

Association Between Cupular Deposits and Otosclerosis

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Objective: To evaluate whether otosclerosis is an underlying mechanism for the production of cupular deposits and to study the association between cupular deposits and dysequilibrium in otosclerosis.

Design: Retrospective human temporal bone (TB) study. The incidence of cupular deposits in these 70 TBs was analyzed. Correlations between cupular deposits and vestibular symptoms, endosteal involvement of the otosclerotic focus, stapedial fixation, and clinical history of stapes surgery were evaluated.

Setting: Otolaryngology laboratory in a tertiary academic medical center.

Patients: The study material consisted of 35 human TBs with otosclerosis and 35 age-matched controls.

Main Outcome Measures: Morphometric evaluations of the incidence of cupular deposits, endosteal involvement of the otosclerotic focus, and stapedial fixation were made by light microscopy. Clinical records were reviewed retrospectively for clinical history of stapes sur-

gery and prevalence of vestibular symptoms. The incidence of cupular deposits was compared between the otosclerotic and control groups. Correlations between cupular deposits and vestibular symptoms, endosteal involvement of the otosclerotic focus, stapedial fixation, and clinical history of stapes surgery were evaluated in the subjects with otosclerosis.

Results: The incidence of cupular deposits in TBs with otosclerosis was significantly higher than in those without whereas there was no correlation between the incidence of the deposits and dysequilibrium in cases of otosclerosis. An increase in deposits did not correlate with stapedial fixation, stapes surgery, or endosteal involvement.

Conclusions: Our results suggest otosclerosis as an underlying mechanism for the production of cupular deposits; however, we did not find an association between these deposits and vestibular symptoms.

Arch Otolaryngol Head Neck Surg. 2006;132:1331-1334

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OTOSCLEROSIS HAS BEEN ASSOCIATED with an increased incidence of vestibular symptoms.¹⁻³ Several histopathologic studies^{2,4,5} have shown otosclerotic involvement of the vestibular apparatus to be a cause of vestibular symptoms owing to invasion and degeneration of the vestibular nerve. Other reports^{6,7} postulate that disequilibrium might be caused by changes in the biochemical composition of the perilymph. It seems logical to assume that vestibular symptoms in patients with otosclerosis can occur from a variety of etiologies.

Clinically, vestibular symptoms relating to otosclerosis can include transitory, recurrent, rotary, positional, or spontaneous vertigo,^{2,3,8-10} and they have even been correlated with an increased incidence of benign paroxysmal positional vertigo (BPPV).¹¹ Although the etiology of BPPV is still a subject of controversy,^{12,13} tem-

poral bone (TB) studies have revealed basophilic deposits that adhere to the surface of the cupula of semicircular canals and are thought to be one of the causes of BPPV.¹⁴ These deposits have no relationship to postmortem preservation status, including the time interval between death and fixation.¹⁵ Because, to our knowledge, there have been no reports regarding the deposits of basophilic material on the cupulae of the semicircular canals as a cause of vertigo in patients with otosclerosis, we attempted to address details of the etiology related to vestibular symptoms by focusing on the pathologic changes at this site.

METHODS

SUBJECTS

Human TBs with otosclerosis were selected from 1756 TBs (905 cases) from the collec-

