Diagnosis and management of intralabyrinthine schwannoma: case series and review of the literature

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Summary. Intralabyrinthine schwannoma (ILS) is a rare benign tumor affecting cochlear and vestibular nerves, whose symptoms are generally unspecific and frequently responsible for a late diagnosis. Radiological examinations, with particular reference to magnetic resonance imaging (MRI), represent the only diagnostic technique to identify ILS. On computed tomography ILS can only be indirectly suspected by the presence of surrounding bone remodeling, whereas MRI provides direct visualization of the neoplasm as a filling defect within the labyrinth with vivid contrast enhancement. At the same time, MRI is also helpful in defining ILS anatomical extension into adjacent structures and in planning therapeutic management. Here we report three representative cases of ILS with new pictorial imaging features to improve ILS early detection and optimize subsequent therapeutic management. (www.actabiomedica.it)

Keywords: Schwannoma, Labyrinth, Magnetic Resonance Imaging, Differential Diagnosis

Introduction

Intralabyrinthine schwannoma (ILS) was first described by Meter in 1917 as a rare benign tumor, affecting cochlear and vestibular nerves (1). Most tumors show a modification in intracellular pathways (2-8). It can variably involve vestibule, cochlea, or semi-circular canals (9). Its symptoms are generally unspecific due to the slow growth pattern, frequently causing a late diagnosis. In most cases, it occurs with unilateral progressive sensorineural hearing loss (95%); more inconstant symptoms include tinnitus (51%), imbalance (35%), vertigo (22%), or fullness (2%), alone or in combination (1, 10). Magnetic Resonance Imaging (MRI) and Computed Tomography (CT) are the primary imaging tool for a variety of conditions and diseases, both for diagnostic and interventional purposes, especially in the neuroradiological field (11,12).

The most common differential diagnoses include Ménière’s disease and vestibular neuritis (1), and neuroradiological investigation with magnetic resonance imaging (MRI) (13-18) represents the reference method to identify ILS diagnostic features.

CT imaging, indeed, could only raise the suspicion of ILS in the case of surrounding bone remodeling. Conversely, MRI shows a filling defect within the labyrinth with relatively high signal on T1w images, low signal on T2w, and vivid contrast enhancement.
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after contrast media administration. MRI is also helpful in defining ILS anatomical epicenter and extension into adjacent structures, as well as in planning therapeutic management (16, 19, 20). Here we report three representative cases with striking imaging features to improve ILS early diagnosis and optimize therapeutic management. All patients had written informed consent, and all the performed procedures were by the 1964 Helsinki declaration and its later Amendments.

Materials And Methods

A 29-year-old woman came to our observation for the first episode of subjective vertigo; she also complained about right-sided tinnitus and hearing loss in the last year. A previous audiometric examination had revealed right fluctuating sensorineural hearing loss with modest pan-tonal hypacusia, classified as suspected for Meniere’s disease for which she was administered Betaistina 24mg/2die. ENT showed normal otoscopic findings, whereas audiometry revealed a worsening of the known sensorineural hearing loss for acute frequencies (moderate-to-severe), still limited to the right side (Figure 1A). An oral exam showed a right-sided slight reduction in detection threshold and alteration in word discrimination (15). Tympanogram was Type A bilaterally, while vestibular examination revealed a deficit on the right ear at Head Impulse Test (HIT). Contrast-enhanced MRI scan of the temporal bone was therefore performed, showing a small mass within the proper vestibule, reducing the regular representation of endocochlear fluids (Figure 1B). Homogeneous and intense enhancement was observed after contrast media administration (Figure 1C); thus the suspicion of ILS was raised. The patient refused to undergo surgery, so a wait-and-scan approach was decided. At present, after a 1-year follow-up, no significant lesion growth was observed. A 56-year-old man complained tinnitus and right-sided hearing loss persisted for 3 years. He underwent his first otoscopic examination was negative on both sides. Audiometric tests showed right-sided progressive (moderate-to-severe) sensorineural hearing loss for low frequencies (Figure 2A), with a slight reduction in detection threshold but no alteration in word discrimination. No spontaneous nystagmus was evoked at the vestibular examination; the Romberg test was negative, and neu-
rological functions were normal. HIT showed slight hyporeflexia on the affected side. Subsequent contrast-enhanced MRI scan showed the presence of a right ear small intralabyrinthine mass limited to the vestibule without the involvement of the semi-circular canals and vivid enhancement (Figure 2B-C), accounting for the diagnosis of ILS. Due to the limited lesion volume and patient’s refusal, surgery was temporarily excluded to avoid hearing loss; after a 2-years follow-up, neither audiometry deterioration nor ILS growth was observed. A 29-year-old man complaining recent onset of right ear hearing loss without tinnitus/vertigo came to our attention for ENT evaluation. Otoscopic examination revealed normal findings bilaterally. Audiometry showed right-sided deep pan-tonal sensorineural hearing loss (Figure 3A), while the vestibular examination was normal. The patient, therefore, underwent contrast-enhanced MRI showing a right intracochlear mass, involving medium and apical turns of the snail on T2w images (Figure 3B) with intense contrast enhancement (Figure 3C); also in this case, the suspicion of ILS was raised, but the patient refused surgery. After a 3-years follow-up, audiometry confirmed a further deterioration of sensorineural hearing loss, but no significant ILS growth was observed at MRI examination, so wait-and-scan approach was continued.

