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Conservative management of vestibular schwannomas – second review of a prospective longitudinal study

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Vestibular schwannomas have been traditionally managed with microsurgical removal and in recent years, stereotactic radiotherapy. However, there is a group of patients in whom a conservative management approach might represent a desirable alternative. The aim of this study was to determine the natural history and outcome following the conservative management of 72 patients with unilateral vestibular schwannomas. This is a prospective cohort review of a previously published group of patients [*Clin. Otolaryngol.* (2000) **25**, 28–39] with unilateral vestibular schwannoma that were initially analysed at our institution in 1998 [Walsh R.M., Bath A.P., Bance M.L. *et al.*, *Clin. Otolaryngol.* (2000) **25**, 28]. The mean duration of follow-up was 80 months (range 52–242 months). All the patients in the study underwent serial magnetic resonance imaging (MRI) for assessment of tumour growth. Patients were deemed to have failed conservative management if there was evidence of rapid radiological tumour growth and/or increasing signs and symptoms, which necessitated active intervention. The mean tumour growth rate for the entire group at the second review was 1 mm/year (range −0.84–9.65 mm/year). The mean growth rate for cerebellopontine angle tumours (1.3 mm/year) was significantly greater than that of internal auditory canal (IAC) tumours (0 mm/year) ($P = 0.005$). The majority of tumours (87.14%) grew <2 mm/year. There was significant tumour growth seen in 38.9%, no or insignificant growth in 41.7%, and negative growth in 19.4%. Twenty-three patients (32%) failed conservative management at the second review. There was no difference in the outcome of these failed patients in comparison with patients who underwent primary treatment without a period of conservative management. The mean growth rate of tumours in patients that failed conservative management (3.1 mm/year) was significantly greater than that in patients who did not fail (0.2 mm/year) ($P < 0.001$). No factors predictive of tumour growth or failure of conservative management were identified. Hearing deterioration with pure tone averages (0.5, 1, 2, 3 kHz) and speech discrimination scores occurred irrespective of tumour growth. This prospective study further emphasizes the role of conservative management in selected cases of vestibular schwannomas. Tumours in this study confined to the IAC typically demonstrated minimal or no growth on serial MRI scanning. Regular follow-up with interval scanning is mandatory in all patients.

Keywords *vestibular schwannoma* *cerebellopontine angle* *magnetic resonance imaging*

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Microsurgical removal and stereotactic or focussed radiotherapy continue their dominance as the mainstay of treatment for vestibular schwannomas. However, since 1985 there have been many reports in the literature investigating the role for the conservative management of vestibular schwannomas.[1–21]

Increasing knowledge regarding the natural history of these tumours and improved imaging primarily through magnetic resonance imaging (MRI) scans has improved our ability to follow these patients conservatively.

Vestibular schwannomas are typically slow-growing, oncologically benign tumours, the majority of which grow at <2 mm/year.[4,6,14,22] Spontaneous involution has also been reported by various authors.[2,4,15,18–20,23] Active treatment in the form of surgery or stereotactic radiotherapy can be associated with significant functional and psychological morbidity besides the small risk of mortality.[5, 24, 25] The majority of small intracanalicular tumours when diagnosed early are relatively asymptomatic or minimally symptomatic (generally related to auditory dysfunction) at presentation a factor to be taken into consideration when deciding on the management of the patient. Rapid growth over a short period of time is a slight risk involved with the conservative management of vestibular schwannomas. Nevertheless delay in treatment does not necessarily result in an adverse neurological outcome.[2]

Materials and methods

STUDY GROUP

Seventy-two patients with a radiological diagnosis of unilateral vestibular schwannoma managed conservatively in the Departments of Otolaryngology and Neurosurgery (University Health Network), Toronto General and Western Divisions (University of Toronto) between 1987 and 1998 underwent an initial analysis of results in 1998. Entry criteria for conservative management included age, small tumour size, poor general health, patient preference, minimal or no symptoms and tumour in the only/better hearing ear. Eleven patients had failed conservative management at first review. The remaining 61 patients have been followed prospectively till April 2002. Of the 11 patients deemed to have failed conservative management at their first review in 1998, five patients were treated with stereotactic radiotherapy and have also been followed prospectively to assess tumour growth and any associated post-treatment morbidity.

