Chapter 8
Perilymphatic Fistula

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Introduction and Definition

Broadly defined, a perilymphatic fistula (PLF) is any communication between the inner ear/perilymphatic space and outside the otic capsule. This definition would encompass essentially all third mobile window disorders (TMWD), including superior semicircular canal dehiscence (SSCD) and temporal bone fractures inclusive of the otic capsule. However, more specifically, PLF has come to define an abnormal opening in the areas of the oval or round window between the inner ear and middle ear space. The diagnosis of a PLF has been controversial since its initial reports as a complication from stapedectomy surgery. There is no controversy about the existence of PLF as a clinical entity after stapes surgery or trauma. The controversy surrounds its diagnosis, particularly in suspect cases that had not undergone stapedectomy or trauma, otherwise known as "spontaneous perilymphatic fistula." This term, "spontaneous perilymphatic fistula," is actually a misnomer. More appropriately, the term should be, "PLF without a known cause." An analogy would be the development of an inguinal hernia. Some hernias occur from a particular activity and others develop without a known activity. To a lesser extent, controversies surround appropriate treatment and its relative frequency.

In the era prior to awareness of TMWD, almost certainly, patients had been diagnosed with PLF who had other types of TMWD, such as SSCD. We have witnessed patients like this in our own practice—initially diagnosed with PLF, only to be later

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identified as having SSCD. However, the traditional surgical treatment of PLF has included reinforcement of the areas of the oval window (OW) and round windows (RW), which has often alleviated symptoms in patients with other TMWD.

The current thinking is that the pathophysiology of TMWD (see Chap. 3) is based on the simple presence of a bony defect in the otic capsule producing abnormal fluid dynamics of the inner ear, thus producing TMWD symptoms. However, this theory does not explain the presence of asymptomatic bony defects, progressive hearing loss in TMWD cases, sensorineural hearing loss in TMWD, vertigo spells that last longer than the duration of the known triggers of sound or straining (i.e., vertigo spells lasting hours) or a Ménière's type presentation. Another aspect of the pathophysiology could stem from individual anatomy with relatively direct connection between the cerebrospinal fluid space and the perilymphatic space. These patients would have a higher fluid pressure in the inner ear, known as perilymphatic hypertension. These exceptions to the current theory raise the question as to whether PLF may play a role in the pathophysiology of TMWD.

One notable case early in our career raised this question:

In October 1996, a 39-year-old female presented with sudden right-sided profound hearing loss (only hearing ear pre-injury) and vertigo which occurred after a grand mal seizure with head injury. She had normal premorbid hearing in the right ear and profound loss in the left ear. This episode left her profoundly deaf bilaterally. She had an uncontrolled seizure disorder with a history of multiple head injuries from grand mal seizures. The hearing loss and vertigo failed to respond to bedrest and high-dose prednisone. She was referred to us for further evaluation and treatment nine days out from her event. Her vertigo spells were provoked by straining and typically lasted 15 min per episode, occurring 1–3 times a day. Her physical exam demonstrated a left-beating spontaneous nystagmus, and the office fistula test was subjectively abnormal in the right ear, although it was difficult to interpret objectively due to the ongoing spontaneous nystagmus. A middle ear exploration was performed with reinforcement of the oval and round windows, and an endolymphatic sac decompression was performed on the following day. Postoperatively the patient had immediate relief from episodic vertigo although disequilibrium persisted and concomitant BPPV was treated later. More impressive was a dramatic improvement in the hearing in the operative ear—to a mild loss (30 db) in the low frequencies, sloping to a profound loss in the high frequencies. She was vertigo free and had stable hearing until March 2000 despite repeated seizures with head injuries. After another head injury, she again developed profound right hearing loss and episodic vertigo. A CT scan at that time demonstrated bilateral SSCD. (Our first SSCD repair was done in January 1998.) A right-sided middle fossa SSCD repair (capping) with oval and round window reinforcement was performed. Postoperatively, the episodic vertigo resolved but there was minimal improvement in hearing. She remained free of vertigo until she passed away nine months later from a presumed intracranial hemorrhage. Did this patient have a PLF and the SSCD was incidental, or vice versa? Was PLF part of the SSCD pathophysiology causing her strain-induced vertigo? Without the seizures and head injuries, would she have remained asymptomatic? Was the prior left profound hearing loss related to the left SSCD or some other subtle congenital defect that was undetectable at that time, e.g. modiolar defect?

