De Novo Development and Progression of Endolymphatic Sac Tumour in von Hippel–Lindau Disease: An Observational Study and Literature Review

Nwaneka Eze¹ Alexander Huber¹ Bernhard Schuknecht²

¹ Department of Otorhinolaryngology-Head and Neck Surgery, University Hospital Zurich, Zurich, Switzerland

² Department of Radiology, MRI Zurich, Medical Radiological Institute, Zurich, Switzerland

Address for correspondence Nwaneka Eze, MD, FRCS (ORL-HNS), Department of ENT, Auditory Implant Centre, 2nd Floor Lambeth Wing, St Thomas' Hospital, Westminster Bridge Road, London SE1 7EH, United Kingdom (e-mail: nnekaeze@yahoo.co.uk).

J Neurol Surg B 2013;74:259–265.

Abstract

Endolymphatic sac tumors (ELST) are rare invasive lesions of the temporal bone that are commonly associated with von Hippel–Lindau disease. This report describes serial magnetic resonance imaging (MRI) and computed tomography (CT) findings over a period of 6 years in a 12-year-old patient who developed an ELST after 3.5 years surveillance for a cerebellar hemangioblastoma. A 1.5 × 8 mm tumor was identified on MRI within the endolymphatic duct when the patient presented with audiovestibular symptoms due to intralabyrinthine hemorrhage. The tumor demonstrated subsequent growth over 25 months until the patient agreed to undergo surgical resection by subtotal petrosectomy. De novo development and the natural history have been described only in six previous cases. MRI is regarded to be unreliable with respect to the ability to demonstrate an ELST in the presence of intralabyrinthine hemorrhage, with only two out of four previously reported patients demonstrating positive MRI findings. Little is known about the precise origin (endolymphatic duct versus sac), growth, and symptom correlation. This case highlights that new audiovestibular symptoms are a potential clinical clue and intralabyrinthine hemorrhage is a neuroimaging indicator for the presence of an ELST, which based on high-resolution MRI appears to originate in the endolymphatic duct rather than sac.

Keywords

- ▶ endolymphatic sac tumor
- ▶ von Hippel–Lindau disease
- ▶ magnetic resonance imaging
- ▶ temporal bone

Introduction

Endolymphatic sac tumors (ELST) are benign but invasive tumors of the temporal bone that may occur sporadically but are commonly associated with von Hippel–Lindau disease (vHL). There is a reported incidence of 11 to 16% of ELST in patients with vHL disease, with approximately 30% occurring bilaterally.¹ Awareness of this manifestation has grown since the confirmation of ELST as part of the disease spec-

trum of vHL in 1997.¹ Symptoms include hearing loss, which may be sudden, or stepwise progressive, tinnitus, vertigo, and rarely facial palsy.^{2–5} Prior to the availability of high-resolution magnetic resonance imaging (MRI) and computed tomography (CT), tumors tended to be large and invade the membranous labyrinth and temporal bone. Due to different mechanisms of labyrinthine involvement, neuroimaging studies show little correlation between tumor size and audiovestibular symptoms.⁶ With specific protocols,

received
February 23, 2013
accepted
March 11, 2013
published online
May 28, 2013

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Stuttgart · New York

DOI <http://dx.doi.org/10.1055/s-0033-1347900>.
ISSN 2193-6331.

Fig. 1 T1 Gd-enhanced MRI: right cerebellar hemangioblastoma. Normal temporal bone.

contrast-enhanced MRI and temporal bone CT are likely to offer the chance to establish the diagnosis of ELST at an early stage.⁶ Intralabyrinthine hemorrhage may be the first clue of an ELST.²

The precise origin, growth, mechanism of symptoms, and indication for surgery of these tumors is still controversial. Review of the English literature revealed only two publications derived from the same institution, with a total of six cases^{7,8} that describe the de novo development of the ELST in patients with vHL. Similarities and differences in clinical/radiological presentation and management between this case and the other reports in the literature will be discussed.