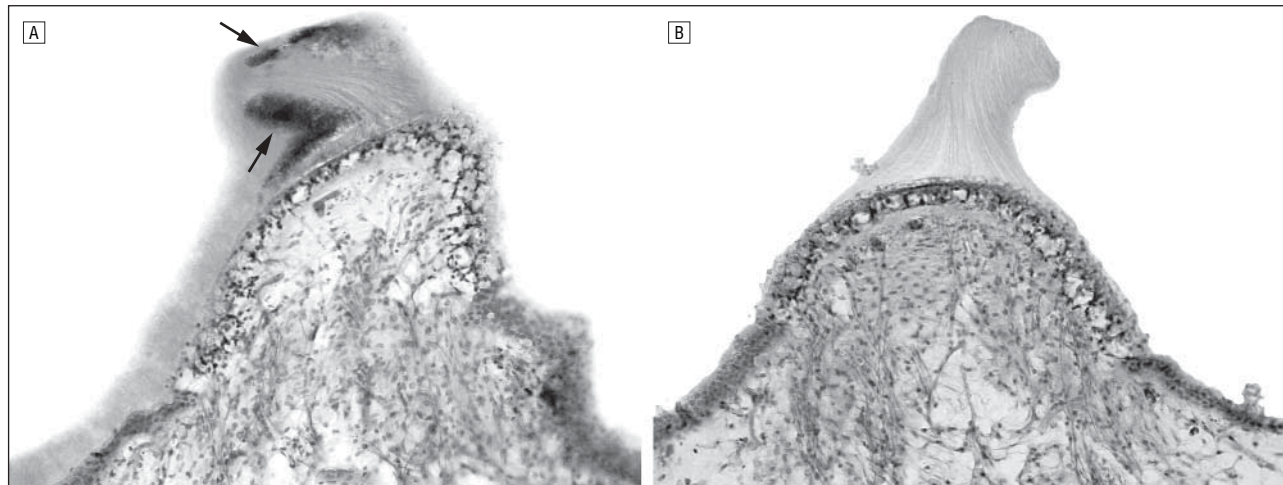


Figure 1. A, Large, amorphous, and basophilic deposits (arrows) on the cupula of the posterior semicircular canal; B, no cupular deposits are seen in the posterior canal from an 89-year-old man without otosclerosis (hematoxylin-eosin; original magnification $\times 200$).

tion at the Otopathology Laboratory, University of Minnesota, Minneapolis. All TBs were harvested at autopsy and fixed in a solution of 10% buffered formalin. The fixed tissues were decalcified in either ethylenediaminetetraacetic acid or trichloroacetic acid for 6 weeks, dehydrated through a graded ethanol series, and embedded in celloidin. The specimens were serially sectioned along a midmodiolar axis in the horizontal plane from superior to inferior at a thickness of 20 μm . Every tenth section was stained with hematoxylin-eosin and examined under light microscopy.

There were 181 TBs from 102 cases with histological otosclerosis. From these, TBs with histopathological findings of inner ear malformation; gross labyrinthine destruction (eg, invasion of the otic capsule by neoplastic involvement or cholesteatoma); inner ear infection; endolymphatic hydrops; or those from subjects with a clinical history of treatment with aminoglycoside antibiotics, of head trauma, or of clinically diagnosed Ménière's disease were excluded. Specimens were further precluded if 1 of 3 cupulae was not available owing to damage from removal, or if it was missed owing to the cutting angle. As a result, we obtained 35 TBs from 26 cases with histological otosclerosis. Thirty-five TBs from 26 age-matched individuals without otosclerosis served as controls. Our inclusion criteria for these age-matched controls were (1) no documented medical history of ear disease except presbycusis, (2) histologically normal TBs except for presbycusis-associated changes, and (3) availability of 3 cupulae.

CLASSIFICATION OF CUPULAR DEPOSITS

Classification of cupular deposits were evaluated as small if the deposits were up to half the width of the base of the cupula and large if they were larger than half the width of the cupula.¹⁶ If TBs included 2 or more cupular deposits and 1 of them was large, it was classified as large.

HISTOLOGICAL ASSESSMENTS AND REVIEW OF CLINICAL RECORDS

Each cupula was carefully observed by light microscopy at a magnification of $\times 40$, and further observation was made at higher magnifications for confirmation. The incidence of basophilic deposits on the cupula was calculated and analyzed in each group. Vestibular involvement of otosclerosis was categorized as endosteal involvement when the normal align-

ment inside the bony labyrinth was not preserved. Clinical records of these subjects were then reviewed retrospectively for clinical history of stapes surgery and prevalence of vestibular symptoms. The associations between the incidence of cupular deposits and vestibular symptoms, endosteal involvement, stapedia fixation, and clinical history of stapes surgery were analyzed in bones with otosclerosis. The TBs after stapedectomy were excluded from the evaluation of stapedia fixation. Each of these associations and correlations was further analyzed individually depending on the size of the deposits.