ANALYSIS OF TUMOUR SIZE AND GROWTH RATE

All patients in this study underwent clinical neurotological examination every 6 months. Radiological assessment of tumour size and growth rate was primarily undertaken with high resolution MRI (gadolinium enhancement and T2-weighted images). Computed tomography (CT with/without enhancement) was performed in some patients early in the series and later in the few selected cases who were unfit to undergo an MRI scan (i.e. claustrophobia, pacemaker inserted, etc.). Imaging was carried out at 6-month intervals in the first year after radiological diagnosis. The scanning interval after the first year was dictated by the clinical status of the patient, the tumour growth rate in the first year and the size of the tumour. The duration of follow-up was defined as the interval between the first scan and the final scan. All scans were consistently evaluated for tumour dimensions by the first author using a computerized scale to measure the maximum antero-posterior (A-P) and medial-lateral (M-L) diameter.

Tumour size was determined using the 1995 guidelines of the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS).[26] The extracanalicular component of cerebellopontine angle (CPA) tumours was determined as follows: the axial image with the largest extracanalicular tumour diameter was selected and the maximum A-P and M-L tumour diameters were calculated with a micrometer in the initial series and more recently calculated on screen by computer calibration. The A-P measurement was calculated parallel to the posterior surface of the petrous bone and the M-L measurement was calculated perpendicular to it. The size of the tumour was calculated as the square root of the product of these two diameters.

The size of the tumour limited to the internal auditory canal (IAC) was calculated as the length of the tumour along the axis of the canal, from the fundus to the porus. Tumour volume was not measured. Tumours in the CPA were categorized as small (<15 mm), medium (15–30 mm) or large (>30 mm). The annual growth rate (mm/year) was calculated as the change in tumour size between the first and the last scan, divided by the duration of follow-up in months, and multiplied by 12. Total tumour growth >1 mm/year was considered significant, as originally defined by Nedzelski *et al.*[4] In those tumours demonstrating growth, intervening scans were also analysed to determine when the growth had taken place. Tumours were described as solid, cystic or mixed. Evidence of calcification or tumour necrosis was also noted. Tumour effects such as brain stem/cerebellar compression, displacement of fourth ventricle and hydrocephalus were also noted. Patients were deemed to have failed conservative management if there was evidence of continuous or rapid radiological tumour growth and/or increasing symptoms or signs suggestive of tumour growth.

AUDIOMETRIC ASSESSMENT

Audiometric assessments were carried out during the period of conservative management. The mean pure tone average (PTA) (0.5, 1, 2, 3 kHz) and speech discrimination scores (SDS) were recorded in accordance with the AAO-HNS guidelines (1995).[26]

DATA PRESENTATION AND STATISTICS

The data are presented as a mean ± SD. Statistical analysis was performed using the Independent samples *t*-test (two-

tailed) for comparison between groups and the paired *t*-test for comparisons within a group with a 95% significance level ($P \leq 0.05$). The association between variables was analysed using the Pearson's correlation coefficient. Nonparametric equivalents, i.e. the Mann–Whitney *U*-test, Wilcoxon signed ranks test and Spearman's ranked correlation coefficient were used for data not normally distributed.

Results

STUDY GROUP

Seventy-two patients with a radiological diagnosis of unilateral vestibular schwannoma have been prospectively followed and managed conservatively between 1987 and 2002. At their first review in 1998 (mean follow-up 39.8 months), 11 had failed conservative management. Sixty-one of the 72 patients who continued with conservative management have been followed prospectively and analysed on an intention to treat basis ending in April 2002. Two patients who initially consented to continue conservative management at the first review have since failed to attend for serial scans. These patients have been included as failures in the final analysis. In the initial series there were 32 men and 40 women with a mean age of 60.8 years at presentation (range 36–78 years) (Table 1). The mean duration of follow-up was 80 months (range 52–234 months) (Table 1).

CLINICAL PRESENTATION

The presenting symptoms were unilateral sensorineural hearing loss (98.6%), tinnitus (62.5%), unsteadiness/vertigo (38.9%), facial nerve or trigeminal nerve symptoms or signs (8.3%), lower cranial nerve (IX-XII) symptoms or signs (2.7%), and various combinations of these (80.5%).

REASONS FOR CONSERVATIVE MANAGEMENT

Reasons for conservative management included advanced age (48.6%), small tumour size (45.8%), patient preference (43%), poor general health (19.4%), no or minimal symptoms (2.8%), tumour in an only hearing ear (1.4%), and various combinations of these (62.5%).

TUMOUR DIAMETER

There were 54 CPA and 18 IAC tumours at the start of the study. The mean tumour diameter at diagnosis for the overall group was 9.4 ± 5.1 mm, 9.8 ± 5.4 mm for CPA tumours and 7.8 ± 3.4 mm for tumours confined to the IAC (Table 1). At the time of diagnosis, 68 of the tumours were small CPA or intracanalicular tumours, four were medium-sized and none was large. After the first review, there were 61 patients with 43 CPA tumours and 18 IAC tumours who continued with this conservative management stratagem.

