Published in final edited form as:

Otol Neurotol. 2016 August ; 37(7): 859–864. doi:10.1097/MAO.0000000000001094.

FOCAL ENDOLYMPHATIC HYDROPS AS SEEN IN THE PARS INFERIOR OF THE HUMAN INNER EAR

Joseph B. Nadol Jr., MD

Human Otopathology Laboratory, Department of Otolaryngology, Massachusetts Eye and Ear Infirmary, Harvard Medical School

INTRODUCTION

Endolymphatic hydrops may be defined as a pathological distention of the endolymphatic spaces of the pars superior (semicircular canals and utricle) and/or the pars inferior (sacculle and organ of Corti) of the inner ear. Hallpike and Cairns (1) and Yamakawa (2) reported the presence of endolymphatic hydrops in the inner ear of patients who had suffered Meniere's syndrome during life. Endolymphatic hydrops had been previously described by Wittmaack (3) as caused by labyrinthitis, and over the years it has been described in humans in a variety of disorders in addition to Meniere's syndrome including syphilis (4); polyarteritis (5); Cogan's syndrome (6); autoimmune inner ear disease (7,8); obstruction of the endolymphatic duct or sac by an endolymphatic sac tumor (9) or by otosclerosis (10); surgical trauma following cochlear implantation (11); or as a response to an unoperated acoustic neuroma (12).

Variation in the degree of hydrops in the cochlear and vestibular systems has been described (13, 14). Thus in the human, endolymphatic hydrops was more common in the pars inferior than in the pars superior, and the most severe hydrops as judged by the degree of distention of the endolymphatic compartment was found in the sacculle followed by the cochlea, utricle, and the three semicircular canals (14). The most severe hydrops in the human cochlear duct was described in the apical turn of the cochlea followed by the hook portion, the middle turn, and the basal turn (14).

Focal cochlear endolymphatic hydrops, that is hydrops limited to focal locations within the cochlear duct, was found in one case (case 19) of Okuno and Sando (14). In this case, endolymphatic hydrops was described in the apex and sacculle with collapse of Reissner's membrane in the middle and basal turns of the cochlea and no pathologic finding in the hook portion of the cochlea. The occurrence of focal apical endolymphatic hydrops was described by Yamashita and Schuknecht (15) in nearly 16% of 495 temporal bones, suggesting that apical hydrops alone has no pathologic or functional significance. In fact, Makarem et al (16) described hydrops limited to the most apical turn as "endolymphatic pseudohydrops" of the cochlear apex. These investigators attributed the appearance of hydrops limited to no more than the most apical four sections (80 micrometers) of the cochlea to be caused by a

transition of the shape of the cochlear duct from one that is conical at the very apex to a triangular shape in the lower apex and therefore not pathologic. Endolymphatic hydrops limited to the cochlear duct was also described by Lindsay and Von Schulthess (17) and Altmann et al (18), although focal endolymphatic hydrops limited to one portion of the cochlear duct was not mentioned in these descriptions. However, in a guinea pig model, in which endolymphatic hydrops was induced by obstruction of the endolymphatic duct, considerable variation of the cross sectional area of the scala media was seen with severe hydrops in the basal turn and transitioning to a near normal appearance in the second turn as evaluated by magnetic resonance microscopy (19).

The present study reports 13 human temporal bone specimens from the collection at the Massachusetts Eye and Ear Infirmary in which endolymphatic hydrops was located focally in the pars inferior.

MATERIALS AND METHODS

A computer-assisted search of all cases in which “endolymphatic hydrops” was found in the pars superior and/or pars inferior of the inner ear generated 225 cases with endolymphatic hydrops in one or both ears. Those cases in which endolymphatic hydrops was limited to the apical turn of the cochlea were excluded since they probably do not reflect pathology of the endolymphatic compartment (15, 16). All cases with endolymphatic hydrops limited to the pars inferior and demonstrating a focal distribution, that is some segments of the pars inferior showing endolymphatic hydrops whereas other segments of the pars inferior showed no evidence of hydrops, were included. This generated a list of 13 ears in which there was good evidence of focal endolymphatic hydrops of the pars inferior (cochlear duct and saccule) (Table 1). All temporal bones were fixed in formalin, dehydrated in graded alcohols, embedded in celloidin, and cut in an axial (horizontal) plane at a thickness of 20 micrometers. The semi-serial sections (every 10th section) of all 13 temporal bones were reviewed in order to generate the localization data reported herein.

