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Endolymphatic Hydrops in the Setting of Vestibular Schwannoma: A Temporal Bone Study

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Abstract

Hypothesis: Vestibular schwannoma (VS) may be associated with endolymphatic hydrops (EH). EH may account for symptomatology in a subset of patients with VS.

Background: Presenting symptoms of VS and EH overlap and MRI evaluation of the membranous labyrinth in some patients with VS demonstrates EH. The aim of the current study is to evaluate whether EH is present in temporal bones of patients with VS.

Methods: The NIDCD and House Temporal Bone Laboratory at UCLA Eccles database was queried for the diagnosis of “acoustic neuroma”. Exclusion criteria included concomitant ear disease and surgery. Temporal bones were analyzed for EH of the basal, middle and apical turns and vestibule. Pre-mortem audiometric and clinical data were gathered.

Results: Of 43 human temporal bones with VS, 6 met inclusion criteria. All temporal bones demonstrated VS that was undisturbed by surgery. 3/6 demonstrated EH of at least one cochlear turn as well as vestibular hydrops. Three patients had severe to profound hearing loss. One patient carried a diagnosis of Meniere’s Disease.

Conclusions: EH is demonstrated in the setting of VS in human temporal bones. EH may be one mechanism of hearing loss and dizziness in patients with VS.

Professional Practice Gap & Educational Need: The underlying mechanisms of symptoms of VS may be multifactorial. The association of EH in some patients with VS would modify our clinical approach to management.

Learning Objective: To discover if EH may be associated with VS.

Desired Result: To broaden understanding of pathophysiologic mechanisms in patients with VS.

Level of Evidence: Level IV

IRB Approved: UCLA IRB#10–001449

Background

Patients with vestibular schwannoma (VS) may present with fluctuating hearing[1] and sometimes with vertigo, symptoms also common in patients with endolymphatic hydrops (EH),[2]which is the histologic marker for Meniere's Disease (MD). Hearing loss in the setting of VS can recover with steroids, similar to patients with MD as well.[3] There are multiple mechanisms of hearing loss in the setting of VS, including cochlear nerve compression,[4] restriction of blood supply to the cochlea[5] or increased protein levels in perilymph caused by the tumor.[6] EH has not been fully investigated as a possible marker for hearing and balance symptoms in patients with untreated VS.

Imaging studies have also supported the association of EH with VS in patients with episodic vertigo and VS. Moayer et al. describe two patients in whom EH was seen in 3-dimensional delayed contrast MRI and whose symptoms improved with diuretic use.[7] Others have demonstrated EH in patients with VS using non-contrast-enhanced 3D FLAIR MRI sequences;[8] patients with EH on this imaging modality also had symptoms of vertigo. A more recent study demonstrated EH in 16.7% of 66 patients with VS using intratympanic (IT) gadolinium-enhanced MRI.[9] IT gadolinium allowed for volumetric quantification of EH in these patients.

In a review of the literature, it is unclear if the association of EH and VS is viewed as two separate disease processes in the same ear, or rather, whether intralabyrinthine changes related to VS can result in EH. Secondary EH[10] is well known in the setting of several inflammatory or traumatic causes, including post-operative to cochlear implantation,[11,12,13] acoustic or mechanical trauma,[1] and after stapedectomy.[14]

The current study aims to document the association of EH in some human temporal bone specimens with VS and suggest EH as a candidate marker for audiovestibular symptoms in a subset of patients with VS.

Methods

The Institutional Review Board (IRB) approved this study (IRB protocol #10–001449), and all methods used in this study are in accordance with NIH and IRB guidelines and regulations. This work was supported from by NIDCD/NIH Grant (U24 DC015910). The NIDCD and House Temporal Bone Laboratory at UCLA Eccles database was queried for the diagnosis of "acoustic neuroma" (this term was used in categorization of temporal bones specimens). Temporal bones from patients Neurofibromatosis Type II (NFII) were excluded as well as those with ear disease ipsilateral to the tumor. Temporal bones with VS that were operated were also excluded, therefore none of the temporal bones included in this study had undergone surgical intervention.

