Review

Sneezing and Perilymphatic Fistula of the Round Window: Case Report and Systematic Review of the Literature

Francesco Comacchio, Marta Mion

Department of Neurosciences, Institute of Otolaryngology, Padova University School of Medicine, Padova, Italy

INTRODUCTION

The term perilymphatic fistula (PLF) refers to an abnormal communication between the middle ear and perilymphatic space through the oval window (OW) and round window (RW). It can be due to a congenital otologic disorder, such as malformations or syndromic diseases, or can be an acquired condition that is provoked by factors, such as iatrogenic or physical injuries [1].

The first report of a nonsurgical PLF was presented by Fee [2], followed by Stroud and Calcaterra in 1970 [3]. Goodhill [4] proposed an etiological theory on the basis of idiopathic rupture of OW and/or RM membranes: implosive (as during Valsalva’s maneuver) or explosive (as for increased intracranial pressures) force can cause membranous lacerations with consequent formation of fistulas.

In case of rupture of RW, patients complain about hearing loss of different grades (even profound deafness), tinnitus, and vertigo with various intensities, alone or in combination. The variety of manifestations and controversial diagnostic tests lead to a difficult classification of this pathological entity.

The aim of our study was to analyze the clinical characteristics, management, therapeutic options, and consequent results of PLF using a case of RW membrane rupture that occurred after sneezing and systematically reviewing the literature pertaining to this topic.

CASE REPORT

A 52-year-old woman consulted the ear-nose-throat emergency unit for sudden left hearing loss and instability following a sneeze. An otoscopic examination was unremarkable. Pure tone audiometry demonstrated a profound (>90 db) flat sudden sensorineural hearing loss (SSHL) of the left ear; tympanogram was type A bilaterally, whereas left cochlear stapedial reflex was absent on ipsilateral and contralateral stimulation of the right ear. No spontaneous or positional nystagmus was described on bedside examination with Frenzel glasses. After a week of oral corticosteroid (CS) therapy, SSHL persisted; hence, the patient came to our hospital. Pure tone audiometry conducted at our unit showed a severe flat SSHL of the left ear. On infrared videonistagmoscopy (ICS Chartr...
a low-amplitude horizontal, left-beating spontaneous nystagmus was noted with positional geotropism. The nystagmus was inhibited by fixation. A fistula test with pressure on the left ear canal increased the intensity of the nystagmus, so an explorative tympanotomy (ET) was performed a day later under general anesthesia due to a suspected PLF. A transcanal approach with tympanomeatal flap elevation enabled the observation of a perilymphatic leakage from RW (Figure 1a and b), which was packed with pericondrium reinforced by fibrin glue (Tissucol; Baxter AG, Wien, Austria). Dizziness and instability immediately disappeared with spontaneous nystagmus; however, unfortunately, the hearing loss persisted 1 month after the surgery.

**Search strategy for the review of the literature**
The search strategy was designed to include articles based on their topic.

The inclusion criteria were based on the type of the study: articles on clinical manifestations, diagnostic tools, possible therapies, and pitfalls of PLF of RW caused due to sneezing.

To identify relevant studies, as the first step, a search was conducted on Google and MEDLINE databases using a combination of MeSH terms and keywords related to PLF of RW (e.g., spontaneous or idiopathic PLF, barotraumas and PLF, rupture of round window, sennutatory event, sneezing, sudden sensorineural hearing loss).

This first step enabled the identification of a list of potential citations for inclusion in this review. Titles and abstracts of these articles were then screened.

The data regarding the demographic features of the sample population, symptoms, diagnostic tools, medical versus surgical therapy, and results were arranged in descriptive tables.