Wackym et al. [1] proposed the entity of a CT negative otic capsule dehiscence in which the patients present with similar clinical findings and test findings as other TMWD but have no identifiable bony defect on CT scan. Presumably, these patients represent either patients who had a bony defect not yet identified or have PLF. Gadre et al. [2] reported on membranous and hypermobile stapes cases successfully treated with OW reinforcement. These were identified on preoperative high-resolution CT scan using gray-scale inverse windowing technique. Recently, Gianoli et al. [3] reported an as yet identified labyrinthine dehiscence of the horizontal semicircular canal where the tympanic segment of the facial nerve crosses near its ampullated end, adjacent to the oval window. See Fig. 8.1. This anatomic defect was linked to TMWD presentation with abnormal fistula testing and cVEMP testing. These patients would have been considered PLF patients in the past and would have undergone OW/RW reinforcement with likely similar outcomes. Given these above findings, we propose the clinical definition of PLF should be as noted in Fig. 8.2.

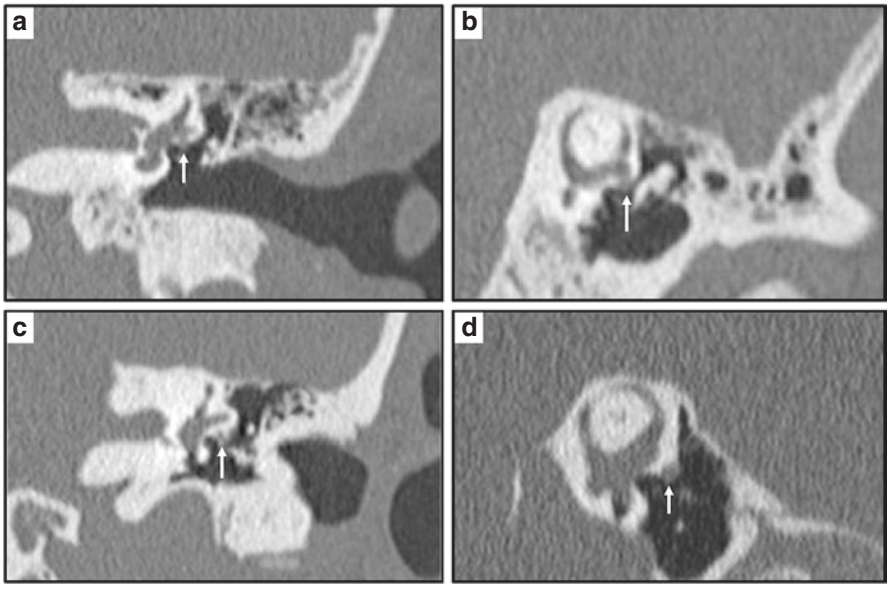

Fig. 8.1 CT scan demonstrating (**a**) HSC-FND on coronal imaging, (**b**) HSC-FND on Poschl imaging, (**c**) normal HSC and facial nerve anatomy on coronal imaging, and (**d**) normal HSC and facial canal on Poschl imaging

Clinical Definition of Perilymphatic Fistula:

1. History and physical findings consistent with TMWD
2. Objective Testing consistent with TMWD
3. CT scan that does not demonstrate a bony defect of the otic capsule

Fig. 8.2 Clinical definition of PLF

The presence of a bony defect would imply the bony defect is integral in the pathophysiology for the patients' disorder but does not preclude the possibility of PLF being part of the pathophysiologic process. However, the inability to identify a bony defect/dehiscence does not exclude the presence of a yet unidentified otic capsule lesion. Several anomalies of the otic capsule have been reported that could be the source for such patients and there may be more yet to be identified. Subtle defects identified include membranous or hypermobile stapes, abnormal Internal Auditory Canal-Cochlear patency, Modiolar defects, horizontal semicircular canal-facial nerve dehiscence, an enlarged internal auditory canal, and cochlear-facial dehiscence. Kohut et al. [4] proposed microfissures of the fissula ante fenestram and the floor of the round window as areas for a possible PLF source. Figure 8.3 demonstrates an

