CASE REPORT

Perisaccular Vascular Obstruction During an Acute Attack of Meniere's Disease

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OBJECTIVE: To shed some light on the morphological findings underlying the occurrence of Meniere's attack.

MATERIALS AND METHODS: An endolymphatic sac sample was taken during ablation surgery from a patient who was experiencing a disabling stage with recurrent vertigo attacks from Meniere's disease. The sample consisted of the most proximal extraosseous portion of the ES, including both walls. The specimen was sent to Transmission Electron microscopic examination and the analysis was in particular focused on the subepithelial region.

RESULTS: No evidence of epithelial damage was observed, and the sample showed signs of high metabolic activity in all cellular components. The most striking findings were found at the level of the subepithelial space, where diffuse signs of vascular thrombosis were identified. The intravascular occlusion was variously represented by sludged erythrocytes and an amorphous, lipid-like material.

CONCLUSION: The occlusion of perisaccular vessels might be regarded as a pathognomonic finding, concurring to the manifestation of acute Meniere's disease.

The pathogenesis and treatment Meniere's disease (MD) are still unknown. Although endolymphatic hydrops (EH) has long been regarded as the pathologic hallmark of MD[1,2], the correlation of EH with either the clinical stages of MD (acute crisis, recurrence, natural course of the disease) or various morphologic features of the endolymphatic sac (ES) has not been established.

All the functional roles (pressure and volume regulation[3], immunomodulation[4], and local secretion of glycoproteins[5]) attributed to the ES within the inner ear environment converge on the key function of endolymph absorption[6]. As a result, this nonsensory, functional pole of the inner ear has been the focus of past and recent surgical and experimental studies. Surgery using a variety of techniques has long been the treatment of choice for providing relief from the effects of excess endolymphatic volume[7-9]. Despite some controversy in the late 1980s[10], ES surgery is still suggested as the first surgical option for the treatment of MD-induced incapacitating vertigo.

In this report, the ultrastructural findings of a surgically ablated ES in a patient with impending intractable vertigo attacks are presented, and the morphologic changes in that organ are correlated with the effects of active disease.

MATERIALS AND METHODS

A relatively large specimen (8 _ 12 mm) from the extraosseous portion of the ES was obtained from a patient with MD who underwent ES removal during a symptomatic period of disease. This 46-year-old male patient had a 5-year history of MD that had proven refractory to medical treatment based on a low-salt diet and diuretic therapy. An audiogram revealed a flat 55 PTA threshold with a 100% speech discrimination score, the results of a depletive test were positive, and electrocochleography (EcochG) showed a pattern with an SP/AP ratio greater than 0.51[11]. The patient's persistent vertigo of 3 months' duration, which was manifested in 2 to 3 violent vertiginous episodes per week, prompted us suggest surgical treatment (ES ablation). The patient agreed, and that procedure was performed as follows: After wide exposure of the posterior cranial fossa dura, the anatomic region of the ES was identified, and the exit site of the ES from the operculum (ie, the entrance to the extraosseous interface; Figures 1, a and b) was noted. Both walls of the extraosseous ES were then cut in a single piece with microscissors at the level of the operculum. The specimen was immediately fixed in phosphate-buffered 2.5 % glutaraldehyde, was immersed for 24 hours, and was then routinely processed for examination via transmission electron microscopy (TEM). Ultrathin transversely cut sections were observed and photographed with a Morgagni Transmission Electron Microscope (Philips, Eindhoven, The Netherlands).