Patient characteristics during life were collected from the clinical charts, including hearing status and tumor details. Each temporal bone was examined for endolymphatic hydrops of the basal, middle and apical turns. Distention of Reissner's membrane towards the modiolus was used to classify temporal bones as those with EH as previously described by Cureoglu et al.[15] Mild hydrops isolated to the apical cochlear turn was not classified as hydrops as this can be seen in normal temporal bones. Vestibular hydrops was also evaluated based on distention of the utricular and saccular membranes. Where available, contralateral temporal bones were examined for hydrops. Hydropic and non-hydropic temporal bones were photo documented and images of the VS were also taken.

Results

The NIDCD and House Temporal Bone Laboratory at UCLA Eccles database query resulted in 43 temporal bones carrying with VS. Of these, only six temporal bones were included that had VS undisturbed by surgery. Table 1 describes patient and tumor characteristics. Temporal bone #2 did not have an associated clinical chart and lacked clinical information. The average patient age was 89 years old. Most tumors appeared to be small (Figure 1A and 1C), involving the internal auditory canal (IAC). Temporal bone #4 and #5 had VS which were intracochlear and #6 had a tumor within Scarpa's ganglion. The full extent of the tumor volume outside of the IAC could not be completely assessed due to limitations in temporal bone preparation.

Although some temporal bones with VS had normal cochlear morphology (Figure 1B), Table 2 shows that half of the temporal bones with undisturbed VS demonstrated EH of at least one cochlear turn (temporal bones #4, #5 and #6) (Figure 2A). Those bones with EH of the cochlea were also found to have EH of the vestibule (Figure 2C). Contralateral temporal bones were available for review for all bones with EH, and no cochlear or vestibular hydrops was found on the non-tumor side (Figure 2B).

PTA and word discrimination were recorded for the ear ipsilateral to the VS. The average PTA in those patients in whom pure tones were measurable was 57 dB (Table 3). Temporal bone #1 was from a patient deaf since childhood and did not have measurable hearing. Word discrimination scores ranged from no response to 92%.

Most patients did not have documented symptoms consistent with EH in the clinical chart. However, temporal bone #6 was from a patient with documented episodes of vertigo and carried a diagnosis of Meniere's Disease.

Subanalysis of the temporal bones with intralabyrinthine schwannoma (TB #4 and #5) is detailed in Table 4. The tumor did not directly involve the endolymphatic duct or sac, but TB #6 (tumor in Scarpa's Ganglion) did have new bone formation involving the duct (the only possible mechanical source of EH identified). The ductus reuniens was unremarkable in these specimens except for the saccular membrane rupture in TB #4, which extended to the ductus reuniens. Tumor cells did appear to involve the basilar membrane in TB #4 and #5 (Figure 3). Ganglion cell counts were not significantly less than the unaffected ear, as seen in Table 4.

Discussion

The current study concurs with previous reports that EH may occur in the setting of VS.[6,7] Evaluation of patient symptoms related to EH is limited in this study because clinical charts did not all contain complete information about vestibular symptoms, fluctuating hearing and tinnitus. Subject 6 carried a diagnosis of Meniere's disease (MD) during her lifetime, with documented fluctuating hearing loss and episodes of vertigo. The diagnosis of MD in the setting of VS has been previously described,[16] and patients who meet the diagnostic criteria of MD based on the AAO-HNS Committee on Hearing and Equilibrium[17,18] have been considered to carry dual diagnoses. The association of EH in a subset of VS patients as detailed below raises the question of whether EH can occur as a result of changes in the inner ear related to the tumor.

Previous work on temporal bone histopathology of undisturbed VS was a combined effort of Massachusetts Eye and Ear Infirmary, University of Zurich, University of Minnesota, and the House Institute collections and demonstrated inner and outer hair cell loss and cochlear neuronal loss.[4] Endolymphatic hydrops was seen in 25% of temporal bones with VS in that study; all temporal bones with EH had cochlear hydrops and 4/7 demonstrated saccular membrane distention. The study found a decrease in pure tone average in the affected ear as compared to the ear contralateral to the tumor. This combined study excluded patients without measurable hearing and those with intralabyrinthine schwannomas. The current study adds to the literature as it demonstrates EH in the setting of intralabyrinthine VS.[19] Although the current study also used the NIDCD House Temporal Bone Collection, there was only one patient included in both studies.

