Sex	Ear	Pre	Post	Pre	Post	Pre	Post	Pre	Post
P43	47	F	L	33.8	10	9	0	+	–	+	–
P34	33	F	L	46.3	28.8	17	0	+	–	+	–
P36	46	F	R	61.3	80	25	0	+	–	+	+
P35	48	F	L	58.8	58.8	10	0	+	+	+	+
P37	61	F	L	45	52.5	9	0	+	+	+	+
P38	47	M	R	43.8	40	16	1	+	+	+	+
P33	42	F	R	78.8	87.5	13	2	+	+	+	+

+ Indicates hydrops positive according to the criteria.
*Hearing is expressed as the average of the pure-tone hearing threshold by air conduction at 0.25, 0.5, 1, and 2 kHz.
†Vertigo attack indicates the number of definitive vertigo spells in the 6 months before (Pre) and between 6 and 12 months (Post) after surgery.

surgery in MD patients with frequent episodes of vertigo. We aimed to clarify whether hydrops could be a reversible change, and whether the symptomatic relief after the surgery could be obtained by the resolution of hydrops.

Material and methods

Seven patients (six females and one male, aged 33–61 years) with unilateral definite MD (AAO-HNS [12]) participated in this study from January to October 2011. All patients had frequent episodes (at least once a month for the last 6 months on average, the maximal interval of two spells was less than 2 months) of definitive vertigo spells defined by AAO-HNS [12], and had developed unilateral hearing impairment. The number of vertigo spells and the hearing level of each case are listed in Table I. After confirmation of both cochlear and vestibular hydrops by Gd-enhanced MRI and giving informed consent, the patients underwent surgery. Some cases used diuretics and vitamin B12 for MD before surgery, but ceased using them within 6 months after the surgery. Other oral medication for diseases other than MD was continued before and after the surgery (cases P37 and P43 for rheumatoid arthritis, P38 for depression). At 6 months after the surgery, MRI was performed again.

We used two types of Gd administration; one intratympanically and the other intravenously. The intratympanic method used Gaddiamide hydrate (Omniscan$^{(R)}$) diluted eightfold in saline, injected into the tympanic cavity with a 23 gauge needle and syringe through the tympanic membrane. The patient stayed in the affected ear up lateral spine position for 30 min, and at 24 h after the injection, MRI was performed [6,7]. The intravenous method used a double dose of gadoteridol compared with general use (Prohance$^{(R)}$ 0.4 ml/kg), injected intravenously, and at 4 h after the injection, MRI was performed [13]. The intratympanic method was only used in early cases (preoperative MRI in cases P34 and P35). Since comparable images could be obtained by the intravenous method, it was used for later cases. The hydrops detection rate was not different between these two methods in our previous study [8].

Images of two-dimensional fluid attenuated inversion recovery (2D-FLAIR) obtained with a 3 Tesla MRI unit (Sigma Excite HD 3T, GE Healthcare) were used for hydrops evaluation. Axial view images of 2 mm thickness were adjusted parallel to the anterior commissure-posterior commissure line the same as a routine MRI. To increase the number of evaluable images, a 2D-FLAIR sequence was done twice with a 1 mm gap in cases P35, P37, P38, and P43.

In the inner ear, only the perilymphatic space was contrast-enhanced by the Gd agent, while the endolymphatic space was evaluable as a low signal intensity area [6,7]. Our criteria for hydrops were basically based on Nakashima et al. [14] but modified to adjust the level of image quality of our device. Cochlear hydrops was qualitatively judged positive when the low intensity signal areas corresponding to the cochlear duct were clearly noticed. The area should be at the edge of the cochlea, and should be distinguished from the bony partition. Vestibular hydrops was judged positive when more than 33.3% of the vestibule was occupied by a low signal area [6–8]. Two of the authors (T.I. and T.K.) independently examined MRI images prepared by others (A.U.) without any information about the clinical course. Outlines of the endolymphatic space were traced on the images (as expressed in Figures 3 and 4) and the

