Vestibular schwannoma: a review of contemporary diagnosis and management strategies

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Vestibular schwannomas are uncommon, benign intracranial tumors that present a management challenge based on their intimate association with the brainstem and the cranial nerves affecting hearing and facial nerve function. Modern strategies for managing vestibular schwannomas have been characterized by improved diagnostic accuracy and reduced morbidity and mortality rates. Observation with serial imaging, open microsurgical tumor resection, stereotactic radiosurgery, or a combination of both modalities represent viable management options. Treatment should be individualized based on the unique characteristics and expectations of each patient.

Vestibular schwannomas are associated with hearing and balance deficits due to compression of the brainstem and vestibulocochlear nerve. Magnetic resonance imaging is used for definitive diagnosis, and computed tomography as well as audiometry are generally used as part of patient evaluation. Open microsurgery, which was previously regarded as the mainstay of therapy, is associated with relatively high rates of hearing loss, facial nerve injury, cerebrospinal fluid leakage, and damage to neural structures when compared to stereotactic radiosurgery. As a result, stereotactic radiosurgery has become a critical treatment option for older patients, for those with medical co-morbidities, and for younger patients with good preoperative hearing function. Younger patients with very large tumors resulting in significant brainstem compression still generally require open surgery to decompress the brainstem. In our experience, many such patients will benefit from a combined approach including debulking of the tumor to decompress the brainstem followed by radiosurgery to treat residual tumor adherent to critical structures.

As surgical approaches for vestibular schwannoma have improved, most patients undergoing treatment can expect reasonable preservation rates of both hearing and facial nerve function. Optimal care should be determined on an individualized, case-by-case basis, may involve a combined surgical/radiosurgical approach, and should ideally be delivered in high volume, multi-disciplinary centers.

Introduction

Vestibular Schwannomas (VS) are rare, generally benign tumors with an annual incidence of 1 in 100,000; a total of 2,000 to 3,000 new cases are identified in the United States each year, comprising 6-7% of intracranial tumors.1,2 The detection of VS has improved in recent years, likely as a consequence of increased access to and use of magnetic resonance imaging (MR) imaging.3

The last century has seen a dramatic shift in the treatment of VS. Due to historically poor surgical outcomes, with mortality rates exceeding 50% until the mid-1900s, a “wait and see” approach was often taken. Subsequent advances in neurosurgical techniques reduced surgical mortality rates to 20%,4 and microsurgical excision became more commonplace. Current surgical methods offer mortality rates of 0-1%,5 yet the development and advancement of stereotactic radiosurgery has reduced the need for open microsurgical excision.6 As a result, patients affected by VS today can generally be managed successfully and typically have an excellent prognosis.

Clinical presentation

VS are slow-growing, benign tumors, and therefore symptoms are generally slow in onset.21 The most common symptoms in VS patients include unilateral, progressive sensorineural hearing loss, tinnitus (ears “ringing”), and balance disturbance.21,22 In one study, the mean length of time from onset of signs or symptoms to diagnosis was 31.6 +/- 50.96 months, with a median of 12 months.24

Patients may occasionally present with more acute symptoms such as sudden sensorineural hearing loss.22 Less common symptoms include headache, feelings of head fullness, and facial numbness, weakness, or pain.22,25 Due to the wide range of symptoms, VSs are often mistaken for Meniere’s disease,22 migraine,21 or other conditions.4 The use of MR imaging (Figure 1) and an array of diagnostic testing, including auditory brain stem response (ABR) and audiometry (Figure 2), have greatly increased the sensitivity and specificity of VS diagnosis.1,2
Assessment and diagnosis
When hearing symptoms persist, patients are usually referred to an otolaryngologist, and audiometry is performed revealing unilateral high-frequency sensorineural hearing loss. While it is common to develop a high-frequency sensorineural hearing loss with advancing age, typical aging does not lead to asymmetries in hearing, and unilateral hearing loss will typically prompt MR imaging to rule out a VS.

Radiologic imaging is typically undertaken using T1-MR, T2-MR, and 3D FLAIR imaging with administration of gadolinium as a contrast agent offering a diagnostic accuracy of 96% sensitivity and 88.2% specificity. MR images can help determine the exact location of the lesion and whether it is compressing other brain structures, such as the brainstem. Computed tomography (CT) imaging is often used as a part of the pre-surgical work up as well.