Case Presentation

The following figures depict the history of a 12-year-old female patient with a known family history of vHL disease who underwent imaging surveillance for a 4-mm right cerebellar hemangioblastoma (►Fig. 1). Serial audiograms and MRIs of the temporal bone were normal prior to the onset of left-sided hearing loss and vertigo at the age of 17. When the patient became symptomatic, the audiogram showed a moderate loss in the low and high frequencies with preservation of thresholds in the mid frequencies (►Fig. 2a). Vestibular assessment revealed left vestibular hypofunction. MRI depicted hemorrhage into the left vestibule and abnormal contrast enhancement of the endolymphatic duct corresponding to an ELST of 1.5×8 mm extending within the bony vestibular aqueduct (►Fig. 2b, c). The joint management decision by the multidisciplinary team and the patient was to continue with surveillance MRI. Over a period of 25 months MRI and CT depicted a mild progression with increasing inhomogeneous enhancement of the endolymphatic duct and expansion of the vestibular aqueduct on CT with progressive retrolabyrinthine osseous invasion (►Fig. 3b–d) consistent with an ELST. After 25 months, at age 19, sudden and profound hearing loss occurred (►Fig. 4a), and the MRI showed recurrence of hemorrhage into the vestibule

Fig. 2 (a) Loss of low and high frequencies with preservation of mid frequencies in the left ear. Normal hearing in the right ear. (b) T1 2 mm noncontrast MRI depicts hemorrhage into left vestibule (top), contrast enhancement (c) of left endolymphatic duct.

Fig. 3 (a) Further loss of the mid frequencies in the left ear. (b) T1 contrast-enhanced MRI: increase in size of the tumor within endolymphatic duct. Persistent inflammatory enhancement of vestibule. (c, d) Axial and coronal high resolution CT. Sharply delineated enlargement of vestibular aqueduct and progressive extension anteriorly and inferiorly into retrolabyrinthine bone.

(► **Fig. 4b**) due to a progressive, partially solid, partially microcystic enlarging tumor within the endolymphatic duct, sparing the labyrinth. However, progressive extension was noticed into the retrolabyrinthine bone approaching the tympanic sinus and mastoid part of the facial nerve canal (► **Fig. 4c–d**).

Persistent vertigo was successfully treated with intratympanic gentamycin. Twenty-five months after the diagnosis of ELST, progressive increase in tumor size and potential encroachment on the mastoid segment of the facial nerve led to the patient's approval for surgical intervention. Surgery consisted of resection of the tumor from the endolymphatic duct by subtotal petrosectomy (► **Fig. 5**), blind sac closure of the external auditory canal, and closure of the Eustachian tube with bone wax. The middle ear and

surgical cavity were obliterated with abdominal fat. A passive cochlear implant electrode was inserted via the round window to maintain access to the cochlea should an active electrode be needed in the event of contralateral tumor development.

Histopathology showed a papillary tumor with cuboidal epithelial cells and nonviable bone chips consistent with an aggressive endolymphatic sac tumor. Follow-up has been unremarkable for 2 years after surgery.

Discussion

Two previous publications by one group^{7,8} report de novo clinical and imaging detection of an ELST associated with vHL in five cases and one case, respectively (► **Table 1**). The

Fig. 4 (a) Loss of all hearing in the left ear. (b) Noncontrast T1 image reveals new intralabyrinthine hemorrhage. (c, d) Axial and coronal CT show progressive retrolabyrinthine extension toward the vestibule and mastoid segment of facial nerve.

patients underwent surgical tumor resection by retrolabyrinthine posterior petrosectomy (RLPP). The tumors ranged in size from 3 to 19 mm and were followed up for 6 to 18 months.

The presence of intralabyrinthine hemorrhage is a common feature in this case, and in three out of the five patients presented by Kim⁷ and the single patient described by Jaganathan.⁸ In the latter case, intralabyrinthine hemorrhage was detected only on an MRI flair sequence but not on a noncontrast T1-weighted image, probably indicating post-hemorrhagic inflammation of the vestibule rather than acute or subacute hemorrhage.

In one patient reported by Kim et al, subsequent imaging suggested the diagnosis of ELST due to the presence of intralabyrinthine hemorrhage, but the tumor itself was not

visible and was only confirmed during surgery. In another case, the tumor was identifiable on MRI 12 months after the identification of intralabyrinthine hemorrhage.