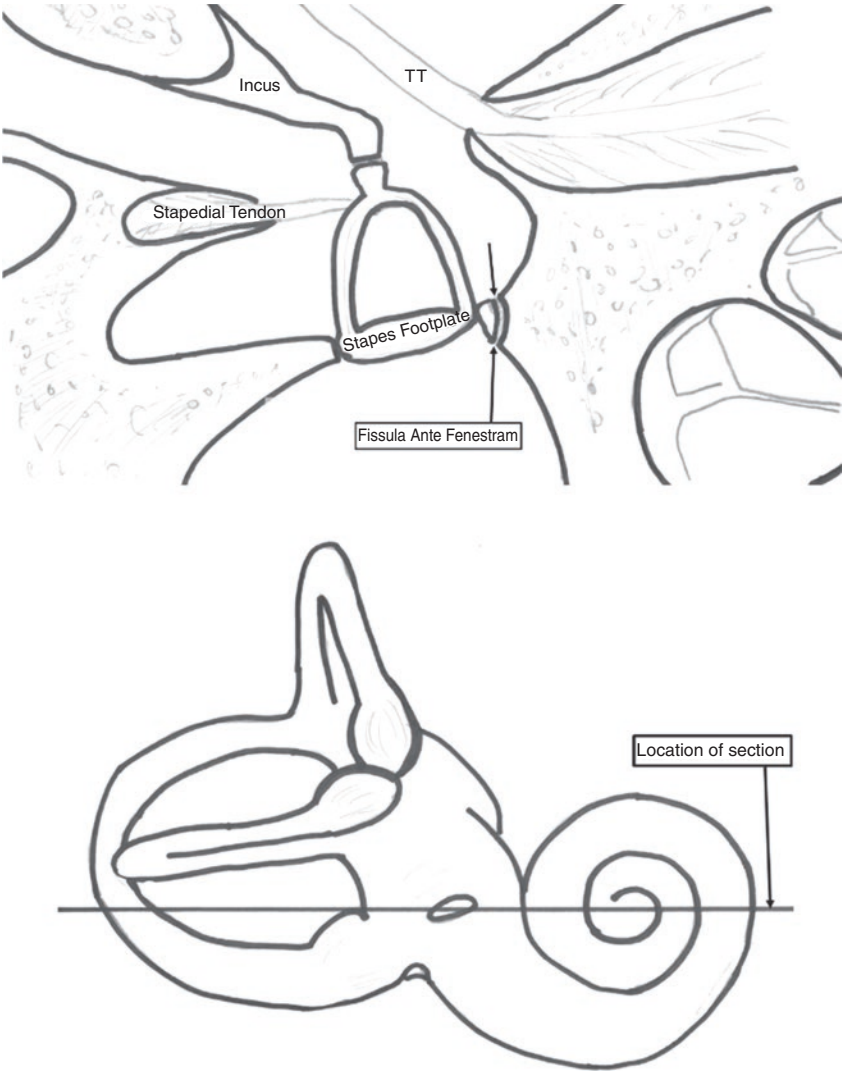

Fig. 8.3 Fissula Ante Fenestram—anatomic diagram. Adapted [4]

artist's rendition of the fissula ante fenestram, located anterior to the oval window. It projects from the junction of the vestibule and scala vestibuli that extends to the periosteum of the middle ear just beneath the cochleariform process, where the tendon of the tensor tympani muscle turns laterally toward the malleus. The fissula ante fenestram is typically not visible on CT scan but, due to its location, can be a source for what would otherwise be presumed to be an oval window PLF. A histologic section of the fissula ante fenestram can be seen on the Mass Eye and Ear Otopathology website, L-181: https://tinyurl.com/56cy3naw

Etiology

The etiology of PLF can be categorized as either resulting from an identified cause (post-stapedectomy, trauma) or an unidentified cause ("spontaneous") [5] (Fig. 8.4). The first case of PLF was reported in 1959 following a stapedectomy; it was found that the polyethylene prosthesis used in the procedure was displaced inferiorly, which resulted in a lack of contact to the incus and PLF [6]. More recently, Ashman and Jyung [7] reported a case of a 50-year-old female where they discovered a pseudomeningocele-like presentation following a stapedectomy. They used a Nitinol prosthesis secured to the incus and followed with a circumferential tragal perichondral graft with Gelfoam packing. This resulted in an improvement of symptoms. Post-stapedectomy PLF has become a well-recognized complication of stapes surgery, with its frequency less common with tissue seals and small fenestra approaches rather than total footplate removal.

Trauma is also a well-recognized cause for PLF, including both implosive and explosive trauma. Goodhill described explosive trauma as increased subarachnoid space and central pressure that transmits through a pre-existing defect to the inner ear [8, 9]. He described the implosive route of trauma as increased middle ear pressure or direct tympanic membrane pressure causing the oval or round window to rupture. Activities such as weightlifting and vaginal delivery cause sustained bouts of increased intracranial pressure and have been implicated as a source for explosive

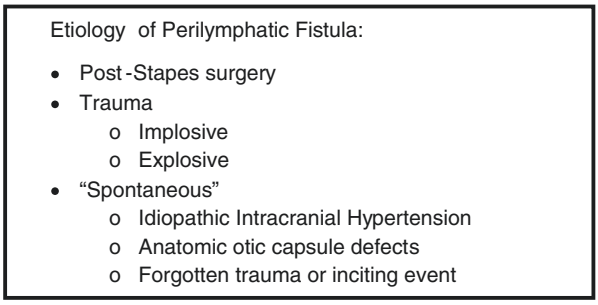

Fig. 8.4 Etiology of PLF

trauma. Patients with pseudotumor cerebri may be more susceptible due to their already elevated intracranial pressure.

