Effectiveness of Conservative Management of Acoustic Neuromas

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Objective: The goal of this study was to assess the effectiveness of the conservative management in patients with acoustic neuroma (vestibular schwannoma).

Study Design: This retrospective study was performed in a university hospital.

Patients: Patients were selected for this wait-and-see policy on the basis of age, general condition, audiometric results, tumor size, and patient preference. The study group included 97 patients, 87 of whom had at least two neuroradiologic examinations. The mean age of this population was 63 years (29 to 89 years). The mean length of follow-up of this population was 31 months. Eighty-seven of these patients had at least two radiologic examinations (magnetic resonance imaging or computed tomography). The mean interval between the initial and follow-up radiologic examinations was 15 months.

Main Outcome Measures: Tumor size was measured by use of two-dimensional data in all patients. The mean tumor size was 12 mm. The growth rate of the tumor was estimated by comparison of the results of the measurements from the initial and follow-up neuroradiologic examinations.

Results: Of the 97 patients studied, 6 patients required surgery and 6 required radiotherapy. Sixty patients (62%) were still being treated conservatively at the end of the study period. Three patients of 28 who were classified as candidates for hearing preservation surgery lost their candidacy during the observation period. The mean annual tumor growth rate was 1.52 mm/year. The tumor was stable in size in 36% of patients, regressed in 11% of patients, or grew in 53% of patients. The growth patterns of the acoustic neuroma fell into five categories: continuous growth in 15% of patients, negative growth in 5%, growth followed by negative growth in 40%, negative growth followed by growth in 20%, and no variation of tumor size in 20%.

Conclusion: Conservative management of acoustic neuromas carries difficulties: long-term follow-up of the patients and unpredictability of the tumor growth pattern. A reliable and reproducible radiologic method for evaluating tumor size is of great importance.

Key Words: Acoustic neuroma—Magnetic resonance imaging—Computed tomography.

Acoustic neuroma (AN) is a benign tumor of the eighth cranial nerve that is found in the cerebellopontine angle and internal auditory canal.

Improvements in surgical techniques such as modern transtemporal microsurgical techniques, as well as improved postoperative care, have greatly reduced both the morbidity and mortality previously associated with the removal of AN. Lower cranial nerve and trigeminal nerve palsies have become rare and generally isolated events (1). Facial palsy is rare in small and medium-sized tumors (2). Hearing preservation can be achieved in 29% to 69% of patients (3). Consequently, these improvements may indicate surgical removal of all AN after diagnosis.

On the other hand, progress in radiologic evaluation, especially gadolinium-enhanced magnetic resonance imaging (MRI), has resulted in the detection of small, less symptomatic AN. For 30 years, some authors have proposed a wait-and-see policy as a reasonable alternative to immediate surgical excision (4, 5). The goal of this therapy, based on the usually slow progression of symptoms, is to minimize therapeutic risks and complications and to preserve an optimal quality of life in selected patients. Therefore, indications for the conservative management of AN were mostly oriented toward elderly patients in whom nonoperative management seems desirable and to patients with a poor life expectancy—that is, those with significant cardiovascular or pulmonary disease or who are in poor general condition. Extension of the indications for a wait-and-see policy has later included patients with minimal symptoms or with a small or middle-sized acoustic tumor in the only hearing ear.

So far, clinical decisions have been based on the two-dimensional measurements of AN diameter (4–7). Radiologic follow-up have shown that some neuromas may grow fast or slowly or may remain stable. The paramount
importance of an accurate assessment of the growth of the tumor has led some authors to calculate volume rather than to observe the diameter of the neuroma. Some have calculated the volume of the tumor using a mathematical formula (8), and others have calculated volume using specific software (9). Even though volumetric calculation of tumor growth is theoretically more accurate, the choice of the most efficient method remains debatable.