**Literature search**
A total of 221 citations were retrieved from the first phase of the search, of which 194 were excluded after screening the titles and abstracts. Full texts of the remaining 27 articles were retrieved, along with four additional full-text articles that were identified as potentially relevant by the second-step search expansion. Based on the inclusion criteria, five articles were selected for inclusion in this review (Figure 2).
c) References (β2 transferrin, Cochlin-tomoprotein detection test, idiopathic cases)

d) Differential diagnosis (inner ear diseases with known causes)

e) Definite diagnosis (ET, detection of perilymph-specific protein) [10]

The main challenge in the diagnosis of PLF is the similarity of symptoms with those of Ménière syndrome [11] and most-ly variable clinical history. While there are several clinical signs and symptoms that may suggest the diagnosis of PLF, definitive diagnosis is often difficult and may require specific imaging studies such as CT or MRI scans. In addition, the presence of PLF may be confirmed by the presence of otoacoustic emissions, which are cochlear microphonics, or by the presence of perilymph-specific protein in the cerebrospinal fluid or endolymphatic fluid.

Table 1. Summary of reviewed studies

<table>
<thead>
<tr>
<th>Auth.</th>
<th>n.pat</th>
<th>Sex</th>
<th>Mean age (y)</th>
<th>PLF of OW</th>
<th>PLF of RW</th>
<th>Vertigo</th>
<th>SHL</th>
<th>Tinnitus</th>
<th>Side + audiom.exam</th>
<th>Fistula test</th>
<th>Imaging</th>
<th>VNG</th>
<th>Reconst. material</th>
<th>Results: vertigo</th>
<th>Results: SHL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Althaus 1977 [6]</td>
<td>6</td>
<td>4M (66%) 2F (33%)</td>
<td>44.33 (29-55)</td>
<td>5 (83%) 1 (16%)</td>
<td>100% 100%</td>
<td>50%</td>
<td>100%</td>
<td>1 otic meningitis</td>
<td>1/</td>
<td>1 pos. (16%)</td>
<td>66% left-beating positional Ny</td>
<td>100% fat</td>
<td>83% improved</td>
<td>50% improved</td>
<td></td>
</tr>
<tr>
<td>Alfesl et al. 2011 [5]</td>
<td>2</td>
<td>M</td>
<td>1) 43 2) 45</td>
<td>-</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>1) Right mixed HL then SHL</td>
<td>1) Pos.</td>
<td>1) CT: dilated stapes</td>
<td>1) no Ny</td>
<td>2) left vestib. deficit</td>
<td>Temp. fascia</td>
<td>1) improved</td>
<td>2) not improved</td>
</tr>
<tr>
<td>Haubner et al. 2012 [8]</td>
<td>4</td>
<td>M</td>
<td>43</td>
<td>-</td>
<td>100%</td>
<td>44.9%</td>
<td>100%</td>
<td>50.7%</td>
<td>56.3% left SHL</td>
<td>43.9% right HL</td>
<td>Exp.lymph: 59.4% no PLF</td>
<td>18.8% RW PLF</td>
<td>21.7 doubt</td>
<td>-</td>
<td>81.2% fat</td>
</tr>
<tr>
<td>Nagai and Nagai 2012 [9]</td>
<td>34</td>
<td>M (56%) 19</td>
<td>(median) 47.4</td>
<td>9 (26%)</td>
<td>3 (8%)</td>
<td>18 (33%)</td>
<td>-</td>
<td>100%</td>
<td>100%</td>
<td>45.7% severe*</td>
<td>42.8% profound*</td>
<td>11.4% total*</td>
<td>23 (66%)</td>
<td>both Ow and RW PLF</td>
<td>CT neg.</td>
</tr>
</tbody>
</table>

Pyykkö et al. 2011 [10] | 5 | M | 42 | - | 100% | 44.9% | 100% | 50.7% | 56.3% left SHL | 43.9% right HL | Exp.lymph: 59.4% no PLF | 18.8% RW PLF | 21.7 doubt | - | 81.2% fat | 11.5% temp. fascia | 7% both |