STATISTICAL ANALYSIS

A χ^2 test for independence and Fisher exact probability test were used to compare these incidents. An unpaired *t* test was used to compare the ages of the subjects. Significance was set at $P = .05$.

RESULTS

AGES OF SUBJECTS

The mean ages of subjects with otosclerosis was 66.4 years (range, 20-90 years) and for the controls was 66.7 years (range, 20-92 years) ($P > .10$ by unpaired *t* test).

INCIDENCE OF CUPULAR DEPOSITS

Temporal bones with and without cupular deposits are shown in **Figure 1**. The incidence of cupular deposits is shown in **Figure 2**. The incidence of cupular deposits in all 3 canals combined and posterior canals in otosclerotic bones was significantly higher than in those of controls ($P = .046$, with χ^2 test for independence). Four cupular deposits in otosclerotic bones and 2 cupular deposits in controls were classified as large. The number of large deposits located in the superior canal was 0; in the lateral canal, 0; and in the posterior canal in otosclerotic bones, 4; whereas in controls the incidence in the superior canal was 0; in the lateral canal, 2; and in the posterior canal, 0. The incidence of large deposits was not statistically different between the TBs with otosclerosis and controls.

PREVALENCE OF VESTIBULAR SYMPTOMS

Thirteen (37.1%) of 35 otosclerotic TBs had a documented medical history of vestibular symptoms; dizziness and unsteadiness were generally noted, but only 4 reported vertigo. There was no medical history of vestibular symptoms in the controls. Two of 4 subjects with vertiginous episodes were noted as positional; however, neither symptoms nor results of disequilibrium tests manifested features associated with BPPV. Cupular deposits were observed in 3 (23.1%) of 13 otosclerotic TBs with vestibular symptoms and in 11 (50.0%) of 22 otosclerotic TBs without ($P > .10$ by χ^2 test for independence). Large cupular deposits were seen in 2 otosclerotic TBs (15.4%) with vestibular symptoms and in 2 (9.1%) without ($P > .10$ by Fisher exact probability test).

VESTIBULAR INVASION

The most common site of the otosclerotic foci was anterior to the oval window. The endosteum of the vestibule and superior semicircular canal with or without involvement of the superior vestibular nerve or its cribrosa area were the 2 most common sites of the vestibular apparatus invaded by otosclerosis. Endosteal involvement was observed in 18 (51.4%) of 35 otosclerotic TBs. Cupular deposits were observed in 9 (50.0%) of 18 otosclerotic TBs with endosteal involvement and 5 (29.4%) of 17 without involvement ($P > .10$ by χ^2 test for independence). Large cupular deposits were seen in 2 otosclerotic TBs with endosteal involvement and 2 without ($P > .10$ by Fisher exact probability test).

STAPES SURGERY

There was a clinical history of temporal bone surgery in 10 (28.6%) of 35 otosclerotic TBs: 5 had a stapedectomy, 2 had stapes mobilization, 2 had stapes mobilization and stapedectomy separately, and 1 had stapedectomy/sacculotomy concomitantly. Cupular deposits were seen in 4 (40.0%) of 10 otosclerotic TBs with surgery and 10 (40.0%) of 25 without ($P > .10$ by Fisher exact probability test). Cupular deposits were seen in 3 (37.5%) of 8 otosclerotic TBs with stapedectomy and 11 (40.7%) of 27 without ($P > .10$ by Fisher exact probability test). No large deposits were detected in otosclerotic TBs with stapes surgery whereas 4 otosclerotic TBs without surgery demonstrated large deposits ($P > .10$ by Fisher exact probability test).

STAPEDIAL FIXATION

Apparent bony ankylosis was observed in 6 (22.2%) of 27 otosclerotic TBs. Cupular deposits were seen in 4 (66.7%) of 6 otosclerotic TBs with apparent bony ankylosis at the stapediostapedial joint and 7 (33.3%) of 21 otosclerotic TBs without ($P > .10$ by Fisher exact probability test). Of the 6 otosclerotic TBs with both bony ankylosis and cupular deposits, 2 deposits (33.3%) were classified as large whereas 2 (9.5%) of 21 otosclerotic TBs without stapediostapedial fixation were large ($P > .10$ by Fisher exact probability test).

