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REVIEW ARTICLE

Vestibular Schwannomas: A Narrative Review on Imaging and Treatment Perspectives

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Abstract

Vestibular schwannomas, the predominant neoplasms within the cerebellopontine angle, have experienced an evolution in therapeutic objectives over the last century, transitioning from the goal of total excision to one of functional preservation. Present-day treatment modalities encompass surgical resection, stereotactic radiosurgery, and observation. Imaging is pivotal for the initial screening, thorough evaluation, and ongoing assessment of vestibular schwannomas. Radiologists, by discerning and understanding management goals, treatment methodologies, anticipated post-treatment results, and potential complications, play an integral role in multidisciplinary medical teams. Their expertise yields essential insights for planning treatment and evaluating outcomes. The authors present an extensive discussion that includes surgical management, the role of radiation therapy, observation strategies, imaging differentials, and both pre- and post-treatment imaging findings pertinent to vestibular schwannomas.

Key words: Diagnosis, Management, Pathology, Schwannoma, Vestibular

Introduction

Vestibular schwannoma (VS), also known as acoustic neuroma, is a benign tumor originating from Schwann cells of the vestibulocochlear nerve. These tumors make up 85% of intracranial growths at the cerebellopontine angle (1, 2). The Koos grading scale classifies tumor size based on extra-meatal extension and brainstem compression (3). While "VS" and "acoustic neuroma" are often used interchangeably, this research prefers "vestibular schwannoma" since most tumors arise from the vestibular part of the vestibulocochlear nerve and consist of Schwann cells (4, 5).

Despite being benign, VS can affect intracranial structures due to its mass effect. Over 60% of patients experience gradual hearing loss and tinnitus as primary symptoms. Larger tumors may cause hydrocephalus and brainstem compression, leading to symptoms. such as facial paresthesia, vertigo, and headache (6). The VS accounts for about 8% of all brain tumors, with an annual incidence of

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10.4 per million (7). Most tumors are unilateral and sporadic; with less than 5% of neurofibromatosis type 2 (NF2) cases showing bilateral disease, indicating a genetic condition. Patients typically present between ages 20-40, while those with NF2 may show symptoms earlier (8). The rising incidence of VS is attributed to increased reporting, driven by the widespread use of MRI for tinnitus and early medical consultation (9). The present study seeks to offer a current review of our knowledge regarding the pathogenesis and diagnosis of VS, emphasizing contemporary management strategies. It also delves into emerging treatment options.

Methods

A thorough database review (PubMed, Scopus, and search engine of Google Scholar) was conducted using the keywords "Vestibular," "Schwannoma," and "surgery," covering literature from 1900 to 2024. The review focused on studies that explored the applications of endoscopic surgeries, their outcomes, limitations, and future prospects. Only studies published in English were considered.

Results

Histopathology

Most VS tumors originate from the inferior vestibular nerve, with occasional cases arising from the superior vestibular or cochlear portions. Characteristic histologic features include bipolar spindle cells arranged in distinctive Antoni A and Antoni B tissue types (10).

Molecular Pathogenesis

Mutations in the NF2 tumor suppressor gene, located on chromosome 22, play a critical role in the development of both sporadic and neurofibromatosis type 2 (NF2)-related vestibular schwannomas (VS) (11). The loss of function of the NF2 protein, Merlin (schwannomin), leads to the disruption of several intracellular signaling pathways, such as Rac1, Ras, PAK1, and mTORC1. Furthermore, the inactivation of additional tumor suppressor genes, including LZTR1, SMARCB1, and COQ6, is linked to the pathogenesis of schwannomas (12, 13). Recent large-scale genomic sequencing studies have confirmed the significant role of NF2 mutations. Notably, there is evidence that NF2-associated vestibular schwannomas exhibit a distinct polyclonal mutation pattern [14]. This variation may account for the differences in treatment outcomes between NF2-associated and sporadic VS(15).

Diagnosis

Vestibular schwannoma (VS) is commonly diagnosed based on a combination of otological and neurological symptoms. Otological symptoms such as progressive sensorineural hearing loss, unilateral tinnitus, and vertigo are more prevalent than neurological symptoms, which may include trigeminal and facial nerve impairment, headaches, and hydrocephalus [5, 6, 16, 17]. Approximately 20% of patients presenting to Ear, Nose, and Throat (ENT) clinics exhibit symptoms suggestive of a lesion at the cerebellopontine angle [18]. Consequently, these patients typically undergo otoscopy, pure tone audiometry, and MRI of the internal acoustic meatus. While brainstem-evoked response audiometry has been used as a screening tool for suspected VS due to the early presentation of hearing loss, it is no longer considered a first-line investigation because of its high false-negative rate (up to 30% for small schwannomas) and a false-positive rate of 10% [19].