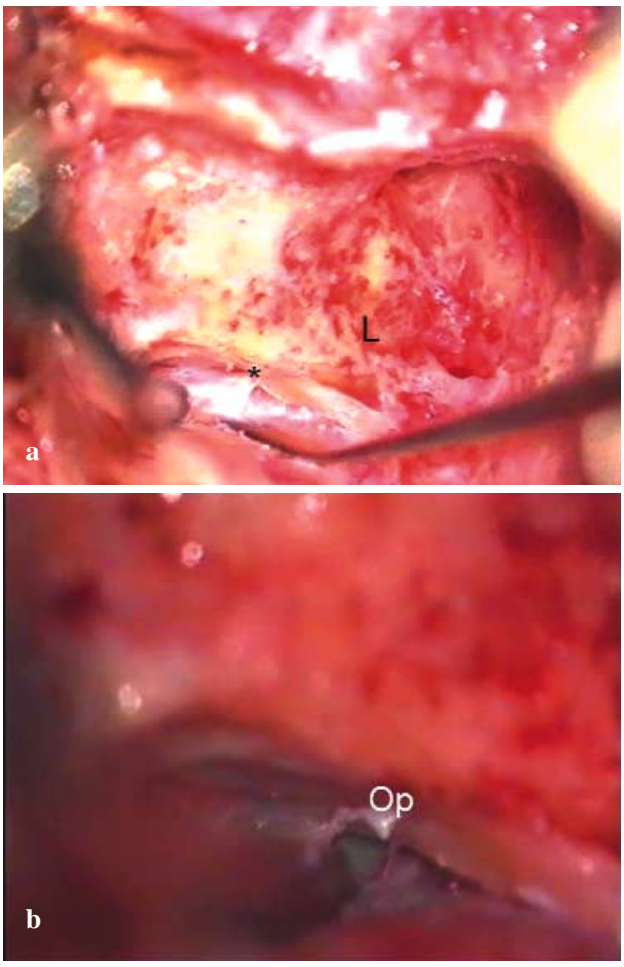

Figure 1, a and b: Left endolymphatic sac surgical ablation. a) The posterior cranial fossa dura and the labyrinthine block (L) have been exposed. The endolymphatic sac (asterisk) projects from the operculum opening. b) At a higher magnification, it is possible to visualize the ES stump (Op) after the intraosseous-extraosseous interface region has been cut.

RESULTS

A tubular epithelial structure lined by flat-to-cuboid cells was identified (Figure 2). Against the background

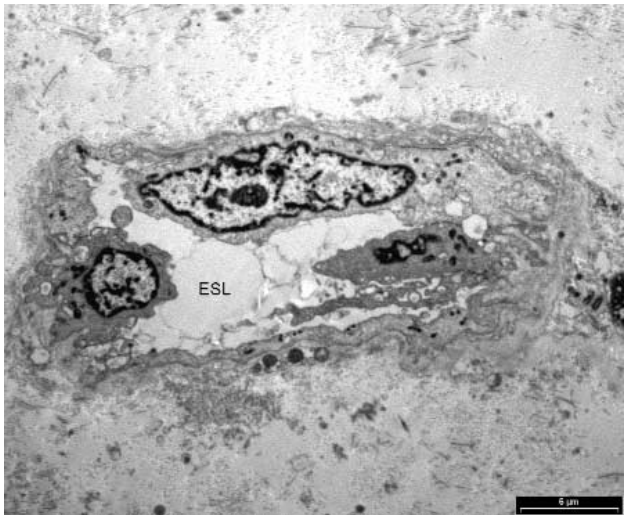

Figure 2: An electron micrograph of the extraosseous portion of a human ES. Note the small tubular structure with a flat-to-cubic epithelial layer that faces the endolymphatic lumen (ESL).

of cytoplasmic content, the epithelial cells were visible as light-stained or dark-stained cells. Regardless of cytoplasmic staining, those cells were shown to contain several mitochondria with compressed cristae that were located primarily at the basocellular level, and fibrillar content and small vacuoles prevailed at the apical cellular level (Figure 3). The nucleus of the epithelial