Nagai and Nagai 2012 [11] | 34 | M (56%) 19 | (median) 47.4 | 9 (26%) | 3 (8%) | 18 (33%) | - | 100% | 100% | 45.7% severe* | 42.8% profound* | 11.4% total* | 23 (66%) | both Ow and RW PLF | CT neg. | - | 100% temp. fascia | Improved SHL | 53% severe* | 73% profound* | 25% total* |

Park et al. 2012 [12] | 9 | M | 32 | - | Yes | Yes | - | Left SHL | - | - | 100% | 100% | 100% | 10% | 100% | 100% | 10% spontaneous horizontal Ny | Soft tissue | 100% resolved | Not improved |

Our | 1 | F | 52 | - | Yes | Yes | - | Left SHL | - | - | - | - | - | - | - | - | Pericond. - | - | - | - |

Auth = authors; n = number; pat = patients; y = years; OW = oval window; PLF = perilymphatic fistula; RW = round window; SHL = sensorineural hearing loss; tinn = tinnitus; audiom = audiometric; VNG = videonystagmography; reconst= reconstruction; M = male; F = female; pos = positive; RX = radiography; neg = negative; Ny = nystgamus; CT = computed tomography; vestib = vestibular; temp = temporals; exp.lymph = exploratory tympanotomy; doubt = doubtful; pericond = pericondrium

*severe = <60–89 dB; profound = <90–110 dB; total = <111 dB
Table 2. Causes and therapeutic choices of reviewed studies on PLF of the RW

<table>
<thead>
<tr>
<th>Authors</th>
<th>Causes of PLF of the RW</th>
<th>CS therapy</th>
<th>Exploratory tympanotomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Althaus 1977 [6]</td>
<td>Heavy lifting</td>
<td>No</td>
<td>First therapeutic choice</td>
</tr>
<tr>
<td></td>
<td>2) Nose blowing</td>
<td>2) Yes (1 week)</td>
<td>2) After 2 weeks*</td>
</tr>
<tr>
<td>Haubner et al. 2012 [8]</td>
<td>89.8% ?</td>
<td>Yes</td>
<td>After 48 h*</td>
</tr>
<tr>
<td></td>
<td>10.2% physical exercise, diving, head trauma, noise exposure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nagai and Nagai 2012 [9]</td>
<td>26.4% head trauma</td>
<td>Yes</td>
<td>After 8.5 days (median)*</td>
</tr>
<tr>
<td></td>
<td>20.5% heavy lifting</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>11.7% nose blowing</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.6% noise exposure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Park et al. 2012 [7]</td>
<td>20% slap</td>
<td>66% yes</td>
<td>From 2 days to 47 days*</td>
</tr>
<tr>
<td></td>
<td>20% head trauma</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>10% heavy lifting</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>30% nose blowing</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>20% intense Valsalva maneuver</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Our Sneeze Yes (1 week) After 8 days*

CS: corticosteroid

*from symptoms’ onset

References retrieved yelectronic search trategy
Total: n=221

Excluded studies based on abstract n=194
- PLF in children (n=7)
- Sperimental induced PLF (n=51)
- PLF after surgery (n=9)
- PLF in scabudivers (n=14)
- PLF in airplane travelers (n=2)
- Only SSHL (n=17)
- Not spontaneous PLF (n=18)
- Not on topic (n=11)
- Only abstract available (n=65)

Included studies relevant to review themen theb axis of title and abstract n= 27

Additional studies identified by references linkage n= 4

Excluded studies not meeting inclusion criteria n= 12

Inclusion full textarticles (effectives studies) fordetail evaluation of eligibility n= 19

Excluded studies n=14
- Based on study design (n=8)
- PLF of oval window (n=2)
- PLF not found (n=1)

studies included in the review n= 5

Figure 2. Flow diagram
Regarding audiometric findings of PLF, Park et al. [7] noted a descending configuration in most cases, indicating that the basal cochlear turn was more prone to damage because of its closeness to OW and RW. There is an experimental demonstration of alteration in the vestibular function of the cells in the organ of Corti due to an abrupt pressure imbalance provoked by the presence of PLF of RW; the consequent change in the summating potential may be an etiological factor for SSHL in case of PLF [19].