TUMOUR GROWTH

Total group

Tumour growth <2 mm/year was recorded in 87.14% of the remaining patients at their second review (83% at first review). Significant tumour growth (defined as growth >1 mm/year) was observed in 38.9% of patients (36.4% at first review). Negative tumour growth was recorded in 19.4% of patients (13.6% at first review). The mean tumour growth for the whole group was 1 ± 2.2 mm/year (range −0.84–9.65 mm/year). In patients who failed conservative management, the mean growth rate was 3.1 mm/year (4.2 mm/year at first review) as against 0.2 mm/year (0.5 mm/year at first review) in those who did not fail. Neither the age of the patient nor the mean tumour diameter at diagnosis was predictive of tumour growth, i.e. there was no significant difference between the mean age of patients ($P = 0.34$) nor between the mean tumour diameter at diagnosis ($P = 0.13$) with and without tumour growth (Table 1). Only 16 patients (22.2%) showed significant growth to be advised intervention.

CPA and IAC tumour groups (n = 72)

The mean growth rate of tumours, which extended into the CPA (1.3 ± 2.4 mm/year) with a range of −0.84–9.65 mm/year, was significantly greater than that of tumours limited to the IAC (0 ± 0.2 mm/year), with a range of −0.36–0.45 mm/year ($P = 0.005$) (Table 1). This could not be attributed to a difference in length of follow-up of the two tumour types ($P = 0.33$) (Table 1).

In the CPA group, 50% showed significant growth, (defined as total growth >1 mm/year) 29.6% had no or insignificant

Table 1. Study group characteristics of conservatively managed vestibular schwannomas

	Total group	CPA group	IAC group
No. of patients	72	54	18
Age at diagnosis (years)	60.8 (36–78)	61.9 (36–78)	57.8 (38–71) ($P = 0.34$)
Male:female	32:40	24:30	8:10
Follow-up (months)	80 (52–234)	80 (52–234) ($P = 0.33$)	80.5 (53–148)
Tumour diameter at diagnosis (mm)	9.4 ± 5.1 (3–24.4)	9.8 ± 5.4 (3–24.4)	7.8 ± 3.4 (3–16)
Tumour growth rate (mm/year) at 2nd review	1 ± 2.2 (−0.84–9.65)	1.3 ± 2.4 (−0.84–9.65) ($P = 0.005$)	0 ± 0.2 (−0.36–0.45)

Table 2. Tumour growth characteristics at 2nd review

	Total group	CPA group	IAC group
Growth (>1 mm)	38.9%	50%	5.5%
No/insignificant growth (0–1 mm)	41.7%	29.6%	77.8%
Negative growth (<0 mm)	19.4%	20.4%	16.7%

growth, and 20.4% demonstrated negative growth. Only one tumour (5.5%) confined to the IAC showed significant growth, 77.8% demonstrating no or insignificant growth and 16.7% showed negative growth (Table 2).

FAILURE OF CONSERVATIVE MANAGEMENT

Eleven patients (15.3%) failed conservative management at the first review in 1998 after a mean duration of 23.8 months (range 6–67 months). At the second review in April 2002, 12 of the remaining 61 patients (19.6%) had failed conservative management after a mean duration of 47.1 months (range 24–83 months). The mean duration to failure for the entire series was 34.9 months (range 6–83 months). Two patients failed follow-up since the first review and have been included as failures in the overall results. Overall 23 of the 72 patients (32%) had failed conservative management over an average follow-up of 80 months (Table 3). Nine patients have died since the first review, eight of whom died because of causes unrelated to their vestibular schwannoma. One patient with a continuously growing tumour that reached 4 cm in size at the time of her last follow-up, refused surgery repeatedly ignoring our advice. This patient later died of bronchopneumonia elsewhere from increasing tumour size associated with cerebral oedema and has been included in the failed group for analysis. A single patient who had failed at the first review and undergone a V-P shunt subsequently died of other unrelated causes.