In addition to ascertaining the localization of endolymphatic hydrops in the pars inferior, the sections were reviewed for evidence of a previous inflammatory process (such as fibrosis or new bone formation) that might be related to, or causative of, focal endolymphatic hydrops. The rationale for this search was the common association of endolymphatic hydrops with various inflammatory processes, such as syphilis, polyarteritis, Cogan’s syndrome, autoimmune inner ear disease, and trauma.

RESULTS

The demographic data for the 13 temporal bone specimens are presented in Table 1. Four specimens (5 and 6, 4 and 12) were generated from two temporal bone donors. In all of the remaining 9 specimens only one temporal bone was generated per donor. The localization of the focal hydrops in the pars inferior is shown in Figure 1. Endolymphatic hydrops of the saccule was present in 10 of the 13 specimens. In the remaining three specimens, the saccule was collapsed in one specimen (#2); in two others (specimens #3 and 4) there was no

endolymphatic hydrops in the saccule despite the presence of hydrops in at least part of the cochlear duct.

In areas of the cochlear duct in which there was no hydrops present, the transition between hydrops and no hydrops was often abrupt. For example, in specimen 1, hydrops was present in the cochlear duct and saccule with the exception of a small segment of the lower basal turn in which hydrops was absent (Fig. 1, 2A). In some specimens, the portion of the cochlear duct in which there was no hydrops was several millimeters in length (specimens #2, 3, 9, 11, and 13) while in another specimen (#12) only the apical turn and saccule demonstrated hydrops (Fig. 1). In one specimen (#8), only the apical turn was free of endolymphatic hydrops. In specimen #10, hydrops was limited to the saccule and mid-portion of the middle turn and apex of the cochlear duct while the base was completely free of hydropic change. In specimens #5, 6 and 7 massive hydrops was found in the saccule and hook portion of the cochlear duct only whereas the remainder of the cochlear duct demonstrated either no or minimal hydrops (Figs. 1, 2B).

There was no histologic evidence of obstruction of the endolymphatic duct or sac in the 13 specimens.

Inflammatory Change

Evidence for previous inflammation was found in 6 of 13 specimens (Table 1). The cause of this inflammation was idiopathic in three specimens (#5, 6 and 7) and was secondary to trauma in two (temporal bone fracture in specimen #11 (Fig. 3A) and traumatic stapedectomy in specimen #13), and one was attributed to an idiopathic sudden sensorineural hearing loss (#3). In the three specimens in which the cause of inflammation was idiopathic and progressive (#5, 6, 7), the inflammatory process was found at the labyrinthine surface of the stapes footplate adjacent to a ballooning saccular wall (Fig. 3B). In addition in one specimen (#5), the inflammatory change was seen not only at the stapes footplate but also in the hook portion of the cochlea and in the lower basal turn of Rosenthal's canal (Fig. 4A). Evidence of an inflammatory process was seen in the scala vestibuli of two specimens (#3 and #6) in the form of osteoid (Fig. 4B, 4C). When evidence of an inflammatory process was present, it was always located in the perilymphatic compartment and was frequently immediately juxtaposed to severe endolymphatic hydrops in the saccule or the cochlear duct, suggesting a possible causal relationship between the inflammatory process and the focal endolymphatic hydrops.

Prevalence of Vestibular Symptoms

Despite the presence of endolymphatic hydrops in all 13 specimens, in only 7 of 13 specimens (54%) were there any associated vestibular symptoms, and in no patients were the symptoms typical of Meniere's syndrome.

Etiology of Deafness

The etiology of deafness varied among the 11 donors of 13 specimens (Table 1). In one it was due to Alport's syndrome, in another to transverse temporal bone fracture, in another to otosclerosis with a traumatic stapedectomy, and in one to idiopathic sudden sensorineural

hearing loss. In one patient hearing loss was attributed to a viral labyrinthitis. In the remaining donors there was a progressive sensorineural hearing loss of idiopathic origin.

DISCUSSION

Pathogenesis of Endolymphatic Hydrops

One theory concerning the pathogenesis of endolymphatic hydrops posits obstruction of “longitudinal flow” of endolymph from the pars superior and from the pars inferior to the endolymphatic duct and sac where endolymph is presumably resorbed (20, 21, 22). Specifically for the pars inferior, it has been assumed that endolymph is produced all along the cochlear duct and that flow occurs via the ductus reuniens to the saccule, then to the utriculo-saccular duct, and finally to the endolymphatic duct and sac.

