Since the introduction of MR imaging technology, the number of patients with relatively small, incidentally found, asymptomatic VS has increased. A recent study estimates the incidence of VS at 0.2% of all scans done in asymptomatic patients. Observation management is an important part of any pretreatment discussion with patients who have VS, because excision or radiosurgical treatment can potentially compromise function. Despite the availability of published data highlighting clinical, radiographic, and biological parameters of significance when managing VS conservatively, deciding between early treatment and expectant management remains a significant challenge for practitioners. Most studies to date have been small to modest in size, frequently from a single institution, lacking statistical power, and subject to practitioner bias.

Our own review of the literature on this topic revealed impressive variations in reported outcomes for patients in whom conservative management was used. For example, we found 3 different case series reporting hearing preservation rates ranging from 11% to 57% to 100% during observation for patients with VS over comparable follow-up periods. Clearly, the wide range of reported outcomes does not provide the clinician with a consensus estimate of expected outcomes when counseling patients. For this reason, we performed an extensive review of the English-language literature to analyze the results in patients with VS who were treated conservatively. Using a disaggregated database of patients from...
studies that met our inclusion criteria, we evaluated the impact of tumor growth rate and size at initial presentation on hearing outcome.

Methods

Article Selection

Articles were identified via a PubMed search by using the key words “vestibular schwannoma,” “observation,” “facial nerve function,” “acoustic neuroma,” “conservative management,” and “hearing preservation,” alone and in combination. We then searched all references in these papers. This query identified 254 papers, describing > 50,000 patients, from which all data regarding patients treated conservatively were assessed to see if they satisfied our inclusion criteria.

Inclusion criteria for articles were as follows: 1) hearing preservation rates were reported specifically for VS; 2) hearing status was reported using the AAO-HNS or Gardner-Robertson classification; 3) tumor growth rate was monitored by serial MR images; and 4) initial tumor size was documented. In all papers “tumor size” was defined as the largest measurable diameter of the tumor.

Data Extraction

Data from individual and aggregated case series were extracted from each paper. Patients with loss of hearing (AAO-HNS Class C or D, or Gardner-Robertson Class III, IV, or V) at time of presentation were excluded. “Hearing preservation” was defined as having AAO-HNS Class A or B hearing or Gardner-Robertson Class II or better hearing at the end of the follow-up period. “Facial nerve preservation” was defined as having House-Brackman Grade I or II function at the end of the follow-up period. “Conservative management” was defined as no initial surgery or radiotherapy at the time of diagnosis. “Intervention” was defined as surgery or radiation therapy after an intended course of observation management. Data were analyzed as a whole and stratified into 2 groups based on the average growth rate of the tumors, with a cutoff of 2.5 mm/year.

Statistical Analysis

Comparisons of hearing preservation rates and subsequent intervention were made between the 2 groups by using the Pearson chi-square test. Comparison of initial tumor size between patients in whom hearing was preserved and not preserved was made using the Wilcoxon rank-sum test. Correlation analyses between length of follow-up, rates of hearing preservation, and rate of tumor growth were performed using the Pearson correlation test. For all tests, the p value was considered significant at the 5% level (that is, p < 0.05). Unless otherwise stated, all continuous values presented are expressed as the mean ± SD.

Results

Results of the Literature Search

A total of 34 articles involving 982 patients met our inclusion criteria and were evaluated. The overall hearing preservation rate reported in the studies was 54%. Intervention during the study periods with either surgery or radiosurgery occurred in 16% of all patients. The overall mean growth rate was 2.9 ± 1.2 mm/year. Length of follow-up for these studies ranged from 26 to 52 months. There was no statistically significant correlation between length of follow-up and rates of hearing preservation (p = 0.56), or between length of follow-up and rates of tumor growth (p = 0.43).

Effect of Initial Size and Tumor Growth Rates on Hearing Preservation

Of the studies in which hearing preservation was reported, a total of 151 patients had tumors with an average growth rate measuring ≤ 2.5 mm/year, and a total of 461 patients had tumors with an average tumor growth rate of > 2.5 mm/year. The hearing preservation rate was markedly higher for patients in the group who had tumors with an average annual growth rate of ≤ 2.5 mm/year, compared with those with higher growth rates (75 vs 32%, p < 0.0001) (Fig. 1 upper). In contrast, patients with preserved hearing at latest follow-up had a statistically larger initial tumor size than those whose hearing declined during the observation period (11.5 ± 2.3 mm vs 9.3 ± 2.7 mm, p < 0.0001) (Fig. 1 lower), suggesting that larger initial tumor sizes did not impact hearing preservation rates.