Several different mechanisms have been proposed for the formation of EH in general, as well as in the setting of VS. Roosli et al demonstrated precipitate in the endolymph and perilymph of temporal bones with VS.[3] Cochlear precipitate in the setting of VS has been previously described histopathologically[20] as well as on MRI fluid-attenuated inversion recovery (FLAIR) images and is thought to relate to protein shed by the tumor.[21] Increased FLAIR signal in the cochlea has also been associated with decreased preoperative hearing levels in patients with VS. Interestingly, 5 of the 7 temporal bones with EH and VS from the above combined study demonstrated an increase in endolymphatic and perilymphatic precipitate.

In the current study, two of the three temporal bones with EH and VS had intralabyrinthine tumors involving the modiolus or the basal turn of the cochlea (TB #4 and #5). Another clinical review of 8 patients with intralabyrinthine tumors described a high rate of positional vertigo in these patients and attributed that symptom to mass effect on the cochlea.[22] It is unclear whether the higher rate of EH in the setting of VS in the current study (50%) is related to the higher rate of intracochlear tumors. Histopathologic review of temporal bones with intralabyrinthine tumors showed ganglion cell counts in these bones comparable to the contralateral unaffected ear. Interestingly, tumor cells appeared to involve the basilar membrane in these specimens (TB #4 and #5). If EH is, in fact, related to the presence of intralabyrinthine tumor, the mechanism of EH formation requires further investigation. Intralabyrinthine tumors might affect function of the endolymphatic sac,

which is involved in the homeostasis and fluid balance of the inner ear.[23] Temporal bones with intralabyrinthine tumors showed a mechanical source of EH only in TB #6, in which neoossification involved the endolymphatic duct. Disruption of the endolymphatic duct and sac is known to lead to EH,[24,25] and endolymphatic sac shunt and decompression, although controversial given histopathologic findings, remains a treatment option for patients with MD and intractable vertigo.[26] VS, and most certainly intracochlear VS, may disrupt intracochlear fluid balance by disruption of sac function.

Some authors have suggested that increased permeability of the blood-labyrinth barrier as a possible mechanism of EH in MD.[22] This mechanism could also be entertained for the formation of EH in the setting of intracochlear VS or VS proximal to the cochlea which could affect cochlear microcirculation.

Finally, some cases of secondary EH have been suggested to be a result of changes in cerebrospinal fluid (CSF) pressure[9] because perilymph is in continuity with CSF, although the underlying mechanism of this process has not been described.[27] This is also a possible mechanism for the formation of EH in the setting of VS.

Whatever the link is between EH and VS, the recognition of this association is important for patient care. Whether EH results from VS or they arise concurrently, treatment of EH may improve symptoms in these patients. Patients presenting with small VS and dizziness are often offered microsurgery for tumor excision as well as improvement of vestibular function.[28] The reasoning behind this treatment paradigm is that a patient will have improved function with a stable vestibular loss rather than fluctuating vestibular function related to the tumor.[29] In vertiginous patients with VS in whom EH is identified, medical management for MD may be considered. In fact, some authors have had successful vertigo control with diuretics.[6] Similarly, benign positional vertigo and migraine-related vertigo have been diagnosed and treated successfully in some patients with VS.[30]

The current study has several limitations. As mentioned previously, gathering clinical data in temporal bone specimens is limited by the completeness of the clinical chart. This is also a retrospective analysis which can lead to selection bias. Moreover, temporal bones are gathered more frequently in patients with significant otologic history—this may affect findings we see in temporal bones in subjects with occult VS because their temporal bones may have been pledged for study of other otologic complaints. Moreover, the small number of temporal bones included in the study allows a suggestion of a correlation of EH with VS but not a robust association. Whether the EH seen in this study is caused by VS or is only associated with VS in some cases, treatment of EH in the setting of VS may be successful. This could allow for tumor observation of small tumors and potentially to a longer period of useful hearing.[31] Despite progress made in imaging techniques,[6–8] temporal bone histopathology is still the most definitive method of evaluating EH. The histopathologic association of EH in untreated VS calls for further investigation of EH in patients with VS.