Discussion

Schwannoma is the most common benign neoplasm affecting the internal auditory canal and pontocerebellar angle (up to 6% of all intracranial tumors), rising from the ends of cochlear and vestibular nerves (21, 22). ILS is a subtype of schwannoma originating from the perineural Schwann cells of the vestibule-cochlear nerve proximal to the membranous labyrinth (cochlea and vestibule) without any outer extension (23). Although considered a rare disease, its prevalence is higher in some patients’ subgroups (i.e., in patients with symptoms accounting for Meniere’s disease who underwent MRI, ILS was found in 0.4% patients) (1, 23). A revision of all the ILS cases described in current scientific literature is reported in Table 1. Kennedy et al. (21, 22) further classified ILS into 7 categories according to anatomical localization (Table 2): intra-cochlear, when confined to the cochlear loops; intra-vestibular, when confined to the vestibule with or without extension into semi-circular canals; vestibule-cochlear, when involving both vestibule and cochlea; trans-macular, when extending from the vestibule to IAC through the lamina cribrosa; trans-modiolar, when extending through the modiolus into the inner auditory canal; tympano-labyrinthine; trans-otic, when involving posterior labyrinth, IAC, and middle ear. In 2013 Van Abel et al. identified 2 more types, respectively, trans-labyrinthine and trans-otic variant into a cerebellopontine angle (1, 10) (Table 2).

In recent years, the ILS incidence has increased thanks to the use of more accurate and advanced imaging techniques (14, 19, 22).

In this regard, imaging techniques have assumed a primary role in the study and treatment planning of numerous pathologies (24-27). In particular, MRI represents the golden standard for the diagnosis of ILS, ensuring an accurate depiction of dimension, shape, margins, signal intensity and relation with adjacent structures (21); moreover, MRI is important in pre-surgical planning, as well as in follow-up when a
Table 1. Literature review of intralabyrinthine schwannoma cases reported in current scientific literature

