Background: Auditory and vestibular symptoms and signs are common in patients with migraine, yet little is known about the pathogenesis of these symptoms and signs.

Objective: To perform clinicopathological correlation in a patient with migraine, sudden deafness, and delayed endolymphatic hydrops.

Methods: A patient with long-standing migraine with aura developed sudden hearing loss in the left ear at the age of 50 years and Meniere disease on the right side at age 73. At age 76, he had a flurry of sudden drop attacks typical of oto-lithic crisis. He died of unrelated causes at age 81. The brain and temporal bones were removed approximately 24 hours after death. The cochlea and vestibular end organs were dissected after the surrounding bone was carefully removed.

Results: The brain and cerebrovasculature were normal. The left cochlea showed prominent fibrosis consistent with an old infarction. The right inner ear showed hydrops, with relatively good preservation of the hair cells in the cochlea, saccular macule, and cristae of the semicircular canals. However, the utricular macule was denuded of hair cells.

Conclusions: The sudden left-sided deafness likely resulted from ischemia, possibly due to migraine-associated vasospasm. Presumably, the right ear suffered only minimal damage when the patient was 50 years old, but this damage later led to the development of delayed endolymphatic hydrops on the right. Otolithic crises are thought to result from pressure changes across the utricular macule. We speculate that loss of hair cells in the utricular macule resulted from a collapse of the utricular membrane onto the macule.

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Migraine is a common disorder whose most readily recognized manifestation is headache. However, many patients with migraine also suffer from episodic vertigo. Infrequently, episodic vertigo may even be the only manifestation of migraine (a migraine equivalent). Although auditory symptoms are generally considered to be less common than vestibular symptoms with migraine, migraine can cause fluctuating low-frequency hearing loss and sudden deafness. Vasospasm of labyrinthine arteries might explain all of these inner ear symptoms.

Delayed endolymphatic hydrops occurs in patients with long-standing unilateral profound hearing loss. Presumably, minor damage to the endolymphatic sac at the time of the deafness leads to impaired endolymphatic resorption and the development of hydrops years later. Schuknecht et al noted that hydrops often develops in the ear that is contralateral to the deaf ear and speculated that a systemic viral infection could cause the deafness and subclinical damage to the endolymphatic sac in either ear. Some patients with delayed endolymphatic hydrops manifest dramatic drop attacks that are thought to result from sudden pressure changes across the oto-lithic receptors (otolithic crises). However, to our knowledge, inner ear abnormalities have not been reported in such patients.

We present a clinicopathological correlation in a patient with life-long migraine with aura but without other vascular risk factors who developed sudden deafness in his left ear at the age of 50 years. Twenty-three years later, he developed endolymphatic hydrops in his right ear, along with typical oto-lithic crises. Based on the findings, we propose that migraine-associated vasospasm caused the sudden deafness in the left ear and the subclinical damage to the endolymphatic sac in the right ear, predisposing to the development of delayed endolymphatic hydrops. A severe loss of hair cells in the utricular macule on the right side probably resulted from collapse of the utricular membrane onto the macule.

REPORT OF A CASE

The patient first began having episodes of migraine with aura at the age of 15 years. He described a classic scintillating scotoma typically beginning in the right visual field and gradually evolving over about 20 minutes, followed by a left-sided throb-
bing headache with nausea and vomiting. These episodes occurred at irregular intervals throughout his life and were commonly triggered by stress, an irregular diet, or lack of sleep. At age 50, he had the sudden onset of profound hearing loss in his left ear that was unassociated with vertigo or any other neurological symptoms. He was given a trial of high-dose steroids, without benefit, and the profound hearing loss remained unchanged throughout the remainder of his life. At age 73, he began having episodes of vertigo, typically lasting 2 to 3 hours and initially unrelated to any auditory symptoms. However, after having several isolated attacks of vertigo, he began noticing a sense of plugging in his right ear, along with fluctuating hearing loss during the attacks of vertigo. These episodes occurred on average about once a month. At age 76, he reported 4 sudden falling spells, with a sensation as though he were being pushed to the ground even though there was no one around him. These episodes were not associated with vertigo or alteration in consciousness, and there were no residual neurological symptoms.

