REVIEW ARTICLE

CONTINUUM AUDIO INTERVIEW AVAILABLE ONLINE

Selected Otologic Disorders Causing Dizziness

By Gail Ishiyama, MD

ABSTRACT

PURPOSE OF REVIEW: **This article details updated clinical presentations and current treatment paradigms of the common otologic disorders that may present to the neurologist for vertigo, including Ménière disease, superior semicircular canal dehiscence syndrome, perilymphatic fistula, barotrauma, cholesteatoma, Ramsay Hunt syndrome, enlarged vestibular aqueduct syndrome, and autoimmune inner ear disease including Cogan syndrome.**

RECENT FINDINGS: **The recent data on modern imaging techniques with three-dimensional delayed IV contrast in Ménière disease, findings on the clinical and testing parameters to diagnose semicircular canal dehiscence and barotrauma, and clinical findings in Ramsay Hunt syndrome, cholesteatoma, and enlarged vestibular aqueduct syndrome are discussed in the article. The most recent findings on the treatment and evaluation of autoimmune inner ear disease and Cogan syndrome are also covered.**

SUMMARY: **This article discusses the common clinical otologic entities in patients who may present to the neurologist for vertigo, and it can be used as a guide in the diagnosis of these conditions with the use of auditory, vestibular, and imaging results.**

CITE AS:
CONTINUUM (MINNEAP MINN) 2021;27(2, NEURO-OTOLOGY): 468–490.

Address correspondence to Dr Gail Ishiyama, Reed Neurological Research Center, UCLA Department of Neurology, Division of Neurotology, 710 Westwood Blvd, Box 951769, Los Angeles, CA 90095, gishiyama@mednet.ucla.edu.

RELATIONSHIP DISCLOSURE:
Dr Ishiyama has received research/grant support from the National Institutes of Health/National Institute on Deafness and Other Communication Disorders (10-001449).

UNLABELED USE OF PRODUCTS/INVESTIGATIONAL USE DISCLOSURE:
Dr Ishiyama reports no disclosure.

INTRODUCTION

This article presents several otologic diseases in patients who may present to the neurologist for vertigo and dizziness. Within each diagnosis, key clinical issues may serve as red flags that should alert the neurologist to which diagnoses require immediate treatment, as well as the clinical presentation and current diagnostic criteria.

PATHOPHYSIOLOGY OF MÉNIÈRE DISEASE

This section focuses on the pathophysiology of Ménière disease; for more information about its clinical features, refer to the article "Episodic Spontaneous Dizziness" by Scott D. Z. Eggers, MD,[1] and for more information about the treatment of Ménière disease, refer to the article "Tinnitus, Hyperacusis, Otalgia, and Hearing Loss" by Terry D. Fife, MD, FAAN, FANS, and Roksolyana Tourkevich, MD,[2] both of which are in this issue of *Continuum*.

Evidence of the pathophysiology of Ménière disease was first noted in archival human temporal bones, which nearly universally revealed endolymphatic

hydrops, a ballooning of the endolymphatic space. The ballooning of the endolymphatic space of the saccule in an archival human temporal bone of a patient with a history of Ménière disease can be seen in FIGURE 8-1; the cochlear duct and utricle were also dilated. Of note, isolated saccular hydrops has been recently demonstrated to be associated with the full spectrum of Ménière disease.[3] Clues to the pathologic mechanisms of Ménière disease can be found in MRI studies developed since 2007. High-resolution three-dimensional 4-hour delayed IV contrast MRI has been developed to visualize the histopathologic hallmark of Ménière disease: endolymphatic hydrops; the evaluation of hydrops is based on the fact that gadolinium is taken up in the perilymph but not in the endolymph.

An incidental finding first noted by Tagaya and colleagues[4] was that, in a patient with Ménière disease, the ipsilateral affected ear compared with the contralateral unaffected ear has an increased uptake of gadolinium, indicative of a breach of the blood-labyrinthine barrier in Ménière disease. It was unclear whether this was a finding specific to Ménière disease because this was noted in several different otologic diseases. However, comparisons between patients with unilateral Ménière disease and patients with unilateral sudden sensorineural hearing loss show that a significantly greater degree of gadolinium uptake occurs in the ipsilateral Ménière disease–affected inner ear.[5] The ipsilateral increased gadolinium uptake in the left inner ear in Ménière disease can be seen in FIGURE 8-2. Histopathologic studies confirmed that on electron microscopy the ultrastructural pathology of the vestibular end organ from patients with intractable Ménière disease displays severe degenerative changes in the microvasculature: vacuolization in the endothelial cells, excessive transcytosis and vesicles, pericyte migration, and thickening and disorganization of the overlying basement membrane.[6] In 2018, Ishiyama and colleagues[7] demonstrated the overexpression of inducible nitric oxide synthase and the presence of nitrotyrosine in the neuroepithelium and within the microvasculature, indicating that oxidative stress likely mediates the damage to the vascular endothelium, as well as the sensory neuroepithelium. Further studies reveal widespread structural damage to the microvasculature, indicating that a possible pathophysiology of Ménière disease is oxidative damage to the microvasculature of the blood-labyrinthine barrier causing neurodegenerative changes.[8]

KEY POINT

- Ménière disease may be caused by oxidative damage of the microvasculature resulting in degeneration of the blood-labyrinthine barrier.

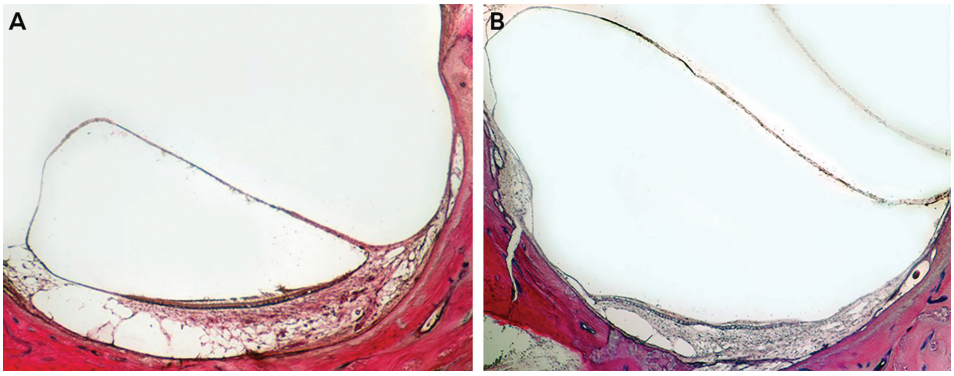

FIGURE 8-1
Archival celloidin-embedded human temporal bone demonstrating saccular hydrops in unilateral Ménière disease. *A*, Normal endolymphatic space in the saccule. *B*, "Ballooning out" of the endolymphatic space, causing distension of the membranous labyrinth.

KEY POINTS

- Tumarkin attacks occur in some patients with Ménière disease and are important to recognize because the falls are unpredictable and may lead to serious injury and are nearly always an indication for ablative treatment.
- The normal acoustic reflex helps distinguish the conductive hearing loss of superior semicircular canal dehiscence from that of otosclerosis, which is associated with an absent acoustic reflex.
- The demonstration of a thinning or dehiscence of the superior semicircular canal on CT of the temporal bone does not necessarily indicate the presence of superior semicircular canal dehiscence syndrome.
- All cases of superior semicircular canal dehiscence should have radiographic evidence, but CT alone overestimates the diagnosis by 6-fold to 20-fold. Patients diagnosed with superior semicircular canal dehiscence should meet criteria based on clinical presentation and audiologic and vestibular testing.
- The absence of a fistula sign at bedside testing does not rule out the diagnosis of a perilymphatic fistula.

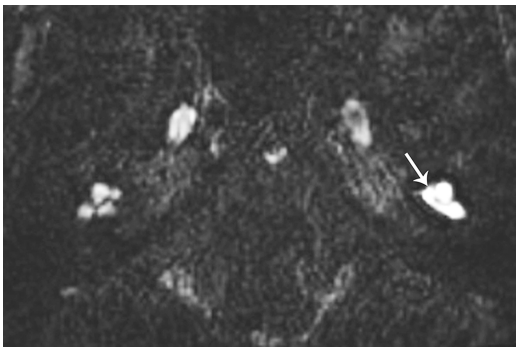

FIGURE 8-2
High-resolution delayed IV contrast axial MRI through the labyrinth in a case of left-sided Ménière disease (endolymphatic hydrops). The delayed contrast T2 fluid-attenuated inversion recovery (FLAIR) demonstrates significantly greater contrast enhancement within the membranous labyrinth on the left side (*arrow*) compared with the right. This indicates breakdown of the blood-labyrinthine barrier. This patient had unilateral Ménière disease on the left associated with spells of vertigo, left-sided aural fullness, and fluctuating hearing loss.

On a clinical note, some patients with Ménière disease experience sudden falls, called *Tumarkin falls* (also known as *vestibular drop attacks* or *otolithic crises*) (CASE 8-1). These drop attacks are sudden violent falls without loss of consciousness described subjectively as if being pushed by an external force.[9] A video (edhub.ama-assn.org/jn-learning/video-player/18471263) of a Tumarkin fall captured at a patient's workplace security camera can be seen in an article by Chen and colleagues.[10] It is important to recognize the cause of these falls because of the unpredictable and forceful nature and the fact that many Tumarkin falls are associated with trauma. Thus, these sudden falls are nearly always an indication for ablative treatment if localized to the inner ear vestibular system. These spells are also called *otolithic attacks*, and they are believed to be caused by a sudden stimulation of the vestibulospinal reflex generated from the otolithic organs: the utricle and saccule. Indeed, pathologic evidence exists for disruption of the otolithic membrane in Tumarkin falls (FIGURE 8-3).[11] Ablative surgery is curative of these dangerous falls and the vertigo spells. In a study of patients older than 65 years of age who underwent vestibular ablation for dangerous Tumarkin falls, these patients derived benefit and were able to compensate well after vestibular ablation.[12]

A second clinical point is the common dissociation of the head impulse test[13] (normal in Ménière disease) and the vestibular caloric response (often abnormally diminished on the ipsilateral side).

SUPERIOR SEMICIRCULAR CANAL DEHISCENCE

Superior semicircular canal dehiscence was first described by Minor and colleagues[14] in 1998. Patients with superior semicircular canal dehiscence report vestibular hypersensitivity, including vertiginous symptoms in the setting of a loud noise (Tullio phenomenon) and pressure sensitivity with Valsalva maneuvers (eg, coughing, sneezing, straining, lifting heavy objects) or with positive pressure placed over the external ear (the Hennebert sign). Conductive hyperacusis can manifest with hearing one's voice in the affected ear (autophony), hearing eye movements or stomach sounds, or pulsatile tinnitus. Careful neuro-otologic assessment may reveal the slow phase of the nystagmus directed upward and away from the affected ear when stimulated by pneumatic otoscopy, a Valsalva maneuver against the pinched nostrils, or loud sound to the affected ear. However, this sign is not noted in all patients, and the induced nystagmus is not always in the plane of the superior semicircular canal or the affected canal.