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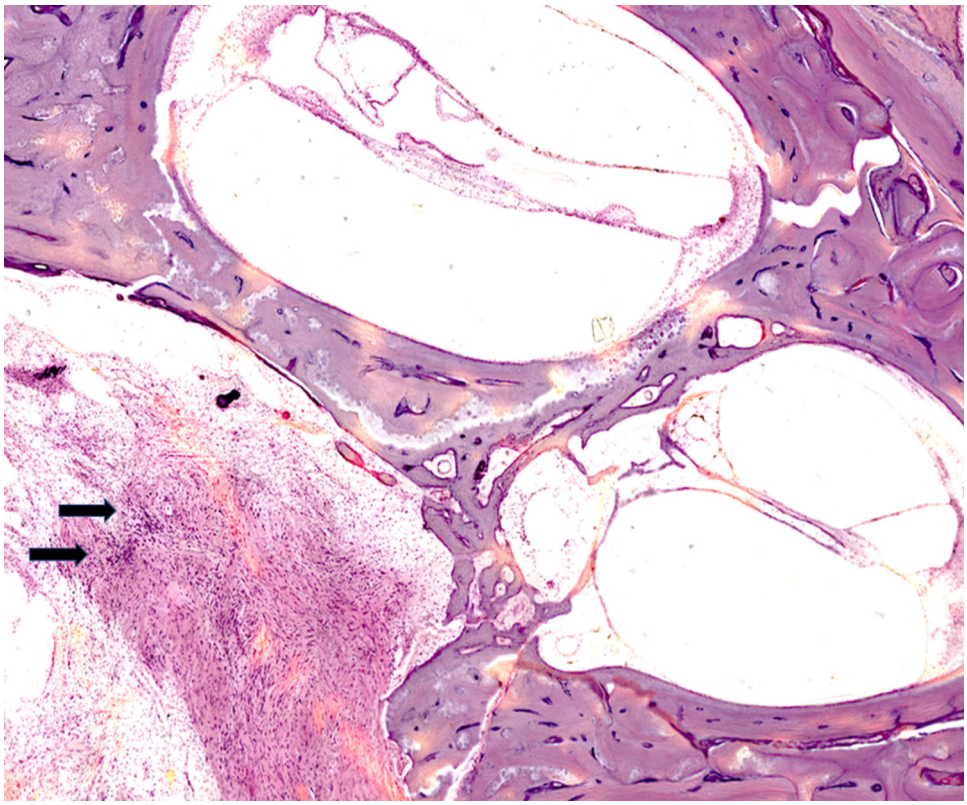
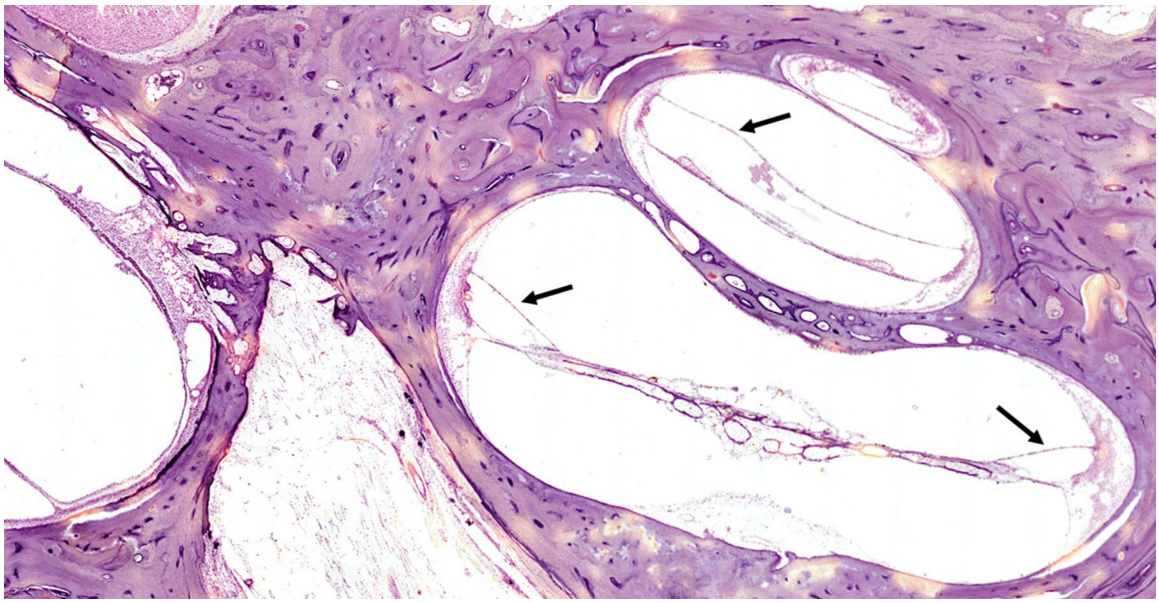