Pathogenesis
VS are benign neoplasms of the nerve sheath surrounding the eighth cranial nerve (CN VIII or the vestibulocochlear nerve). Most VS occur in sporadic fashion without associated genetic abnormalities. VS may be associated with neurofibromatosis type 1 (NF1)—this subtype is also considered a sporadic VS—or with neurofibromatosis type 2 (NF2) which is typically associated with bilateral VS.

Neurofibromatosis 1
NF1 has been shown to be associated with the development of nerve sheath tumors, including VS based on mutations of a Ras GTPase gene on the long arm of chromosome 17 that regulates cell proliferation. Sporadic VS have demonstrated a connection with deregulation of p53 in several studies, but further research is needed to determine the range of pathogeneses of sporadic VS. NF1-related and sporadic VS are rarely bilateral, differentiating them from NF2-associated VS.

Neurofibromatosis 2
For VS associated with NF2, the strongest genetic marker is a loss-of-function mutation in the tumor suppressor gene NF-2 on chromosome 22. Tumor development, proliferation, and survival have been associated with multiple intracellular signaling molecules, including MAP kinase, AKT, p21-activated kinase, and others. However, there has been no conclusive evidence for the causative role of these pathways in the development of VS. Furthermore, genetic alterations are insufficient to describe or predict tumor growth or clinical manifestations in these patients.

Therapeutic strategies
Treatment options for VS include a “wait-and-see” approach, microsurgical tumor removal, stereotactic radiosurgery (SRS), and combined microsurgery-SRS.

The “wait-and-see” approach, which consists of serial MR imaging typically performed on an annual basis to monitor tumor growth, was initially proposed as a method for addressing the historically high morbidity and mortality rates associated with surgical removal of these tumors. In one study of 123 patients managed conservatively, 28% were ultimately operated on due to tumor growth, 6% received SRS and/or shunt insertion, and 6% died of tumor compression. Therefore, the risks of this approach primarily relate to the delayed consequences of tumor growth causing functional deficits and potentially increasing the risks of treatment once the tumor has reached a larger size. This approach makes sense in older patients with smaller tumors that may never reach a size of consequence to the patient. Generally, a course of watchful waiting is recommended for a significant percentage of newly diagnosed patients, since many VS are now being diagnosed in older patients or while their size is quite small due to the increasing utilization of MR imaging.

Open microsurgery
When treatment is recommended, microsurgery has been shown to both control tumor growth and potentially preserve hearing, depending on the approach used. Microsurgical resection is often recommended in younger patients, in patients with substantial dizziness that may not respond well to SRS, and in those with larger tumors causing symptoms due to mass effect on the brainstem (see Figure 3). However, resection carries the risk of permanent facial nerve palsy, hearing loss, CSF leak, meningitis, and headache. Over the past 50 years, the goal of treatment for VS first shifted from preservation of life to preservation of facial nerve function with improving surgical techniques. More recently, the goal has become preservation of hearing, an option that would not have been considered feasible in the past but has become a real possibility with further refinements in surgery and with the advancement of SRS options.

Surgery may be carried out through translabyrinthine, retrosigmoid, or middle fossa approaches. The translabyrinthine approach is generally used to treat tumors of the internal auditory canal (IAC) or cerebellopontine angle (CPA) in patients who have already lost their hearing ability as the approach itself results in complete hearing loss due to removal of the inner ear structures. The greatest advantages of this approach include the need for only minimal brain retraction and the ability to visualize tumors that extend all the way to the internal auditory canal.
the lateral-most aspect of the internal auditory canal.4,5 The retrosigmoid approach is used to resect VS primarily involving the CPA and is often preferred for larger lesions with significant brainstem compression.1,4,32 Hearing preservation is possible with this approach. The middle fossa approach is used to resect small tumors within the IAC when hearing is excellent.1,4,32,33 This approach allows for the possibility of hearing preservation but carries an elevated risk of facial nerve injury.4,33

The major disadvantages of open surgery include the relatively high rates of hearing loss, the potential for injury to the facial nerve causing temporary or permanent facial weakness, and the risk of CSF leak postoperatively. In our practice, surgery is performed by a team that includes a skull base neurosurgeon and a neuro- otologist. The specific approach is tailored to meet the needs of each individual case. Over time, we have gained a better sense of which tumors can be completely resected without subjecting the patient to significant facial nerve palsy. In those patients with tumors particularly adherent to the facial nerve, we will often perform a subtotal resection, removing most of the tumor and decompressing the brainstem. This can be followed by SRS to treat any residual tumor while minimizing risk to the facial nerve.