In contrast, the underlying etiology for implosive trauma involves inadequate pressure equalization between the middle ear and pressure external to the body. Increases in ambient pressure occur when a person moves from a low to a high pressure such as scuba diving or air travel [10]. Increased ambient pressure can also result from direct trauma to the external auditory canal, such as a slap to the ear or an explosion. In a case presented by Sheridan et al. [11], a 28-year-old male had resurfaced after SCUBA diving 35 feet under water, with complaints of hearing loss, nausea, and imbalance. His audiogram revealed sensorineural hearing loss and he was managed conservatively. Subsequently his symptoms had returned and he underwent exploratory tympanotomy. Middle ear exploration discovered an oval window perilymph leak. The window was patched using temporalis fascia.

Direct trauma has also been associated with PLF, including direct penetrating trauma and general head trauma. The mechanism for penetrating trauma is a simple direct breach usually at the oval window. This has been reported in Q-tip trauma and even due to intratympanic steroid perfusion [12]. The mechanism for blunt head trauma resulting in PLF is presumed to be due to a traveling wave of pressure from the intracranial space through the inner ear resulting in a window breach, which represents another type of an explosive event.

The so-called spontaneous PLF is one where there is no obvious provocateur for the pathology—no trauma, stapes surgery, implosive event, or explosive event. In this case, some patients, especially if the symptoms are of long duration, may have forgotten the antecedent event. An alternative explanation is an anatomic anomaly that allows for increased pressure transmission from intracranially to the inner ear, making the round or oval window more susceptible to breach. There have been several anatomic anomalies that could fulfill this distinction and includes most of the TMWD identified in this textbook.

The last etiology to consider is erosive processes. Infectious erosive processes such as otosyphilis and mass lesions eroding into the otic capsule must also be included in the spectrum of disorders presenting with TMWS. In the past, these have been referred to as labyrinthine fistulas and were described as presenting similar to how a PLF would present. Now, they would more likely be referred to as a part of the spectrum of TMWD. Cholesteatoma is the most common of erosive processes that we encounter. These can be acquired or congenital in origin, but the TMWS may be delayed until a critical amount of erosion has occurred. Patients typically present in a comparable manner with strain-induced dizziness, ear fullness, and conductive or mixed hearing loss, but will also typically have otorrhea.

Pathophysiology

The cochlear aqueduct can be defined as a bony channel, which contains the fibrous periotic duct and connects the perilymphatic space with the subarachnoid space

[13]. It is suggested that the cochlear aqueduct provides a direct connection between CSF and perilymph fluid in both a normal labyrinth and in malformations [14]. The length and patency of the cochlear aqueduct varies between subjects. With age the cochlear aqueduct grows in length and the arachnoid tissue contained in the aqueduct becomes denser. Thus, explaining the varying patency of the cochlear aqueduct among different age groups [15, 16].

The round and oval windows are separated by the rigid osseous spiral lamina and basilar membrane. Other than the neurovascular bundles, the remainder of the labyrinth is encased in bone. When pressure is applied to the stapes it travels through the scala vestibuli, eventually reaching the elastic membrane of the round window. The interaction of the flexible basilar and tectorial membrane induces shearing of the cochlear inner hair cells. Vestibular hair cells are enclosed in the bony labyrinth and are protected from sound induced movement of perilymph [17].

Activities that increase intracranial pressures can transmit pressure through a patent cochlear aqueduct to the inner ear. An additional possible connection is through the internal auditory canal (IAC) and in fact has been demonstrated to occur with CSF contrasted CT scan. Increases in hydrostatic pressure of perilymph are released by the opening of the otic capsule or a breach of the oval or round windows. CSF pressure leads to an efflux of perilymph from CSF entering the scala tympani through the cochlear aqueduct [18]. This suggests that perilymph flow is the direct result of increased intracranial pressure forcing CSF through the cochlear aqueduct.

Space occupied by CSF is part of a dynamic pressure system, which determines intracranial pressure. The normal physiologic pressure of CSF is 3–4 mmHg (4–5.4 cm H_2O) before the age of one, and in adults pressure ranges from 10 to 15 mmHg (13–20 cm H_2O) [19]. As we age, the middle and inner ear becomes more adaptive to intracranial pressure changes. The length of the cochlear aqueduct increases and the density of arachnoid in the lumen increases. These adaptations are suggested to dampen the effects of sudden pressure changes in the subarachnoid space thus protecting the inner ear from rapid changes in pressure [15]. If pressure is transmitted to the vestibular organs, it must do so without causing endolymph to flow. When endolymph is caused to flow, vestibular stimulation results [17]. The complete enclosure of perilymph ensures that pressure is equally distributed and aids in the prevention of inappropriate pressure being transmitted to the vestibular sensors.