CASE 8-1

A 57-year-old woman presented with recurrent spells of rotational vertigo with intractable nausea and vomiting, associated with tinnitus on the right side, and fluctuating hearing loss. Her most recent audiogram demonstrated nonserviceable hearing with 75-dB hearing loss on the right. However, she still had spells with increased tinnitus to a loud roar, followed by spinning vertigo and vomiting. Recently, she began having sudden violent falls, always to the right side, and the last fall caused a dislocated shoulder; thus, she was referred to a neurologist for urgent evaluation.

Videonystagmography demonstrated 43% reduced vestibular response on the right and a normal head impulse test bilaterally. High-resolution three-dimensional 4-hour delayed IV contrast MRI demonstrated endolymphatic hydrops of the utricle, saccule, and cochlear duct and hyperintensity on gadolinium uptake on the right side. She underwent labyrinthectomy, and otolithic debris was noted within the vestibule (FIGURE 8-3). On follow-up 5 years after surgery, she had no further spells of drop attacks or vertigo.

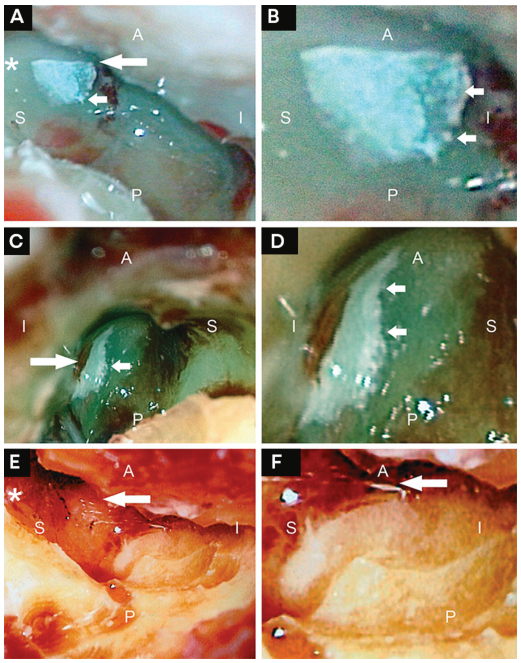

FIGURE 8-3

Representative intraoperative images in three different patients with Tumarkin crises and intractable unilateral Ménière disease about to undergo labyrinthectomy that demonstrate disintegration of the utricle. *A*, Right ear of patient 1 showing disintegration (*small arrow*) of the utricular membrane (*large arrow*). *B*, High-magnification view of panel A, also showing freely mobile otoconia (*arrows*). *C*, Left ear of patient 2 demonstrating more severe disintegration (*small arrow*) of the otolithic membrane (*large arrow*). *D*, High-magnification view of panel C, also showing aggregates of displaced otoconia (*arrows*). *E*, Right ear of patient 3 showing atrophy of the utricular membrane (*arrow*). *F*, High-magnification view of panel E revealing completely absent otoconia and otoconial membrane (arrow points to the area of the utricle). The *asterisk* in panels A and E indicates the superior semicircular canal.

A = anterior; I = inferior; P = posterior; S = superior.

COMMENT

This is a common clinical picture of Ménière disease affecting the right ear and points out how specialized MRI procedures are emerging as helpful adjuncts to diagnosis and to identifying the side that is causing the vertigo and vestibular attacks.

The sensitivity of the auditory and vestibular system to loud noise and pressure is hypothesized to occur due to the presence of a "third window." In normal inner ear anatomy, two windows allow for the sound pressure waves: the oval window and the round window. The osseous covering of the superior semicircular canal is most often the area of bony defect, which allows for a "third window." In the normal inner ear, sound waves from the ossicular movement on the oval window pass through the incompressible perilymph within the scala vestibuli and scala tympani and produce an outward movement of the round window. In superior semicircular canal dehiscence, the sound waves create pressure that is shunted to the vestibular system, resulting in hypersensitivity and vertigo. This shunting effect is often associated with bone conduction hyperacusis confirmed by bone conduction hearing thresholds that are less than 0 dB, autophony, and pulsatile tinnitus.[15]

Workup should include vestibular-evoked myogenic potentials and temporal bone CT with a slice thickness of less than 1 mm (ideally 0.625 mm or less) reformatted in the planes of the superior semicircular canal (Pöschl view) and orthogonal to it (Stenvers view).

A special note regarding cervical-vestibular evoked myogenic potentials: threshold values distinguish patients with superior semicircular canal dehiscence from controls with a sensitivity of 85% to 91% and a specificity of 90% to 96%. In a retrospective cohort of 65 patients, at 500-Hz tone bursts, vestibular-evoked myogenic potential thresholds were 66 dB for ears with superior semicircular canal dehiscence and 85 dB for ears without superior semicircular canal dehiscence. Thus, using a threshold of 65 dB or less had 91.4% sensitivity and 95.8% specificity.[16] Using the corrected cervical vestibular-evoked myogenic potential amplitudes with a cutoff at greater than 2.5 standard deviations

CASE 8-2

A 43-year-old woman presented with pulsatile tinnitus, vertigo induced with loud sounds in the right ear, and the perception of hearing her voice in her right ear. Coughing, sneezing, and straining were associated with a brief sense of tilting and vertiginous sensation. She also reported a sensation of right aural fullness but did not note drops in hearing and did not describe hearing loss.

At bedside testing, the struck 512-Hz tuning fork on the forehead (or even on the ankle) was heard in her right ear. On audiologic testing, she had low-frequency conductive hearing loss on the right side, and vestibular-evoked myogenic potentials revealed a threshold for activation on the right of 65 dB compared with 95 dB on the left and an amplitude twice that of the left. The acoustic reflexes were normal bilaterally. CT of the temporal bone revealed thinning of the bone overlying the superior semicircular canal on the right. After undergoing the transmastoid approach to patch the dehiscence, she no longer experienced the vertigo attacks with a Valsalva maneuver.

COMMENT

This case demonstrates the key clinical findings in superior semicircular canal dehiscence and meets the diagnostic criteria.[15,20]

from normal distinguished patients with superior semicircular canal dehiscence from controls with a sensitivity of 100% and specificity of 93%.[17] Fife and colleagues[18] concluded that cervical vestibular-evoked myogenic potential threshold values and cervical vestibular-evoked myogenic potential amplitudes may be used to distinguish patients with superior semicircular canal dehiscence.

Workup should include pure tone audiometry, with the audiometer calibrated to test for bone conduction below the 0-dB hearing level. Bone conduction thresholds with negative decibel values are indicative of a conductive hyperacusis, consistent with semicircular canal dehiscence. On pure tone audiometry, an air-bone gap with bone hearing better than air hearing may be seen at 250 Hz, 500 Hz, and 1000 Hz in superior semicircular canal dehiscence. Acoustic reflexes should be tested because an absent acoustic reflex would be consistent with otosclerosis as the cause of a conductive hearing loss.

Most cases of canal dehiscence or "third window phenomena" are due to dehiscence affecting the superior semicircular canal, but other locations of dehiscence may also occur and present with similar clinical findings except that the temporal bone CT shows a different location of the dehiscence. The posterior canal may also exhibit bony dehiscence and is associated with a high-riding jugular bulb and fibrous dysplasia.[19] Fife and colleagues[20] proposed an algorithm that can be applied for the evaluation of patients presenting with signs or symptoms of superior semicircular canal dehiscence syndrome, such as autophony, Tullio phenomenon, Valsalva maneuver–induced vertigo, or conductive hyperacusis (CASE 8-2).

A review of the literature demonstrates four surgical approaches: middle fossa craniotomy, transmastoid, endoscopic approach, and transcanal with reinforcement of the round or oval window[21]; the 2019 multicenter study demonstrated that the transmastoid approach for correction of superior semicircular canal dehiscence was associated with a significantly shorter duration of hospitalization and lower recurrence rate compared with a middle fossa craniotomy. Patients in both groups had improvement in the Tullio phenomenon, autophony, and pulsatile tinnitus, and no difference was seen in audiometric outcomes between the transmastoid approach and the traditional middle fossa craniotomy approach.[21]

It is important to note that the demonstration of a thinning or dehiscence of the superior semicircular canal on CT of the temporal bone does not necessarily indicate the presence of superior semicircular canal dehiscence syndrome. By using 0.5-mm-resolution CT, the incidence of radiographic evidence of thinning or dehiscence of the superior semicircular canal is reported to be from 3% to 10%.[22] However, true histopathologic dehiscence of the superior canal occurs in only 0.5% of normative cases in studies of the human temporal bone, indicating that the CT diagnosis of dehiscence overestimates the diagnosis of superior semicircular canal dehiscence by 6-fold to 20-fold.[23] Furthermore, even if dehiscence of the temporal bone is present, it is likely that it is not always symptomatic. The diagnosis of clinically significant superior semicircular canal dehiscence should be reserved for patients who meet certain criteria of symptoms and signs on testing (TABLE 8-1).[15,19]

PERILYMPHATIC FISTULA

A perilymphatic fistula is an abnormal communication between the fluid-filled inner ear and the air-filled middle ear, causing a leakage of fluid at the oval or

KEY POINTS

- In trauma associated with hearing loss and/or vertigo, the CT should be evaluated in the coronal view for air bubbles (pneumolabyrinth), which is evidence of a traumatic perilymphatic fistula. Pneumolabyrinth, ossicular fracture or dislocation, or a temporal bone fracture through the otic capsule may be indications for urgent surgical exploration to preserve inner ear function.
- Clinicians should have a high level of suspicion in children presenting with hearing loss and should rule out perilymphatic fistula in the setting of inner ear anomaly as etiology.
- Mild symptoms consistent with perilymphatic fistula may be treated conservatively with avoidance of a Valsalva maneuver or with rest. However, conservative treatment is not recommended for traumatic perilymphatic fistula secondary to penetrating inner ear injury, temporal bone fracture, or ossicular damage.
- Acoustic hyperacusis with bone conduction thresholds less than 0 dB, autophony, and abnormal cervical vestibular-evoked myogenic potentials can help distinguish superior semicircular canal dehiscence from perilymphatic fistula.
- Barotrauma related to scuba diving is often associated with hearing loss (90%) and variably associated with vertigo (averaging 50%).

round window, with the etiology described as being congenital, acquired related to closed head trauma, or related to a penetrating inner ear injury. Congenital perilymphatic fistula is often related to middle ear defects, for example, abnormal stapes or cochlea or vestibular dysplasia, and a dilated vestibular aqueduct.[24] The rupture in the round window was proposed to be caused by either explosive (increased intracranial pressure) or implosive (Valsalva maneuver–induced) mechanisms.[25] Some of the more common causes of perilymphatic fistula include barotrauma (discussed later), stapedectomy with slippage of the stapes prosthesis, temporal bone fracture, and, less commonly, a penetrating inner ear injury. In the case of a penetrating perilymphatic fistula injury, immediate surgical exploration and intervention are indicated (CASE 8-3[26]). Other less dramatic causes can occur with relatively innocuous "trauma," such as blowing the nose hard, a slap to the ear, and other minor Valsalva maneuvers.