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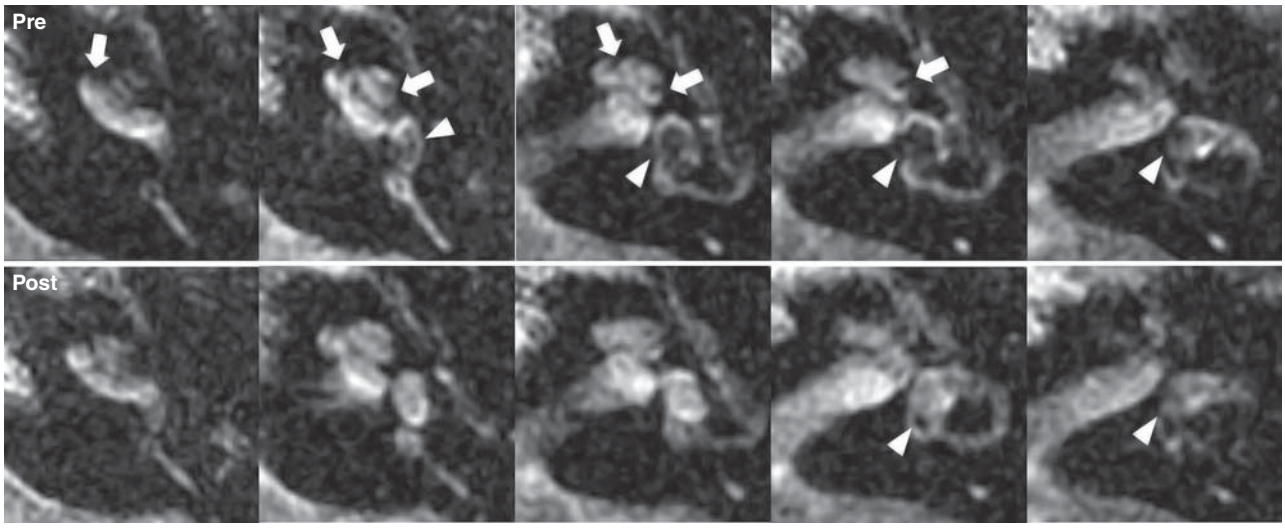

Figure 1. An example of reduced endolymphatic hydrops (case P43). Upper panels are images taken before, and lower panels 6 months after, sac surgery. From the left to the right, caudal to rostral axial views of the inner ear are depicted by Gd-contrasted perilymphatic space. Gd contrast medium was applied intravenously for both examinations. Arrows indicate low signal intensity areas corresponding to the cochlear duct, apparently indicating cochlear hydrops. As for the vestibule, low intensity areas indicated by arrowheads occupy more than 33.3% of the vestibule, indicating vestibular hydrops in the preoperative MRI. The postoperative MRI did not show either cochlear or vestibular hydrops.

proportion of the area in the cochlea or the vestibule was calculated. As the area of the vestibule, the semicircular canals and the ampullae were not included. For comparisons between preoperative and postoperative images in the same case, the extent of hydrops was also assessed, following a positive/negative judgment. Adobe Photoshop CS5 software was used for the image processing.

Our procedure for sac surgery with steroid instillation was described in a previous report [11]. Briefly stated, following an L-shaped incision on the lateral wall of the endolymphatic sac, prednisolone powder