Inner ear trauma occurs when rapid pressure changes are transmitted to the inner ear from either the middle ear space or the cerebral spinal fluid [10]. This can result in a tear of the basilar membrane, perilymphatic fistula or hemorrhage. Thus, the explosive route suggests that sudden increases in CSF pressure are transmitted through the cochlear aqueduct, the IAC, or some other otic capsule defect to the scala tympani, leading to rupture of the round window or basilar membrane [8]. The implosive route is the result of sudden increases in tubotympanic pressure with round window or oval window ligament rupture. There may also be disruption of internal labyrinthine membranes that would result in hearing loss, vertigo, and tinnitus [8].

Vestibular symptoms can be divided into either intermittent or persistent. Like other TMWS, there can be quite a variation in the description of vestibular symptoms, but a common feature is exacerbation or provocation of vestibular symptoms with activities that raise intracranial pressure. It is also not unusual for PLF patients to have concomitant BPPV as a secondary pathology, making positional exacerbation of vestibular symptoms another feature. In these cases, presumably the pressure effects that caused breach in the oval or round window areas also caused a dislodgement of otoconia from the utricle.

Third window syndromes, including perilymphatic fistulas, can occur as a consequence of traumatic head injury. This is commonly mistaken for a traumatic brain injury or a post-concussive syndrome [2]. Head trauma has been proposed as one of the "second events" that provokes the onset of TMWS in patients with anatomic dehiscence present since childhood. Similarly, head trauma has been identified as a mechanism by which PLF may occur. The proposed theory is the traveling wave theory of pressure transmitted from intracranially through the inner ear, resulting in labyrinthine concussion, intralabyrinthine hemorrhage, endolymphatic hydrops, and PLF.

Clinical Presentation

Patients with suspected PLF can present with sudden or fluctuating sensorineural hearing loss, tinnitus, aural fullness, rotational vertigo, lightheadedness, disequilibrium, and motion intolerance. A patient can present with complaints of purely auditory, vestibular or a combination of both. Seltzer and McCabe [20] collected data on 91 patients with a confirmed diagnosis of PLF and found that 82% had auditory symptoms and 8% had auditory symptoms as the sole complaint. Eighty one percent of the patients had vestibular symptoms and 12% complained of only vestibular symptoms. The audiologic and vestibular symptoms were widely variable. The typical vestibular symptoms are chronic disequilibrium with episodes of vertigo provoked by straining. The chronic disequilibrium is akin to what is seen with an uncompensated vestibular loss.

Post-stapedectomy PLF symptoms can occur in as little as a week or can present years after surgery [21]. A diagnosis of PLF should be suspected in a patient presenting with sensorineural hearing loss and dizziness following a stapedectomy. The diagnosis can be commonly mistaken for Ménière's disease, with a similar presentation of vertigo and sensorineural hearing loss. In some cases, a CT scan may show fluid in the middle ear and/or pneumolabyrinth [22]. CT scan is the preferred method of imaging since it will also help rule out otic capsule defects. However, the finding of pneumolabyrinth is a rare but specific finding strongly suggestive of a breach in the labyrinth. In the absence of a bony defect, a window breach is presumed.

The variable signs and symptoms of PLF, and their similarities to other pathologies, contribute to the controversy surrounding the missed or misdiagnosed PLF. A thorough history and physical exam are pertinent for an accurate diagnosis. One should maintain a high index of suspicion for PLF among patients who present with

sudden sensorineural hearing loss and/or vestibular symptoms following explosive trauma (Valsalva maneuver, weightlifting), implosive trauma (bomb explosions, hand slap to the ear canal) or barotrauma (deep-sea diving, air travel). Hearing loss associated with trauma is often sudden, progressive/fluctuant but can have a delayed presentation.

There is a strong association between barotrauma and the production of perilymphatic fistulas. Patients with a history of deep-sea diving or recent airline travel presenting with sensorineural hearing loss should be suspected of having a perilymphatic fistula. Pullen [23] found 48 cases of PLF out of 62 patients who had experienced barotrauma from deep-sea diving. The results corroborated previous findings. The majority of the cases were found to have a round window PLF.

After an inciting event that has produced a PLF, the patient will usually experience hearing loss and vertigo. Nausea and vomiting are usually associated with vertigo. Audiometric examination may reveal a sensorineural hearing loss. Fluctuating symptoms can be reproducible or exacerbated by performing the Valsalva maneuver, which increases intracranial and intralabyrinthine pressure. A preferential leaning to one side has also been noted. Between vertigo spells, the patients often report chronic disequilibrium as would be reported by those experiencing an uncompensated vestibulopathy.

While symptoms presenting immediately after a traumatic event make for a more confident diagnosis, most cases are not so straightforward. The onset of symptoms can occur weeks to months or even years after an inciting event and the symptoms experienced by the patient can fluctuate. This makes it difficult for the patient to precisely recall an event that may have caused the trauma. The fluctuation of symptoms may be difficult for the patient to explain to the physician. Trigger avoidance also changes the clinical presentation, with patients either consciously or unconsciously avoiding straining, masking the most classic symptoms.