The patient’s medical history was negative for hypertension, coronary artery disease, and stroke. His family history revealed that his mother had migraine headaches. The results of his general and neurological examinations at age 76 were normal except for the profound left-sided hearing loss. The results of a fluorescent treponemal antibody absorption test were negative, and the erythrocyte sedimentation rate was normal. Audiometric testing showed a severe sensorineural hearing loss in the left ear and a moderate sensorineural hearing loss in the right ear. Vestibular function testing performed with rotation in the dark at multiple frequencies and peak velocities showed only a mild decrease in gain and an increase in phase lead at low frequencies of rotation. Gain and phase at higher frequencies of rotation were normal. The findings of magnetic resonance imaging of the brain revealed no abnormalities. A diagnosis of delayed endolymphatic hydrops involving the right ear was made, and the patient was started on a salt restriction diet. He had no further drop attacks but continued to have occasional spontaneous vertigo attacks with fluctuating right-sided hearing. He died of complications from cancer at the age of 81 years.

The brain and both temporal bones were removed approximately 24 hours after death. The general procedures of autopsy and tissue preparation have previously been described. After fixation with 10% formalin for 2 weeks, both temporal bones were immersed in a solution of 1% osmium tetroxide for 1 hour. The cochlea and vestibular end organs were carefully dissected after decalcification with 10% acetic acid solution; then, they were serially dehydrated and imbedded in resin. Unfortunately, all the vestibular end organs on the left side, except the saccular macule, were destroyed in the process of removal. Thin sections (5 mm) were obtained from each of the remaining end organs and stained with toluidine blue.

RESULTS

BRAIN AND MAJOR ARTERIES

Other than normal age-related changes, no gross or microscopic abnormalities were identified in the cerebral cortex, brainstem, or cerebellum. The major arteries at the base of the brain, including the vertebrobasilar system, anterior inferior cerebellar arteries, and internal auditory arteries, were patent throughout their course.

LEFT EAR

The left cochlea showed prominent degenerative changes throughout the organ of Corti. Hair cells, spiral ganglion neurons, and cochlear nerve fibers were all gone (Figure 1). The basilar membrane was intact, but the tectorial membrane and Reissner membrane were absent. There was prominent fibrosis in the stria vascularis and spiral ligament (Figure 1). By contrast, the saccular macule on the left side was essentially normal, with a normal layer of hair cells and supporting cells.

RIGHT EAR

The right cochlea showed prominent endolymphatic hydrops (Figure 2). The scala media was expanded, and Reissner membrane came in contact with the bony walls of the scala vestibuli. There was some loss of hair cells at the base of the cochlea, with corresponding drop out in spiral ganglion neurons and cochlear nerve fibers, thought to be consistent with the patient’s age. The stria vascularis was mildly atrophic compared with the prominent fibrosis seen in the left cochlea. The neuroepithelium of the cristae of the semicircular canals and the saccular macule were within normal limits for the patient’s age. By contrast, there were prominent degenerative changes in the neuroepithelium of the utricular macule, with a severe loss of hair cells (Figure 3).

COMMENT

Sudden unilateral deafness occurring in a young patient without cerebrovascular risk factors is usually thought to be due to an isolated viral infection of the cochlea, even though a viral cause is rarely proved in any given case. Although the term sudden deafness is used to describe the syndrome, there is frequently a subacute onset over hours, and about 50% of patients will have symptoms of a systemic viral illness near the time of the onset of the hearing loss. A more abrupt onset of unilateral hearing loss can be seen in patients with known cerebrovascular disease or in patients with hypercoagulation syndromes, such as polycythemia and macroglobulinemia. The left-sided hearing loss in our patient came on abruptly, but there were no known vascular risk factors other than possibly the migraine with aura. Because of the long interval between the sudden deafness and the postmortem examination, it is difficult to be certain of the cause of the sudden hearing loss, but the prominent fibrosis seen in the stria vascularis and spiral ligament is the characteristic histopathological finding associated with an ischemic vascular insult. Viral infections of the cochlea typically lead to prominent atrophy of the stria vascularis and spiral ligament. Unfortunately, the only vestibular end organ that we were able to examine from the left ear was the left saccular macule, but this organ was normal, and since there was no vertigo with the sudden hearing loss, we can reasonably assume...
that the initial insult that occurred when the patient was 50 years old mainly damaged the left cochlea.

