Endolymphatic Sac Tumour: A Neoplastic Cause for Meniere's Syndrome

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Abstract Patients with intractable vertigo often present a diagnostic dilemma to the treating physician. A wide spectrum of diseases, ranging from those of the labyrinth onto the central nervous system, may present predominantly with vertigo. In some cases, it requires the clinical acumen of an experienced neuro-otologist, to decipher these vertiginous symptoms and arrive at a definitive diagnosis. Meniere's syndrome is one such phenomenon, where the endolymphatic hydrops may be attributable to varied aetiology. We report a case of sporadic (non-syndromic) Endolymphatic Sac Tumor which presented to us, mimicking a classical Meniere's syndrome. We discuss its clinical presentation, diagnostic modalities, operative technique and histo-pathological features. The case is reported along with a review of the world literature on this tumor, highlighting the diagnostic and management protocols advocated for this rare entity. Endolymphatic sac tumor is a rare entity which may masquerade as a classical case of Meniere's syndrome, wherein the triad of symptoms (as in endolymphatic hydrops) may not be alleviated by the usual treatment protocols. Tracing the aetiology of these symptoms, remains the most crucial factor in treating such patients.

Keywords Vertigo · Endolymphatic hydrops · Endolymphatic sac tumor (ELST) · Von Hippel–Lindau's disease (VHL)

Introduction

Endolymphatic sac tumor (Heffner's tumor) [1] is a rare, hyper-vascular and locally aggressive papillary neoplasm that originates in the retro-labyrinthine part of the temporal bone. Most papillary endolymphatic sac tumors are sporadic, but recent literature reveals its syndromic association with Von Hippel–Lindau's (VHL) disease in nearly 30% of cases [2]. They classically grow very slowly, resulting in late clinical manifestations with an expansile mass invading temporal bone and extending onto the posterior cranial fossa. The main symptoms produced by these lesions include vertigo, sensori-neural hearing loss and lower cranial nerve deficits [3].

Endolymphatic sac tumors originate in two principal patterns that histologically form follicular, papillary or solid structures and all these patterns are usually manifested in the same tumor. Immuno-histochemical analysis of these tumors, usually reveal cytokeratin, vimentin, epithelial membrane antigen and less frequently S-100 protein or neuron-specific enolase [4, 5]. Surgical excision is often curative for most endolymphatic sac papillary tumors. Current world literature favors surgery and long-term follow-up. Few reports have suggested a role for adjuvant radiotherapy, but the outcomes are debatable [6, 7]. We report a case of sporadic endolymphatic sac tumor (ELST), discuss the management protocols and review the present literature on this rare condition.

Case Report

A 33 year old gentleman presented to our institution, with symptoms suggestive of a classical Meniere's syndrome in the left ear, since 3 years duration. He vividly described

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spells of aural fullness preceding episodic vertigo, associated with fluctuant hearing loss, tinnitus and imbalance on walking or travel. He had visited several ENT surgeons and neurologists elsewhere and had been treated with prolonged doses of vestibular sedatives, betahistine and diuretics, which gave him only momentary relief from his symptoms. His previous investigations had shown mild sensori-neural hearing loss and poor vestibular function in the affected left ear. His clinical examination was unremarkable and he had no signs of acute vestibular dysfunction at the time of presentation.

A comprehensive oto-neurological evaluation was performed at our institution which included radio imaging studies along with an objective audio-vestibular assessment. The audiological test battery including electrophysiological tests, proved that he had moderate sensori-neural hearing loss in the affected left ear. Vestibular system assessment by bithermal caloric testing with video oculography showed a hypo-active left labyrinth. Vestibular Evoked Myogenic Potentials confirmed normal saccular function.