MRI remains the gold standard for diagnosing vestibular schwannoma in patients with unilateral tinnitus or sensorineural hearing loss [5, 16, 17]. A systematic review and cost-effectiveness study by Fortnum et al. [20] demonstrated that gadolinium-enhanced T1-weighted MRI, although the gold standard, shows minimal difference in sensitivity and specificity compared to non-contrast T2-weighted scans. Additionally, non-contrast T2-weighted MRI scans are considered more cost-effective for clinical practice.

CT scans can be useful for identifying moderate to large vestibular schwannomas; however, small intracanalicular tumors may be missed. On CT imaging, solid VS appears isoattenuating relative to cerebellar parenchyma and usually shows enhancement. Unlike meningiomas, vestibular schwannomas do not contain calcifications [21].

Current Treatment Options

Various strategies exist for managing patients with vestibular schwannoma (VS). These include observation, often referred to as the 'watch and rescan' approach, surgical excision, and radiotherapy. The main goal of interventional treatment is to excise or reduce the tumor size to alleviate its mass effect [5, 16, 17].

Conservative Management

Observational management is a recommended approach for specific patients, particularly those aged 60 and older with significant comorbidities, small tumors, and no symptoms. Patients are routinely monitored through serial MR imaging at intervals of 6 to 12 months. Additionally, this approach may be suitable for patients at risk of hearing loss from other causes or those who prefer

a conservative management strategy.

However, it is important to note that progressive hearing loss can occur due to the slow growth of most vestibular schwannomas. Tumors that grow at a rate of 2.5 mm/year or more tend to have higher rates of hearing deterioration compared to those that grow more slowly [22]. Therefore, if maintaining hearing function is a treatment goal, earlier intervention may be more beneficial [23, 24].

Surgery

In recent years, the goals of surgical management for vestibular schwannoma (VS) have shifted from achieving total resection to prioritizing long-term functional preservation [25, 26]. Subtotal resection followed by observation or stereotactic radiosurgery (SRS), particularly for large VS, has shown effective long-term tumor control while preserving cranial nerve (CN) function [25, 27]. The management approach for small-to-medium VS (typically measuring less than 3 cm) differs from that for larger tumors, with surgery often being favored over SRS for larger VS.

Although some researchers have successfully treated large VS using SRS [28], concerns remain about potential complications, including compressive ischemia of CN VII and brainstem compression [29, 30]. The optimal treatment strategy for VS, especially small-to-medium lesions, remains a topic of debate, with preferences varying among different medical centers.

Gross total resection is generally recommended for younger patients with persistent dizziness, those with small anatomically favorable tumors and intact hearing, cystic tumors, and larger tumors causing symptoms related to mass effect [30]. Surgical resection, unlike SRS, provides a definitive histopathologic diagnosis. However, due to post-radiation effects on tissue, SRS following surgical resection is generally more favorable than performing SRS before surgery [30].

It is crucial to recognize that surgery presents a higher risk of permanent facial nerve palsy when compared to stereotactic radiosurgery (SRS). Additional risks of surgical resection encompass iatrogenic hearing loss, cerebrospinal fluid (CSF) leaks, meningitis, headaches, and complications related to anesthesia. After gross total resection, the recurrence rate of vestibular schwannoma (VS) within five years can be as high as 10% [22]. Ten-year tumor control rates for gross total and subtotal resection are 78% and 82%, respectively [22].

Translabyrinthine craniotomy (TL) is a surgical technique involving a posterior route through the mastoid temporal bone, situated in front of the sigmoid sinus. Following a simple mastoidectomy, the vertical facial nerve canal is revealed, and a labyrinthectomy is performed to reach the internal auditory canal (IAC) located behind the vestibule [31]. The cerebellopontine angle (CPA) can be accessed by excising bone behind the porus acusticus. Throughout the procedure, facial nerve monitoring is conducted, and the tumor is debulked and microdissected. The craniotomy is sealed by positioning temporalis fascia at the aditus ad antrum and packing the mastoidectomy defect with abdominal fat. Fat is favored over muscle because of its easy availability and lower associated morbidity. Moreover, the fat signal can be effectively suppressed on follow-up contrast-enhanced MR imaging. TL offers sufficient exposure of the IAC and posterior fossa (PF) with minimal brain retraction. However, if there is a significant PF component, the retrosigmoid (RS) approach may be preferable. TL is usually reserved for patients with total hearing loss or an unfavorable hearing prognosis [31].