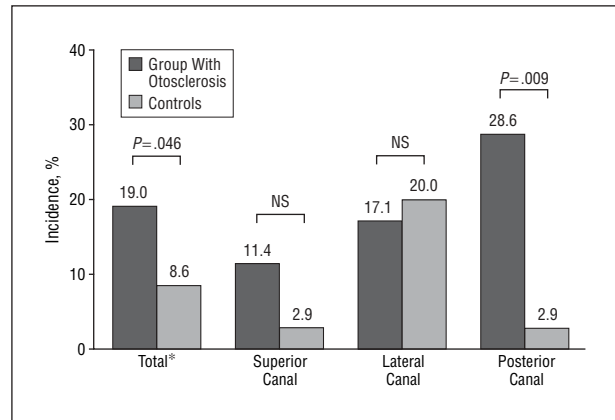


Figure 2. The incidence of cupular deposits. An asterisk denotes the incidence of cupular deposits in all 3 canals combined; NS, not significant.

COMMENT

Although previous reports^{15,17-19} described the incidence of basophilic deposits on the surface of cupula as approximately 6.1% to 26.4% in the superior semicircular canal, 10.5% to 41.4% in the lateral, 21.5% to 36.8% in the posterior, and 12.7% to 34.9% in all 3 canals combined, these findings were not related to cases with otosclerosis. In our study, the incidence of basophilic deposits in otosclerotic TBs was lower and probably resulted from our methods; we did not consider diminutive deposits as important because it has been suggested that a large amount of deposit is necessary to cause vestibular symptoms.¹⁸ Also, we excluded subjects with inner ear infection and with a medical history of treatment with aminoglycoside antibiotics and of head trauma because these factors have been suggested to facilitate the occurrence of cupular deposits.^{16,20} Our results demonstrated a significantly higher incidence of cupular deposits in TBs with otosclerosis compared with those without. Sando et al⁴ reported cupular deposits in 2 of 4 otosclerotic bones. Their result seems to support this association.

Studies have suggested the otoconia of the otolithic membrane in the utricle as the possible origin of these deposits.^{14,18,19} They are believed to detach and migrate through the endolymphatic system and finally appear on the "sticky" surface of the cupula of the semicircular canals. The mechanisms by which the deposits are produced in otosclerotic TBs are assumed to be the result of changes in the biochemical composition of the endolymph or deterioration of conduction of sound waves. However, in our study, neither endosteal involvement of the otosclerotic focus nor stapediostapedial fixation contributed to the promotion of cupular deposits. Cupular deposits have been suggested to be occasionally generated after TB surgery.²⁰ In our study, there was no difference between the incidence of cupular deposits after stapedectomy alone or general stapes surgery compared with those without surgery.

Temporal bone studies have reported basophilic deposits to be one of the causes of BPPV¹⁴; however, we found no significant correlation between either the incidence or size of cupular deposits and dysequilibrium in subjects with otosclerosis.

Submitted for Publication: February 17, 2006; final revision received May 9, 2006; accepted June 19, 2006.

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Author Contributions: All authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Hayashi, Cureoglu, Schachern, Oktay, Fukushima, Sone, and Paparella. *Acquisition of data:* Hayashi. *Analysis and interpretation of data:* Hayashi, Schachern, and Fukushima. *Drafting of the manuscript:* Hayashi, Schachern, and Sone. *Critical revision of the manuscript for important intellectual content:* Hayashi, Cureoglu, Schachern, Oktay, Sone, and Paparella. *Statistical analysis:* Hayashi and Fukushima. *Obtained funding:* Schachern and Paparella. *Administrative, technical, and material support:* Schachern, Oktay, Fukushima, and Paparella. *Study supervision:* Cureoglu, Schachern, Sone, and Paparella.

Financial Disclosure: None reported.

Funding/Support: This study was supported by the Japan Health Sciences Foundation, the International Hearing Foundation, the Hubbard Foundation, and the Starkey Foundation.

Acknowledgment: We thank Carolyn Sutherland for her help with preparing the temporal bone slides used in this study.

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