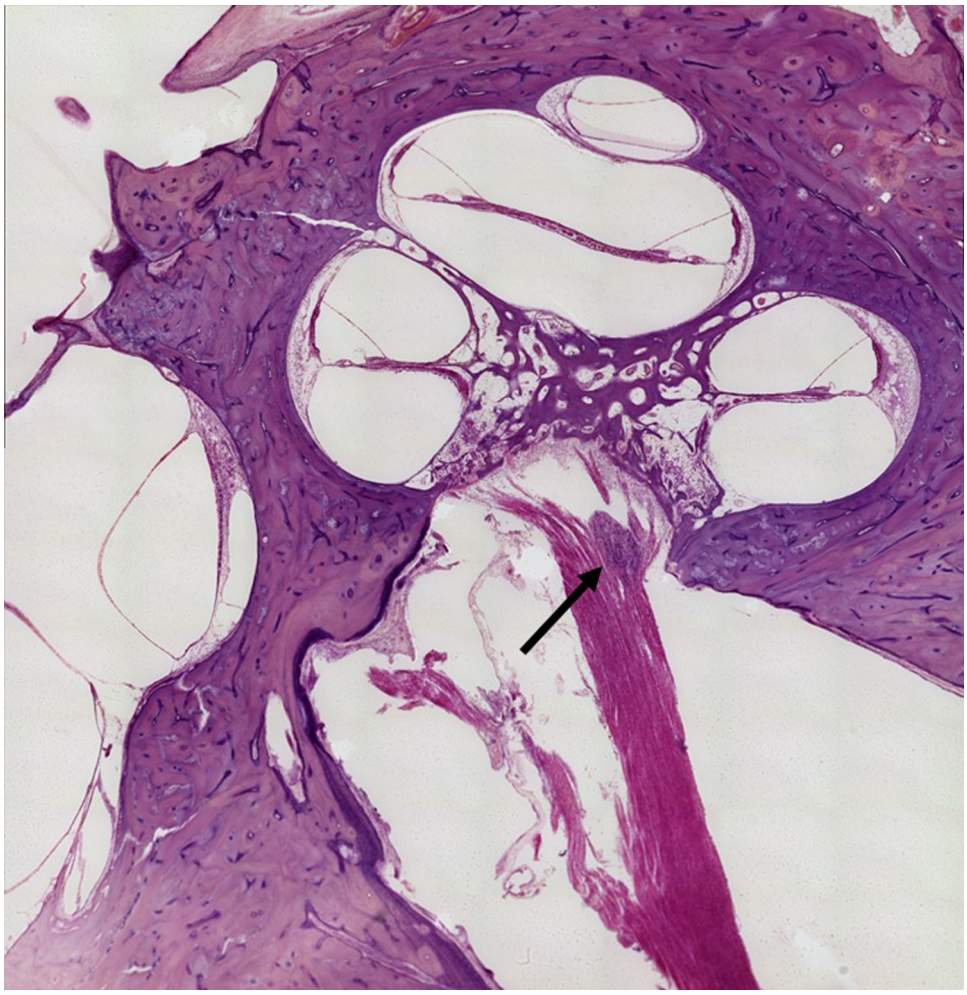
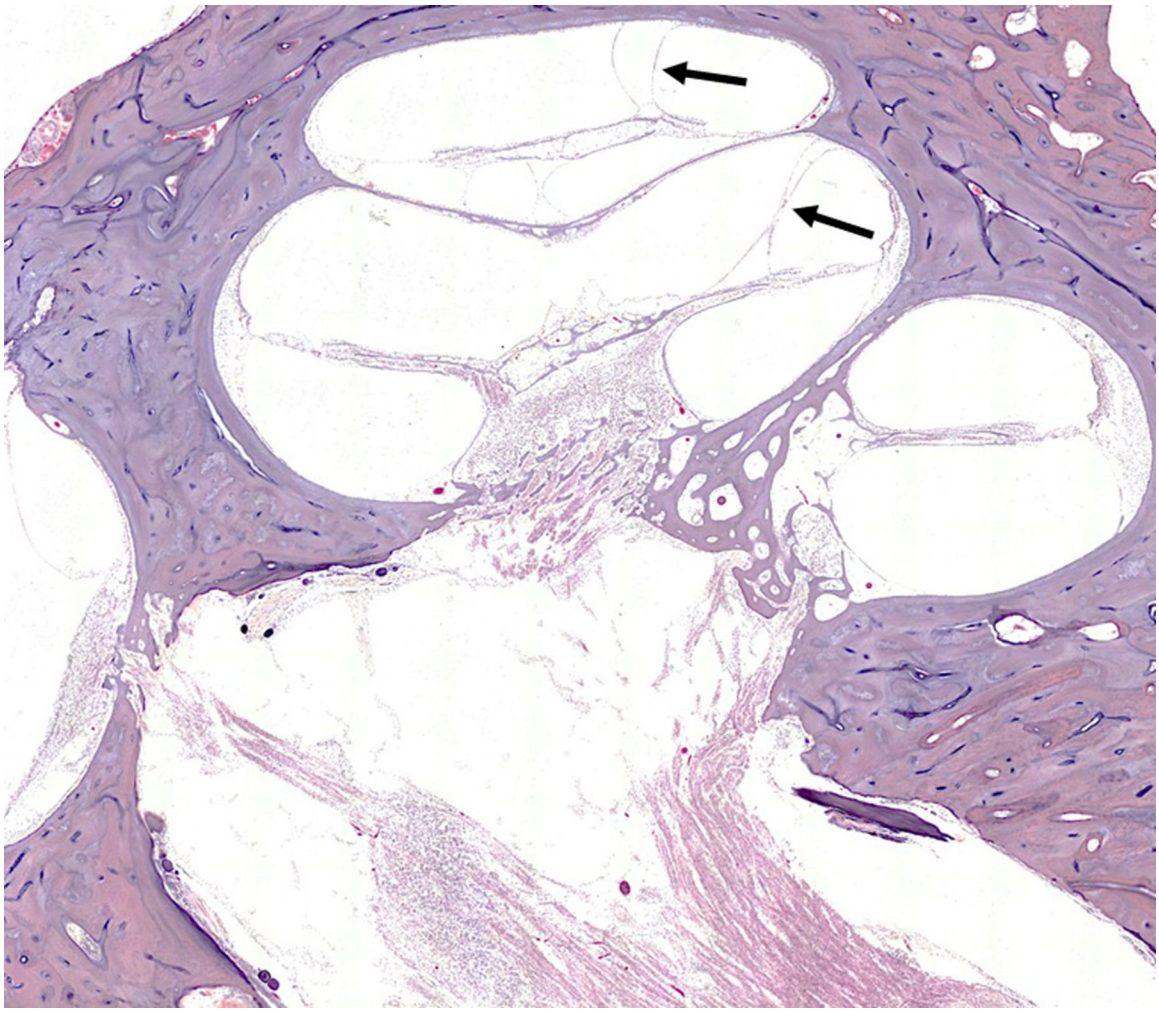