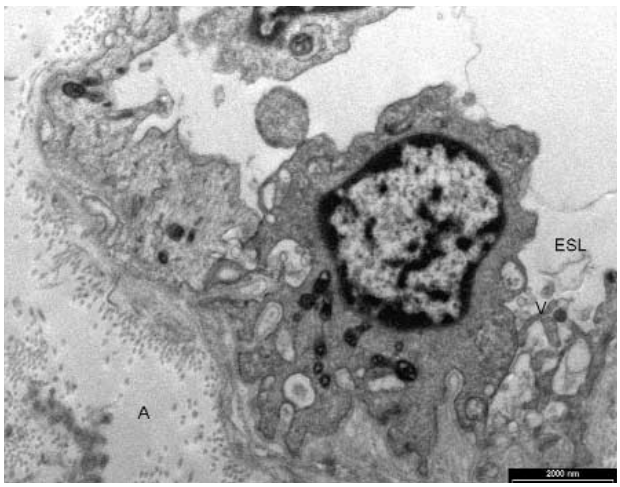

Figure 3: Left inset of Figure 2. A dark-stained epithelial cell with many compressed mitochondria at the basocellular level. The subepithelial region appears to contain amorphous material (A) that separates multiple bundles of collagen fibers. Note the villous formations (V).

cells showed the accumulation of euchromatin in both cell types. Villous formations with slightly dilated lateral intercellular spaces were also identified near multiple intercellular junctions (Figure 4). A thin, continuously intact basal lamina was also noted.

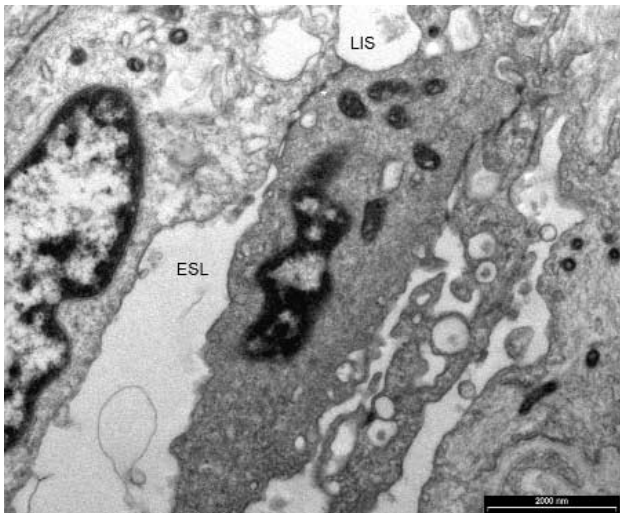

Figure 4: Right inset of Figure 2. Dilated lateral intercellular spaces (LIS) are noticed near multiple cell junctions (white asterisk).
ESL, Endolymphatic sac lumen.

At the subepithelial level, variously oriented collagen fibers were abundantly represented within a loose, areolar subepithelial tissue. Large areas of accumulated amorphous material caused the separation of bundles of collagen fibers, which were pushed toward the basal lamina (Figure 4). Diffuse signs of vascular thrombosis were also observed. The vascular lumen of the vessels surrounding the ES epithelial tubule appeared to be obstructed by sludged erythrocytes and an amorphous, lipid-like material (Figure 5). Other vessel-like structures demonstrated complete endoluminal occlusion caused by an accumulation of amorphous material and waste products (Figure 6).

DISCUSSION

An intraoperative biopsy enables the thorough study of inner ear morphology that may reveal unknown aspects of labyrinthine disorders[12]. To date, knowneldge about the several issues related to MD is scanty, including the relationships between MD and the