Hennebert[27] described a nystagmus triggered by positive pressure and negative pressure into the ear canal. The presentation of vertigo triggered by pressure changes is sometimes called the *fistula sign.* However, the fistula sign is reported in only 29% to 71% of cases of perilymphatic fistula. Other causes of a positive Hennebert sign include superior semicircular canal dehiscence, cholesteatoma causing a destructive lesion of the labyrinthine capsule (discussed later), barotrauma, and a phenomenon of a "slipped strut problem" in which the stapes prosthesis used in stapedectomy surgery has entered into the inner ear, causing a perilymphatic leak. The Hennebert sign can be elicited at the bedside by pressing on the tragus or during vestibular testing by using a pneumatic otoscope to elicit vertigo or nystagmus, indicative of a possible perilymphatic fistula.

TABLE 8-1 **Diagnostic Criteria for Superior Semicircular Canal Dehiscence[a]**

High-resolution CT imaging with ≤0.625-mm slice thickness reformatted in the plane of the superior semicircular canal demonstrating dehiscence

At least one of the following symptoms

- Bone conduction hyperacusis (autophony, audible eye movements, audible footsteps, etc)
- Tullio phenomenon: sound-induced vertigo
- Pressure-induced vertigo (via nasal or glottic Valsalva maneuver or pressure applied to the external auditory canal)
- Pulsatile tinnitus

At least one of the following diagnostic tests indicating a mobile third window

- Negative bone conduction thresholds on pure tone audiometry
- Enhanced vestibular-evoked myogenic potential responses (low cervical vestibular-evoked myogenic potential thresholds or high ocular vestibular-evoked myogenic potential amplitudes)
- Elevated summating potential to action potential on electrocochleography in the absence of sensorineural hearing loss

CT = computed tomography.
[a] Reprinted with permission from Ward BK, et al, Front Neurol.[15] © 2017 Ward, Cary, and Minor.

Ikezono and colleagues[28] developed a novel test for human cochlin-tomoprotein, which is present in perilymph but not in CSF or serum, yielding high specificity and sensitivity. However, cochlin-tomoprotein testing is not routinely available, so perilymphatic fistula remains predominantly a clinical diagnosis, confirmed and treated in exploratory surgery.

In cases of traumatic penetration into the inner ear, the CT may demonstrate pneumolabyrinth (ie, tiny air bubbles in the labyrinthine fluid in the vestibule, semicircular canals, and scala vestibuli of the cochlea). It is believed that both the perilymphatic fluid loss and the air bubbles within the labyrinth cause audiovestibular dysfunction. It is important to be aware that children with anomalies of the inner ear, such as malformation of the cochlea, may be susceptible to perilymphatic fistula–induced hearing loss, and, therefore, imaging is always indicated in unknown causes of sudden hearing loss in children.

For patients without severe hearing loss or severe vertiginous symptoms, some neuro-otologists may recommend conservative treatment, which includes bed rest for 5 to 7 days, elevation of the head of the bed, and avoidance of Valsalva maneuvers or straining.

The hearing is followed up with serial audiograms, and if hearing loss is present, the patient should be counseled that earlier intervention is associated with a higher likelihood of hearing recovery. Friedland and Wackym[29] reviewed the surgical cases in a multi-institutional study and reported improvement in vestibular symptoms in 90% of the patients presenting with disabling vertigo due to perilymphatic fistula. Perilymphatic fistula and superior semicircular canal dehiscence can present similarly: pressure-induced vertigo or sound-induced vertigo, both of which represent a vestibular hypersensitivity. One distinction is that superior semicircular canal dehiscence is much more likely than perilymphatic fistula to present with acoustic hyperacusis, documented by a bone conduction threshold that is less than 0 dB and autophony.

INNER EAR DAMAGE RELATED TO SCUBA DIVING

Two main types of inner ear damage may occur secondary to scuba diving. Inner ear barotrauma is related to pressure changes being transmitted to the inner ear, such as when attempting to equalize the pressure with a forceful Valsalva maneuver. Inner ear decompression damage is related to air emboli or a supersaturation of inert gasses. It is important to distinguish between these two entities because the treatment differs greatly, and inner ear decompression is an indication for immediate hyperbaric oxygen treatment (TABLE 8-2[30]).

Inner Ear Barotrauma

Inner ear barotrauma generally refers to damage to the inner ear that causes auditory and vestibular symptoms related to underwater diving. Inner ear barotrauma can occur when pressure changes within the middle ear are transmitted to the cochlea. The function of the round window is to compensate for changes in pressure by flexing in and out to prevent damage to the inner ear membranes. In deep-sea diving, especially during ascent or descent, or during equalization attempts with a forced Valsalva maneuver, sudden changes in the pressure can occur, causing damage to the inner ear. For barotrauma, mechanisms of damage can be both explosive and implosive. During descent, the external pressure increases, and if the eustachian tube has "locked" and a forceful Valsalva maneuver is attempted, the sudden perilymphatic fluid pressure

KEY POINTS

- High-resolution CT of the temporal bone is always indicated in audiovestibular loss in the setting of diving to rule out anatomic risk factors, ossicular disruption, hemorrhage, or pneumolabyrinth.
- Vestibular symptoms and vertigo in inner ear barotrauma should be referred to an otologic surgeon because surgical correction results in a high rate of symptom relief.
- The distinction between barotrauma and decompression inner ear syndromes in diving is critical, as inner ear barotrauma can be managed with an observational period. In contrast, decompression inner ear disease, which presents with a predominance of vestibular symptoms, should be treated with hyperbaric oxygen within 5 hours of injury as any further delay usually results in permanent inner ear damage.
- Early recognition of chronic otitis media and invasive cholesteatoma is critical. Because of the proximity of the middle ear canal to the facial nerve, the horizontal semicircular canal, and overlying dura, invasive cholesteatoma can cause hearing loss, vertigo, facial paresis, meningitis, and intracranial abscess.
- Surgical eradication of cholesteatoma is indicated and aims to prevent the extension through the dura membrane and the associated intracranial complications.

increase can rupture the round window. A sudden opening of the eustachian tube can cause an implosive injury, tearing the oval or round window, disrupting the Reissner membrane and the basilar membrane, or causing inner ear hemorrhage, the last two being examples of intralabyrinthine membrane rupture. Other than surgical exploration and visualization, the diagnosis of inner ear barotrauma can be difficult to make.

For the workup and evaluation of patients with suspected inner ear barotrauma, pure tone audiometry may reveal varied patterns of hearing loss,

CASE 8-3

A 45-year-old man fell from a bicycle while on a trail and had an immediate onset of severe rotational vertigo with intractable vomiting, headache, hearing loss, and tinnitus in his left ear. He was taken to the local emergency department, and CT was conducted. The physician noted the presence of a twig impaling the tympanic membrane. The temporal bone CT revealed a twig through the tympanic membrane (FIGURE 8-4A) and air bubbles in the vestibule in all three semicircular canals and in the scala vestibule and basal turn of the cochlea (FIGURE 8-4B). The patient was transferred to a university center hospital for further treatment.

Examination revealed a spontaneous, continuous, right-beating nystagmus in the primary position, and the bedside Weber test lateralized to the right side indicative of a profound unilateral sensorineural hearing loss on the left. The patient was immediately taken to the operating room where it was discovered that one twig pierced the oval window and a smaller twig penetrated the vestibule. The oval window was repaired, and a stapes prosthesis was placed. Postoperatively, he had improvement in the vertigo with only minimal spontaneous nystagmus in the primary position, a speech reception threshold of 30 dB on the left, and symmetrical responses to rotational testing on vestibular nystagmogram (FIGURE 8-5).

Modified from Kita et al, Clin Pract Cases Emerg Med.[26] © 2019 Kita et al.

COMMENT

This case demonstrates a traumatic perilymphatic fistula with pneumolabyrinth on CT, hearing loss, and vestibular loss with preservation of audiovestibular function by rapid surgical intervention.

most often a flat or down-sloping hearing loss in patients presenting with hearing loss.[30] Electronystagmography is useful in quantifying vestibular damage and has been reported to have a sensitivity and specificity of 77% in cases of inner ear barotrauma.[31] In studies of inner ear barotrauma, the incidence of vertigo ranged from 28% to 77% and was overall found in 71 of 156 cases (46%). Hearing loss is common for barotrauma with perilymphatic fistula in up to 228 of 253 cases (90%).[30] High-resolution CT of the temporal bone is critical to evaluate for

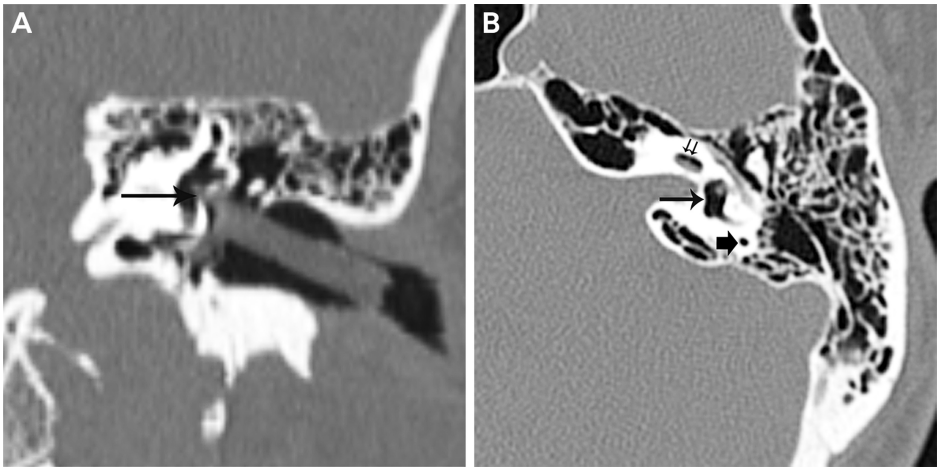

FIGURE 8-4

Penetrating ear trauma and perilymphatic fistula of the patient in CASE 8-3. *A*, A reconstructed oblique coronal image shows a linear foreign body projecting from the external auditory canal to the oval window, with a small projection into the vestibule (*arrow*). Extensive intralabyrinthine air is present. *B*, Axial CT image through the left temporal bone shows air in the vestibule (*long arrow*), the posterior semicircular canal (*wide arrow*), and the scala vestibuli compartment of the cochlear basal turn (*double arrows*). Air was also seen in the lateral and superior semicircular canals (*not shown*).