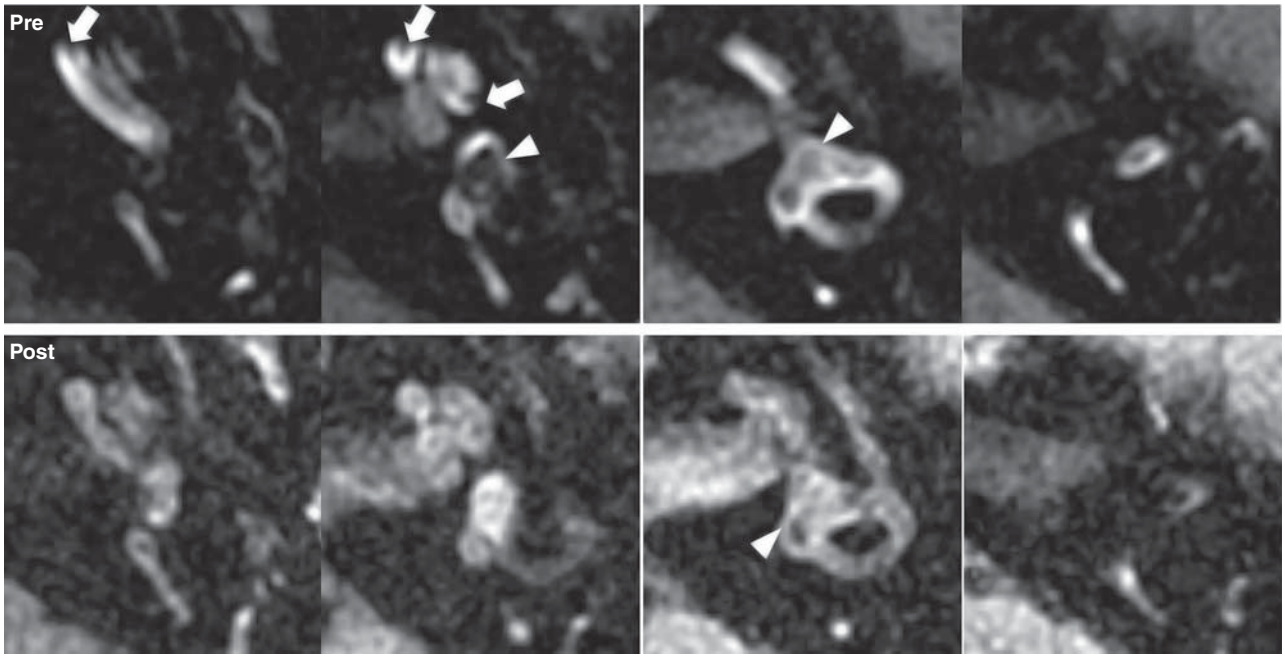

Figure 2. Another example of reduced hydrops (case P34). Upper panels are 2D-FLAIR MR images of Gd contrast medium applied intratympanically before sac surgery. Lower panels are images of Gd contrast medium applied intravenously in the same patient 6 months after surgery. The intratympanic application gave clearer contrast images, but the intravenous application was comparable. Cochlear and vestibular hydrops were clearly seen before surgery, but both disappeared after the surgery. Arrows and arrowheads indicate the endolymphatic space in the cochlea and the vestibule, respectively.

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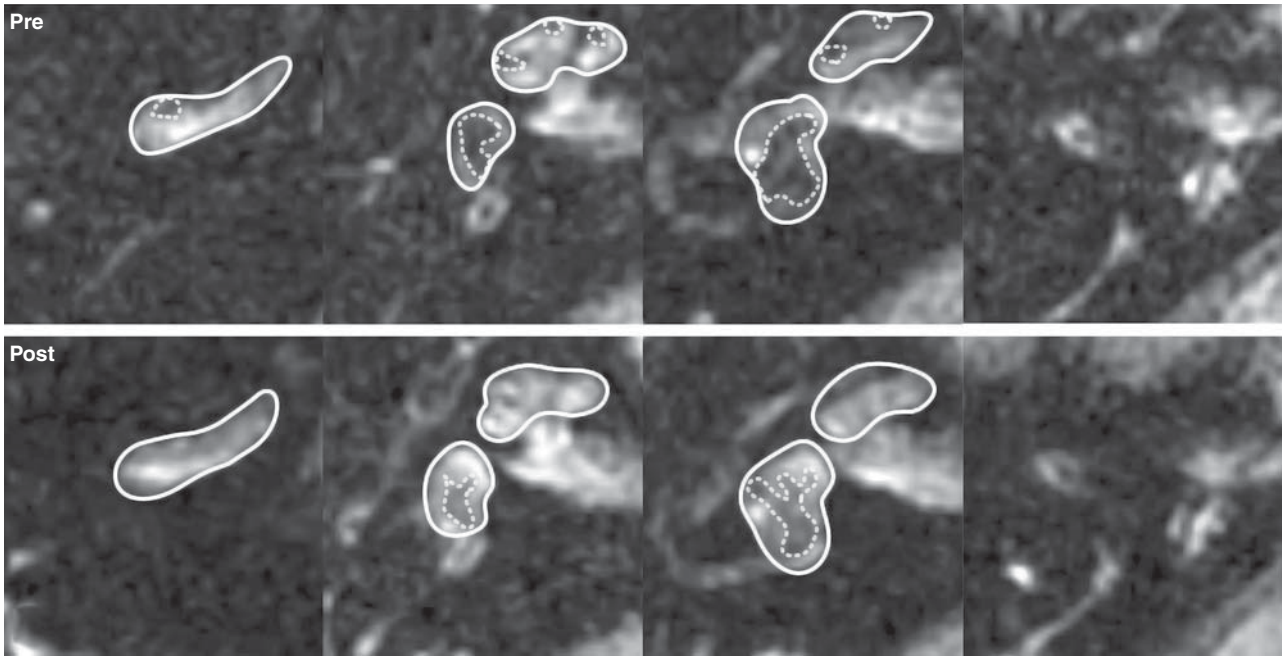