In this study, the authors present the selection criteria for conservative management of AN, the follow-up, and the outcome in these patients. They also describe the results of the radiologic assessment and the follow-up of these patients.

MATERIAL AND METHODS

Study group

Between January 1989 and December 1998, a population of 282 patients with posterior fossa tumor, including AN, were followed up or treated in our department. Among them, 179 patients (64%) were operated on, 6 patients (2%) underwent radiation therapy, and 97 (34%) patients were initially observed. Before patients were included in the latter group, all the advantages and disadvantages of all the existing methods for the treatment of AN were fully explained to them.

The group whose tumors were managed conservatively had a mean age of 63 years (range 29–89) and included 34 men and 63 women. There were 4 patients aged <40 years, 18 patients between 40 and 60 years, 48 patients between 60 and 70 years, and 27 patients aged >70 years. One patient had bilateral AN caused neurofibromatosis type 2. The length of follow-up ranged from 4 months to 10 years (mean 31 months). The initial presenting symptoms are given in Table 1. Hearing loss was the most common initial symptom, followed by vertigo and tinnitus. In 9% of the patients, sudden deafness inaugurated the symptoms. Twenty-eight patients had moderate deafness (mean pure-tone average [PTA] 0–30 dB), 48 patients had moderate to severe deafness (PTA 30–70 dB), 12 patients had severe deafness (PTA 70–90 dB), and 9 patients had total deafness (PTA >90 dB).

The reasons for choosing initial conservative treatment are listed in Table 2 and are detailed here. In 28 patients (29%), general anesthesia was contraindicated because of general disease; 24 patients (25%) refused surgery, and 18 (19%) elderly patients (>70 years) were treated conservatively because of their age. In 9 patients, AN was asymptomatic; in 5 patients, we found a local contraindication to surgery; in 3 patients, the tumor was found in the only hearing ear. Other reasons are listed in Table 2 for the remaining 10 patients.

The clinical stage of AN was determined according to Koo's classification ((10)) for the 97 patients (98 tumors): stage I (intracanalicular tumor with a longitudinal diameter of 1–10 mm): 30 AN; stage II (intracanalicular and intracisternal tumor with a longitudinal diameter ≤20 mm): 47 AN; stage III (intrameatal and intracisternal tumor with a longitudinal diameter ≤30 mm): 13 AN; and stage IV (intrameatal and intracisternal tumor with a longitudinal diameter ≥30 mm): 8 AN. The mean size of the AN in the population was 12 mm; it was 10.37 mm in patients aged <60 years and 14.48 mm in those aged >60 years. Stage I and II AN in patients aged >60 years occurred in 62% of the population.

The conservative management consisted in clinical follow-up every 6 months with pure-tone and speech audiometry, and MRI at 1 year. Follow-up MRI was obtained every 1 or 2 years.

AN growth rate analysis

Among the untreated patients, 87 underwent at least 2 neuroradiologic examinations of the cerebellopontine angle. If a patient underwent radiation therapy or surgery, the latest radiologic examination taken into account was the one performed before the procedure. The radiographic study performed for the initial and follow-up examinations varied with the evolution of imaging techniques for the diagnosis of AN. Among these 87 patients, size measurement of the tumor was based primarily on MRI and secondarily on computed tomography (CT). The imaging measurements were made by the same observer (C.C.).

In our center, MRI is done with a Siemens (Paris, France) Magnetom Vision 1.5 Tesla. Sequences were acquired according to the following protocols: axial T1-weighted images, axial T1-weighted gadolinium-enhanced images with saturation of fat (Fat-Sat), axial T2-weighted images, three-dimensional Fourier-transform constructive interference in the steady state (CISS 3D), and flash 3D for the large tumors. A correlation between two MRI was performed in 84%, between an initial CT and a MRI in 14%, and between two CT in 2%. The mean interval between the initial and control radiologic examinations was 1.3 years.