The predilection for the left side noted in the literature may be related to larger left cochlear aqueducts found in most human skulls, but this still remains a conjecture [8].

Kohut et al. [11] recognized some objective diagnostic criteria for PLF: presence of sudden or fluctuating hearing loss (unresponsive to CS therapy), vestibular symptoms mimicking a positional vertigo, and constant disequilibrium. These represent very unspecific findings; furthermore, fistula test is a very specific but poorly sensitive diagnostic tool. Positive test results strongly suggest the presence of PLF, but negative results cannot rule out the presence of such a lesion [9]. However, our case underlined the importance of evaluating patients using videonystagmoscopy because the nystagmus may be of very low amplitude.

Based on the above discussion, it is mandatory to identify and select candidates for surgical exploration, considering the possibility of using less invasive diagnostic tools, such as the detection of perilymph-specific protein [20-22], neurophysiological tests (electrocochleography), multifrequency tympanometry [23], instrumental examination (vestibular-evoked myogenic potentials) [24], and low-frequency sound stimulation during posturography [25].

According to Nagai et al. [9], the indication for ET in case of SHL is progressive hearing loss, acute hearing loss with vertigo, acute hearing loss with the presence of positional nystagmus in a spinal position, or unresponsiveness to CS therapy. On the contrary, our report demonstrated that a prolonged CS therapy in patients with strongly suspected PLF and consequently delayed ET can lead to an irreversible hearing damage and failure of relief from vestibular symptoms. Furthermore, in our opinion, not all patients with SHL who have progressive hearing loss or are unresponsive to CS therapy are candidates for ET.

While performing surgical exploration, the criteria to confirm PLF of RW are as follows: actual observation of fluid leakage from RW, direct inspection of membrane rupture, and no simultaneous transmission of pressure from OW to RW [9]. Despite these clear definitions, assessment of PLF can remain doubtful in some circumstances [9], provoked, for instance, by scarred membranes or solid ridges in the proximity of the site of interest. The use of alternative methods, such as intratympanic fluorescein, remains controversial [9].

Previous studies have underlined how vestibular outcomes are generally better than hearing outcomes after surgery [7, 26, 27], and our report confirmed this aspect.

In all the five studies analyzed in our review, there was no correlation between the material used for RW membrane reconstruction and possible healing.

The timing for ET and surgical outcomes were variable; however, the findings suggested that an early fistula repair can increase the chance of hearing recovery. In fact, persistent perilymphatic leakage can lead to an irreversible damage of the inner ear, as shown in our case report. Moreover, all other active therapeutic options, which are more or less invasive, including the use of autologous intratympanic blood patch, can be considered [28, 29].

CONCLUSION

The heterogeneity of clinical presentations, often combined with inaccurate history, makes the diagnosis of PLF challenging for ENT specialists. Among the causes of PLF, sneezing is a well-known entity, but our report represented a rare case. The cornerstone in PLF management remains the correct selection of patients for surgical exploration and early surgical repair of the membrane rupture for better hearing outcomes. In particular, when PLF is strongly suspected in case of history of trauma, followed by hearing loss associated with vestibular symptoms, especially disequilibrium rather than vertigo or dizziness, the use of ET is justified [10].

Informed Consent: Written inform consent was obtained from patients who participated in this study.