This theory is supported by animal models of endolymphatic hydrops in which obstruction of the endolymphatic duct (23) or of the ductus reuniens (24) resulted in endolymphatic hydrops. More recently the theory of longitudinal flow has been challenged by the observations of Salt and his co-workers (25, 26). These studies have suggested that homeostasis of the endolymphatic and perilymphatic spaces occurs all along the cochlear duct and is facilitated by aquaporin regulated water channels (27). This theory suggests that homeostasis of endolymph is largely controlled by a local ion transport mechanisms and that flow within the cochlear duct occurs only in rare situations (26, 28).

The findings of the current study suggest that the pathogenesis of endolymphatic hydrops, at least in these 13 cases, is unlikely to be due to a distal obstruction of flow such as in the ductus reuniens or endolymphatic sac, given the finding of focal occurrence of endolymphatic hydrops within the cochlear duct in these human cases.

These findings do not preclude a causal relationship between obstruction of the endolymphatic duct or sac, such as caused by tumor (9) or otosclerosis (10), and the presence of endolymphatic hydrops. However, the findings do suggest that the pathogenesis of endolymphatic hydrops cannot be attributed solely to interruption of longitudinal flow of endolymph (20-22).

The findings in this study are consistent with the findings of Salt et al (19) in which the cross-sectional area of the endolymphatic space in a guinea pig model of endolymphatic hydrops demonstrated abrupt transition from normal to an adjacent area of severe hydrops. Salt and co-workers (19) suggested that other factors such as variable distensibility of Reissner’s membrane or local solute homeostatic mechanisms, (29, 30) may cause wide variation in the degree of hydrops.

Focal Inflammatory Change in the Cochlea and Saccule

Of the 13 specimens with focal endolymphatic hydrops, in six there was histopathologic evidence of a focal inflammatory process. In 1 of these 6, the inflammatory change consisted of new bone and fibrous tissue secondary to temporal bone fracture; in one there was fibrosis following a traumatic stapedectomy. In the four remaining specimens, the cause of the inflammatory changes was idiopathic. Some of the inflammatory changes in these four

idiopathic cases was similar to that described in Meniere's syndrome, congenital syphilis, and suspected viral labyrinthitis (13, 14, 31). It is tempting to hypothesize that at least in these 6 cases, a focal inflammatory process during life was responsible for the development of endolymphatic hydrops. In support of this hypothesis is the fact that in all six specimens, evidence of focal inflammatory change was juxtaposed to an area of the saccule and/or cochlear duct with severe endolymphatic hydrops. The mechanism by which focal inflammation might produce an alteration in the fluid homeostasis of the inner ear is hypothetical. In all cases, the inflammatory change detected was in the perilymphatic space, and therefore osmotic forces due to a putative inflammatory increase in solute content in the perilymph would not be expected to create an expansion of the endolymphatic space. As an alternative hypothesis, disruption of the local physiologic water permeability mechanisms mediated by aquaporins should be considered (27).

Acknowledgments

Supported by: National Institute on Deafness and Other Communication Disorders (NIH: Grant #: U24DC013983)