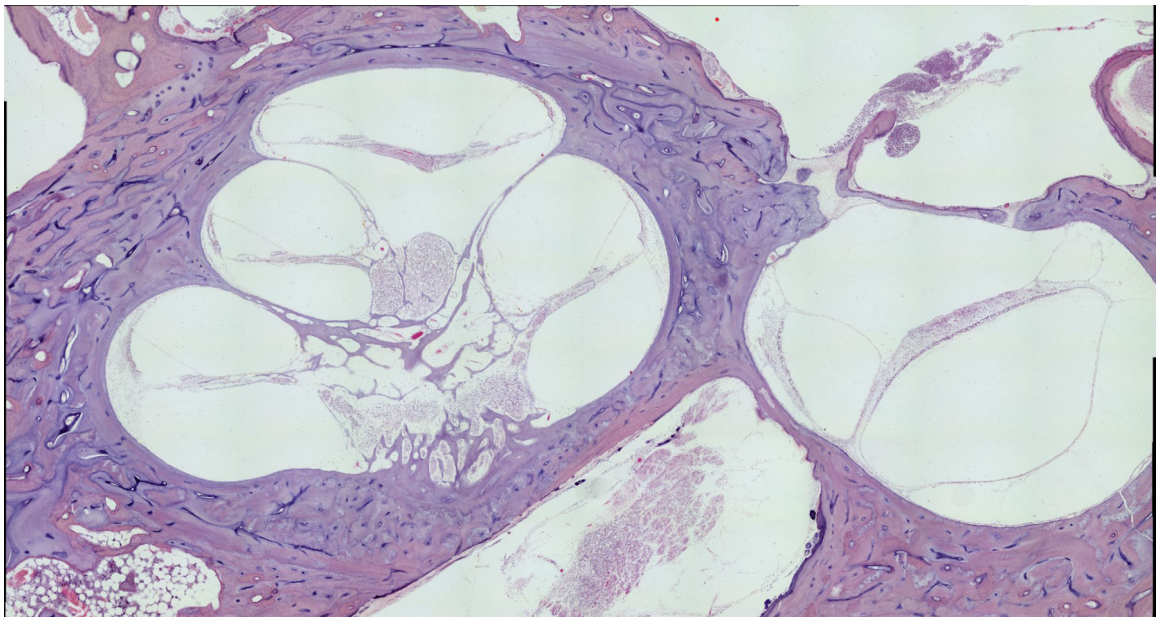