Reprinted from Kita AE, et al, Clin Pract Cases Emerg Med.[26] © 2019 Kita et al.

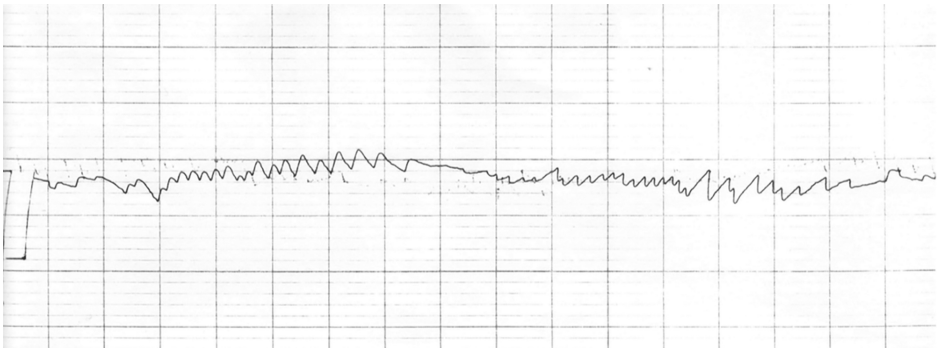

FIGURE 8-5

Vestibular testing for the patient in CASE 8-3 conducted 1 month after the penetrating ear trauma. The sinusoidal rotational vestibulo-ocular reflex at 0.05 Hz and a peak velocity of 60 degrees per second revealed normal and symmetrical gain and phase lead. This demonstrates recovery of vestibular and auditory function with rapid intervention in the case of penetrating inner ear trauma.

anatomical risk factors, ossicular disruption, intralabyrinthine hemorrhage, or other potential causes.

Conservative management of inner ear barotrauma includes initial observation and medical therapy, including high-dose steroids with a taper for a total duration of therapy of 18 days, and exploratory surgery with patching if clinical deterioration with vertigo or a sudden drop in hearing occurs. Many surgeons opt for exploration, especially in the case of bothersome vertigo. After barotrauma diagnosis, the patient should consult with a specialist before conducting more diving. It is important to note that surgical intervention in inner ear barotrauma led to dramatic improvement in vertigo in 12 of 13 patients, and thus many otologic surgeons intervene for vestibular symptoms.[31]

Inner Ear Decompressive Damage in Scuba Diving

Inner ear decompressive damage must be distinguished from inner ear barotrauma. In the case of inner ear decompressive damage, the damage to the inner ear is believed to be secondary to either of two mechanisms: (1) the local supersaturation of inert gases, with the vestibular system more at risk than the cochlear system because of its lower arterial perfusion and (2) slower inert gas washout or right-to-left air emboli.[32] Deep technical diving using helium and oxygen and trimix breathing gases appears to confer a higher risk of inner ear decompression sickness.

As an aid in determining inner ear barotrauma from decompression inner ear disease, key differences are delineated in TABLE 8-2.[30] Decompression inner ear damage, in contrast to barotrauma with perilymphatic fistula, presents with a preponderance of vestibular symptoms soon after surfacing from the dive, after an average of 36 minutes and ranging from 13 to 206 minutes after surfacing. Of note, in 75% of cases, inner ear decompression presents with a pure vestibular disorder and nearly 18% with a vestibular and cochlear disorder.[33,34] In cases of decompression inner ear syndrome, clinicians should arrange for rapid

TABLE 8-2 **Distinguishing Inner Ear Barotrauma From Inner Ear Decompression Illness With HOOYAH Criteria[a]**

Criterion	Description	Inner ear barotrauma	Inner ear decompression
H	Hard to clear	Descent or ascent: difficulty with Valsalva maneuver	Not associated
O	Onset	Descent, ascent, or after diving	Often soon after ascent, average 36 minutes
O	Otoscopy	Can be abnormal if the middle ear is involved	Normal
Y	Your dive profile	Fast ascent or descent	Missed decompression stops, repetitive dives, technical diving
A	Additional symptoms	Isolated to the inner ear	Other decompression symptoms, "the bends" but only in 17% in some studies
H	Hearing	Very common	Vestibular only in 75%, vestibulocochlear in 18%, cochlear in 6%

[a] Reprinted with permission from Rozycki SW, et al, Diving Hyperb Med.[30] © 2018 The authors.

transport to the nearest center for hyperbaric oxygen treatment, ideally within 5 hours, during which the patient should be given 100% oxygen. Steroids can reduce edema, and low-molecular-weight dextran may improve microcirculation.[35]

CHOLESTEATOMA AS A CAUSE OF VESTIBULAR SYMPTOMS

An acquired cholesteatoma is a mass of keratinizing epithelium that accumulates in the middle ear, often a sequela of chronic otitis media beginning as an inward growth often from the lateral epithelium of the tympanic membrane. This area of the tympanic membrane has no annulus (the fibrous thickened edges of the tympanic membrane that anchor it) and, thus, is susceptible to the development of chronic otitis and cholesteatoma (CASE 8-4).[36] This area of the middle ear canal is adjacent to the horizontal semicircular canal, and an acquired cholesteatoma can cause erosive changes invading into the labyrinth, causing vertigo and hearing loss and eroding into the facial canal causing facial paralysis.

Erosion into the fallopian canal of the facial nerve and facial nerve paralysis associated with chronic otitis media are other red flags for impending intracranial complications. Because of the bone-eroding properties of cholesteatoma, erosion into the central nervous system can also occur and be associated with life-threatening intracranial infections or complications, including lateral sinus thrombosis, brain abscess, or cranial nerve damage.

In the case of recurrent vertigo spells in the setting of a history of otalgia and partially treated persistent ear infections, a cholesteatoma eroding into the round window, causing perilymphatic fistula, or eroding into the labyrinthine structures, causing dehiscence of the horizontal semicircular canal, is most

CASE 8-4

A 23-year-old man presented with drainage from the right ear and ear pain, unilateral tinnitus on the right, and dizziness. He was seen by his local otolaryngologist who prescribed a 10-day course of antibiotics. However, 12 days later, he presented to the emergency department with headache, vertigo, vomiting, and lethargy.

Examination in the emergency department revealed a pearly mass in the right "attic space" behind the pars flaccida region of the tympanic membrane. MRI revealed an abscess in the right temporal lobe, and the mastoid space was filled with granulation tissue and a large cholesteatoma. During surgery, a defect in the mastoid tegmen (the thin plate of bone separating the mastoid and middle ear from the brain) and invasion of the cholesteatoma through the dura were discovered.

COMMENT

Clues in this case include a patient presenting with new-onset vertigo spells, having a history of persistent otalgia or otorrhea with odor, and otorrhea that persists beyond 3 weeks of antibiotic therapy or a recurrence of infection within 2 weeks after treatment. This should trigger the clinician to rule out bone-invading cholesteatoma and to refer the patient urgently to an otologic surgeon.

commonly the cause of vertigo. In one study of cholesteatoma-induced labyrinthine fistula, the horizontal canal was involved in 87% of cases.[37] Invasive cholesteatoma is an indication for surgical resection to prevent complications and intracranial spread. In the case of cholesteatoma, the debris from the keratinizing mass may block the fistula site, and thus the fistula test may be negative.

A case report of a man presenting with hearing loss, tinnitus, and vertigo reported a positive fistula test in a left-sided cholesteatoma producing a left-beating nystagmus with positive pressure pushing on the tragus (a video of a positive Hennebert test is available at cmaj.ca/lookup/suppl/doi:10.1503/cmaj.180799/-/DC1)[38]; intraoperatively, a left lateral (horizontal) semicircular canal dehiscence was noted in this patient. High-resolution CT of the temporal bone is usually able to define the location and size of the fistula. However, in the setting of asymmetry of hearing and vertigo, MRI with contrast of the internal auditory canal is indicated to rule out other causes.

A patient with facial paralysis must not be given the diagnosis of Bell's palsy without a thorough evaluation of the clinical history and detailed examination. In cases of true Bell's palsy, the paralysis should occur over less than 24 to 48 hours, often upon awakening, and should be complete. However, a gradual onset of facial paralysis may occur in the setting of a tumor or an infection spreading from otitis media or cholesteatoma. On a clinical note, in bacterial meningitis, the

CASE 8-5

A 47-year-old man presented with a history of right ear pain, fluid-filled vesicular rash in the external auditory canal, hearing loss, vertigo, and complete facial paralysis on the right.

On examination, a spontaneous left-beating nystagmus was present in the primary position, with an increase in amplitude and frequency of nystagmus with gaze to the left and a decrease with gaze to the right. The head impulse test[13] demonstrated catch-up saccades when the patient's head was turned quickly to the right. Test of hearing using a 512-Hz tuning fork demonstrated that the Weber test lateralized to the left. MRI with gadolinium revealed enhancement of the right facial nerve, and T2 fluid-attenuated inversion recovery (FLAIR) images revealed swelling of the facial nerve. The patient was treated with IV acyclovir and prednisolone. Eight months later, the patient exhibited a House-Brackmann score of III, partial facial palsy, and mild imbalance when walking, especially with his eyes closed. Videonystagmography revealed a 70% caloric paresis.

COMMENT

This patient presented with the classical triad of Ramsay Hunt syndrome of vesicles, hearing loss, and facial paresis. Vestibular involvement is variable. It is important to recognize and treat Ramsay Hunt immediately because earlier intervention portends a better outcome. Several aspects of this case highlight the importance of looking carefully for vesicles of varicella-zoster virus: the complete facial paralysis associated with ipsilateral otalgia and the associated audiovestibular disturbance. In this case, only the external canal near the tympanic membrane exhibited vesicles, requiring otoscopic examination to visualize.

clinician should rule out chronic otitis media or cholesteatoma as the source of infection. The signs of meningitis, including nuchal rigidity and fever in a patient with cholesteatoma invading into the dura, may be masked by chronic antibiotic use, which may have partially treated the infection.