Table 3. Failure of conservative management and subsequent active management

Total no of failed patients	23 (32%)
No. of patients requiring treatment	21 (29.2%)
No. of patients without follow-up	2 (2.8%)
Time to failure (months)	34.9 (6–83)
Refused surgery (death secondary to cerebral oedema)	1
Treatment	
Microsurgery	7
Translabyrinthine approach	5
Retrosigmoid approach	2
Ventriculo-peritoneal shunt	1
Radiotherapy	12
Gamma knife	8
Gamma knife + V-P shunt	1
Linear accelerator (LINAC)	3

Table 4. Comparison between failed and the continued (successfully) conservatively managed groups. Growth rates at 2nd review

	Failed group	Success group
Patients (%)	23 (32%)	49 (68%)
Time to treatment(months)	34.9 (6–83)	
Growth rate (mm/year)	3.1 ± 3.3	0.2 ± 0.5 ($P < 0.001$)

The growth rate of tumours in patients who failed conservative management (3.1 ± 3.3 mm/year) was significantly greater than that in patients who did not fail (0.2 ± 0.5 mm/year) ($P < 0.001$) (Table 4). Neither the age of the patient nor the mean tumour diameter at diagnosis was predictive of the eventual need for treatment, i.e. there was no significant difference between the mean age of patients ($P = 0.20$) nor between the mean tumour diameter at diagnosis of patients ($P = 0.23$) who required treatment and those who did not. Amongst patients who had radiological tumour growth, only 22.2% had growth significant enough to be advised treatment while 6.9% of patients either on their own volition or as the result of increasing symptomatology, despite no growth in their tumour underwent active treatment.

TREATMENT AND OUTCOME OF PATIENTS WHO FAILED CONSERVATIVE MANAGEMENT ($n = 23$)

Seven patients underwent microsurgical excision (five – translabyrinthine approach; two – suboccipital or retrosigmoid approach); 12 patients underwent stereotactic radiotherapy (eight – gamma knife; three – linear acceleration (LINAC) radiotherapy; one – gamma knife with V-P shunt) (Table 3). One patient with hydrocephalus had a V-P shunt inserted. One patient with a large and rapidly growing tumour refused surgery and eventually died of bronchopneumonia from associated cerebral oedema. Two patients placed in the failure category for lack of follow-up had growth rates of 1.2 and 0 mm/year at their last recorded visit.

Tumour removal was total in all cases except for an 81-year-old lady with a medium sized vestibular schwannoma and an associated arachnoid cyst who underwent subtotal removal and decompression of the cyst. The mean duration of follow-up post-treatment was 41.6 months (range 12–91 months). Only one patient died following treatment. There has been no evidence of recurrence in those tumours who were totally excised nor increased growth in the patients managed by subtotal removal or V-P shunting. Of the eight patients who underwent gamma knife stereotactic radiotherapy, five patients have shown further growth of their tumours although not significant enough to warrant further treatment at the second review. Two of the patients who have undergone gamma knife treatment have shown a negative growth following treatment while one patient has shown no growth

at all. All three patients who underwent LINAC have shown further significant growth with one of them likely to require further intervention in the near future. A transient grade 2/3 facial weakness (House and Brackmann grading system) occurred in four patients following surgery. All four reverted to a grade 1 ultimately. No attempt was made to preserve hearing in the two patients whose tumour was excised via the retrosigmoid approach as the hearing was not serviceable preoperatively. Six patients experienced mild balance disturbance. Of the 12 patients who were working prior to treatment, seven have returned to work. There were no serious intracranial or lower cranial nerve complications.

AUDIOLOGICAL RESULTS

Total, CPA and IAC tumour groups

Fifty-five patients had audiological measurements available for comparison at the time of diagnosis and last follow-up. At the time of diagnosis, the mean PTA (0.5, 1, 2, 3 kHz) for the overall group was 47.6 dB and the mean SDS was 60.4%. Over the follow-up period of 80 months, there has been a significant deterioration in both mean PTA and SDS for the total group, mean PTA being 76 dB (62.5 dB at first review) and the SDS being 22.1% (37.4% at first review) ($P < 0.001$) (Table 5). The mean PTA and SDS for the CPA group at the second review were 80.4 dB and 17.3%, and that for the IAC group were 63.1 dB and 36.6% respectively. There was a significant longitudinal deterioration in the PTA and SDS for both CPA ($P < 0.001$) and the IAC ($P < 0.008$) groups.

Growth versus no-growth groups

A significant deterioration in the mean PTA and SDS occurred following conservative management in both the radiological tumour-growth and no-growth groups (Table 6). There was significant difference in the change in mean PTA between the tumour-growth and no-growth groups ($P = 0.001$) (no association at first review) although similar statistical significance was not observed with the SDS scores ($P = 0.15$) (Table 6).

Discussion

The incidence of occult vestibular schwannomas in human temporal bones has been shown to be between 0.57% and 0.87% or equivalently 570–870 patients per 100 000 of the population.[27] Yet, the incidence of clinically apparent vestibular schwannomas is certainly less reported at 13 per 1 000 000 of the population.[28, 29] Although 0.87% may be a biased figure (as the temporal bones studied were known to have otological disease), if correct then potentially <1% of all vestibular schwannomas demonstrate enough growth to become clinically active. With the development of increasingly more sophisticated imaging techniques, the chances of finding a vestibular schwannoma that would never become clinically significant has increased tremendously.