Volume measurement

Tumor size was calculated by estimating the mean of the greatest anteroposterior and mediolateral tumor extent as described by Nedzelski et al. ((7)) and therefore was not estimated only by the largest diameter of the tumor, including its intrameatal root (Figs. 1 and 2):

\[ \text{Tumor size} = \frac{(AP + ML)}{2} \]

The growth per annum was calculated by dividing the change in tumor size (mm) by the follow-up period (year). Tumor growth pattern was determined for all patients for whom three neuroradiologic exams were performed.

Of these 87 patients, we also studied the volume of the tumor of 6 patients, for whom the mean interval between the first and
second examinations was 13 months (range 3–23) and between the second and third examinations 18 months (range 4–27).

Tumor volume was measured by determining the area of the tumor with a computer program. In this method, the outline of the tumor was drawn on each slice (Fig. 1). We averaged each slice and obtained an average area measurement. The averaged slice area was multiplied by slice interval to obtain a slice volume, and slice volumes were added to obtain a tumor volume (Fig. 2). The growth per annum was calculated by dividing the change in tumor volume (mm$^3$) by the follow-up period (year).

We compared the results of this volume measurement made in our center with a method based on mathematical formulas as reported by Charabi et al. (8).

Statistical analysis

Statistical analysis was performed classic bivariate tests: unpaired and paired Student’s $t$ tests, one-way analysis of variance (ANOVA), and Pearson’s correlation coefficient. We also used Student’s test, the Mann-Whitney $U$ test, and Spearman’s rank correlations for the other parameters. The level of significance was 5%.

Clinical outcome

Of the 97 patients studied, 6 required surgery and 6 required stereotactic radiotherapy. Surgical intervention was required for above-average growth of the tumor. Among the irradiated group, one of the patients who benefited from gamma-knife surgery was later operated on because his tumor grew rapidly (growth ≥5 mm). Evolution was stable for three patients after a follow-up period ranging from 3 to 6 years. For two other patients, a slight increase (<2 mm) was observed. Despite this slow progression, one patient underwent a ventriculoperitoneal shunt because hydrocephaly developed. He underwent a chemical labyrinthectomy because he was experiencing major dizziness. Twenty-five patients decided to interrupt the follow-up program: 6 refused to undergo serial MRI, and 19 patients did not return to their semiannual or annual appointment. Finally, 60 patients (62%) were still being treated conservatively at the end of the study period. The overall evolution in the group not operated on is summarized in Table 3.

Concerning the evolution of the hearing level in this population, 16% of the patients considered as potential candidates for hearing preservation surgery, with a grade I or grade II neuroma and a useful hearing (mean PTA <30 dB), lost their eligibility for such surgery.

Acoustic neuroma growth rate in the untreated group

The mean annual AN growth rate for the untreated group of 87 patients was 1.52 mm/year (extreme range: from a regression of 13 mm/year to an increase of 18 mm/year). The growth rate was 1.9 mm/year for patients aged <60 years and 1.1 mm for patients aged >60 years. We did not find a statistically significant correlation between the mean growth rate of the AN and, successively, patient age, gender, and AN stage.

In the group of 87 patients who did not undergo surgery, the tumor remained stable in size in 36% of patients, regressed in 11%, or grew in 53% (Table 4).

Acoustic neuroma growth pattern

When three neuroradiologic examinations were available, we classified the pattern of evolution of the AN in five categories: continuous growth in 15%, negative growth in 5%, growth followed by shrinkage in 40%, negative growth followed by growth in 20%, and no variation in tumor size in 20%.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No surgery</td>
<td>60 (62)</td>
</tr>
<tr>
<td>Surgery</td>
<td>6 (6)</td>
</tr>
<tr>
<td>Stereotactic radiotherapy</td>
<td>6 (6)</td>
</tr>
<tr>
<td>Quit the follow-up program</td>
<td>25 (26)</td>
</tr>
</tbody>
</table>