Conflict of Interest: No conflicts of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

REFERENCES

2. Fee GA. Traumatic perilymph fistulas. Arch Otolaryngol 1968; 88: 477-80. [CrossRef]
4. Goodhill V. Sudden deafness and round window rupture. Laryngoscope 1971; 81: 1462-74. [CrossRef]
6. Althaus SR. Spontaneous and traumatic perilymph fistulas. Laryngoscope 1977; 87: 364-71. [CrossRef]
11. Kohut RI, Hinojosa R, Thompson JN, Ryu JH. Idiopathic perilymphatic fis-
tulas: a temporal bone histopathologic study with clinical, surgical, and
121: 412-20. [CrossRef]

12. Shea JJ. The myth of spontaneous perilymph fistula. Otolaryngol Head
Neck Surg 1992; 107: 613-6. [CrossRef]

13. Pyykkö I, Selmani Z, Zou J. Low-frequency sound pressure and transtym-
panic endoscopy of the middle ear in assessment of “spontaneous” peri-
lymphatic fistula. ISRN Otolaryngol 2012; 2012: 137623. [CrossRef]

membrane sealing in the treatment of idiopathic sudden unilateral hear-
ing loss. Clin Exp Otorhinolaryngol 2015; 8: 20-5. [CrossRef]

15. Yenigun A. Sudden post-traumatic sensorineural hearing loss re-
verted to normal by sneezing. SAGE Open Med Case Rep 2014; 2:
205313X14564774.

16. Azem K, Caldarelli DD. Sudden conductive hearing loss following sneez-
ing. Arch Otolaryngol 1973; 97: 413-4. [CrossRef]

17. Whitehead E. Sudden sensorineural hearing loss with fracture of the sta-
pes footplate following sneezing and parturition. Clin Otolaryngol Allied
Sci. 1999; 24: 462-4. [CrossRef]

18. Bonfils P, Laccourreye O, Durand FX, Malinvaud D, Bensimon JL. Sudden
deafness following a steretatory attack. Eur Ann Otorhinolaryngol Head
Dis 2011; 128: 103-5. [CrossRef]

perilymphatic fistula. Am J Otolaryngol 1988; 9: 244-55. [CrossRef]

20. Bluestone CD. Implications of beta-2 transferrin assay as a marker for
perilymphatic versus cerebrospinal fluid labyrinthine fistula. Am J Otol
1999; 20: 701.

21. Ikezono T, Shindo S, Sekiguchi S, Morizane T, Pawankar W, Watanabe
A, et al. The performance of Cochlin-tomoprotein detection test in the
[CrossRef]

chlin-tomoprotein (CTP) detection test identified perilymph leakage pre-
[CrossRef]

in the assessment of perilymphatic fistulas. Audiol Neurootol. 1997; 2:
391-402. [CrossRef]

vestibular evoked myogenic potentials (VEMPs) also be useful in the di-
agnosis of perilymphatic fistula? Eur Arch Otorhinolaryngol 2006; 263:
552-5. [CrossRef]

25. Selmani Z, Ishizaki H, Pyykkö I. Can low frequency sound stimulation
during posturography help diagnosing possible perilymphatic fistula in
patients with sensorineural hearing loss and/or vertigo? Eur Arch Otorhi-
nolaryngol 2004; 261: 129-32. [CrossRef]

26. House JW, Morris MS, Kramer SJ, Shasky GL, Coggan BB, Putter JS. Peri-
lymphatic fistula: surgical experience in the United States. Otolaryngol
Head Neck Surg 1991; 105: 51-61. [CrossRef]

gical management of perilymphatic fistula: a Portland experience. Am J

28. Foster PK. Autologous intratympanic blood patch for presumed perilym-
phatic fistulas. J Laryngol Otol 2016; 130: 1158-61. [CrossRef]

29. Shinohara T, Gyo K, Murakami S, Yanagihara N. Blood patch therapy of
the perilymphatic fistulas—an experimental study. Nihon Jibiinkoka Gak-
kal Kaiho 1996; 99: 1104-9. [CrossRef]

30. Hornibrook J. Perilymph fistula: fifty years of controversy. ISRN Otolaryn-
gology 2012; 2012: 281248. [CrossRef]