Numerous previous studies have documented that migraine can lead to permanent auditory and vestibular deficits.3,8,21 Vasospasm definitely occurs with migraine, although there is controversy regarding its role in the production of symptoms.22 For example, vasospasm is associated with the classic migraine visual aura, but there is convincing evidence that the visual aura results from a metabolic defect that slowly spreads across the occipital cortex and that the associated vasospasm is caused by the hypometabolism.23 By contrast, there is convincing evidence that vasospasm is a primary cause of retinal injury with migraine.24 Some patients with migraine experience transient episodes of monocular blindness, and, when the patients are examined during these episodes, vasospasm can be identified in the retinal arteries.25 Rarely, blindness due to infarction of the retina will occur.27 Antispasmodic agents, such as calcium channel blockers, often dramatically prevent the episodes of monocular blindness.26 The histopathological findings suggest that the sudden left-sided deafness in our patient resulted from ischemia, and we speculate that the ischemia most likely was due to migraine-associated vasospasm. Since the damage was confined to the cochlea, the vasospasm probably was primarily localized to small arterioles within the cochlea, just as it can involve only a subset of arterioles in the retina with retinal migraine.

Endolymphatic hydrops (Ménière disease) is a disease of middle age and rarely presents in the eighth decade of life. Although it is possible that the right-sided endolymphatic hydrops in our patient was unrelated to the earlier left-sided deafness, this pattern of endolymphatic hydrops developing in the ear that is contralateral to an ear in which hearing was lost many years earlier has been well described.19 A leading theory is that whatever
the mechanism of the initial hearing loss, the same mechanism results in subclinical involvement of the endolymphatic sac of the ear on the other side. As noted earlier, Schuknecht et al\textsuperscript{10} thought that a viral infection involving both ears provided the best explanation, but other mechanisms are possible. Since some cases of endolymphatic hydrops are thought to be autoimmune, damage to one inner ear from any cause might potentially trigger an autoimmune process that would later attack the normal-hearing ear.\textsuperscript{27} Regardless of the underlying mechanism, the result is a progressive dilatation of the endolymphatic space, as was seen in the right ear of our patient.

Sudden drop attacks have been reported in patients with both primary and secondary endolymphatic hydrops.\textsuperscript{11} These dramatic episodes were called \textit{otolithic catastrophes} by Tumarkin\textsuperscript{28} based on his suspicion that they represented acute stimulation of one of the otolith organs from the hydrops. Patients typically report a feeling as though they are being pushed to the ground by some external force. Episodes can occasionally be confused with drop attacks associated with vertebrobasilar insufficiency, particularly when seen in older patients, such as our patient.\textsuperscript{11} Although the pathogenesis of these drop attacks is unknown, a sudden pressure differential across one of the macules could explain the patient’s report of a sudden linear displacement. Some patients are thrown to the ground, possibly owing to a sudden stimulation of vestibulospinal pathways. Surprisingly, we found a marked loss of hair cells in the utricular macule on the right side, while the other sensory receptors on that side were intact. Collapse of the utricular wall onto the utricular macule could explain such a loss of hair cells. The collapse could result either from a rupture of the utricular wall or from pressure from a ballooning saccular wall. The saccular wall is much thinner than the utricular wall, and the saccule expands to a much greater degree than the utricle.\textsuperscript{29} Schuknecht and colleagues observed that the wall of the utricle collapsed onto the macule and produced patchy areas of atrophy and hair cell loss in the temporal bone specimen from a 53-year-old woman with primary endolymphatic hydrops. The patient had experienced constant unsteadiness and sensations of being tilted. The saccule was markedly dilated, compressing the utricular membrane against the utricular macule. The saccular macule was normal, as in our case.\textsuperscript{30}

We speculate that the sudden drop attacks experienced by our patient resulted from intermittent pressure on the utricular macule from a collapsing utricular membrane. Eventually, the utricular wall collapses against the utricular macule, denuding it of hair cells.

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\textbf{REFERENCES}