| Author            | Year | n  | Clinical picture               | Location                                      |
|-------------------|------|----|--------------------------------|-----------------------------------------------|
| Lee et al.        | 2019 | 16 | Progressive HL, vertigo        | 37.5% intracochlear                           |
|                   |      |    |                                | 18.75% intravestibular                        |
|                   |      |    |                                | 18.75% intravestibular-cochlear               |
|                   |      |    |                                | 12.5% transmodiolar                           |
|                   |      |    |                                | 6.25% transmacular                            |
|                   |      |    |                                | 6.25% nc                                      |
| Withers et al.    | 2019 | 1  | Bilateral HL                   | Intracochlear                                 |
| Venkatasamy et al.| 2019 | 3  | Progressive hearing loss, vertigo|                                              |
| Pan et al.        | 2019 | 1  | Unilateral HL, vertigo         |                                              |
| Park et al.       | 2019 | 1  | HL, vertigo                    | Intravestibular-cochlear                      |
| Thapa et al.      | 2019 | 30 | 72% gradual HL, 51% tinnitus, 21% dizziness, 9% facial nerve paresthesia, 12% SNHL |                                              |
| Marchioni et al.  | 2018 | 8  | 100% HL, 62.5% vertigo, 75% tinnitus | 62.5% intracochlear                           |
| Marinelli et al.  | 2018 | 14 | 29% sudden HL, 36% vertigo, 29% aural fullness, 21% neurofibromatosis type 2 | 25% transmodiolar                             |
| Bae et al.        | 2018 | 9  |                                |                                              |
| Mazzoni et al.    | 2017 | 8  | Severe HL, vertigo             | 37.5% transmodiolar                           |
|                   |      |    |                                | 12.5% transotic + CPA                        |
|                   |      |    |                                | 25% transmacular transmodiolar                |
|                   |      |    |                                | 12.5% transmacular                            |
|                   |      |    |                                | 12.5% intracochlear                           |
| Plontke et al.    | 2017 | 12 | Hearing fluctuating, vertigo   |                                              |
| Covelli et al.    | 2017 | 1  | Sudden hearing loss            |                                              |
| Fukushima et al.  | 2017 | 1  | Sudden hearing loss            |                                              |
| Plontke et al.    | 2017 | 1  | Sudden hearing loss            |                                              |
| Sabatino et al.   | 2017 | 1  | Rapidly progressive hearing loss, vertigo |                                              |
| Jerin et al.      | 2016 | 5  | 40% progressive hearing loss, 40% sudden hearing loss, 20% vertigo |                                              |
| Shupak et al.     | 2016 | 7  | 95% progressive hearing loss   |                                              |
| Gosselin et al.   | 2015 | 66 | No description                 | 50.9% intracochlear                           |
|                   |      |    |                                | 38.2% intravestibular                         |
|                   |      |    |                                | 10.9% intravestibulocochlear                  |
| Lee et al.        | 2015 | 1  | Sudden hearing loss, vertigo   |                                              |
| Dubernard et al.  | 2014 | 110| 94.5% progressive hearing loss, 59.1% vertigo | 50% intracochlear                            |
|                   |      |    |                                | 19.2% intravestibular                         |
|                   |      |    |                                | 14.5% transmodiolar                           |
|                   |      |    |                                | 11.8% intravestibulocochlear                  |
|                   |      |    |                                | 2.7% transmacular                             |
|                   |      |    |                                | 1.8% tympanolabyrinthine                      |
| Bittencourt et al.| 2014 | 1  | Hearing fluctuating and tinnitus |                                              |
| Kim et al.        | 2013 | 1  | Sudden hearing loss            |                                              |
| Schutt et al.     | 2013 | 1  | Hearing fluctuating, ear fullness and vertigo |                                              |
### Table 1. Literature review of intralabyrinthine schwannoma cases reported in current scientific literature

| Author                | Year | n  | Clinical picture                      | Location                                      |
|-----------------------|------|----|---------------------------------------|-----------------------------------------------|
| Van Abel et al.       | 2013 | 234| 84% progressive hearing loss          | 51% intracochlear                             |
|                       |      |    | 3% hearing fluctuation                | 29% intravestibular                           |
|                       |      |    | 43% vertigo                           | 9% intravestibulocochlear                     |
|                       |      |    |                                       | 5% transmodiolar                              |
|                       |      |    |                                       | 1% transmacular                               |
|                       |      |    |                                       | 1% translabyrinthine                          |
| Salzaman et al.       | 2012 | 45 | 60% progressive hearing loss          | 31.11% intracochlear                          |
|                       |      |    | 31.11% sudden hearing loss            | 28.88% transmodiolar                          |
|                       |      |    | 8.89% hearing fluctuating             | 15.55% intravestibular                        |
|                       |      |    | 35.56% vertigo                        | 11.11% intravestibulocochlear                 |
|                       |      |    |                                       | 8.88% transmacular                            |
|                       |      |    |                                       | 4.47% transotic                               |
| Gordts et al.         | 2011 | 1  | Hearing fluctuating and tinnitus      |                                               |
| Magliulo et al.       | 2009 | 1  | Sudden hearing loss and vertigo       |                                               |
| Brozek-Madry et al.   | 2009 | 1  | Sudden hearing loss and vertigo       |                                               |
| Tieleman et al.       | 2008 | 52 | 83.67% progressive hearing loss       | 80.7% intracochlear                           |
|                       |      |    | 14.28% sudden hearing loss            | 13.5% intravestibular                         |
|                       |      |    | 19.23% vertigo                        | 5.8% intravestibulocochlear                   |
| Jia et al.            | 2008 | 4  | 75% progressive hearing loss          |                                               |
|                       |      |    | 25% sudden hearing loss               |                                               |
|                       |      |    | 75% vertigo                           |                                               |
| Nishimura et al.      | 2008 | 1  | Sudden hearing loss and tinnitus      |                                               |
| Lella et al.          | 2007 | 7  | 71.42% progressive hearing loss       |                                               |
|                       |      |    | 28.5% sudden hearing loss             |                                               |
|                       |      |    | 57.14% vertigo                        |                                               |
| Kennedy et al.        | 2004 | 28 | 61% progressive hearing loss          | 32% intracochlear                             |
|                       |      |    | 32% sudden hearing loss               | 21% intravestibular                           |
|                       |      |    | 7% hearing fluctuating                | 32% transmodiolar                             |
|                       |      |    | 71% tinnitus                          | 11% transmacular                              |
|                       |      |    | 29% vertigo                           | 4% transotic                                  |
| Green et al.          | 1999 | 4  | 75% progressive hearing loss          |                                               |
|                       |      |    | 25% sudden hearing loss               |                                               |
|                       |      |    | 75% vertigo                           |                                               |
| Deux et al.           | 1998 | 3  | Progressive hearing loss, tinnitus,   |                                               |
| De Lozier et al.      | 1994 | 1  | Progressive hearing loss, tinnitus    |                                               |