The newest imaging application for cholesteatoma is the use of non–echo planar diffusion-weighted imaging (DWI) MRI to evaluate both primary and postoperative recurrence of middle ear cholesteatoma. DWI can delineate the size, location, and extent of cholesteatoma because the keratin content of the cholesteatoma demonstrates restricted diffusion on DWI (bright) and a lower value on the apparent diffusion coefficient map. One of the largest meta-analyses, which included 26 studies and 1152 patients in total, noted a sensitivity of 91% and a specificity of 92% for middle ear cholesteatoma, and the specialized DWI sequence can be used for both preoperative primary diagnosis (usually combined with temporal bone CT) and for postoperative surveillance.[39] A clinical note is that cholesteatoma in children is characterized by more severe recurrence, and thus, second-look surgery to evaluate for recurrence or residual disease after the first surgery is often recommended. MRI can be used to follow cholesteatoma by using the DWI hyperintensity property of cholesteatoma to evaluate for recurrence and severity. MRI was used to follow a teenage child with recurrent ear infections after a resection at an outside institution, and the imaging revealed a recurrence of cholesteatoma that was cleared intraoperatively. Some of the congenital syndromes associated with a high incidence of cholesteatoma potentially include Down syndrome, microtia (congenital deformity of the outer ear), Treacher Collins syndrome, and Turner syndrome.[36] These patients may present initially with vertigo, nausea, and vomiting due to vestibular labyrinthine involvement (often the horizontal semicircular canal), which portends an impending breach of the overlying dura membrane and possible intracranial complications with high morbidity and mortality. The dictum is that any patient with chronic otitis media with an exacerbation of otorrhea, ear pain, or pain in the temporal region, or headache with high fever and vomiting, has an intracranial complication from invasive cholesteatoma until proven otherwise.

RAMSAY HUNT SYNDROME WITH VERTIGO

Ramsay Hunt syndrome is theorized to be a reactivation of the varicella-zoster virus in the geniculate ganglion or facial nerve presenting with a vesicular rash and often involves the eighth cranial nerve, causing hearing loss, tinnitus, vertigo, and imbalance (CASE 8-5). Ramsay Hunt syndrome is the second most common cause of atraumatic peripheral facial paralysis; a retrospective review reported that 12% of 1507 consecutive patients with atraumatic facial palsy had Ramsay Hunt syndrome, and an incidence of approximately 5 per 100,000 per year, and an age older than 50 years renders a patient more susceptible.[40] Ramsay Hunt syndrome is a peripheral facial nerve palsy accompanied by an erythematous vesicular rash on the ear (zoster oticus) or in the mouth.

Ramsay Hunt syndrome with vertigo, hearing loss, and facial palsy without a rash is known to occur, termed *zoster sine herpete*. In a case report, severe prolonged vertigo lasting several days, with nausea and vomiting similar to that seen in vestibular neuritis without facial palsy was the initial presentation of atypical Ramsay Hunt syndrome, with zoster oticus appearing later; the diagnosis was confirmed by varicella-zoster virus DNA extracted from the lesions.[41]

KEY POINTS

- Evaluation for fistulization of the bony labyrinth may be tested at the bedside with the fistula test using a pneumatic otoscope (the Hennebert test). However, the fistula test may be falsely negative in the case of a cholesteatoma abundantly filled with keratin debris.
- The patient presenting with a gradual onset of facial weakness, often incomplete in the setting of otalgia and otorrhea, likely has chronic otitis media with cholesteatoma causing dehiscence of the facial nerve canal.
- The classical signs of meningitis may be masked in the patient with invasive cholesteatoma due to antibiotics.
- A diffusion-weighted imaging sequence on MRI can be used to follow a cholesteatoma, which will be hyperintense on diffusion-weighted imaging.
- Chronic otitis media with headache, nausea, and vomiting should trigger a workup for meningitis.
- Areas of vesicular rash eruption in Ramsay Hunt syndrome involve the sensory distribution of the facial nerve, which can include vesicles in the ipsilateral ear (concha and antihelix, antitragus, and a portion of the lobule and adjacent mastoid), ipsilateral hard palate, and anterior two-thirds of the tongue, which has the special taste sensory fibers.

A 2020 comprehensive study used a computer search of patient records for 120 patients with Ramsay Hunt syndrome and questionnaires with long-term follow-up, ranging from 1 to 17 years (median of 6.6 years), in 81 patients.[42] The vesicles could be present before, concomitant with, or after the facial palsy. A clinically important note is the high frequency of a feeling of an ache around the affected ear in 77% of the patients, which should alert the clinician to the possibility of Ramsay Hunt syndrome.[42] Ramsay Hunt syndrome (ie, varicella-associated zoster virus causing facial nerve weakness) can present with vesicles before and after the facial weakness. The ear canal and tympanic membrane should be examined for vesicles because external ear vesicles may not be visible. The outer ear was the primary and sole location of vesicles in 58%, but vesicles were present solely in the ear canal or on the eardrum in some cases.

Regarding auditory and vestibular involvement in patients with Ramsay Hunt syndrome, 52% had acute hearing loss on audiogram, but for those answering the questionnaire, only 22% felt they had any hearing loss as a result of Ramsay Hunt syndrome.[42] In 31% of the records obtained from the hospitalization, patients reported vertigo, nausea, and vomiting, likely indicative of vestibular nerve and ganglion involvement. Of the patients who answered a questionnaire that had been sent out, 51% mentioned vertigo and dizziness, and 32% reported persistent vertigo or dizziness after a minimum of 1 year of recovery.[42]

Treatment for Ramsay Hunt syndrome generally consists of antiviral drugs (acyclovir or famciclovir) combined with corticosteroid treatment. Murakami and colleagues[43] studied outcomes in 80 patients with Ramsay Hunt syndrome treated with either IV or oral acyclovir and prednisone taper; they reported 75% recovered if treated within 1 to 3 days of symptom onset, but only 30% recovered if treated after more than 7 days. For this reason, it is imperative that the clinician recognize the possibility of Ramsay Hunt syndrome to evaluate and start treatment immediately. Of note, other cranial nerves have been reported to be involved in Ramsay Hunt syndrome, but clearly cranial nerve VIII, associated with vertigo and hearing loss, is the most frequently involved cranial nerve in Ramsay Hunt syndrome other than the facial nerve; other nerves involved include cranial nerves V and IX through XII and cervical nerves 2 through 4.

ENLARGED VESTIBULAR AQUEDUCT SYNDROME

The vestibular aqueduct in normal human anatomy is a slitlike aperture forming a bony canal running from the vestibule to the endolymphatic sac within the osseous labyrinth. The opening on the cranial side is located close to the internal auditory canal opening in the posterior surface of the petrous temporal bone. The vestibular aqueduct contains the endolymphatic duct and the endolymphatic sac, which are believed to be the areas of endolymph absorption. The enlarged vestibular aqueduct was initially reported by Valvassori and Clemis[44] in 1978 and noted to be associated with bilateral sensorineural or mixed hearing loss, but the pathophysiology of the hearing loss is unknown. Up to 10% to 15% of children with sensorineural hearing loss have enlarged vestibular aqueduct syndrome.[45]

An enlarged vestibular aqueduct is the most common imaging finding in children with a congenital inner ear anomaly, and the likely etiology is an arrest in development in the fifth to eighth week of gestation when the endolymphatic sac and duct are forming and the vestibular aqueduct develops. In at least half of the cases of hearing loss associated with an enlarged vestibular aqueduct, a sequence alteration of the *SLC26A4* gene, which encodes for pendrin, an anion

exchanger, is present.[46] Pathogenic sequence alterations in the *SLC26A4* gene are the second most common cause of autosomal recessive nonsyndromic hearing loss, and up to 71% of these patients have recurrent spells of episodic vertigo. Mutations in the pendrin gene (*SLC26A4*) can be associated with nonsyndromic deafness with an enlarged vestibular aqueduct and may be associated with goiter and vestibular symptoms.

The enlarged vestibular aqueduct can serve as a third window mechanism, and the cervical vestibular-evoked myogenic potentials exhibit abnormally low thresholds and high amplitude as is noted with superior semicircular canal dehiscence syndrome.[47] However, the vertigo associated with the Tullio phenomenon (sound-induced) and Hennebert sign (pressure-induced) is less prominent than in the superior semicircular canal dehiscence syndrome, and, more commonly, recurrent spells of vertigo last hours or longer, similar to the presentation of Ménière disease, with unknown pathophysiology. And although the hearing loss usually begins in early childhood, the vestibular symptoms can begin in childhood or may be delayed until adulthood.[48] Suzuki and colleagues[49] studied the phenotype in 39 patients with hearing loss with *SLC25A4* mutations and reported that 24 (70.6%) of the patients with *SLC25A4* mutations had episodes of vertigo. A retrospective chart review of 22 patients with an enlarged vestibular aqueduct revealed 14 (64%) had dizziness, with half of the patients having recurrent spells of vertigo.[50] An enlarged vestibular aqueduct is also associated with other inner ear malformations including the cochlea.[44,45]

Workup and evaluation of a suspected enlarged vestibular aqueduct should include an audiogram, otoacoustic emissions, vestibular testing with cervical vestibular-evoked myogenic potentials, and an imaging modality. Classically, previous studies relied on high-resolution CT of the temporal bone to evaluate for an enlarged vestibular aqueduct. The CT image at the 45-degree oblique plane Pöschl view was used for calculation. Now, the axial image can be used to define an enlarged vestibular aqueduct if the width at the operculum is ≥2 mm or the width at the midpoint is ≥1 mm.[51] Because the most widely used modality for imaging in the evaluation of hearing loss is MRI and because of the potential sensitivity of a pediatric patient to the effects of ionizing radiation, MRI is considered the modality of choice to evaluate the inner ear. A large study comparing MRI and CT showed 93% agreement in the diagnosis of an enlarged vestibular aqueduct.[52] In a study of 96 pediatric patients without sensorineural hearing loss, the mean midpoint width was 0.527 mm ± 0.08 mm, ranging from 0.353 to 0.887 mm.[53] Similar findings, including a mean midpoint width of 0.48 mm ± 0.17 mm, were noted in a study of 27 normal temporal bones of patients aged from 28 to 102 years.[54]

Patients diagnosed with an enlarged vestibular aqueduct are often advised to avoid sports or activities or to wear helmets because of the hypothesis that even minor head impacts may be associated with drops in hearing; however, a more recent meta-analysis reported that no strong data prove an association of hearing loss with trauma.[55] Brodsky and Choi[56] recommend that providers should make families aware of the possible association between an enlarged vestibular aqueduct and sudden hearing drops due to head trauma, but the family should make their own decisions on whether contact sports should be permitted given that head trauma may not significantly impact the risk of overall hearing loss progression.[56] They concluded that, currently, evidence is insufficient to support a recommendation that physicians should explicitly restrict patients from playing

KEY POINTS

- In addition to evaluation of the external ear for vesicles in Ramsay Hunt syndrome, the clinician should evaluate the back of the ear and conduct an otoscopic examination of the external canal and the tympanic membrane.
- Facial paralysis occurs in nearly all and hearing loss in up to half of patients with Ramsay Hunt syndrome. About 30% to 50% have vestibular neuritis–like vertigo and subsequent imbalance.
- A key factor in the recovery of cranial nerve function after Ramsay Hunt syndrome appears to be an earlier onset of treatment. Treatment within 1 to 3 days of symptom onset ensures 75% of patients recover function, but only 30% recover if treated after 7 days.
- Up to 15% of children with sensorineural hearing loss have an enlarged vestibular aqueduct.
- An enlarged vestibular aqueduct and pathogenic sequence alteration in the *SLC26A4* gene are associated with bilateral hearing loss and recurrent spells of episodic vertigo.
- An enlarged vestibular aqueduct, like superior semicircular canal dehiscence, can present with cervical vestibular-evoked myogenic potentials with low thresholds and high amplitudes, but the Tullio phenomenon and the Hennebert sign are generally less prominent. A Ménière disease–like presentation with recurrent spells of vertigo can be associated with an enlarged vestibular aqueduct.