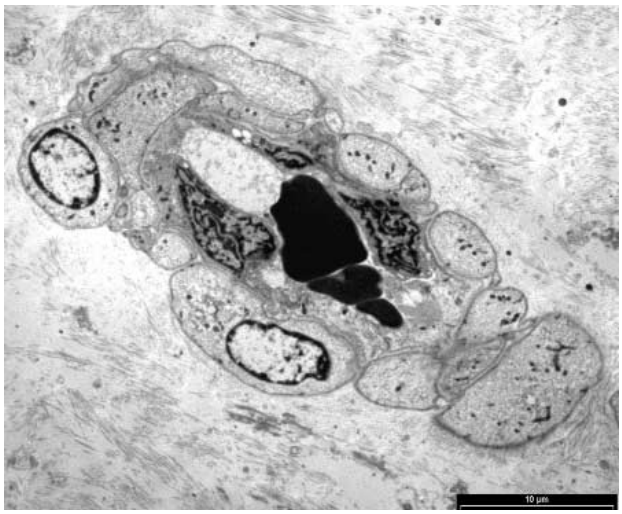

Figure 5: ES human subepithelial tissue. A small vessel appears to be totally occluded by sludged erythrocytes and an amorphous material. The surrounding connective tissue appears loose and contains collagen bundles of differing orientations.

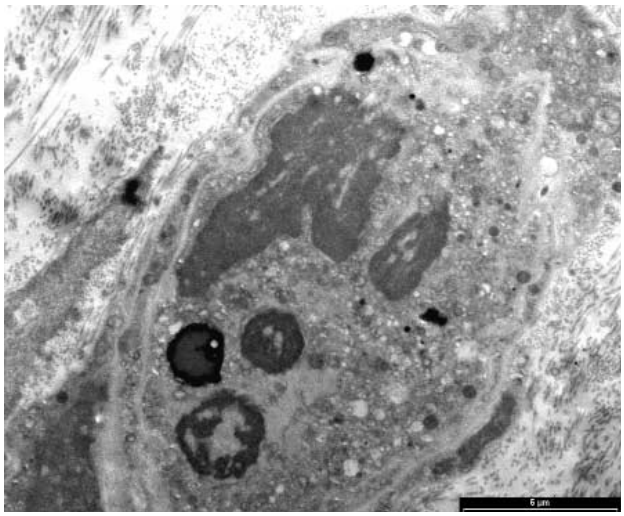

Figure 6: ES human subepithelial tissue. A capillary vessel is totally occluded by amorphous material. A thrombus-like formation is also evident.

ES (which has often been the subject of ultrastructural investigation). ES biopsies have been performed during major otoneurosurgical procedures[13] as well as during ES surgery[14]. From an anatomic point of view, a translabyrinthine or transpetrosal approach enables the excision of portions of both the extraosseous and the intraosseous ES and duct in an intact single piece encased in a tiny shell of bone. A slightly longer than usual time is required for that surgical dissection[15], which ensures that the intermediate and proximal ES portions (where water and ionic exchange and absorption are thought to primarily occur) are included in the sample[16], although in this circumstance intraoperative removal is carried out in non menieric patients. A biopsy during ES surgery, however, is usually performed in the extraosseous portion to prevent damage to the inner ear. The material obtained via biopsy usually depends on the type of ES surgery: the lateral aspect of the extraosseous ES portion is biopsied during ES shunt surgery, and both ES walls are biopsied in cases of ES ablation[17] or unidirectional valve shunt surgery[18]. When both ES walls are included in the specimen, information pertaining to the unknown aspects of ES-related inner ear disorders, such as MD, is likely to be revealed because the luminal space is usually represented.

In a study by Gibson, the ES biopsy was performed during the ablation procedure[17]. This same technique has been applied in this study on a patient for whom, on the grounds of his clinical picture, an acute, hydropic, fluctuating stage of the disease could be suggested.

EH is considered to be the most reliable pathologic sign of MD, and although different degrees of EH severity have been described in experimental animals[19], little is known about the correlation of EH severity and the duration and/or stage of MD.

In our patient, the ES had a rounded, tubular shape and a diameter of about 25 μm. Whether this diameter coincides with the whole ES lumen or with 1 of the canaliculi[20] cannot be ascertained due to the extreme variability that ES usually shows in size and location. That size is, however, characteristic of a small ES, which has been associated with a poorly pneumatized mastoid and little absorptive capability[5, 21].