Vestibular schwannomas tend to be slow-growing tumours as confirmed by studies outlining the natural history of these tumours.[4,6,14,22] The results of conservative management of these tumours has been widely reported from numerous retrospective series in the literature dating back to Wazen *et al.* in 1985[30] to Hoistad *et al.* in 2001.[21] To date there has been only one reported small prospective series investigating the value of conservative management of these tumours.[18] Data from our study has looked prospectively at 72 patients with vestibular schwannomas over an average follow-up period of 80 months (or approximately 6.7 years).

EVALUATION OF TUMOUR GROWTH AND TUMOUR GROWTH RATE

How to measure the size and growth of vestibular schwannomas varies widely in the literature.[15,31–34] The most accurate way to determine the size of a tumour would be to use an MRI based calculation with a computer-assisted

Table 5. Comparison of mean pure tone average (PTA) (0.5, 1, 2, 3 kHz) and speech discrimination score (SDS) at 2nd review

	Mean PTA		Mean SD	
	First audio (dB)	Last audio (dB)	First audio (%)	Last audio (%)
Total group	47.6 ± 19.9 ($P < 0.001$)	76 ± 26.6	60.4 ± 36	22.1 ± 31
CPA group	50.6 ± 21.8 ($P < 0.001$)	80.4 ± 27.1	53 ± 37	17.3 ± 28.1
IAC group	40.7 ± 13.5 ($P = 0.008$)	63.1 ± 20.7	77 ± 28	36.6 ± 35.7

Table 6. Change in mean PTA and mean SDS in tumour growth and no growth groups at 2nd review

	Tumour growth group	No growth group
Change in mean PTA (dB)	(+) 36.7 ± 20.7 ($P < 0.05$) ($P = 0.001$)	(+) 16.7 ± 15.9 ($P < 0.05$)
Change in mean SDS (%)	(−) 33.6 ± 38.7 ($P < 0.05$) ($P = 0.15$)	(−) 18 ± 32.3 ($P < 0.05$)

measurement that calculated the area of each tumour slice multiplied by the slice thickness.[31] More recently, Niemczyk *et al.*[32] have shown that the growth of vestibular schwannomas can be demonstrated by the use of volumetric studies despite no apparent change to the tumour diameter measurements. Notwithstanding, serial volumetric measurements may be more accurate for detecting tumour growth rates. However, Charabi *et al.*[15] found no difference in tumour growth using tumour diameters and volume. More recently, Fiirgard *et al.*[33] concluded that measurement of the maximal diameter of a vestibular schwannoma on MRI was a better parameter for comparison of tumour size than calculation of real volume. In our series the growth rate for tumours extending into the CPA was higher (mean 1.3 mm/year, range −0.84–9.65 mm/year) compared with the tumours limited to the IAC (mean 0 mm/year, range −0.36–0.45 mm/year) ($P = 0.005$) (Table 1).

This study endorses the view that the majority of vestibular schwannomas grow slowly with only 38.9% of the tumours (whole group) showing significant radiological growth (usually defined as total tumour growth >1 mm/year).[4] Most vestibular schwannomas grow at <2 mm per year,[4,6,14,22] although there is a wide variation in tumour growth rates.[2,4,35] Although most tumours are slow-growing, a few may demonstrate rapid growth due to oedema, haemorrhage, cyst formation or rapid cell mitosis. Deen *et al.* have demonstrated two distinct growth patterns in the first year of conservative management.[16] Those that did not require intervention (85%) had a growth rate of 0.36 mm/year while those requiring intervention had a growth rate of 3 mm/year. In our series, 68% of patients, not requiring active intervention over an 80-month follow-up period demonstrated a mean growth rate of 0.2 mm/year against those that required treatment which demonstrated a mean growth rate of 3.1 mm/year (Table 4). However, there is a group which demonstrates tumour regression. Tschudi *et al*.[20] have recently reported tumour regression in 16% of their patients managed conservatively over a 3 yr period. Luetje *et al.*[23] have reported spontaneous involution in 13% of vestibular schwannomas in their series. In this study, tumour regression was also observed in 19.4% of patients undergoing conservative management (Table 2). Regression may be caused by ischaemic necrosis secondary to intratumoural thrombosis and may be the expression of a normal involution of tumours that have reached their maximal growing power.[36]

FACTORS PREDICTING TUMOUR GROWTH

Although generally slow-growing, vestibular schwannomas are still somewhat unpredictable as regards their growth patterns. Charabi *et al.*[15] have reported rapid growth following a long period of no growth in some cases in their series. However, some studies assessing the natural history of vestibular schwannomas have reported that growth rate measured during the first year of observation is predictive of growth in the following year[2,4,14] and of the eventual need for treatment.[16] As exact certainty regarding tumour growth remains unknown, in our opinion prudent medical practice for the conservatively managed patient entails life long follow-up for these patients.