In this patient, imaging confirmation of a small tumor within the endolymphatic duct occurred in conjunction with identification of intralabyrinthine hemorrhage. High-resolution MRI may be a decisive factor for early detection of the tumor, which is usually small (1.5 mm in this patient). In concurrence with the two previously reported patients with positive MRI findings (3-mm tumor in case 4 of Kim et al⁷; 2-mm tumor in Jagannathan case⁸) the origin appears be the endolymphatic duct rather than the sac. The endolymphatic sac may only become secondarily involved when the tumor increases in size. A patient with intralabyrinthine hemorrhage and macroscopic labyrinth sparing on MRI is

Fig. 5 (a) Normal thresholds right ear. No hearing left ear. (b) T1 contrast-enhanced postoperative MRI depicts total tumor resection by petrosectomy. Right cerebellar hemangioblastoma is visible.

particularly likely to harbor an ELST in this particular location. Therefore, contrary to the term endolymphatic sac tumor, the lesion is better described as an endolymphatic duct tumor. This has implications for the initial identification by imaging. As shown in our patient, the CT will become positive only when the margins of the bony vestibular aqueduct become eroded.

Due to the proximity of the endolymphatic duct to the labyrinth, audiovestibular symptoms are common. Hearing loss may occur suddenly (43%), in a rapidly progressive (43%), slowly (14%) progressive, or in a stepwise fashion. It is invariably permanent though may respond to steroid treatment. Mechanisms of hearing impairment may be acute intralabyrinthine hemorrhage, endolymphatic hydrops, or by direct invasion of the labyrinth. Intralabyrinthine hemorrhage appears to be a common mechanism. In this patient, hearing loss was relatively stable with preservation of the midfrequencies over an 18-month period until a second episode of labyrinthine hemorrhage led to a sudden and complete loss of hearing. Endolymph hydrops may cause symptoms in small tumors that obstruct perilymph flow or resorption prior to the occurrence of hemorrhage. In previous reports, tumors tended to be too small to be detected by imaging at this stage.^{7,8} Advancements in MRI technique may result in earlier and smaller tumor

detection. Small tumors are expected to be located within the endolymphatic duct and may be managed with hearing-preservation surgery, via a RLPP approach, prior to the onset of significant hearing loss.⁷ The management of larger tumors unsuitable for hearing-preservation surgery, in patients with functional hearing, is less clear. There have been published reports recommending observation of these tumors if they are already associated with significant hearing loss, as they can be slow growing.⁹ Hearing loss and the threat of facial nerve palsy were the main factors in the decision for the patient in this report to agree to surgery.

Conclusions

Based on sequential imaging observations and contrary to current terminology, endolymphatic sac tumors appear to initially arise from the endolymphatic duct. Audiovestibular symptoms in the presence of intralabyrinthine hemorrhage may be regarded as an early indicator to the presence of a small tumor. Recognition of the existence and location of the tumor requires a high degree of clinical suspicion and thin-slice, high-resolution, contrast-enhanced MRI. Surgery may be advocated to avoid tumor progression into the labyrinth and hearing loss.

Table 1 Summary of the clinical findings, surgery, and postoperative course in the current and previously published patients

Case no.	Age (y), sex	Tumor side	Tumor diameter (mm)	Preop symptom	Presence of intralabyrinthine hemorrhage	Time between hemorrhage and tumor identification on MRI	Surgical approach	Postop result	Follow-up (mo)
1	17, F	L	8	Hearing loss (SRT 100 dB), tinnitus, vertigo	yes	1y	Trans labyrinthine subtotal petrosectomy and passive CI electrode insertion	Resolution of tinnitus and vertigo	24
2	42, M	L	5	Hearing loss (SRT 60 dB), vertigo, tinnitus	Yes	0	RLPP	Stable hearing, resolution of tinnitus and vertigo	18
3	40, M	L	19	Hearing loss (SRT 35 dB), vertigo, tinnitus, aural fullness	Yes	0	RLPP	Stable hearing, resolution of tinnitus, vertigo, and aural fullness	18
4	27, F	L	11	Temporary mild hearing loss (SRT 25 dB), vertigo	No	N/A	RLPP	Stable hearing, resolution of vertigo	12
5	34, F	L	3	Hearing loss (SRT 40 dB), vertigo, tinnitus, aural fullness	Yes	1y	RLPP	Stable hearing, resolution of tinnitus, vertigo, and aural fullness	12
6	31, M	L	7	Vertigo	No	N/A	RLPP	Stable hearing, resolution of vertigo	6
7	33, M	L	2	Hearing loss, tinnitus, vertigo	yes	N/A (tumor identified during surgery)	RLPP	NR	NR

Abbreviations: CI, cochlear implant; RLPP, retrolabyrinthine posterior petrosectomy; SRT, speech reception threshold.

Case 1: this report.

Cases 2–6 Kim⁷: five patients.Case 7 Jagannathan⁸: one patient.

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