Various morphologic features of the ES region can contribute to the development of inner ear disorders (such as EH), which jeopardize the fluid environment of the inner ear. Although in our patient the ES lumen appeared empty except for some unspecific waste products, the epithelial cell layer, in which both light-stained and dark-stained cells were identified, was characterized by signs of intense activity indicated by

the mitochondrial shape and location. We concluded that in our patient, longstanding MD did not cause major damage to the ES as a whole. The lack of intraluminal ES precipitate further supports the presence of EH, which has been shown to increase the enzymatic degradation of the homogenous substance normally produced into the ES lumen[22].

The most interesting findings of our study were found in the subepithelial ES region. It is well known that pinocytotic vesicles in the epithelial dark-stained cells, enlarged lateral intercellular spaces, "leaky" intercellular junctions, and fenestrated capillaries are required to ensure the proper absorption of endolymph[23, 24]. The vascular system is represented primarily at the level of the distal ES portion, where the ES capillaries originate in the branches of the posterior meningeal artery and the ES venules drain into the adjacent sigmoid sinus[25, 26].

In our sample, we found partial or total occlusion of the perisaccular vessels, as have other authors in their research[27]. The occlusion was not uniformly distributed. In some vessels, the occlusive material consisted only of sludged erythrocytes, and in others, a lipid-like material was either prevalent in or was the sole cause of the thromboid occlusion. Whether the occlusion of the ES vasculature was a cause or an effect of EH, of the clinical stage of MD, or of any other factor remains a matter of speculation.

We believe that the following dynamics may have occurred in the ES region of our patient. The positive EcochG pattern and the patient's medical history suggest the presence of EH (it is impossible to obtain cochlear morphologic material from a living human). In an individual with those pathologic characteristics, increased functional activity of the ES is likely to occur in an attempt to maximize the absorption of excess endolymph. Although that activity is known to take place primarily in the endolymphatic duct and the proximal portion of the ES[23], even the extra-osseous ES sample in our patient revealed remarkable findings. No major signs of ES damage were recorded in our patient. In fact, the flat-to-cuboid epithelial cell layer typical of the ES region appeared intact, and a high level of mitochondrial activity was revealed in both light-stained and dark-stained cells. The presence of villous formations and the wide area of surface contact between the ES epithelium and the ES lumen support the theory of the active absorption of excess endolymph in our patient. The same wide area of contact was also observed between the abluminal epithelial cell layer and the underlying subepithelial tissue, and a normally thin and intact basal lamina ruled out the previously described ES inflammatory process during the acute phase of MD[28]. The loose aspect of the ES subepithelial space appeared to be somewhat distorted by the accumulation of dense, amorphous material, and collagen fibers had been pushed toward the basal lamina. An anatomofunctional barrier, which had been created between the epithelial layer and the perisaccular vascular network, revealed the most striking alterations of the whole specimen: All the vessels had been more or less affected by endoluminal subtotal or total occlusion. ES ischemia has been reported to cause EH in experimental animals[29], but to our knowledge whether EH or ES vascular occlusion develops first remains unknown. ES perisaccular thrombosis did not seem to be caused by other factors such as temporal bone drilling or sample dissection, because these factors have been ruled out when ES samples from non menieric patients were reported[27]. The occluding material found in our ES specimen varied in amount and type: The thrombus-like formation shared the luminal space with sludged erythrocytes in some vessels, and in others, it was the only endoluminal component. The same findings were described after an experimentally induced hyperosmolar condition[30]. It is difficult to say whether such a variability of endoluminal content would stand for a dynamic condition somewhat in relationship with the hydropic, fluctuating stage found in the patient of the present study. On the basis of previous, though scanty, data in the literature, it is possible to conclude that perisaccular vascular occlusion is a major ultrastructural finding in patients with MD. Further studies are needed to establish whether perisaccular vascular occlusion is a key sign in acute MD crisis.

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