The American Journal of Otology, Vol. 21, No. 6, 2000
Volume
In six patients, we compared the volume calculation from mathematical formulas based on anteroposterior and mediolateral measures as reported by Charabi et al. (8), with the volume measurement based on a computer program. These two results were not similar, especially for large AN. A paired comparison of the means using a repeated measures ANOVA adjusted on patients made evidence of higher values given by the volume calculated with mathematical formulas ($p = 0.028$) with no significant interaction. This difference between the two series was confirmed by a nonparametric Wilcoxon’s $t$ test ($p < 0.01$). In Table 5, the volume measurement of the tumor with a computer program is compared with the volume calculated with mathematical formulas.

**DISCUSSION**

**Growth of acoustic neuromas**

Wait-and-see policy results in AN have been reported since Wazen et al. (11). Those authors reported 21 elderly patients monitored with serial CT who had undergone partial tumor removal or had not been operated on. From this beginning, all the authors stated that the majority of the tumors grew during the period of follow-up. Gardner et al. (6) reported on the wait-and-see policy in six patients. Tumor growth rate was 0 mm/year in four patients and <2 mm/year in the two other patients. In 1991, Bederson et al. (12) reported 70 patients with AN and monitored for an average of 26 months. In this report, 40% of tumors remained stable and 53% grew $\sim 3.8$ mm/year. In 1991, Nedzelski et al. (13) reported a study that included 50 patients who benefited from the wait-and-see policy; 78% had a growth rate of $< 2$ mm/year. In 1994, Strasnick et al. (14) analyzed 51 patients selected to undergo initial nonoperative management of their tumors. Thirty-nine patients in this series demonstrated tumor growth rates $< 2$ mm/year, whereas 11 patients demonstrated tumor growth rates $> 2$ mm/year. In 1995, Charabi et al. (8) reported a study on 123 patients over a 20-year period; tumor growth was observed in 90 patients.

The results of this study supported the current thought that vestibular schwannomas are slow-growing tumors (1.52 mm/year). Strasnick et al. (14) reported a growth rate of 1.1 mm/year, Nedzelski et al. (13) 1.1 mm/year, Sterkers et al. (15) 1.4 mm/year, and Bederson et al. (12) 2 mm/year, whereas Charabi et al. (8) reported a mean annual growth rate of 3.2 mm/year. They also confirmed that there was wide interindividual variability in the mean growth rate of the AN. We did not find a statistically significant correlation between the mean growth rate of the AN and, successively, patient age, gender, and AN grade.

In our series, negative tumor growth was observed in 11% of the patients. This is consistent with reports by Charabi et al. (8; 8%) and Bederson et al. (12; 7%). Other authors have reported spontaneous shrinkage and even disappearance of a diagnosed tumor (7,16–18). We think that the wide variability in tumor growth depends more on secondary phenomena (hemosiderin, cystic formation) than on the tumor proliferation index (19).

We have shown that a tumor’s growth changes over time and that some grow after a period of stability. Our results differ from what was claimed by some authors; that is, tumor behavior will become apparent within a short period of follow-up subsequent to diagnosis (7,14,20). Our results support the findings of Charabi et al. (8). However, in this study, we analyzed the overall evolution of the growth pattern and not the specific evolution of a particular pattern of growth.

In this study, we did not find a statistical correlation between the growth of AN and the age of the patient and between the growth of AN and the initial stage of the tumor, although growth rate of the tumor seemed to be

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**TABLE 4. Growth rate of tumor in the group not operated on (N = 87)**

<table>
<thead>
<tr>
<th>Growth</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No growth</td>
<td>31 (36)</td>
</tr>
<tr>
<td>Growth &lt;2 mm</td>
<td>21 (24)</td>
</tr>
<tr>
<td>Growth between 2 and 5 mm</td>
<td>14 (16)</td>
</tr>
<tr>
<td>Growth &gt;5 mm</td>
<td>11 (13)</td>
</tr>
<tr>
<td>Shrinkage</td>
<td>10 (11)</td>
</tr>
</tbody>
</table>