Patients age, gender, clinical presenting symptoms and tumour diameter at diagnosis has no correlation with tumour growth as demonstrated by several studies in the literature as well as the present study.[2,10,14,15,19,21,37] However, Fucci *et al.*[38] in a review of 119 patients found that tumours >2 cm at presentation were more likely to grow than tumours <2 cm. Immunohistochemistry using the nuclear antibody Ki-67[35] and proliferating cell nuclear antigen,[39] chromosomal studies[40] and DNA flow cytometry studies[41,42] have shown some potential to correlate tumour growth but have failed to produce a reliable and reproducible parameter for tumour growth. Beenstock[43] in a recent study has shown much greater growth in left sided tumours and some evidence that tumours that are more stable between the initial two measurements are more likely to remain stable between the second and third measurements. However, this did not apply to tumour growth between the third and fourth measurements.

FAILURE OF CONSERVATIVE MANAGEMENT

This study has shown a 32% failure rate of conservative management of vestibular schwannomas over an 80-month follow-up period. This figure although doubled since the last review is still low considering the long follow-up time. The failure rate in the published series varies widely from 0–50%.[44] Recently Hoistad *et al.*[21] have shown a 37% failure rate over a 28.5-month average follow-up period. The follow-up in most of the above-mentioned series has been limited to around 3 years which is short considering the slow growth of these tumours. Any failure has definite economical implications, as active intervention for these tumours (surgery/radiotherapy) involves extensive infrastructure with its associated costs. On the contrary, when the conservative paradigm is successful serial MRI scanning on a regular basis, although inconvenient for the patient, has minimal monetary implications in comparison.

Intervention has been advised in tumours whose growth rate exceeds 2 mm/year.[4] However, Rosenberg has additionally suggested that it is rapid tumour growth with development of symptoms such as vertigo, ataxia, headache, facial numbness or imbalance that should be used as indicators for intervention.[45] In our study, five patients failed conservative management either because of increasing symptomatology and/or their wish to have the tumour removed despite MRI scans failing to demonstrate significant tumour growth.

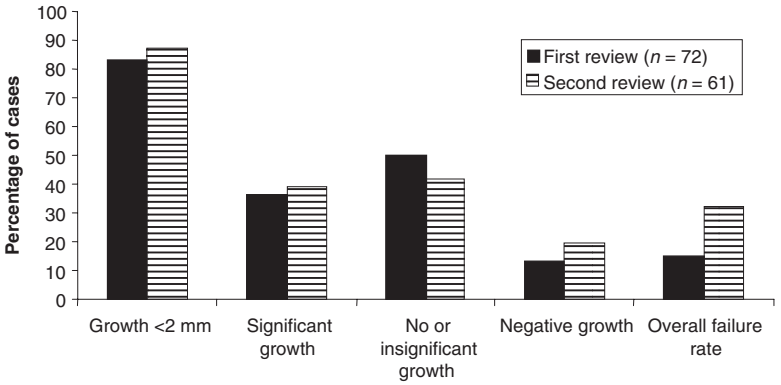

Figure 1. Growth comparison with previous review and overall failure rate.

Studies by Bederson *et al.*[2] and Tschudi *et al.*[20] have shown no difference in the postoperative neurological outcome in patients who failed conservative management, suggesting that the delay in their surgery did not adversely affect the outcome. This study too has further reinforced these findings.

COMPARISON WITH PREVIOUS RESULTS

This prospective series has shown an overall decrease in total tumour growth over time. Eighty-three per cent of tumours showed growth <2 mm/year at the first review while on longer follow-up with the remaining patients this has increased to 87.14%[44] (Fig. 1). There has also been a reduction in the growth rates of both the CPA and the IAC groups (Fig. 2). Although the number of patients with significant tumour growth (defined as total tumour growth >1 mm) has increased from 36.4% to 38.9%, the tumours with a negative growth have also shown an increase (13.6–19.4%)[44] (Fig. 1). The number of patients failing conservative management has doubled since the last review (15.3% to 32%) (Fig. 1). There has been a reduction in the mean growth rate of tumours in patients who failed conservative management (4.2 mm/year to 3.1 mm/year) and those that didn't (0.5 mm/year to 0.2 mm/year) (Fig. 3). Most importantly,