TABLE 8-3 **Characteristic Auditory, Vestibular, and Imaging Findings in Selected Otologic Disorders Causing Dizziness**

Syndrome	Hearing	Vestibular	Image
Ménière disease	Usually low-frequency sensorineural hearing loss unilateral	Often with unilateral reduced caloric vestibular responses but normal head impulse test response	Three-dimensional delayed IV gadolinium demonstrates endolymphatic hydrops and ipsilaterally bright perilymph
Superior semicircular canal dehiscence	Bony hyperacusis: bone conduction <0 dB, pulsatile tinnitus, autophony, air-bone gap in low frequencies	Vestibular hypersensitivity: Tullio phenomenon and Hennebert sign; cervical vestibular-evoked myogenic potential with high amplitude and low threshold	CT demonstrates thinning or dehiscence over the superior semicircular canal; CT should be Pöschl view or Stenvers view, at slices ≤0.625 mm
Perilymphatic fistula			
Traumatic	Can have sudden sensorineural hearing loss	Can have severe vertigo with complete vestibular loss	Pneumolabyrinth may indicate penetrating injury; other potential indications for surgical exploration include ossicular fracture and temporal bone fracture; developmental abnormalities of the cochlea are associated with a higher risk of perilymphatic fistula
Idiopathic	Can be normal	Can be normal	Only seen on surgical exploration
Diving and barotrauma			
Inner ear barotrauma	Often affected	Less often affected	Some are surgically correctable
Inner ear decompression	Rarely solely affected (6%)	Often solely affected (75%)	Needs immediate hyperbaric chamber
Cholesteatoma with vertigo	Often affected	Often affected	CT or MRI may demonstrate cholesteatoma invading the horizontal semicircular canal, diffusion-weighted imaging hyperintensity on MRI
Ramsay Hunt syndrome	About 50% of patients have hearing loss	About 30%-50% of patients have vertigo	Look for vesicles on the external ear and otoscopic evaluation in the setting of facial weakness
Enlarged vestibular aqueduct	10% of all patients with congenital hearing loss have an enlarged vestibular aqueduct	60%-79% have vestibular symptoms, often recurrent prolonged spontaneous vertigo	Both CT and MRI can demonstrate a midpoint width of vestibular aqueduct ≥1 mm or operculum ≥2 mm
Autoimmune inner ear disease	Bilateral, often dropping hearing loss over ≥3 and ≤90 days	About 50% have vertigo, dizziness, and other vestibular symptoms	Normal

CT = computed tomography; MRI = magnetic resonance imaging.

contact sports because of an enlarged vestibular aqueduct alone. It is also important to note that cochlear implantation resulted in significant hearing improvement in patients with an enlarged vestibular aqueduct regardless of morphology, including incomplete partition type II defects and enlarged vestibular aqueduct size. Cochlear implantation is safe in enlarged vestibular aqueduct syndrome and provides improvement of an average of 64 dB in pure tone average and 58 dB in speech reception threshold and 35% improvement in word score.[57]

AUTOIMMUNE DISEASES AND INNER EAR SYNDROMES

A wide range of autoimmune disorders can involve the inner ear and are associated with hearing loss or vertigo. The proposed mechanisms of inner ear dysfunction include (1) antigen antibody–immune complex deposition, (2) autoantibodies directed against inner ear antigens, and (3) specific cytotoxic T cells causing inner ear damage. Following are specific examples of autoimmune inner ear disease that are associated with progressive hearing loss over weeks, Cogan syndrome and Sjögren syndrome.

Autoimmune Inner Ear Disease

In one of the first case series of autoimmune inner ear disease, Lehnhardt[58] hypothesized an antigen-antibody reaction in 13 patients with progressive bilateral sensorineural hearing loss. Nine of the patients had initial unilateral hearing loss and then subsequent involvement of the contralateral ear, which Lehnhardt proposed was secondary to the first cochlear injury triggering antibodies that then secondarily caused the involvement of the contralateral inner ear and hearing. In 1979, McCabe[59] proposed the term *autoimmune inner ear disease* in a series of patients with idiopathic bilateral hearing loss that was responsive to steroids. The differential diagnosis includes syphilis, bilateral Ménière disease, superficial siderosis, ototoxicity, neurofibromatosis type 2, and radiation injury.

The timeframe of the development of hearing loss is key to the diagnosis of autoimmune inner ear disease: typically, the development of deafness occurs over weeks, and not quickly over a day or two, but it also does not progress over years as in age-associated presbycusis.

Autoimmune inner ear disease is defined as bilateral hearing loss with a decline in at least one ear that evolves in longer than 3 days but less than 90 days. It is important to note that, in up to one-third of cases, autoimmune inner ear disease occurs in the setting of a primary rheumatologic disorder, including systemic lupus erythematosis, rheumatoid arthritis, Sjögren syndrome, Hashimoto thyroiditis, granulomatosis with polyangiitis, Behçet disease, and primary neurologic immune-related entities such as multiple sclerosis and myasthenia gravis.[60,61]

Investigating the sera of patients with a history of autoimmune inner ear disease has identified antibodies to inner ear proteins such as cochlin, type II collagen, peripheral myelin protein zero, and β-actin, and the most studied is the antibody directed to 68-kDa inner ear antigen, characterized as heat shock protein 70, which has a high specificity of 90% but low sensitivity of 42%.[62] MRI with and without gadolinium aids in ruling out retrocochlear pathologies: vestibular schwannoma, intracranial metastases, demyelinating diseases, or cerebrovascular ischemia.

Investigators have noted that vestibular symptoms often present as recurrent vertigo spells during the course of autoimmune inner ear disease.[63] A 2018 review

KEY POINTS

- An enlarged vestibular aqueduct can be diagnosed by using either CT of the temporal bone or MRI of the internal auditory canal.
- Many patients with an enlarged vestibular aqueduct have been advised to avoid contact sports, but current data may not support an association with minor head trauma and drops in hearing. Also, cochlear implantation in these patients is safe and effective.
- Deafness associated with autoimmune inner ear disease occurs over weeks and not 1 or 2 days, as in sudden sensorineural hearing loss. One-third of the patients with autoimmune inner ear disease have or will develop a systemic autoimmune disease.
- Up to 50% of patients with autoimmune inner ear disease report vertigo or dizziness or have tinnitus and aural fullness, mimicking Ménière disease.
- Corticosteroids are the mainstay of treatment for autoimmune inner ear disease, with serial audiograms to evaluate hearing with taper. Referral to rheumatology for consideration of steroid-sparing medications and evaluation for systemic autoimmune disease should be considered.

of autoimmune inner ear disease reported vestibular symptoms, with imbalance and motion intolerance, ataxia, and positional or episodic vertigo occurring in 50% of patients with autoimmune inner ear disease.[64] Because 25% to 50% of patients with autoimmune inner ear disease have tinnitus and aural fullness, it can be difficult to distinguish from Ménière disease. Other considerations in bilateral hearing loss with and without vertigo include otologic syphilis, Lyme disease, and Cogan syndrome.

Corticosteroids remain the mainstay of treatment for autoimmune inner ear disease, with the dosing relatively unchanged from the original recommendation: untapered high-dose steroids for 4 weeks followed by attempted tapers depending on clinical outcomes.[61] Referral to rheumatology is nearly always indicated to aid in steroid-sparing interventions and to investigate for primary autoimmune diseases, which are a comorbidity in up to 30% of the cases of autoimmune inner ear disease.[60,65] Of note, autoimmune inner ear disease preceded the development of autoimmune disease as long as months to years later; thus, follow-up with these patients is strongly recommended.[63]

TABLE 8-4 **"Red Flags" When a Patient Presents With Vertigo and These Symptoms**

- Presence of sudden violent falls (ie, Tumarkin falls) with a sense of being pushed in a patient with Ménière disease: indication for consideration of vestibular ablation due to the violent nature of these falls, which can be associated with trauma
- Vertigo triggered by pressure on the tragus (Hennebert sign) or loud sounds (Tullio phenomenon): superior semicircular canal dehiscence or perilymphatic fistula; both are surgically correctable
- Presence of fever and ear pain with draining ear (otorrhea) and vertigo: rule out cholesteatoma invading into the horizontal semicircular canal causing dehiscence syndrome, urgent surgical evaluation
- Severe otalgia and ipsilateral facial weakness: evaluate external canal, pinna, and tympanic membrane for vesicles of Ramsay Hunt syndrome; immediate acyclovir or other antiviral, with corticosteroids; rapid initiation of treatment is important because 75% recover cranial nerve function if given within 1 to 3 days, but only 30% recover if given after 7 days
- Vertigo occurring soon after a complex dive, within 13 to 206 minutes after surfacing (average of 36 minutes): consider inner ear decompression illness, which presents with a pure vestibular disorder in 75% of cases; treatment is hyperbaric chamber as soon as possible with supplemental oxygen while en route
- Presence of pneumolabyrinth on CT (best view to visualize the air bubbles is coronal cuts): may indicate a penetrating trauma causing perilymphatic leak allowing air bubbles to enter into the labyrinth; this requires urgent surgical exploration and reparative surgery
- History of congenital sensorineural hearing loss bilateral, fluctuating course: (1) enlarged vestibular aqueduct is associated with up to 10%-15% of children with sensorineural hearing loss, cochlear implant is restorative of hearing and safe in patients with enlarged vestibular aqueduct; (2) children with congenital cochlear malformations have a much higher incidence of perilymphatic fistula with even minor trauma, such as blowing the nose hard, and surgical exploration may be indicated if cochlear malformation is identified on CT, about one-third of patients with enlarged vestibular aqueduct had recurrent spells of vertigo in one study
- Fluctuating bilateral dropping hearing levels over from 3 days to 90 days: consider autoimmune inner ear disease with institution of high-dose untapered corticosteroids for 4 weeks followed by attempted tapers (vertigo and vestibular symptoms in up to 50% of patients with autoimmune inner ear disease)

CT = computed tomography.