Retrosigmoid Craniotomy (RS) is a surgical technique that utilizes a posterior approach, offering a broad view of the cerebellopontine angle (CPA). The procedure starts with a suboccipital craniotomy situated behind the sigmoid sinus, followed by the medial retraction of the cerebellum to expose the CPA mass and associated neurovascular structures. During dissection, the facial nerve is identified, and the intrameatal portion can be accessed and excised by drilling the posterior meatal lip. Factors such as tumor infiltration of the cochlear nerve, poor preoperative hearing, and larger tumor size decrease the likelihood of hearing preservation [31]. RS allows for the removal of large extrameatal and small medial intrameatal tumors while aiming to maintain hearing function [31, 32]. However, limitations of the RS approach include possible obstruction by a high-riding jugular bulb or labyrinth and the risk of injury to the cerebellar parenchyma [33]. Postoperative headaches following RS may be more common than those after translabyrinthine craniotomy, possibly due to the dissemination of subarachnoid bone dust or the use of a titanium plate [34].

The Middle Fossa Approach (MF) is a lateral surgical technique utilized to access the internal auditory canal (IAC). This technique involves performing a temporal craniotomy above the external auditory canal, lifting the dura from the skull base, and retracting the temporal lobe upward. Key anatomical landmarks for this approach include the arcuate eminence and the greater superficial petrosal nerve. By accessing the IAC from above, the tumor can be removed following the microdissection of the facial and cochlear nerves. Bone wax is used to seal

any exposed mastoid air cells [31]. The MF approach is particularly well-suited for small lateral IAC tumors, especially those extending to the IAC fundus, when the preservation of hearing is a treatment objective. However, this approach is not typically attempted for tumors with a cerebellopontine angle (CPA) component larger than 1 cm due to limited exposure to the posterior fossa. Some surgeons have reported success with larger tumors using this approach. The retraction of the temporal lobe during the procedure carries a small risk of seizures, aphasia, and stroke. The MF approach is most suitable for vestibular schwannomas (VS) originating from the superior division, which displaces the facial nerve anteriorly [31].

Radiotherapy

There are three primary forms of radiotherapy for managing VS: SRS, fractionated stereotactic radiotherapy (FSRT), and proton beam therapy. The SRS and FSRT are the most commonly utilized due to the limited availability and insufficient evidence supporting the efficacy of proton beam therapy (35, 36). The primary goal of radiotherapy is to inhibit tumor growth, making it unsuitable for large tumors with significant mass effect (5). Each radiotherapy method has its advantages and disadvantages. The SRS employs Gamma Knife technology to deliver a single dose of radiation to the tumor and is less suitable for large lesions (>2.5 cm extracanalicular diameter) (37). The FSRT involves multiple sessions of radiotherapy, aiming to target the tumor during the most radiation-sensitive phase of the cell cycle for potentially greater efficacy (38). Additionally, FSRT systems are more widely available in hospitals and can be used for larger lesions (37).

A recent systematic review comparing FSRT and SRS revealed similar tumor control rates, with about 4.8% and 5% of patients, respectively, requiring rescue therapy. Facial and trigeminal nerve deterioration was less common with SRS. However, these comparisons are based on limited evidence and lack randomized controlled trials (RCTs). Only two studies on FSRT were assessed, which limits the validity of these findings. More research is needed to confidently compare these two therapies [39]. Controlled studies have shown comparable progression-free survival rates and side effects, such as nerve palsies and hearing deterioration, between radiotherapy and microsurgery [40-44]. A recent Cochrane review highlighted that these comparisons are based on low-quality evidence, and no RCTs exist comparing surgery and radiotherapy treatments [45]. Furthermore, long-term evidence (>10 years) regarding hearing preservation following radiotherapy is limited. Yang et al. reported an average hearing preservation rate of 57% from data derived from 74 articles, with an average follow-up of only 41.2 months [46]. A more recent case-controlled study found that hearing preservation among patients decreases from 53% at 5 years to 34% at 10 and 15 years across all tumor grades [47]. This emerging evidence suggests that hearing may not be as well preserved as previously thought, with loss occurring due to long-term nerve damage from radiation exposure. These studies also found that the tumor Koos grade is an independent predictor of hearing loss, representing a potential confounder.