Figure 3. A case where cochlear hydrops became negative and cochlear hydrops remained positive but reduced (case P36). Solid traces indicate outlines of the cochlea and the vestibule; dotted traces indicate the endolymphatic space. The area of endolymphatic space in the vestibule was reduced from 50.5% to 37.2% of the vestibule.

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was placed inside, layered gelatin films were inserted, and then small pieces of gelatin sponge soaked in dexamethasone were placed densely in the surrounding area.

This study was conducted under approval of the ethical committee of Osaka University Hospital (IRB #08223, 11341). Some of the preoperative clinical profiles of the cases were presented in a previous report using the same case IDs [8]. All pictures and postoperative case profiles in this article were originally documented.

Results

Table I shows preoperative and postoperative clinical profiles including the number of vertigo spells 6 months preoperatively and postoperatively for 6–12 months, the worst dB hearing level in the corresponding periods, and MRI results. Preoperatively, all seven patients with typical and active unilateral MD showed cochlear and vestibular hydrops in the affected ear. The proportions of the endolymphatic space in the cochlea and the vestibule were 12.5% (± 5.2%) (mean ± standard deviation) and 50.6% (± 5.5%), respectively. Postoperatively, both cochlear and vestibular hydrops became negative in two cases (P43 shown in Figure 1, P34 in Figure 2). The proportion of the endolymphatic space in the vestibule was changed from 42.3% preoperatively to 19.4% postoperatively in case P43, and from 45.6% to 18.3% in case P34. In these two cases, the postoperative hearing level was improved by more than 10 dB and vertigo spells were completely suppressed. In case P36 (Figure 3), cochlear hydrops became negative, postoperative vestibular hydrops was judged positive according to our criteria (the endolymphatic space >33.3% of the vestibule) but the proportion of the endolymphatic space was reduced from 50.5% to 37.2%. Hearing was worsened by more than 10 dB, but vertigo spells were completely suppressed. In case P35 (Figure 4), both hydrops remained positive after the surgery, but the proportions of the endolymphatic space in the cochlea and the vestibule were reduced from 18.3% to 8.2% and from 50.5% to 37.2%, respectively. In the remaining three cases (P37, P38, P33), postoperative images were quite similar to the preoperative ones, and the proportion of the endolymphatic space for both cochlear and vestibular areas were changed by no more than 10 points (%). Even in these cases, the number of vertigo spells was significantly decreased.

Discussion

Endolymphatic hydrops was definitively diagnosed only by histopathologic examination after death until Gd-enhanced inner ear MRI was introduced [6]. Histopathologic endolymphatic hydrops was detected at a high rate in patients with MD, regardless of whether MD was still active or not in the last period

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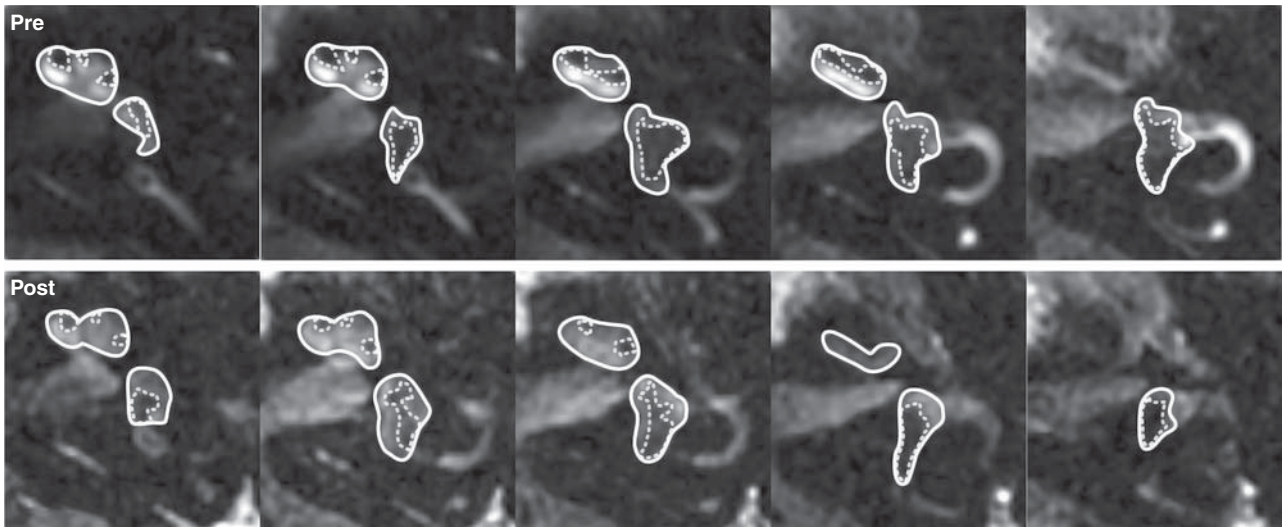