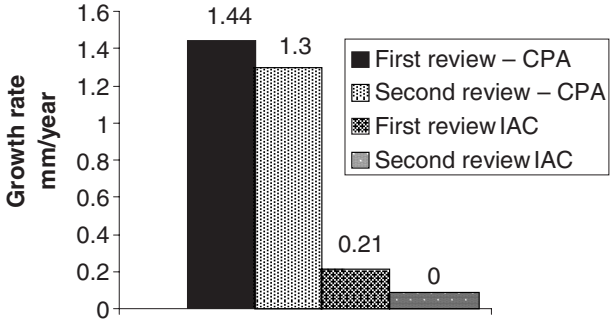

Figure 2. CPA and IAC growth rate comparison between initial (39.8 months) *versus* 2nd review (80 months).

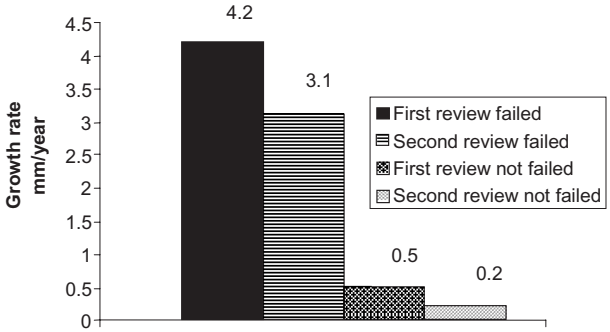

Figure 3. Tumour growth rate comparison in failed and successful conservatively managed patients between initial (39.8 months follow-up) *versus* 2nd review (80 months).

only an isolated IAC tumour has shown significant growth (i.e. growth >1 mm) over a long follow-up. This patient too showed a 2-mm growth at the first review (growth rate 1.85 mm/year) but subsequently has shown no further growth (current growth rate 0.45 mm/year). The vast majority of the IAC tumours (94.5%) have shown no growth, insignificant growth or negative growth.

This study, we believe, conclusively proves the value of conservative management especially in small tumours confined to the IAC if hearing conservation is not a consideration on the proviso that active management can realistically preserve hearing without increasing patient morbidity. Comparison of the hearing results at the second review has demonstrated further deterioration in the mean PTA and SDS scores for the total as well as the individual groups (CPA and IAC) (Fig. 4). This deterioration in hearing has occurred irrespective of tumour growth although patients with definitive tumour growth did have a greater deterioration in hearing in comparison with those who did not demonstrate tumour growth ($P = 0.001$). This is in contrast to the findings at the first review where no association could be demonstrated between tumour growth and change in mean PTA ($P = 0.4$).

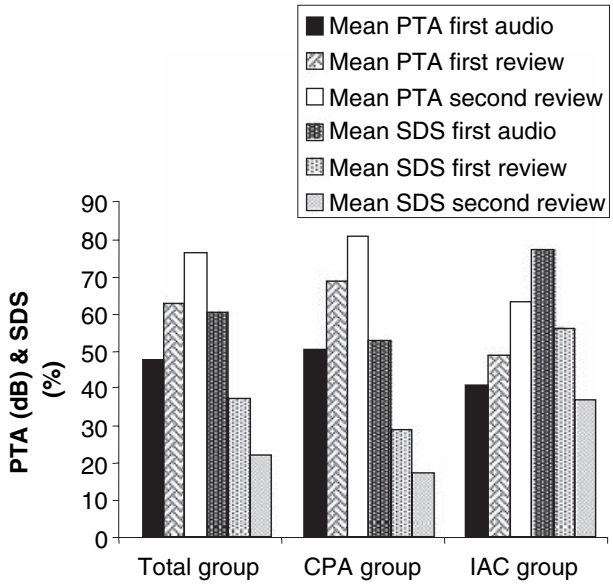

Figure 4. Audiological comparisons between initial *versus* 2nd review.

Tumour growth has occurred at variable times in the series and hence it has not been possible to predict definitive trends from this series. Regular follow-up with serial MRI scanning is absolutely vital to continuing conservative management of these tumours.

HEARING RESULTS

Studies evaluating audiological function in vestibular schwannomas have expressed concerns regards deterioration of hearing, significant enough, to lose eligibility for a hearing preservation operation whilst being observed conservatively (using either the 30/70 or the 50/50 rule).[15] However, there have also been reports of no loss of auditory acuity in five of 12 patients who showed no tumour growth.[18]

Rosenberg[45] in a retrospective series of 72 patients did not find any statistical correlation between initial tumour size and pure tone average or speech discrimination scores. However, this paper demonstrated a trend towards positive correlation between tumour growth and change in PTA among 32 patients who were found to have positive growth. The correlation in Rosenberg's series was even stronger in the 22 patients whose tumour grew more than 10 mm during the conservative management period.[45] Surprisingly there was no statistically significant correlation between tumour growth and speech discrimination scores. The present study too has shown a definite correlation between tumour growth and deterioration in pure tone thresholds ($P = 0.001$) but fails to reach significance with speech discrimination scores (Table 6). Recently Warrick *et al.*[46] in a small study have reported loss of useful hearing with conservative management of vestibular schwannomas.