BIBLIOGRAPHY

1. Hallpike C, Cairns H. Observations on the pathology of Meniere's disease. *J Laryngol Otol*. 1938; 53:523–654.
2. Yamakawa K. Über die pathologische Veränderungen bei einem Meniere-Kranken. *J. Otolaryngol Jpn*. 1938; 44:2310–2.
3. Wittmaack K. Hydrops labyrinthi (labyrinthitis serosa). In: Henke, F.; Lubarsch, O., editors. *Handbuch der speziellen pathologischen Anatomie und Histologie*. Springer, Berlin: 1926. p. 290–307.
4. Belal A Jr, Linthicum FH Jr. Pathology of congenital syphilitic labyrinthitis. *Am J Otolaryngol*. Feb; 1980 1(2):109–18. [PubMed: 7446834]
5. Gussen R. Polyarteritis nodosa and deafness. A human temporal bone study. *Arch Otorhinolaryngol*. 1977; 217:263–271. [PubMed: 21648]
6. Wolff D, Bernhard WG, Tsutsumi S, Ross IS, Nussbaum HE. The pathology of Cogan's syndrome causing profound deafness. *Ann Otol Rhinol Laryngol*. 1965; 74:507–520. [PubMed: 14325863]
7. McCabe BF. Autoimmune sensorineural hearing loss. *Ann Otol Rhinol Laryngol*. 1979; 88:585–589. [PubMed: 496191]
8. Schuknecht HF. Ear pathology in autoimmune disease. *Adv Otorhinolaryngol*. 1991; 46:50–70. [PubMed: 1681708]
9. Megerian CA, McKenna MJ, Nuss RC, Maniglia AJ, Ojemann RG, Pilch BZ, Nadol JB Jr. Endolymphatic sac tumors: Histopathologic confirmation, clinical characterization, and implication in von Hippel-Lindau Disease. *Laryngoscope*. 1995; 105:801–808. [PubMed: 7630290]
10. Yoon TH, Paparella MM, Schachern PA. Otosclerosis involving the vestibular aqueduct and Meniere's disease. *Otolaryngol Head Neck Surg*. 1990; 103(1):107–12. [PubMed: 2117717]
11. Handzel O, Burgess BJ, Nadol JB Jr. Histopathology of the peripheral vestibular system after cochlear implantation in the human. *Otol Neurotol*. 2006; 27:57–64. [PubMed: 16371848]
12. Mahmud MR, Khan AM, Nadol JB Jr. Histopathology of the inner ear in unoperated acoustic neuroma. *Ann Otol Rhinol Laryngol*. 2003; 112:979–986. [PubMed: 14653368]
13. Antoli-Candela, F, Jr. *Acta Otolaryngol*. Stockh: 1976. The histopathology of Meniere's disease; p. 1–42. suppl 340
14. Okuno T, Sando I. Localization, frequency, and severity of endolymphatic hydrops and the pathology of the labyrinthine membrane in Meniere's disease. *Ann Otol Rhinol Laryngol*. 1987; 96:438–445.

15. Yamashita T, Schuknecht HF. Apical endolymphatic hydrops. *Arch Otolaryngol.* 1982; 108:463–466. [PubMed: 7103821]
16. Makarem A, Fayad JN, Linthicum FH. Endolymphatic pseudohydrops of the cochlear apex. *Otol Head Neck Surg.* 2010; 143(2):269–273.
17. Lindsay, JR.; Schulthess, GV. *Acta Otolaryngol.* Vol. 49. Stockh: 1958. An unusual case of labyrinthine hydrops; p. 315-324.
18. Altmann F, Fowler EP Jr. Histological findings in Meniere's symptom complex. *Ann Otol Rhinol Laryngol.* 1943; 52:52–80.
19. Salt AN, Herison MM, Gerwalt SL, Keting AW, DeMott JE, Henson OW Jr. Detection and quantification of endolymphatic hydrops in the guinea pig cochlea by magnetic resonance microscopy. *Hear Res.* 1995; 88:79–86. [PubMed: 8576007]
20. Guild SR. The circulation of the endolymph. *Am J Anat.* 1927; 39:57–81.
21. Schuknecht HF, Ruther A. Blockage of longitudinal flow in endolymphatic hydrops. *Eur Arch Otorhinolaryngol.* 1991; 248(4):209–17. [PubMed: 1859653]
22. Paparella MM, Djalilian HR. Etiology, pathophysiology of symptoms, and pathogenesis of Meniere's disease. *Otolaryngol Clin North Am.* Jun; 2002 35(3):529–45. [PubMed: 12486838]
23. Kimura RS, Schuknecht HF. Membranous hydrops in the inner ear of the guinea pig after obliteration of the endolymphatic sac. *Pract Otorhinolaryngol.* 1965; 27:343–354.
24. Kimura RS, Schuknecht HF, Ota CY, Jones DD. Obliteration of the ductus reuniens. *Acta Otolaryngol.* 1980; 89(3-4):295–309. [PubMed: 6967248]
25. Salt AN, Thalmann R, Marcus DC, Bohné BA. Direct measurement of longitudinal endolymph flow rate in the guinea pig cochlea. *Hear Res.* 1986; 23:141–151. [PubMed: 3745017]
26. Salt AN. Regulation of endolymphatic fluid volume. *Ann NY Acad Sci.* Oct.2001 942:306–12. [PubMed: 11710472]
27. Eckhard, Muller M, Salt A, Smolders J, Rask-Andersen H, Lowenheim H. Water permeability of the mammalian cochlea: functional features of an aquaporin-facilitated water shunt at the perilymph-endolymph barrier. *Arch Eur J Physiol.* 2014; 466:1963–1985.
28. Salt AN, DeMott J. Longitudinal endolymph flow associated with acute volume increase in the guinea pig cochlea. *Hear Res.* May; 1997 107(1-2):29–40. [PubMed: 9165344]
29. Salt, AN.; Thalmann, R. Cochlear fluid dynamics. In: Jahn, AF.; Santos-Sacchi, JR., editors. *Physiology of the Ear.* Raven Press; New York: 1988. p. 341-357.
30. Salt AN, Ohyama K. Accumulation of potassium in scala vestibuli perilymph of the mammalian cochlea. *Ann Otol Rhinol Laryngol.* 1993; 102:64–78. [PubMed: 8420472]
31. Nadol JB Jr. Positive fistula sign with an intact tympanic membrane. Clinical report of three cases and histopathological description of vestibulofibrosis as the probable cause. *Arch Otolaryngol.* 1974; 100:273–278. [PubMed: 4547272]