Figure 4. A case of hydrops that was reduced but still existed in both the cochlea and the vestibule (case P35). The endolymphatic space (dotted traces) was noticed even after surgery, although the proportions in the cochlea and the vestibule (solid traces) were reduced from 18.3% to 8.2% and from 51.8% to 35.4%, respectively.

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of patient observation. A review from the temporal bone collection at the Massachusetts Eye and Ear Infirmary reported that hydrops could be detected in all 28 cases with classical symptoms of MD in at least 1 ear [15]. Does hydrops persist once it has formed? The present study using MRI could show cases of hydrops reduced in a comparison before and 6 months after surgery, which indicated that hydrops was a reversible change in at least some cases.

Sac surgery for MD has controversial efficacy based on the results of a placebo-control study [10]. A temporal bone study of cases after sac surgery showed that the sac shunt was incomplete in many cases and that hydrops persisted in all cases (15/15), even though the vertigo was well controlled [16]. We have modified the surgery with steroid instillation into the opened sac, and reported good results in vertigo control and hearing [11]. In the present study, two cases showed hearing improvement. In these two cases, endolymphatic hydrops was reduced and became negative. Sac surgery with steroid instillation may have the potential to reduce hydrops, although we do not have enough data regarding how hydrops varies with time over the entire life of the patient undergoing surgery, sham-surgery, or other treatment. On the other hand, even in the cases where hydrops was not modified after surgery, vertigo spells were significantly suppressed, which indicates that the effects of sac surgery are not limited to hydrops reduction. The mechanism of vertigo attack is not completely understood, and at least not explained by the state of endolymphatic hydrops alone.

As another treatment option for MD, intratympanic gentamicin therapy is widely used, which was originally based on the concept that lowering the vestibular function of the affected ear suppresses the variation in function, leading to vertigo suppression. A recent modification using low-dose gentamicin is supposed to act on the hydrops, but not destroy the inner ear function. However, intratympanic low-dose gentamicin treatment was reported not to reduce the extent of hydrops on MRI images in even successful cases [17], in contrast with our results after performing sac surgery. It may be possible that sac surgery influences more directly the endolymphatic flow. We use high-dose steroid applied into the opened endolymphatic sac, which may be another possibility to explain the hydrops reduction. On the other hand, vertigo control could be achieved even without the hydrops reduction, which also happened in our study as mentioned above.

Inner ear examination by MRI still has potential for further development. The quality of the inner ear images depends on the device and imaging technique, and is now far less than that of histologic sections. Criteria for endolymphatic hydrops depend on the image quality, and have not been unified yet among research groups [13,17]. Our criteria were still not quantitative. Particularly in the cochlear hydrops evaluation, the area of the cochlear duct (endolymphatic space) in other than hydrops (enlarged) cases was small and difficult to measure quantitatively. Further development of hardware and software and accumulation of control data will be necessary to deal with more precise comparisons.

In conclusion, we showed that after sac drainage surgery with steroid instillation, three cases of hydrops were reduced and the symptoms went

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into remission. Therefore, it can be said that endolymphatic hydrops is reversible, at least in some cases, and that sac surgery may have the potential to ameliorate hydrops. However, vertigo suppression after sac surgery did not always result in a reduction in hydrops. As for the potential for surgery to affect hydrops, a large number of cases with or without surgery should be accumulated and further comparisons are necessary.

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

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