**TABLE 5. Comparison between volume measurement and anteroposterior × mediolateral diameters and calculated volume (N = 6)**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Volume measurement (cm³)</th>
<th>AP × ML (mm)</th>
<th>Volume (cm³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>D.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>7.34</td>
<td>38 × 35</td>
<td>25.4</td>
</tr>
<tr>
<td>2</td>
<td>5.94</td>
<td>38 × 20</td>
<td>10.97</td>
</tr>
<tr>
<td>3</td>
<td>4.7</td>
<td>26 × 20</td>
<td>6.21</td>
</tr>
<tr>
<td>Z.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>1.6</td>
<td>15 × 11</td>
<td>1.11</td>
</tr>
<tr>
<td>2</td>
<td>1.6</td>
<td>15 × 11</td>
<td>1.11</td>
</tr>
<tr>
<td>3</td>
<td>1.4</td>
<td>15 × 11</td>
<td>1.11</td>
</tr>
<tr>
<td>A.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>0.78</td>
<td>13 × 12</td>
<td>1.02</td>
</tr>
<tr>
<td>2</td>
<td>0.78</td>
<td>13 × 11</td>
<td>0.9</td>
</tr>
<tr>
<td>3</td>
<td>2.61</td>
<td>16 × 18</td>
<td>2.56</td>
</tr>
<tr>
<td>L.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>1.4</td>
<td>15 × 15</td>
<td>1.77</td>
</tr>
<tr>
<td>2</td>
<td>1.78</td>
<td>18 × 18</td>
<td>3.06</td>
</tr>
<tr>
<td>3</td>
<td>1.78</td>
<td>18 × 18</td>
<td>3.06</td>
</tr>
<tr>
<td>M.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>1.26</td>
<td>18 × 15</td>
<td>2.32</td>
</tr>
<tr>
<td>2</td>
<td>1.68</td>
<td>22 × 15</td>
<td>3.14</td>
</tr>
<tr>
<td>3</td>
<td>1.58</td>
<td>21 × 15</td>
<td>2.93</td>
</tr>
<tr>
<td>V.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>3.1</td>
<td>20 × 15</td>
<td>2.72</td>
</tr>
<tr>
<td>2</td>
<td>3.1</td>
<td>20 × 30</td>
<td>7.7</td>
</tr>
<tr>
<td>3</td>
<td>3.1</td>
<td>28 × 24</td>
<td>9.12</td>
</tr>
</tbody>
</table>

1, 2, 3, first, second, and third examinations, respectively; AP, anteroposterior; ML, mediolateral diameters of the tumor.

Volume = volume calculation from AP and ML diameters of the tumor.
slower in elderly patients aged >60 years. For Charabi et al. (8), Bederson et al. (12), and Ogawa et al. (21), these figures are higher in a younger population. Our study could not support these findings. It would be interesting to compare this growth rate in a homogeneous population (stages I–II) of young patients with a homogeneous population (stages I–II) of elderly patients.

Difficulties of the conservative management

The first major difficulty is the nonobservance of this management. In our series, 19 patients (20%) did not return to their clinical/radiologic evaluation appointments. Although this nonobservance has not been reported by other authors, we think it represents a major difficulty of this policy. All the parameters for long-term follow-up are gathered in the organization of our center: a specific register is filled, and data are gathered in a software program. This part of the follow-up is performed by one of the authors (I.G.). There are two weekly specific consultations led by the senior author to monitor these patients. If a patient does not come to the appointment, we write and call the patient for another appointment. Some reasons for this nonobservance may be the following: this is an elderly population; despite a detailed explanation, the absence of “classic” treatment (surgery, radiotherapy) may lead patients to obtain a second opinion at another center that applies a different policy; or patients with few symptoms may tend to wait until their hearing worsens. This is a major concern, because we have demonstrated that 16% of the patients with a grade I or II neuroma lost their candidacy during the follow-up.