A high resolution CT scan of the Temporal Bone (Fig. 1) gave us a vital clue to the diagnosis, when it showed an irregular moth-eaten destructive lesion with central calcific speculations centered over the posterior aspect of left petrous temporal bone, just abutting the Jugular fossa in the region of the endolymphatic sac. The middle ear, mastoid, bony labyrinth and internal auditory meatus were all normal. MRI scan of the brain and inner ear (Fig. 2) showed a hyper-intense heterogenous lesion on T2 weighted images, in the left endolymphatic sac region, the vestibule-cochlear nerve bundles, cerebellum and the cerebello-pontine angles were all normal.

Due to proximity of the lesion to the jugular foramen, a high suspicion of a glomus tumor arose and a selective carotid artery/jugular venous angiography was performed, which showed a mild vascular tumor blush in the region of the left endolymphatic sac, but no major feeding vessel was delineated. Since a glomus tumor was excluded, a provisional differential diagnosis for the solitary lytic lesion in the posterior cranial fossa, included an eosinophilic granuloma,

Fig. 1 HRCT Temporal Bone showing an irregular moth-eaten lytic lesion with central calcific spiculations, over the posterior aspect of left petrous temporal bone, abutting the jugular fossa

Fig. 2 MRI Brain showing a hyper-intense lesion on T2 weighted images in the endolymphatic sac region of the left posterior cranial fossa

paraganglioma, hyper-parathyroid lesion, Metastatic deposit (from thyroid, lung or breast) or a primary neoplasm of the endolymphatic sac.

As the possibility of a neoplastic lesion (either primary or metastatic) was present, a meticulous evaluation to identify any other primary site was done. An ultrasound of neck, FNAC thyroid and thyroglobulin studies proved negative. As there is a strong syndromic association of a primary neoplasm of the endolymphatic sac with VHL disease, diagnostic tests for VHL disease including a fundoscopy to rule out retinal haemangiomas, CT abdomen to exclude liver or adrenal tumors, biochemical markers for neuro-endocrine tumors, MR imaging of the brain with spine (to locate any angiomatous lesions) and a genetic study for VHL were performed and found to be normal.

Surgical exploration of the left endolymphatic sac region was performed by a transmastoid–retrolabyrinthine approach. As the endolymphatic sac was exposed a highly vascular, friable and polypoidal tumour was seen with surrounding areas of bony erosion and adhesions up to the dura (Fig. 3). A radical resection of the tumour was completed, while preserving the integrity of the dura of the posterior cranial fossa.

The gross specimen showed a papillary tumor with rugosity of its walls and a cystic component containing a colloid like material within. Histopathological examination confirmed the diagnosis of an endolymphatic sac tumour with characteristic malignant papillary epithelial clusters with hyperchromatic nuclei and a glandular stroma containing eosinophilic colloid like material (Fig. 4).

The patient had an uneventful post operative period and he was referred to the Radiation Oncologist for contemplating adjuvant radiotherapy to the operated site. Subsequently he received a short course of Intensity Modulated

Fig. 3 Intra-operative pictures of a friable and vascular papillary tumor in the endolymphatic sac with surrounding bone erosion

Fig. 4 Histopathological photomicrograph (40× high power) showing Endolymphatic Sac Tumour with characteristic malignant papillary epithelial clusters with hyperchromatic nuclei and a glandular stroma containing eosinophilic colloid like material

Radiotherapy and has been kept under meticulous follow up for the past 1 year. His follow up (post RT) MRI scan shows no evidence of any residual tumor. His hearing remains status quo, while his tinnitus and vertiginous spells have subsided.