Effect of Initial Size and Tumor Growth on the Rate of Subsequent Intervention

Despite the apparently poorer rate of hearing preservation in patients with faster-growing tumors, the intervention rate was not different for patients in either group (18 vs 16% for ≤ 2.5 mm/year vs > 2.5 mm/year growth rate, respectively [p = NS]; Fig. 2 upper). Similarly, tumor size at initial presentation had no impact on rate of intervention; the average tumor size was no different between patients who received intervention and those who did not (12.5 vs 12.9 mm, p = NS; Fig. 2 lower).

Impact of Conservative Management on Facial Nerve Preservation Rate

In general, facial nerve outcomes in the reported literature were excellent for patients undergoing careful observation as a principle management strategy. We found that the facial nerve preservation rate was > 97% regardless of whether the tumor growth rate was > or ≤ 2.5 mm/year (97 vs 98%, p = NS; Fig. 3).

Discussion

Observation management with serial MR images has provided practitioners with useful information about the variability in natural history of untreated VSs. Several investigators have published their institutional results, but to date there have been few efforts to combine these experiences to achieve the statistical power needed to determine the suitability of conservative management for these tumors. In this study we performed a comprehensive review of the literature on the hearing preservation and intervention rates, with special emphasis on tumor growth
Natural history of untreated vestibular schwannomas

rates, in a large population of patients with VS who were treated conservatively.

Patients with tumors that grew \( \leq 2.5 \) mm/year had better hearing outcomes than patients with tumors that grew \( > 2.5 \) mm/year. We did not find a similar relationship between initial tumor size and rate of hearing preservation. In fact, patients with preserved hearing had statistically larger tumors on average at presentation, but the 2-mm difference in average size must be interpreted within the context of limitations associated with imaging resolution and observer reliability. This suggests that for patients with tumors \( \leq 2.5 \) cm, the tumor growth rate is a more important indicator of who is at risk for progressive hearing loss than tumor size at presentation. The mechanism behind this observation is unclear; however, we hypothesize that faster-growing tumors represent a biologically more aggressive subset of lesions, which are more likely to infiltrate and disable the cochlear nerve, regardless of the initial size of the tumor.

Facial nerve outcomes in patients with VS in whom the disease is managed conservatively have been consistently excellent throughout all reported series. For example, Perry and colleagues\(^{21}\) followed 36 patients with VS of various sizes, and reported that House-Brackmann Grade II facial nerve function developed in only 1 patient during the study period. Similarly, we found that the facial nerve preservation rates in both groups were very high (\( > 97\% \) regardless of growth rate) and almost identical. Thus, facial nerve dysfunction seems to be of lesser concern than hearing loss when discussing the risks of
conservative management. Our data show that the patients with faster-growing tumors had a nearly identical reported rate of subsequent intervention to that of patients with slow-growing tumors, despite poorer hearing outcomes. It would appear that the practitioners in the studies we examined did not use tumor growth rate as a metric to trigger intervention.

Conclusions

These data suggest that a tumor growth rate of > 2.5 mm/year is a strong predictor of failure of conservative management at 3-year follow-up in patients with tumors < 25 mm. It should be acknowledged that any aggregation of data is only as good as the composite studies, and may reflect source study biases. Also, due to the diverse range of data presentation, the number of variables able to be studied and controlled for is limited. Variables such as intracanalicular versus extracanalicular growth, which might be of interest, are inconsistently presented and cannot be studied. Additionally, multilogistic regression to control for the effects of important variables, such as age and initial tumor size, is impossible to do across 34 studies that adhere to differing formats of data presentation. Another drawback to our study is that there is no way to assess the impact of patients’ personal choice on the ultimate management decision described in the studies. Despite these limitations, this analysis seems to suggest strongly that medium or small tumors with a growth rate > 2.5 mm/year should be treated with active intervention.

Disclosure

Dr. Parsa was supported in part by the Reza and Georgianna Khatib Endowed Chair in Skull Base Tumor Surgery. The authors report no other conflicts of interest concerning the materials or methods used in this study or the findings specified in this paper.

References

29. Silverstein H, Rosenberg SI, Flanzer JM, Wanamaker HH, Seidman MD: An algorithm for the management of acoustic


Manuscript submitted February 6, 2008. Accepted April 29, 2009. Please include this information when citing this paper: published online June 19, 2009; DOI: 10.3171/2009.4.JNS0895. Address correspondence to: Andrew T. Parsa, M.D., Ph.D., Department of Neurological Surgery, University of California at San Francisco, 505 Parnassus Avenue, San Francisco, California 94143. email: parsaa@neurosurg.ucsf.edu.