Cogan Syndrome

Cogan syndrome is a rare disease of people predominantly between the ages of 20 and 40 years (mean age of onset is 25 years old); it is characterized by autoimmune nonsyphilitic keratitis of the eyes, vertigo, and tinnitus, but, generally, patients maintain normal or near-normal vision, and up to 52% develop profound hearing loss despite immunosuppressive treatment.[66] In atypical Cogan syndrome, progressive hearing loss occurs, and in 15% to 20% of patients, systemic manifestations can occur, such as aortitis of the cardiovascular system, or systemic vasculitis of the neurologic or gastrointestinal system. Recurrent vertigo, similar to that which occurs in Ménière disease, is common, but a distinction is that the hearing loss in Cogan syndrome is bilateral and often progresses to complete deafness in 2 years. Systemic corticosteroids are the mainstay for treatment of the audiovestibular symptoms of Cogan syndrome, but if these are not effective, other immunosuppressants are tried, including azathioprine, cyclosporin A, and methotrexate, among others.[67]

The typical audiovestibular presentation may be Ménière disease–like, with fluctuating hearing loss and vertigo spells, and the audiometric profile is consistent with cochlear, rather than retrocochlear, hearing loss. Of note, deafness occurs in more than half of patients with Cogan syndrome. Temporal bone studies of Cogan syndrome report degeneration of the structures of the vestibular labyrinth and the cochlear duct, including the organ of Corti and stria vascularis, and endolymphatic hydrops. A temporal bone of a patient with Cogan syndrome after successful bilateral cochlear implantation revealed endolymphatic hydrops of all cochlear turns and of the saccule and degenerative and fibro-osseous changes throughout.[68]

Sjögren Syndrome

In a study using temporal bones from patients with a history of Sjögren syndrome, an autoimmune illness associated with 22.5% to 46% occurrence of sensorineural hearing loss, immunoglobulin deposition was identified in the stria

Special Imaging Considerations in Otologic Disorders Causing Dizziness TABLE 8-5

- MRI on 3-tesla delayed IV gadolinium evaluates for endolymphatic hydrops and permeability within the blood-labyrinthine barrier in Ménière disease
- CT evaluates for superior semicircular canal dehiscence; use 0.5-mm CT reformatted in the plane of the superior semicircular canal (Pöschl view) and orthogonal (Stenvers view)
- CT in the coronal view is best to visualize pneumolabyrinth, if present, other red flags in trauma is the presence of ossicular fracture or dislocation: both indicate possible penetrating trauma with damage to the inner ear
- CT is classically used to evaluate for cholesteatoma, and non–echo planar diffusion-weighted imaging is increasingly being used to evaluate for restriction on diffusion-weighted imaging indicative or cholesteatoma
- MRI with gadolinium reveals enhancement, and T2 fluid-attenuated inversion recovery (FLAIR) reveals swelling of the facial nerve in Ramsay Hunt syndrome
- CT in the Pöschl plane, which runs parallel to the longitudinal axis of the vestibular aqueduct, evaluates the diameter at the midpoint; if the vestibular aqueduct diameter is >1.0 mm, it is consistent with an enlarged vestibular aqueduct

CT = computed tomography; IV = intravenous; MRI = magnetic resonance imaging.

KEY POINTS

- **The vasculitis and audiovestibular dysfunction of Cogan syndrome usually respond to high-dose corticosteroids, with the expectation of a beneficial response within 2 to 3 weeks. In intractable Cogan syndrome, the progression to deafness occurs in more than half of patients.**
- **In both autoimmune inner ear disease– and Cogan syndrome–associated deafness, cochlear implantation is often restorative of hearing with good to excellent results.**
- **The finding of immunoglobulin deposition in the stria vascularis and spiral ganglia in Sjögren syndrome associated with hearing loss indicates that the hearing loss in autoimmune inner ear disease and systemic autoimmune disease may be mediated in part by immunoglobulin deposition in the inner ears.**

vascularis of patients with a history of hearing loss but not in those without a history of hearing loss.[69] Sone and colleagues[70] noted multiple studies related to temporal bone findings in patients with a history of systemic autoimmune disease, demonstrating stria vascularis and spiral ganglia neuronal atrophy. In addition, animal models of autoimmune inner ear disease also demonstrate the same histopathologic findings.[68]

CONCLUSION

This article summarizes the most recent clinical findings in the otologic diseases that often present with vertigo including Ménière disease, superior semicircular canal dehiscence, perilymphatic fistula, barotrauma, cholesteatoma, Ramsay Hunt syndrome, enlarged vestibular aqueduct, and autoimmune inner ear disease. TABLE 8-3 is a summary of the auditory and vestibular testing results and imaging findings of these entities. Also, TABLE 8-4 presents a summary of red flags that the neurologist and neuro-otologist should always keep in mind when evaluating a patient with vertigo of unknown etiology. TABLE 8-5 shows important new imaging considerations in these otologic entities. In most cases, auditory and vestibular testing and an imaging study are indicated in the workup of these patients.

REFERENCES

1 Eggers SDZ. Episodic spontaneous dizziness. Continuum (Minneap Minn) 2021;27(2, Neuro-otology:369-401.

2 Fife TD, Tourkevich R. Tinnitus, hyperacusis, otalgia, and hearing loss. Continuum (Minneap Minn) 2021;27(2, Neuro-otology):491-525.

3 Maxwell AK, Ishiyama G, Kaznezis S, Ishiyama A. Isolated saccular hydrops on high-resolution MRI is associated with full spectrum Meniere's disease [published online January 19, 2021]. Otol Neurotol. doi:10.1097/MAO.0000000000003051

4 Tagaya M, Yamazaki M, Teranishi M, et al. Endolymphatic hydrops and blood-labyrinthine barrier in Ménière's disease. Acta Otolaryngol 2011;131(5):474-479. doi:10.3109/00016489.2010.534114

5 Pakdaman MN, Ishiyama G, Ishiyama A, et al. Blood-labyrinth barrier permeability in Menière disease and idiopathic sudden sensorineural hearing loss: findings on delayed postcontrast 3D-FLAIR MRI. AJNR Am J Neuroradiol 2016;37(10):1903-1908. doi:10.3174/ajnr.A4822

6 Ishiyama G, Lopez IA, Ishiyama P, et al. The blood labyrinthine barrier in the human normal and Meniere's disease macula utricle. Sci Rep 2017;7:253. doi:10.1038/s41598-017-00330-5

7 Ishiyama G, Wester J, Lopez IA, et al. Oxidative stress in the blood labyrinthine barrier in the macula utricle of Meniere's disease patients. Front Physiol 2018;9:1068. doi:10.3389/fphys.2018.01068

8 Ishiyama G, Lopez IA, Acuna D, Ishiyama A. Investigations of the microvasculature of the human macula utricle in Meniere's disease. Front Cell Neurosci 2019;13:445. doi:10.3389/fncel.2019.00445

9 Baloh RW, Jacobson K, Winder T. Drop attacks with Menière's syndrome. Ann Neurol 1990;28(3):384-387. doi:10.1002/ana.410280314

10 Chen Z, Zhang Y, Zhang Q. Tumarkin drop attack recorded by video surveillance. JAMA Neurol 2020;77(7):897-898. doi:10.1001/jamaneurol.2020.0884

11 Calzada AP, Lopez IA, Ishiyama G, Ishiyama A. Otolithic membrane damage in patients with endolymphatic hydrops and drop attacks. Otol Neurotol 2012;33(9):1593-1598. doi:10.1097/MAO.0b013e318271c48b

12 Ishiyama G, Ishiyama A, Jacobson K, Baloh RW. Drop attacks in older patients secondary to an otologic cause. Neurology 2001;57(6):1103-1106. doi:10.1212/wnl.57.6.1103

13 Halmagyi GM, Curthoys IS. A clinical sign of canal paresis. Arch Neurol 1988;45(7):737-739. doi:10.1001/archneur.1988.00520310043015

14 Minor LB, Solomon D, Zinreich JS, Zee DS. Sound- and/or pressure-induced vertigo due to bone dehiscence of the superior semicircular canal. Arch Otolaryngol Head Neck Surg 1998;124(3):249-258. doi:10.1001/archotol.124.3.249

15 Ward BK, Carey JP, Minor LB. Superior canal dehiscence syndrome: lessons from the first 20 years. Front Neurol 2017;8:177. doi:10.3389/fneur.2017.00177

16 Zhou G, Gopen Q, Poe DS. Clinical and diagnostic characterization of canal dehiscence syndrome: a great otologic mimicker. Otol Neurotol 2007; 28(7):920-926.