Symptoms associated with PLF are remarkably similar to other TMWD, such that physicians should assess for other TMWD such as superior SSCD, cochlear-facial dehiscence (CFD), and horizontal semicircular canal erosion by cholesteatoma or other mass lesions. These syndromes can present with similar symptoms to PLF and can present concomitantly with PLF. SSCD and other TMWD typically present with hearing loss, strain-induced vertigo, and autophony [24, 25]. The presence of sound and pressure induced vertigo along with autophony should raise the clinician's suspicion of a TMWD [25]. Some have argued the presence of Tullio phenomenon would favor an otic capsule dehiscence over PLF, but others have reported Tullio phenomenon among PLF patients as well, making this distinction more difficult [25–27].

Diagnosis

The controversy surrounding the diagnosis of PLF stems from non-specific symptoms, a lack of trauma or surgery in many cases, no definitive preoperative diagnostic test, and no good gold standard for diagnosis. The symptoms are similar to more

common conditions such as Vestibular Migraine, Ménière's disease, and Vestibular Neuritis. For this reason, without knowledge of an antecedent event to the onset of symptoms, PLF can be commonly misdiagnosed. Unfortunately, the preoperative tests proposed for diagnosis of PLF, are also frequently abnormal in other TMWD further complicating the picture.

The gold standard for diagnosis of PLF, to which other preoperative testing is compared, has been intraoperative identification of clear fluid emanating from the round or oval window areas. However, this has been problematic. The volume of perilymphatic fluid in the inner ear is estimated to be 75 μl. Consequently, the amount of fluid potentially seen would be even smaller, maybe 2–5 μl of clear fluid. This gold standard is compromised by subjective qualifications that can vary tremendously from one surgeon to another. The fluid seen at the time of middle ear exploration may represent transudate or local anesthetic that had been injected preoperatively, which could lead to a false positive diagnosis. Furthermore, an intermittent PLF may not leak at the time of middle ear exploration leading to a false negative diagnosis. There have been no universally accepted means of getting around this problem. Consequently, using intraoperative identification as the gold standard (fluid identification), upon which preoperative testing has been compared, is less than ideal [28, 29].

The primary concern following a traumatic head injury is to rule out possible intracerebral hemorrhage with a non-contrast CT scan of the head. While this type of scan is quick in determining the presence of intracranial hemorrhage, it is not an acceptable means for assessing temporal bone pathologies [30]. A high-resolution CT scan is needed to visualize the subtleties of the inner ear and temporal bone fractures following a traumatic head injury, as well as identifying concomitant labyrinthine dehiscences. Venkatasamy et al. [31] proposed that a combination of CT and MRI is a fast and reliable method for the accurate diagnosis of round and oval window fistulas, with a sensitivity of 80%. Of the 17 participants that were enrolled in the study, the most common sign on imaging was fluid filling the round or oval window area. This seems to be a unique idea since it is difficult to imagine any imaging technique seeing a few microliters of perilymph. However, the presence of pneumolabyrinth on CT is highly suggestive of a Perilymphatic Fistula [31].

Audiometric testing and tuning fork testing may show a unilateral sensorineural hearing loss. The ear that is affected is typically the side where the fistula is located. However, PLF can present with conductive, sensorineural hearing loss or mixed losses [30]. Hearing loss alone, however, is a non-specific finding for PLF.

Platform posturography pressure test (PPT) demonstrated a high sensitivity (97%) in the diagnosis of PLF and a 93% specificity by one group [32]. Pressure is applied to the auditory canal while standing on the posturography platform under sensory organization test 5 (eyes closed and sway referenced surface). The pressure is applied to the external ear canal rapidly from 0 to +400 mm H20. If a fistula is present the changes in pressure are transmitted to the inner ear causing vestibular stimulation. If the postural sway has an amplitude of greater than two standard deviations in any direction from the base, the test is considered positive [30]—representing saccular stimulation and a vestibulospinal reflex. However, Sheppard

et al. [33] used platform posturography to test patients with suspected PLF and other balance disorders. Their data concluded a 56% diagnostic specificity for a confirmed PLF, but using identification of perilymph fluid in the inner ear. Experienced surgeons have questioned the identification of perilymph fluid intraoperatively as "proof" of a PLF as discussed earlier in the chapter [30]. Anecdotally, we have found that other TMWD such as SSCD often have abnormal results on PPT, but this tends to be more specific than sensitive.

Videonystagmography (VNG) is frequently performed for PLF patients. Abnormal results of caloric testing and spontaneous nystagmus have a low sensitivity or specificity in identifying PLF. However, tests such as fistula testing, Valsalva testing or Tullio testing during VNG have a reasonably higher sensitivity. These are not part of most VNG protocols but could be easily incorporated. These tests would objectively support the subjective complaints of patients with sound or strain-induced dizziness. Keep in mind, however, these tests are also frequently abnormal in other TMWD.