Fig. 1.
Focal localization of endolymphatic hydrops in the 13 specimens. In 3 cases (#5, 6, 7) there were segments of the cochlear duct with minimal to no hydrops indicated by a low profile blackened region.

Fig. 2A.
Specimen #1. Endolymphatic hydrops was present throughout (hollow arrows) the cochlea except in a short segment of the basal turn (solid arrow).

Fig. 2B.
Specimen #6. Endolymphatic hydrops was severe in part of the basal turn but absent in an adjacent segment of the basal turn. The boxed area is seen at higher magnification in Figure 4C.

Fig. 3A.
Specimen #11. Transverse fracture (Fx) of the temporal bone through the vestibule. There was endolymphatic hydrops of the saccular wall (SW), in basal end of the cochlea, and in the apical turn.

Fig. 3B. Specimen #6. Evidence of previous inflammation included deposition of fibrous tissue and osteoid (O) between the ballooned saccular wall (SW) and the footplate (FP).

Fig. 4a.
Specimen #5. There was endolymphatic hydrops of the saccule and proximal basal turn. Within Rosenthal's canal innervating the basal turn there was evidence of previous inflammation in the form of deposition of osteoid (O).

Fig. 4b.

Specimen #3. There was a history of idiopathic sudden sensorineural hearing loss. There was endolymphatic hydrops (hollow arrows) in the apical half of the cochlea and none (solid arrow) in the basal half or in the saccule. There was evidence of a previous inflammatory process consisting of prominent deposition of osteoid (O) in the scala vestibuli of the basal and middle turns.

Fig. 4c.

Specimen #6. Higher magnification of the boxed area seen in Fig. 3. There was significant endolymphatic hydrops of the basal turn with evidence of a previous inflammatory process consisting of deposition of osteoid (O) in the perilymphatic space of the scala vestibuli.

TABLE 1

Demographics in 13 Human Specimens with Focal Endolymphatic Hydrops

Specimen # Ear (L, R)	Age M/F	Cause of Hearing Loss	Vestibular Symptoms Y/N	Evidence for Inflammatory Process
1 (L)	76 F	Idiopathic	Yes	None
2 (L)	78 M	Idiopathic	No	None
3 (R)	94 F	Idiopathic Sudden Sensorineural	Yes	Osteoid in scala vestibuli
4 (R)	50 M	Alport's Syndrome	No	None
5 (R)	91 F	Idiopathic, progressive	Yes	Saccular wall at footplate cochlear duct & Rosenthal's canal (hook)
6 (L)	91 F	Idiopathic, progressive	Yes	Saccular wall at footplate
7 (R)	70 F	Idiopathic, progressive	No	Saccular wall at footplate; osteoid in scala vestibuli
8 (R)	83 M	Idiopathic, progressive	Yes	None
9 (L)	83 F	Idiopathic, progressive	No	None
10 (R)	35 M	"Viral Labyrinthitis"	No	None
11 (R)	68 M	Transverse Temporal Bone Fracture	Yes	New bone and fibrous tissue at fracture site
12 (L)	50 M	Alport's Syndrome	No	None
13 (L)	72 F	Otosclerosis	Yes	Fibrosis in Vestibule (Traumatic Stapedectomy)