Figure 1A.
TB #1 showing tumor cells involving nerves in IAC (arrow). 1B) TB #1 demonstrating normal cochlea without EH (Reissner's membrane indicated with arrows). 1C) TB #3 with very small VS in IAC (arrow) and no EH.





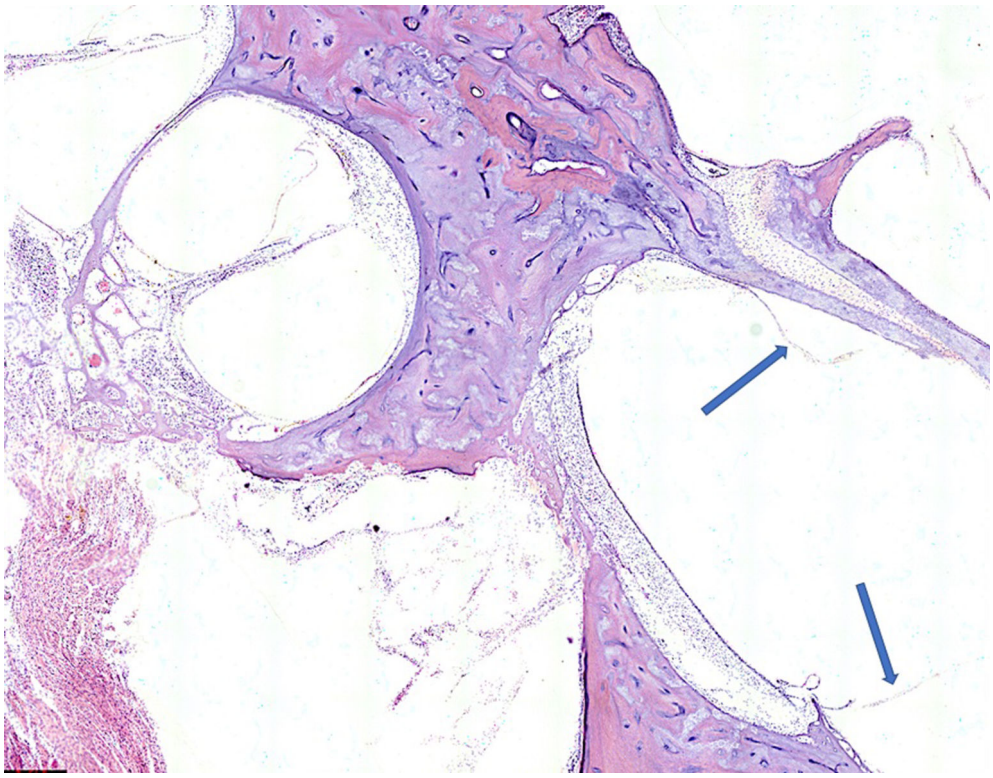


Figure 2A.
TB #6 showing cochlear hydrops with distention of Reissner's membrane. 2B) TB #6 showing contralateral non-tumor ear without EH. 2C) TB #5 demonstrating vestibular hydrops with the saccular membrane distended to abut the stapes footplate.