Another difficulty is to find the appropriate and accurate means for evaluating tumor growth. Since the report by Wazen et al. (11), two-dimensional measurement on CT or MRI has been the first method used (4–7,11,12,16). More recently, volume measurement of the tumor was proposed as an alternative to the two-dimensional measurement. Interest in volume measurement stems from the fact that the relationship between diameter and volume in AN is not equivalent to the relationship of a spherical tumor with the same diameters. In tumors with large diameters, small increases in diameter correspond to much larger increases in tumor volume than would have occurred with similar increases in diameter of small tumors. However, the choice of the most efficient method for volume calculation is still questionable. We analyzed and compared volume calculation with mathematical formulas and volume measurement from the area of the tumor on all slices in six patients. This comparison was not performed for the whole population because this technique was introduced for the last patients included in the study period and required at least three examinations. A paired comparison of the means, by repeated measures ANOVA adjusted on patients, gave evidence of higher values given by the volume calculated with mathematical formulas (p = 0.028). This means that we can consider that the volume calculation method presents a trend toward generating higher values, regardless of the patient. The difference was more evident for large tumors, as seen in patients D. and V. in Table 5. This finding, although made in a small population, stresses the importance of using a single and unique method of volume measurement for the follow-up of one patient. Moreover, both methods are time-consuming for the neuroradiologist to calculate and therefore have to be evaluated in terms of cost efficiency. Computerized assessment of tumor volume based on semiautomated volume calculation with MRI could improve this limitation. Finally, calculation of the systemic error and accuracy should be perfectly delineated, as Long et al. (18) and Niemczyk et al. (20) did. Those authors reported 25% and 15% margin of error, which are still relatively high figures for these slow-growing tumors. As Sarazin et al. (9) have said, the higher the tumoral volume, the lower the margin of error. These latter authors also confirmed a 15% margin of error. Niemczyk et al. (20) state that methods using additional computer software to three-dimensional analysis should be more accurate. Such estimations, though they may be true theoretically, are so far preliminary, and more studies involving larger populations and cost-efficiency data are necessary to validate computer-assisted methods.

Finally, in our practice and at the current time, the authors think that three-dimensional volume measurement from the shape of the tumor is the most efficient and reliable method for assessing tumor growth. Although still hampered by a relatively high margin of error, the methods used seem to be more convincing (9).

The third difficulty is to apply a policy based on the evolution of clinical signs and radiologic findings. In our series, surgery or radiotherapy performed because of tumor growth was required in 12 patients (12%). This figure is lower than in other reports because the decision to modify our attitude is not only dependent on small radiologic variations of volume of the AN. Bederson et al. (12) reported that 19% of their patients required surgical intervention an average of 14 months after the patient initially sought treatment. Strasnick et al. (14) and Charabi et al. (8) reported indications for surgery or radiotherapy in 24% and 34%, respectively, of their patients.

Our decision to modify the management is not based only on the overall growth of the tumor, because we think that the anatomical relations of the AN with the neighboring structures, its anterior extension, and the initial growth rate of the tumor have to be taken into account. Finally, decision-making factors also include modification of symptoms and the patient’s life expectancy.

CONCLUSION

Conservative management of AN is accompanied by these difficulties: long-term follow-up of patients, unpredictability of the tumor growth pattern, and correlations between clinical and radiologic findings. A reliable and
A reproducible radiologic method is of great importance in evaluating tumor size and growth. Further studies are needed to establish the accuracy and reliability of radiologic evaluation of tumor size.

Acknowledgment: The authors thank Professor A. Bonafe, Dr. M. V. Cadene, and Ms. N. Iked for their contributions to this study and Mr. M. Ardente and Mr. M. Bouamra for manuscript preparation.

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