The fistula test is usually performed at bedside but can be performed during VNG recording. The typical VNG fistula test entails using a tympanometer to pressurize the ear canals while recording eye movements, looking for nystagmus. A positive test (presence of nystagmus) is suggestive of a fistula, but the lack of nystagmus does not rule out the presence of a fistula. Hain and Ostrowski [34] found that little nystagmus was produced during fistula testing when a window fistula was present using this method. An alternative method we advocate is the use of a handheld Bruening Otoscope with alternating positive and negative pressure application to the tympanic membrane under direct visualization, while watching concomitant eye movement with infrared video oculography. Phase-locked movement of the eyes (a positive Hennebert's sign) or the patient feeling a shifting sensation or nausea is considered a positive Hennebert's symptom. A positive Hennebert's symptom has about the same sensitivity, 60%, as a positive PPT [30]. The identification of nystagmus is considerably less sensitive.

Performing the Valsalva maneuver causes changes in perilymph pressure. This test can be positive when a fistula is present. This can be performed with a closed glottis (i.e., Glottic Valsalva) or with insufflation (Nasal Valsalva). Resulting nystagmus is considered a positive result. However, this can also be abnormal in other TMWD and in Chiari malformation [35].

The Tullio phenomenon refers to disequilibrium/vertigo induced by sound [36]. Tullio demonstrated that loud sounds produced nystagmus and head movement in dogs and pigeons with surgically fenestrated superior canals [37]. While the Tullio test has been used for the diagnosis of SCD, it has shown diagnostic potential for PLF. However, a positive Tullio test can also be positive in normal subjects. Pyykko [38] conducted testing using low-frequency sound stimulation on fifty-seven control subjects, seven with suspected PLF and seven with other inner ear pathologies, while postural stability was measured on a balance platform. All the patients with PLF exhibited altered postural stability. The controls with a purely sensorineural hearing loss did not exhibit instability. This phenomenon suggests a saccular vestibulospinal stimulation in response to sound. Similarly, the Tullio test can be

performed with infrared video observation to enhance identification of concomitant nystagmus.

The Vibration-Induced Nystagmus test (VINT) is a test that is sensitive to vestibular asymmetry with an abnormal result (i.e., nystagmus) being non-specific to the underlying cause of the asymmetry. However, VINT has also been advocated as a means to detect SSCD by means of the character of the induced nystagmus. Typically, in SSCD, the VINT will produce an upbeat torsional nystagmus, whereas with other pathologies horizontal nystagmus is more commonly encountered. Therefore, although an "abnormal result" does not specifically denote SSCD, an abnormal result with characteristic upbeat torsional nystagmus does correlate with SSCD. One study reported that the combination of VINT with upbeat torsional nystagmus and the presence of high frequency oVEMP (4 kHz) combined, resulted in a high probability of detecting SSCD on CT [39]. A source for potential false positive results we have witnessed is the concomitant existence of SSCD and a unilateral vestibular loss. It must also be pointed out that a positive result indicating SSCD does not in itself exclude the possibility of a concomitant PLF.

VEMP has been proposed for detection of SCD. However, abnormally responsive VEMP responses have been reported in PLF. It is yet to be seen whether this can distinguish between these two entities [40].

Electrocochleography (ECOG) has been used in the identification of Ménière's disease (endolymphatic hydrops) and PLF. An increase in summating potential and the action potential ratio is suggestive of Ménière's and PLF [15]. Some authors have suggested that all PLFs have increased endolymphatic hydrops, the histopathologic finding in Ménière's disease [30]. However, ECOG is also frequently abnormal in SSCD and other TMWD which has been demonstrated to return to normal with successful repair of SSCD [41].

Biomarkers have been proposed for diagnosis of PLF intraoperatively. Cochlintomoprotein (CTP) exists only in the perilymph and is not found in blood, saliva, or CSF [42]. Its detection intraoperatively can be useful for confirmation at the time of middle ear exploration. However, it is not helpful for preoperative identification which limits its benefits.

Another biomarker proposed for the detection of PLF was beta-2 transferrin. It is found in CSF and perilymph. Buchman et al. took samples of perilymph from 20 patients and compared them with negative controls. The results showed that only 5% of the known perilymph samples and none of the control samples were positive for beta-2 transferrin [43]. These results suggest the beta-2 transferrin biomarker may not be a reliable test for the diagnosis of PLF.