The evidence regarding the best treatment options for all categories of VS remains inconclusive. While most small tumors are managed conservatively and larger tumors with surgery and/or radiotherapy, there is uncertainty surrounding the best management options for tumors that fall between these categories [48]. More robust, high-quality RCTs are needed to guide treatment in these scenarios.

Follow-up Assessment

The primary goals of follow-up imaging include the detection of residual or recurrent tumors, evaluation of tumor size, monitoring of response to radiation therapy, and identification of post-treatment complications. Residual tumors are most effectively assessed using fat-suppressed contrast-enhanced T1-weighted imaging, which nullifies the signal from fat packing. As the therapeutic focus has shifted from total resection to functional preservation, residual tumors are often deliberately left adjacent to the facial nerve. The presence of residual enhancing tumors is a common occurrence and can be monitored through serial imaging, with further treatment via SRS as needed. Residual masses typically contract and assume a more rounded shape within 6 to 12 months following the completion of SRS [21].

Evolving Treatment Strategies

With the growing comprehension of the molecular pathology of vestibular schwannoma (VS), targeted biological therapies are gaining prominence in treatment. Among the potential therapeutic options are Bevacizumab, Everolimus, and Lapatinib [49].

Bevacizumab, a monoclonal antibody and vascular endothelial growth factor (VEGF) inhibitor, plays a critical role in angiogenesis, which is essential for tumor growth [50]. Plotkin et al. were trailblazers in investigating Bevacizumab for patients with neurofibromatosis type 2 (NF2) and progressive

disease. Their studies, albeit limited by small sample sizes (n=10 and n=31), showed over 50% of patients experienced improvements in hearing and tumor growth restriction. The subsequent 2012 study was also retrospective, with a median treatment duration of just 14 months [51, 52].

Everolimus, an mTOR complex 1 (mTORC1) inhibitor, is linked to tumor growth due to merlin deficiency, and has demonstrated antiangiogenic effects [53]. Despite its theoretical potential, clinical evidence remains sparse. Phase II trials in NF2 patients have produced mixed results. While Karajannis et al. reported no significant impact on tumor growth or hearing improvement with Everolimus [54], Goutagny et al. observed a 66.5% reduction in tumor growth in ten NF2 patients during treatment with Everolimus, although growth resumed after discontinuation [55].

Lapatinib, an inhibitor of EGFR/ErbB2, has shown promise in inhibiting tumor growth in vitro [56]. According to early clinical evidence, the Central Nervous System (CNS) recognizes Lapatinib as a potential treatment for managing tumor growth and enhancing hearing [57]. A phase II clinical trial involving 21 NF2 patients reported a ≥ 15% reduction in tumor volume in 23.5% of participants and improved hearing in 30.8% of participants, as observed through serial MRI scans. However, only 14 of the 21 participants were eligible for audiological response evaluation, and the absence of a control group limits the findings. Notably, Lapatinib demonstrated low toxicity levels, a significant advantage compared to Bevacizumab, which is known for its adverse side effects [58]. Long-term controlled studies are necessary to provide more robust evidence.

Conclusions

Vestibular schwannomas (VS), benign neoplasms originating from the vestibulocochlear nerve sheath, are the most prevalent tumors in the cerebellopontine angle (CPA). Treatment modalities for VS encompass surgical resection, radiation therapy, and observation. Nevertheless, conservative management is typically reserved for certain patients due to the association of VS with hearing loss. The treatment paradigm has shifted from seeking total resection to striving for long-term tumor control while preserving maximum functionality. Larger VS tumors (exceeding 3 cm) are generally managed through surgical resection, as radiation therapy poses a risk of brain stem compression due to post-treatment edema. Smaller tumors may be addressed with either surgical intervention or radiation therapy. Various lateral skull base approaches—such as translabyrinthine (TL), retrosigmoid (RS), and middle fossa (MF)—are utilized not only for VS but also for other skull base and posterior fossa pathologies. Radiologists play a crucial role by providing imaging findings relevant to initial management decisions, recognizing expected post-therapeutic changes, and identifying potential complications.

Conflict of Interest

The authors declare no conflict of interest.

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