17 Govender S, Fernando T, Dennis DL, et al. Properties of 500Hz air- and bone-conducted vestibular evoked myogenic potentials (VEMPs) in superior canal dehiscence. Clin Neurophysiol 2016;127(6):2522-2531. doi:10.1016/j.clinph.2016.02.019

18 Fife TD, Colebatch JG, Kerber KA, et al. Practice guideline: cervical and ocular vestibular evoked myogenic potential testing: report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Neurology 2017;89(22): 2288-2296. doi:10.1212/WNL.0000000000004690

19 Gopen Q, Zhou G, Poe D, et al. Posterior semicircular canal dehiscence: first reported case series. Otol Neurotol 2010;31(2):339-344. doi:10.1097/MAO.0b013e3181be65a4

20 Fife TD, Satya-Murti S, Burkard RF, Carey JP. Vestibular evoked myogenic potential testing: payment policy review for clinicians and payers. Neurol Clin Pract 2018;8(2):129-134. doi:10.1212/CPJ.0000000000000430

21 Schwartz SR, Almosnino G, Noonan KY, et al. Comparison of transmastoid and middle fossa approaches for superior canal dehiscence repair: a multi-institutional study. Otolaryngol Head Neck Surg 2019;161(1):130-136. doi:10.1177/0194599819835173

22 Linda W, Brewster R, Poe D, et al. Superior semicircular canal dehiscence syndrome. J Neurosurg 2017;127(6):1268-1276. doi:10.3171/2016.9.JNS16503

23 Carey JP, Minor LB, Nager GT. Dehiscence or thinning of bone overlying the superior semicircular canal in a temporal bone survey. Arch Otolaryngol Head Neck Surg 2000;126(2): 137-147. doi:10.1001/archotol.126.2.137

24 Weissman JL, Weber PC, Bluestone CD. Congenital perilymphatic fistula: computed tomography appearance of middle ear and inner ear anomalies. Otolaryngology 1994;111(3 pt 1): 243-249. doi:10.1177/01945998941113P113

25 Goodhill V, Brockman SJ, Harris I, Hantz O. Sudden deafness and labyrinthine window ruptures. Audio-vestibular observations. Ann Otol Rhinol Laryngol 1973;82(1):2-12. doi:10.1177/000348947308200103

26 Kita AE, Kim I, Ishiyama G, Ishiyama A. Perilymphatic fistula after penetrating ear trauma. Clin Pract Cases Emerg Med 2019;3(2): 115-118. doi:10.5811/cpcem.2019.1.37404

27 Hennebert C. Labyrinthite double reflexe moteur otooculaire. Clinique 1905;19:214-215.

28 Ikezono T, Matsumura T, Matsuda H, et al. The diagnostic performance of a novel ELISA for human CTP (cochlin-tomoprotein) to detect perilymph leakage. PLoS One 2018;13(1):e0191498. doi:10.1371/journal.pone.0191498

29 Friedland DR, Wackym PA. A critical appraisal of spontaneous perilymphatic fistulas of the inner ear. Am J Otol 1999;20(2):261-276.

30 Rozycki SW, Brown MJ, Camacho M. Inner ear barotrauma in divers: an evidence-based tool for evaluation and treatment. Diving Hyperb Med 2018;48(3):186-193. doi:10.28920/dhm48.3.186-193

31 Edmonds C. Inner ear barotrauma: a retrospective clinical series of 50 cases. SPUMS Journal 2004;34:11-19.

32 Klingman C. Inner ear decompression sickness in compressed-air diving. Undersea Hyperbaric Med 2012;39(1):589-594.

33 Shupak A, Gil A, Nachum Z, et al. Inner ear decompression sickness and inner ear barotrauma in recreational divers: a long-term follow-up. Laryngoscope 2003;113:2141-2147.

34 Gempp E, Louge P. Inner ear decompression sickness in scuba divers: a review of 115 cases. Eur Arch Otorhinolaryngol 2013;270(6):1831-1837. doi:10.1007/s00405-012-2233-y

35 Livingstone DM, Smith KA, Lange B. Scuba diving and otology: a systematic review with recommendations on diagnosis, treatment and post-operative care. Diving Hyperb Med 2017; 47(2):97-109. doi:10.28920/dhm47.2.97-109

36 Jennings BA, Prinsley P, Philpott C, et al. The genetics of cholesteatoma. A systematic review using narrative synthesis. Clin Otolaryngol 2018; 43(1):55-67. doi:10.1111/coa.12900

37 Copeland BJ, Buchman CA. Management of labyrinthine fistula in chronic ear surgery. Am J Otolaryngol 2003;24(1):51-60. doi:10.1053/ajot.2003.10

38 Hsieh MC, Wu CC, Wang SH. Positive perilymph fistula test with semicircular canal dehiscence from cholesteatoma. CMAJ 2019;191(4):E104. doi:10.1503/cmaj.180799

39 Lingham RK, Bassett P. A meta-analysis on the diagnostic performance of non-echoplanar diffusion-weighted imaging in detecting middle ear cholesteatoma: 10 years on. Otol Neurotol 2017;38(4):521-528.

40 Robillard RB, Hilsinger RL, Adour KK. Ramsay Hunt facial paralysis: clinical analyses of 185 patients. Otolaryngol Head Neck Surg 1986;95(3 pt 1): 292-297. doi:10.1177/019459988609053P105

41 Nakamura Y, Matsumoto H. Case of atypical Ramsay-Hunt syndrome who presented with severe vertigo and vomiting [in Japanese]. No To Hattatsu 2012;44(1):66-68.

42 Kanerva M, Jones S, Pitkaranta A. Ramsay Hunt syndrome: characteristics and patient self-assessed long-term facial palsy outcome. Eur Arch Otorhinolaryngol 2020;277(4):1235-1245. doi:10.1007/s00405-020-05817-y

43 Murakami S, Honda N, Mizobuchi M, et al. Rapid diagnosis of varicella zoster virus infection in acute facial palsy. Neurology 1998;51(4): 1202-1205. doi:10.1212/wnl.51.4.1202

44 Valvassori GE, Clemis JD. The large vestibular aqueduct syndrome. Laryngoscope 1978;88(5): 723-728. doi:10.1002/lary.1978.88.5.723

45 Steinbach S, Brockmeier S, Kiefer J. The large vestibular aqueduct–case report and review of the literature. Acta Otolaryngol 2005;126(8): 788-795. doi:10.1080/00016480500527276

46 Miyagawa M, Nishio SY, Usami S. Mutation spectrum and genotype-phenotype correlation of hearing loss patients caused by SLC26A4 mutations in the Japanese: a large cohort study. J Human Genet 2014;59(5):262-268. doi:10.1038/jhg.2014.12

47 Sheykholeslami K, Schmerber S, Habiby Kermany M, Kaga K. Vestibular-evoked myogenic potentials in three patients with large vestibular aqueduct. Hear Res 2004;190(1-2):161-168. doi:10.1016/S0378-5955(04)00018-8

48 Oh AK, Ishiyama A, Baloh RW. Vertigo and the enlarged vestibular aqueduct syndrome. J Neurol 2001;248(11):971-974. doi:10.1007/s004150170050

49 Suzuki H, Oshima A, Tsukamoto K, et al. Clinical characteristics and genotype-phenotype correlation of hearing loss patients with SLC26A4 mutations. Acta Otolaryngol 2007;127(12): 1292-1297. doi:10.1080/00016480701258739

50 Song JJ, Hong SK, Lee SY, et al. Vestibular manifestations in subjects with enlarged vestibular aqueduct. Otol Neurotol 2018;39(6): e461-e467. doi:10.1097/MAO.0000000000001817

51 Boston M, Halsted M, Meinzen-Derr J, et al. The large vestibular aqueduct: a new definition based on audiologic and computed tomography correlation. Otolaryngol Head Neck Surg 2007; 136(6):972-977. doi:10.1016/j.otohns.2006.12.011

52 Connor SEJ, Dudau C, Pai I, Gaganasiou M. Is CT or MRI the optimal imaging investigation for the diagnosis of large vestibular aqueduct syndrome and large endolymphatic sac anomaly? Eur Arch Otorhinolaryngol 2019;276(3):593-702. doi: 10.1007/s00405-019-05279-x

53 Juliano AF, Ting EY, Mingkwansook V, et al. Vestibular aqueduct measurements in the 45° oblique (Pöschl) plane. AJNR Am J Neuroradiol 2016;37(7):1331-1337. doi:10.3174/ajnr.A4735

54 Sando I, Ikeda M. The vestibular aqueduct in patients with Meniere's disease. A temporal bone histopathological investigation. Acta Otolaryngol 1984;97(5-6):558-570. doi: 10.3109/00016488409132934

55 Alemi AS, Chan DK. Progressive hearing loss and head trauma in enlarged vestibular aqueduct: a systematic review and meta-analysis. Otolaryngol Head Neck Surg 2015;153(4):512-517. doi:10.1177/0194599815596343

56 Brodsky JR, Choi SS. Should children with an enlarged vestibular aqueduct be restricted from playing contact sports? Laryngoscope 2018; 128(10):2219-2220. doi:10.1002/lary.27119

57 Patel ND, Ascha MS, Manzoon NF, et al. Morphology and cochlear implantation in enlarged vestibular aqueduct. Am J Otolaryngol 2018;39(6):657-663. doi:10.1016/j.amjoto.2018.06.006

58 Lehnhardt E. Sudden hearing disorders occurring simultaneously or successively on both sides [in German]. Z Laryngol Rhinol Otol 1958;37(1):1-16.

59 McCabe BF. Autoimmune sensorineural hearing loss. Ann Otol Rhinol Laryngol 1979;88(5 pt 1): 585-589. doi:10.1177/000348947908800501

60 Bovo R, Almoni C, Martini A. Immune-mediated inner ear disease. Acta Otolaryngol 2006;126(10): 1012-1021. doi:10.1080/00016480600606723

61 Rauch SD. Clinical management of immune-mediated inner-ear disease. Ann N Y Acad Sci 1997;830:203-210. doi:10.1111/j.1749-6632.1997.tb51891.x

62 Hirose K, Wener MH, Duckert LG. Utility of laboratory testing in autoimmune inner ear disease. Laryngoscope 1999;109(11):1749-1754. doi:10.1097/00005537-199911000-00005

63 Broughton SS, Meyerhoff WE, Cohen SB. Immune-mediated inner ear disease: 10-year experience. Semin Arthritis Rheum 2004;34(2): 544-548. doi:10.1016/j.semarthrit.2004.07.001

64 Ciorba A, Corazzi V, Bianchini C, et al. Autoimmune inner ear disease (AIED): a diagnostic challenge. Int J Immunopathol Pharmacol 2018;32:2058738418808680. doi: 10.1177/2058738418808680

65 Vambutas A, Pathak S. AAO: autoimmune and autoinflammatory (disease) in otology: what is new in immune-mediated hearing loss. Laryngoscope Investig Otolaryngol 2016;1(5): 110-115. doi:10.1002/lio2.28

66 Gluth MB, Baratz KH, Matteson EL, Driscoll CLW. Cogan syndrome: a retrospective review of 60 patients throughout a half century. Mayo Clin Proc 2006;81(4):483-488. doi:10.4065/81.4.483

67 Illiescu DA, Timaru CM, Batras M, De Simone A, Stefan C. Cogan's syndrome. Rom J Ophthalmol 2015;59(1):6-13.

68 Kamakura T, Lee DJ, Herrmann BS, Nadol JB Jr. Histopathology of the human inner ear in Cogan's syndrome with cochlear implantation. Audiol Neurotol 2017;22(2):116-123. doi:10.1159/000477534

69 Calzada AP, Balaker AE, Ishiyama G, et al. Temporal bone histopathology and immunoglobulin deposition in Sjogren's syndrome. Otol Neurotol 2012;33(2):258-266. doi:10.1097/MAO.0b013e318241b548

70 Sone M, Schachern PA, Paparella MM, Morizonon N. Study of systemic lupus erythematosus in temporal bones. Ann Otol Rhinol Laryngol 1999;108(4):338-344. doi:10.1177/000348949910800404