Treatment

The treatment for PLF can be divided into two categories: conservative or surgical. The decision on which treatment plan to pursue is influenced by several factors including: the etiology of the fistula, severity of symptoms, and whether the patient

is a good surgical candidate. Typically, surgical intervention is the treatment of choice for trauma induced fistulas [44]. A perilymph fistula of idiopathic origin or with no known recollection of trauma may be managed conservatively. Conservative therapy entails bed rest and avoiding activities that can increase intracranial pressure. Maitland [44] suggests that patients on bed rest elevate their heads to a 30-degree angle. Patients are to avoid strenuous activities and are given laxatives to avoid straining when defecating. Gotto et al. [45] looked at 44 cases of PLF and found that 50% were associated with nose blowing, strenuous lifting and air travel. Patients' symptoms are monitored for a few weeks while on conservative therapy and, if there is a lack of improvement, surgical intervention can be considered [25]. While the benefits of conservative therapy have not been well analyzed, the gold standard for the management and treatment of PLF involves selecting good surgical candidates and early surgical repair for the best possible outcomes [46].

Depending on the surgical procedure used to repair a PLF, it can be done in-office or in the operating room. There are a variety of techniques and materials that can be used with the goal of sealing the fistula. Most experienced surgeons use tissue grafts in both the areas of the oval and round window niches [30]. Traditionally the use of temporalis fascia has been the gold standard of grafting material for PLF [47]. The tissue seals need to be applied to areas in the oval and round windows that have been scarified to allow for a permanent scar to form.

Sarna et al. found that in cases where excessive tissue graft was used, conductive hearing loss was a side effect and advocated the use of Gelfoam to seal around the fascia and oval window [25]. However, Gelfoam dissolves over a brief period of time and it has been argued would be a poor choice for a permanent closure. Garj et al. [48] proposed the use of intratympanic blood injections due to feasibility, low cost, and its minimally invasive nature. The procedure involves the application of local anesthetic to the tympanic membrane, then injecting 0.5 mL of blood into the middle ear. Patients are then placed in a semi-recumbent position for 20 min to allow for blood to adequately reach the oval and round windows. Their results showed that two of the three patients had complete resolution of symptoms the very next day. However, this is a limited number of subjects, and blood seals would seem to be as equally temporary seals as Gelfoam.

While conservative and surgical therapies are both viable options, most studies have concluded that if conservative therapy is pursued, for many patients surgical intervention may still be necessary. The timing of surgery after the incident has been shown to be crucial in optimal resolution of symptoms.

Outcome

Many prior studies on the outcome from PLF surgery are almost certainly contaminated by the presence of unrecognized labyrinthine dehiscences that would more than likely be addressed separately in current neurotologic practice. These prior studies need to be evaluated in that context, while newer studies are much less likely

to have such contamination. Furthermore, it is likely that many of the successes of PLF surgery in patients with concomitant dehiscences are integral as to the etiology of recurrent PLF syndrome, much as we have seen with recurrent TMWS after window reinforcement surgery.

Success from PLF surgery has a dichotomous outcome with vestibular symptom resolution much higher than hearing outcomes. The range of successful improvement of vestibular complaints is 85–90%, whereas hearing improvement ranges from 20 to 49% [20, 45, 49]. Controversy regarding the timing of surgery revolves around the question of hearing improvement. Some have argued for immediate surgical intervention with the concern of delay causing further hearing deterioration. While others have argued that the low success in hearing improvement mitigates the need for early surgical intervention, since vestibular symptom resolution does not appear to be so time sensitive.

Complications from PLF surgery are relatively low compared to surgical intervention for direct repair of labyrinthine dehiscences such as SSCD. Some may have residual conductive hearing loss from scarring due to window reinforcement but this can be minimized by using tiny pieces of grafting material. Aside from this, complications are what would be expected from a typical middle ear exploration—infection, perforation, etc. [49].

Conclusion

In summary, we define PLF as a patient who has TMWS (including symptoms and test findings consistent with TMWD) yet has no evidence of a bony dehiscence of the otic capsule. These patients may have an identical presentation as other TMWD. There is a significant question as to whether PLF can be distinguished on physiologic testing from other TMWD, with PLF patients frequently having abnormal fistula testing, Valsalva testing, Tullio testing, ECOG, and VEMP testing. Audiometric testing may demonstrate similar low-frequency conductive gaps, mixed loss, or sensorineural loss, making audiometry unhelpful in distinguishing PLF from other TMWD. Some have looked for a test that differentiates PLF from other TMWD, but there only appears to be one test that differentiates the two entities: a CT scan that demonstrates the presence or absence of an otic capsule defect. Future research may help delineate an anatomic or physiologic basis that defines PLF and distinguishes it from other more recently identified TMWD. The question as to whether PLF plays a part in the pathophysiology of other TMWD is an open one that future research hopefully resolves. Treatment is similar to other TMWD with trigger avoidance being the prime mode of non-surgical management, and window reinforcement as the surgical treatment of choice.

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