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

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 hypoacusia, classified ad 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-
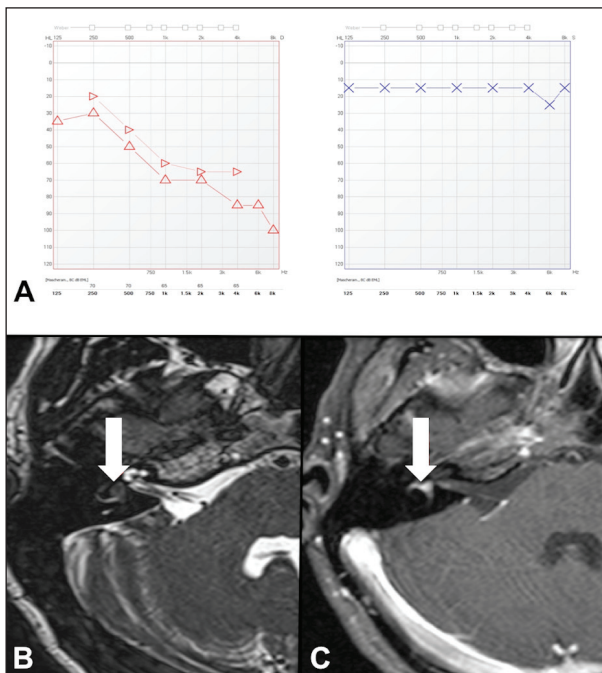

Figure 1. Audiometry results (A), axial volumetric T2w (B) and axial volumetric contrast-enhanced T1w image (C) of Patient#
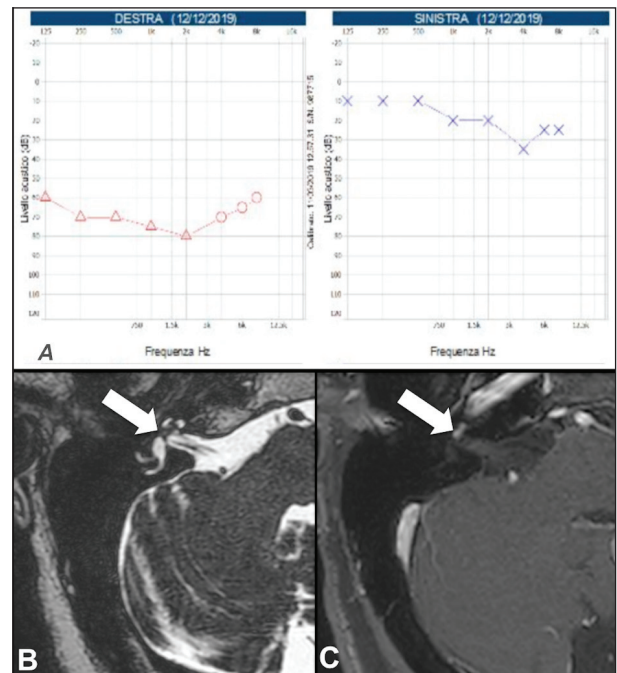

Figure 2. Audiometry results (A), axial volumetric T2w (B) and axial volumetric contrast-enhanced T1w image (C) of Patient#2

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 (**Figure3B**) 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 hear-

Figure 3. Audiometry results (A), axial volumetric T2w (B) and axial volumetric contrast-enhanced T1w image (C) of Patient#3

ing 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
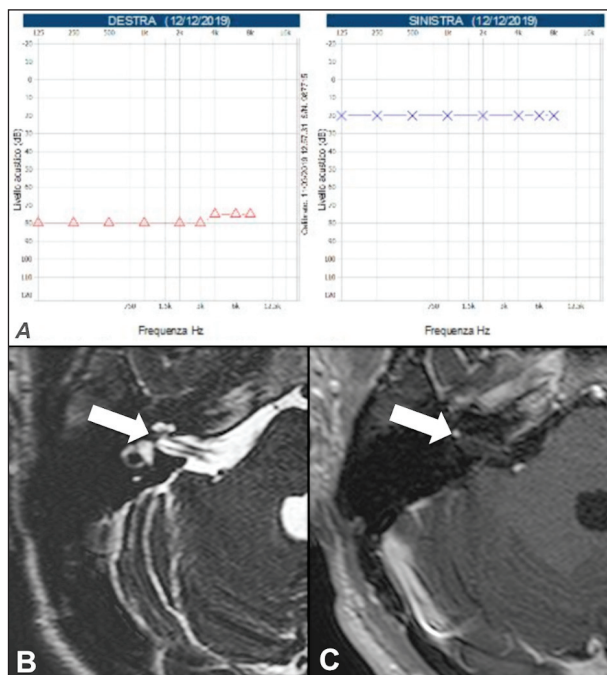
Table 1. Literature review of intralabyrinthine schwannoma cases reported in current scientific literature

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 12.5% intravestibular 25% transmodiolar
Marinelli et al.	2018	14	29% sudden HL 36% vertigo 29% aural fullness 21% neurofibromatosis type 2	
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. [35]	2017	12	100% hearing loss	
Covelli et al.	2017	1	Hearing fluctuating, vertigo	
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% intracoclear 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	

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Author	Year	n	Clinical picture	Location
Van Abel et al.	2013	234	84% progressive hearing loss 3% hearing fluctuation 43% vertigo	51% intracochlear 29% intravestibular 9% intravestibulocochlear 5% transmodiolar 1% transmacular 1% translabyrinthine
Salzaman et al.	2012	45	60% progressive hearing loss 31.11% sudden hearing loss 8.89% hearing fluctuating 35.56% vertigo	31.11% intracochlear 28.88% transmodiolar 15.55% intravestibular 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 14.28% sudden hearing loss 19.23% vertigo	80.7% intracochlear 13.5% intravestibular 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% sudden hearing loss 7% hearing fluctuating 71% tinnitus 29% vertigo	32% intracochlear 21% intravestibular 32% transmodiolar 11% transmacular 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, vertigo	
Weed et al.	1994	1	Progressive hearing loss, tinnitus	
De Lozier et al.[35]	1979	2	Progressive hearing loss, vertigo	

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.

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