### Table 2. Kennedy’s classification of ILSs (modified by Van Abel)

| Class                  | Areas of ear involved                                          |
|------------------------|---------------------------------------------------------------|
| Intra-vestibular (IV)  | Vestibule ± semi-circular canal (SCC)                         |
| Intra-cochlear (IC)    | Cochlea                                                       |
| Vestibulo-cochlear     | Vestibule and cochlea                                         |
| Trans-modiolar (TMO)   | Cochlea and IAC                                               |
| Trans-macular (TMA)    | Vestibule and IAC                                             |
| Trans-otic             | Middle ear and vestibule/cochlea and IAC                      |
| Tympano-labyrinthine   | Middle ear and vestibule/cochlea                              |
| Trans-labyrinthine     | Vestibule and/or SCC + cochlea + Internal auditory meatus (IAM)|
| Trans-otic variant into CPA | CPA ± cochlea ± vestibule and/or SCC ± IAM ± Middle ear |
“watch-an-wait” strategy is preferred (28). However, for diagnostic purposes, MRI is also crucial in providing imaging clues for differential diagnosis from other causes of vertigo, tinnitus, and hearing loss with negative otoscopic findings (29). E.g., when acute labyrinthitis is suspected MRI shows less pronounced enhancement that gradually decreases and progressively disappears at follow-up (23), whereas schwannoma enhancement does not change over time. In more challenging cases, such as intralabyrinthine extension of otomastoiditis or cholesteatoma, MRI can provide differential diagnosis by the use of diffusion-weighted techniques (30-32). Conversely, only in rare cases, CT can be more informative than MRI, as it happens in case of suspected labyrinthitis ossificans (33).

ILS management options primarily include the “wait and scan” approach, surgical removal, and radiotherapy (34). The “wait and scan” approach, based on longitudinal MRI examinations, relies on the slow growth rate of ILS and on the preservation of inner ear functions (1). The surgical removal is reserved to a limited number of cases (about 3% cases) (10), mostly depending on patients’ compliance, tumor size, localization, and growth pattern, and mainly on the presence of intractable symptoms refractory to medical treatment. Surgical ablative treatment results in total hearing loss in 100% of cases; moor inconstant consequences also include facial nerve palsy (4%), cerebrospinal fluid leakage (5.4%), and meningeal inflammation (1.8%) (1, 34). At present only few cases of ILS stereotactic radiosurgery have been reported (1), generally reserved to patients who cannot undergo surgery due to systemic counter-indications and intractable symptoms; however, no significant effect on vertigo was observed, whereas the probability of neurological side-effects and malignant tumor transformation was increased (1). Finally, recent studies reported some cases of ILS treatment by trans-tympanic steroid and intra-tympanic gentamicin injections, improving clinical outcomes in those cases were vestibular impairment was relatively more prominent than hearing loss (1, 35).

In conclusion, although ILS is a very rare pathology, its incidence has increased in recent years due to the availability of more accurate imaging techniques. As well documented in both neurological and other clinical specialties, diagnostic investigations and interventional radiology represent a fundamental integration to clinical evaluation. MRI is the gold standard both for ILS diagnosis and preoperative management, also allowing for differential diagnosis between ILS and possible mimickers. Several algorithms for ILS management have been proposed, but no consensus concerning the best therapeutic strategy was reached. At present, a tailored therapeutic approach based on the multidisciplinary evaluation of every single case should be considered the best option to be pursued.

Conflict of interest: Authors declare that they have no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

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