**Stereotactic radiosurgery**

Stereotactic radiosurgery (SRS) has become an increasingly important alternative to open microsurgery over the past two decades.1,4,34,35 SRS is most often used to treat smaller tumors that demonstrate interval enlargement on serial imaging and is an excellent option for patients with good hearing. SRS has been shown to control tumor growth with higher rates of hearing preservation and decreased risk for facial nerve palsy compared to open microsurgery (see Figure 4).1,4,24 Two popular forms of SRS are Cyberknife (CKRS) and Gamma Knife (GKRS). While both methods apply beams of radiation to lesions; their main difference is in the procedure itself.36 Since GKRS requires the mounting of a head frame with screws inserted into the skull before and during treatment, we have utilized CKRS for the past 15 years. CKRS is frameless and therefore painless, often allowing patients to return to work the day of treatment. The lack of a frame allows for CKRS to be fractionated, which may improve tumor control rates while minimizing the potential for injury to neighboring critical structures.37

Both options provide excellent tumor control rates with hearing preservation rates exceeding those offered by open surgery in those patients who have good hearing before treatment. One study found that GKRS was able to control tumor growth in 97.1% of the patients and 82.7% showed decreased tumor volume at follow-up.24 CKRS has shown excellent tumor control rates, as high as 99.1%.38 Hearing preservation rates in GKRS reportedly range from 55% to 79%,38 while studies evaluating hearing preservation for CKRS have shown that approximately 80% of patients have improved or unchanged hearing post-operatively.38,39

Potential complications reported following GKRS have included cerebral edema, headache, nausea, and facial numbness or weakness.40,41 Also, similar to other forms of standard radiotherapy, there are risks of bleeding and microvascular dysfunction due to endothelial cell damage.42,43 Other potential complications include facial nerve impairment, vertigo, and imbalance, however, these findings are rare, ranging from 0 to 3%.44

Some surgeons have argued against SRS for VS, based on the potential risk of late malignant transformation.45-47 In fact, the statistical evidence suggests that malignant transformation likely only occurs in the setting of NF-2, can occur in NF-2 tumors even without irradiation, and is so uncom-
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**Options in the setting of NF-2**

NF-2 patients are unique in their propensity to develop bilateral VS, often presenting at a young age, and potentially resulting in eventual deafness. In these patients, unique strategies have been developed to maintain hearing function, including the possible use of chemotherapeutic agents to slow tumor growth in an attempt to preserve hearing as long as possible. In patients who suffer bilateral hearing loss, auditory brainstem implantation may allow for some preservation or restoration of hearing. These are best managed in centers that care for a high volume of VS patients to optimize their outcomes. Genetic counseling and patient support groups may also be important, particularly for NF-2 patients, who often struggle with life-long issues from their disease.

**Conclusions**

As microsurgical techniques have improved over time, many VS patients can undergo treatment with the realistic expectation of preservation of hearing and facial nerve function. The increasing use of SRS has revolutionized the management of VS and allowed for a combined approach with microsurgery to debulk the tumor and decompress the brainstem followed by the use of SRS to treat residual tumor adherent to critical structures. Optimal management for VS patients generally occurs in high volume, multidisciplinary centers that include skull base neurosurgery, neuro-otology, and dedicated SRS to offer patients the full spectrum of options and to optimize outcomes.

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**FIGURE 3**

Large vestibular schwannoma before and after open microsurgery.

A) Pre-operative axial T1-weighted MRI showing large enhancing vestibular schwannoma filling the cerebellopontine angle with marked displacement of the brainstem and fourth ventricle to the right. B) CT after removal of a large acoustic neuroma, showing fat graft following resection and improvement in brainstem position.

**FIGURE 4**

Planning stereotactic radiosurgery of a vestibular schwannoma.

A) Axial T1-weighted post contrast MRI showing a homogenously enhancing intracanalicular vestibular schwannoma, prior to stereotactic radiosurgery. B) Treatment plan showing precise targeting of fractionated radiation on axial contrast CT.


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