Discussion

Endolymphatic sac tumours (ELSTs) have been known as an individual tumour entity since 1984. ELSTs may occur either solitarily and sporadically or as a hereditary manifestation associated with VHL disease [1, 2]. The latter association was first observed in 1992 and confirmed by molecular genetic analysis of the VHL gene. VHL disease is a familial, genetically inherited condition which occurs due to germ-line mutations in the VHL tumor-suppressor gene in Chromosome 3p 25/26, that plays a major role in regulating the oxygen-sensing pathway by targeting the hypoxia-inducible factor (HIF) for degradation in cellular

organelles. This results in abnormal growth of multiple tumours in parts of the body which are rich in blood supply (like liver, lung, brain, kidney, pancreas and adrenal gland) [4, 8]. Endolymphatic sac tumors associated with a diagnosis of VHL disease appear to affect a younger population of patients than non-VHL disease cases and occur in women twice as often as in men when associated with VHL disease. In addition, tumors are more frequently bilateral and advanced in the VHL disease patient as opposed to the non-VHL disease patient [3, 9]. Historically, nomenclature of invasive adenoid tumours in the petrous bone has been divergent, the term papillary adenocarcinoma used most frequently. Histologically, they have a follicular or papillary and adenoid pattern that can be easily confused with various other neoplastic conditions including metastatic carcinoma. [6, 10] Papillary ELSTs of the temporal bone are rare, slow growing and aggressive neoplasms, with an incidence of ~1:30,000 in adult population. These tumors had initially been presumed to be of middle ear origin, but recent literature has confirmed their anatomic, morphological and immuno-histochemical characteristics to the endolymphatic sac (of inner ear/neuro-ectodermal origin).

ELST can express a variety of epitopes (including cytokeratin and neuroectodermal markers) which can be detected by immuno-histochemical analysis [4, 5, 8]. They most often develop within the intra-petrosal part of the sac, and spread in two directions: laterally towards the external/middle ear and in the direction of jugular foramen and medially into the CP angle. The symptoms are usually auditory, with a constant sensori-neural deafness of sudden onset in 50% of cases along with tinnitus and vertigo. Those tumors with medial extension result in a cerebello-pontine angle syndrome. The cause of sensori-neural hearing loss has been implicated to the otic capsule invasion, tumor-associated intra-labyrinthine hemorrhage or due to endolymphatic hydrops [11]. Tumors of the endolymphatic sac may be found in association with VHL disease which has a range of presentations including retinal

angiomas, CNS haemangioblastomas, pheochromocytomas and renal cell carcinomas. VHL associated ELSTs usually present as large tumors involving the CP angle, resulting in unilateral fifth to eleventh cranial nerve palsies, progressive ataxia, meningism and a pyramidal or pseudo-bulbar syndrome, in addition to the predominant symptoms of progressive sensori-neural hearing loss, intractable vertigo, referred otalgia, tinnitus and occipital headaches [12–14].

In apparently sporadic cases of ELST, genetic testing for VHL disease is considered mandatory. Surgical excision is the treatment of choice, but sacrifice of the vestibule-cochlear nerve and facial nerve may be needed in advanced cases to achieve complete tumor clearance. Pre-operative super-selective embolization of the feeding vessel in the posterior cranial fossa has been attempted for certain hyper-vascular ELSTs, which has eased the difficulty of tumor excision to a larger extent. If complete resection is not possible due to extensive local invasion, adjuvant radiotherapy is advocated in order to achieve tumor regression and to preserve the integrity of surrounding vital structures in the posterior cranial fossa [7, 15].

Conclusion

It is paramount to perform a meticulous neuro-otological evaluation of patients with intractable Meniere's syndrome, in order to identify the primary pathology. A clinical and imaging surveillance protocol needs to be devised especially in patients diagnosed with VHL disease, in order to provide an early insight into the origin of syndromic ELSTs. The investigative protocol should include objective tests for vestibular function and high resolution radio imaging, to precisely look into the region of the endolymphatic sac. A neoplastic cause like the ELST and its syndromic association with VHL disease should be kept in mind while planning for surgical exploration of posterior cranial fossa/CP angle lesions. Radical resection of an endolymphatic sac tumor is often curative and adjuvant radiotherapy is advocated especially for large tumors with invasion into the cerebellum or cranial nerves in CP angle, wherein complete removal may not be possible. Long term post operative follow up of these patients with periodic audio-vestibular testing and radio-imaging remains vital.

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