In this study, there was a significant deterioration in PTA and SDS in both the CPA and the IAC groups during the observation period (Table 5). These findings further substantiate the long held view that audiological deterioration occurs regardless of tumour growth. Hearing deterioration in non-growing tumours is probably not the result of direct tumour compression on the cochlear nerve but is more likely caused by indirect factors such as ischaemia induced by the blood stealing action of the tumour.[20]

DIFFICULTIES INHERENT IN THE CONSERVATIVE MANAGEMENT OF PATIENTS WITH VESTIBULAR SCHWANNOMAS

The first major difficulty is patient compliance for regular follow-up and serial imaging. Possible reasons for this could be an elderly population with limited mobility, absence of any definitive treatment (surgery/radiotherapy) without complication which leads patients to obtain a second opinion and a different protocol or that patients with very few symptoms often tend to wait until their hearing worsens or other symptoms present themselves. The second difficulty has been to find the most appropriate and accurate means of evaluating tumour growth. There is controversy over two-dimensional measurements and volume measurements for the identification of tumour growth. This has arisen largely as it has been found that in tumours with large diameters, small increases in diameter correspond to much larger increases in tumour volume than would have occurred with similar increases in diameter of small tumours. Shin *et al.*[47] in a recent study analysed and compared volume calculation with mathematical formulas and volume measurement from the area of the tumour on all slices in six patients. A paired comparison of the mean, gave evidence of higher values given by the volume calculated with mathematical formulas. This study emphasizes the lack of an accurate method of assessing tumour growth. The third difficulty has been applying a policy based on clinical symptomology and radiological findings. In our series, not all patients who failed conservative management showed rapid tumour growth and vice versa not all patients who demonstrated tumour growth fail conservative management. Clinical symptoms, patient's choice, age and social factors do influence decision making.

A short follow-up and lack of prospective data has been the drawback of most retrospective series in the literature. Our study too has its drawbacks with it having initially started as a retrospective series which has since been followed prospectively. In the initial part of our study some patients were evaluated by CT scans rather than MRI and throughout we have used two-dimensional measurements of tumour growth

as opposed to volumetric measurements. However, we now have an 80-month prospective follow-up which is the largest follow-up reported to date. A third follow-up study at 120 months (10 years) is currently planned.

In future, a prospective multi centre trial with randomized treatment arms would more clearly elucidate management issues with vestibular schwannomas.

Conclusions

This long-term follow-up prospective study has proved conclusively that vestibular schwannomas tend to be very slow-growing tumours and that conservative management has a definite role to play in a certain select group of patients, i.e. advanced age, poor general health, small tumour size especially those intracanalicular tumours with minimal symptoms, tumours in an only or better hearing ear and/or a combination of the above.

Each patient must be assessed individually and a decision regarding the definitive management protocol made after assessing the growth rate of the tumour at 1 year. Our protocol entails a follow-up MRI at 6 months and 1 year and subsequently at yearly intervals. The indication for intervention is based on a combination of rapid tumour growth and/or the development of symptoms that affect the patient's quality of life. When hearing preservation is a goal of surgery, earlier intervention should be considered.

The majority of vestibular schwannomas at the second review appeared slow growing with 87.14% of tumours demonstrating growth rates <2 mm/year. Only 50% of the CPA tumours showed significant tumour growth (>1 mm) while 94.5% of IAC tumours showed no growth, insignificant or negative growth. The growth rate of the CPA tumours was significantly greater than those confined to IAC ($P = 0.005$). Overall 32% failed conservative management over an 80-month follow-up period. However, in contrast it should be noted that the conservative management in patients with a vestibular schwannoma remained unchanged in 68% of the study group. There was no difference in the surgical or stereotactic radiotherapy outcome of these patients in comparison with those that underwent primary treatment without a period of conservative management. The growth rate of tumours that failed conservative management (3.1 mm/year) was significantly greater than those that did not fail (0.2 mm/year) ($P < 0.001$). Factors predicting tumour growth or failure of conservative management could not be identified. Audiological deterioration during conservative management continued to occurr irrespective of tumour growth.

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