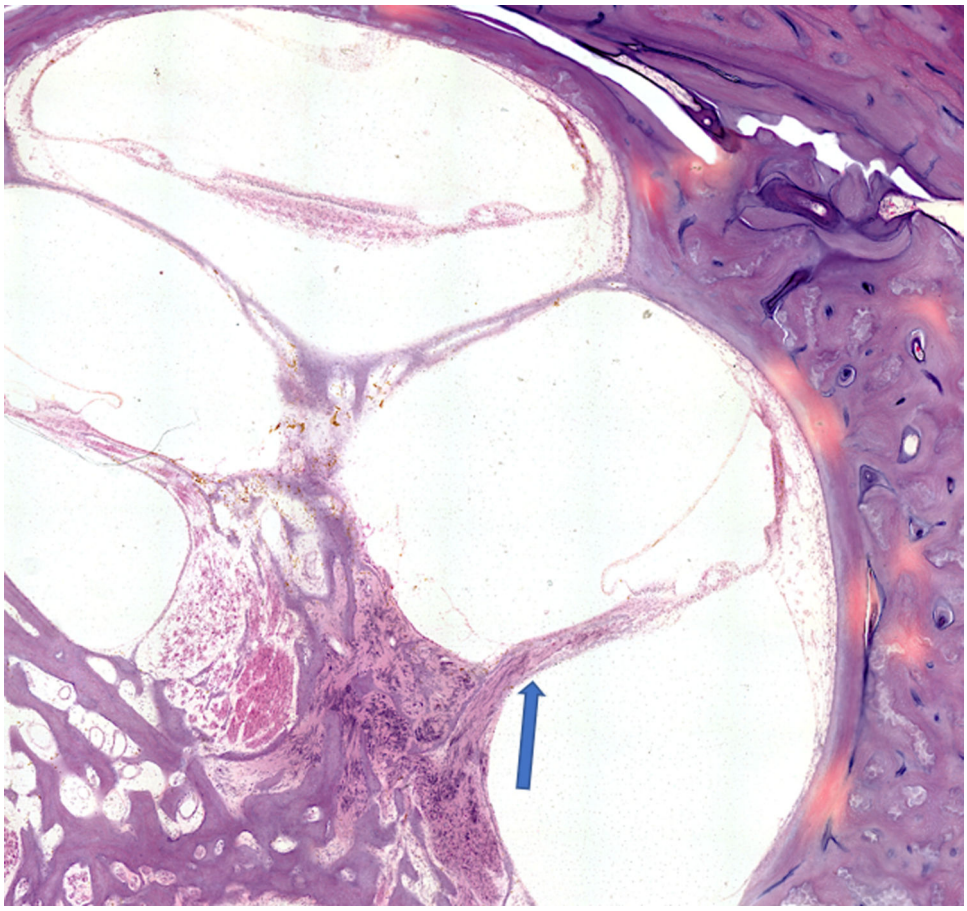


Figure 3.
TB #4 demonstrating tumor cells involving the basilar membrane (arrows).

Table 1.

Patient and Tumor Characteristics

TB#	Age at death	Sex	Tumor side	Tumor location
1	93	M	right	IAC
2	n/a	n/a	left	IAC
3	78	M	left	IAC
4	91	F	left	Modiolus
5	89	M	left	Scala tympani basal turn
6	94	F	right	Inferior Scarpa's ganglion

Table 2.

Endolymphatic Hydrops by Specimen Number

TB#	Basal turn	Middle turn	Apical turn
1	no	no	no
2	no	no	no
3	no	no	no
4	yes	yes	yes
5	yes	no	no
6	yes	yes	yes

Table 3.

Hearing Results by Specimen Number

TB#	PTA (dB)	SDS
1*	NR	n/a
3	43	92%
4	40	92%
5	87	36%
6	59	20%

Table 4.

Histopathology of Intralabyrinthine Schwannomas

TB#	Endolymphatic Duct/Sac	Ganglion Cell Count (GCC)	Contralateral GCC
4	Widened	20,548	16,623
5	Normal	8,425	12,396
6	Obstructed by neoossification	18,357	25,321