Gamma Knife Radiosurgery for Acoustic Schwannoma: Early Effects and Preservation of Hearing

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Abstract

The effects of relatively low dose gamma knife irradiation on acoustic schwannoma were evaluated. The signal intensity change and tumor shrinkage on magnetic resonance (MR) images, change in hearing, and complications in 28 patients (mean age 47.0 ± 13.6 yrs) were studied. Three patients had bilateral tumors. Six were already deaf when treated. The maximum tumor diameter was 35 mm. The mean dose delivered to the tumor was 12.1 ± 1.6 Gy at the periphery, and 25.2 ± 4.3 Gy at the center. The mean follow-up time was 16 months and the longest 24 months. Lowering of the MR signal intensity in the tumor center appeared after 3 months at earliest but generally after 6 months. Signs of tumor shrinkage appeared within 12 months on average. Cyst in the tumor enlarged rapidly after treatment in two patients. The percentage of hearing preservation was 85% (17/20) at 3 months, 80% (16/20) at 6 months, 72% (13/18) at 9 months, 75% (12/16) at 12 months, 67% (8/12) at 15 months, 60% (6/10) at 18 months, and 50% (2/4) at 24 months. Subtle changes in hearing were detected by speech tone audiometry. Temporary facial numbness and weakness was seen in one patient each. No patient had lower cranial nerve paresis. Relatively low dose gamma knife radiosurgery is effective in suppressing growth of acoustic schwannoma with preservation of hearing.

Key words: acoustic schwannoma, gamma knife, radiosurgery, hearing preservation

Introduction

Gamma knife is now widely used for the treatment of acoustic tumors,^{6,7,9,10,12,13,15} not only in elderly patients, but also patients with medical problems, bilateral tumors, a tumor in the only functioning ear, or a recurrent tumor and those who refuse surgical removal. Comparison of the results of radiosurgery with the results of microsurgery suggests that radiosurgery is the treatment of choice.^{13,15} Acoustic schwannoma has been treated by gamma knife radiosurgery with a relatively high radiation dose,^{6,7,9,10} but lower doses have been recommended.^{11,15}

We report our experience in treating acoustic schwannoma with a relatively low radiation dose based on changes in the tumor appearance on magnetic resonance (MR) images and the clinical course, especially changes in hearing acuity.

Subjects and Methods

Twenty-eight patients, 10 males and 18 females aged between 24 and 73 years old (mean $\pm$ SD 47.0 ± 13.6), were treated from May 1991 to December 1992. Three patients had bilateral tumors. The maximum lesion diameter was 35 mm. Six patients had lost hearing acuity on the side of the tumor. Dosimetry was carefully planned on both axial and coronal MR images, especially at the porus of the internal auditory meatus, using computed tomographic (CT) scans to correct the distortion of the MR images. The mean isodose at the periphery was $48.9 \pm 6.3\%$. The dose delivered to the tumor periphery was mean 12.1 ± 1.6 Gy, range 10–17 Gy, and to the center mean 25.2 ± 4.3 Gy, range 17–34 Gy. The time necessary for one fraction was usually between 4 and 7 minutes. The number of fractions was 5.0 ± 2.1 . The mean follow-up time was 16 months and the longest was 24 months.

Three correlations were studied: when the signal change or shrinkage of the tumor was first observed

on MR images, original tumor size (approximate volume), and the peripheral or center dose; the time course of hearing change (or cranial nerve paresis), by correlating the change in auditory acuity, original tumor size, and the dose delivered to the periphery or center, or the dose rate in the periphery; and the change in auditory acuity, the length of acoustic nerve irradiated which is related to the pons-petrous distance, and the dose delivered to the periphery.

The tumor was surgically removed in two patients at 3 and 4 months after gamma knife radiosurgery, because the cyst in the tumor had enlarged, although the solid part had shrunk. Histological examination of surgical specimens was possible in one of these two cases.

Results

I. MR imaging study

The MR signal intensity of the central area of the tumor had lowered in 17 (65%) of the 26 patients excluding the two receiving surgical removal, starting at 3 months at earliest but generally at around 6 months (mean 5.7 mos). Shrinkage of the tumor appeared in six (23%) of 26 patients, beginning at 12 months on average. Four patients showed both tumor shrinkage and lowering of the MR signal intensity in the central area. Two patients showed shrinkage of the tumor without change in the MR signal intensity. In seven (27%) of 26 patients, the MR signal intensity and the tumor size remained unchanged (Fig. 1).

Larger tumors were associated with tumor shrinkage and more rapid appearance of signal changes. There was no definite correlation between

Fig. 1 Onset of MR signal intensity changes in the central area and tumor shrinkage. Closed bars show patients with lowering of the MR signal intensity. Open bars represent patients with tumor shrinkage.

Fig. 2 Change of MR signal intensity, tumor shrinkage, original tumor size, and dose delivered to the tumor periphery. Closed circles show patients with MR signal intensity change in the central area of the tumor without tumor shrinkage. Asterisks show patients with tumor shrinkage with and without MR signal intensity change. Open circles show patients without tumor shrinkage or MR signal intensity change. Closed squares show patients with enlarging cyst in the tumor after treatment.

the signal change in the tumor and the dose delivered to the periphery or center. Even 10 Gy at the periphery induced a lowering of the MR signal intensity in the central area of the tumor (Fig. 2).

II. Clinical study

Follow-up examination found trigeminal neuropathy and facial weakness in only one patient and this was temporary. No patient developed lower cranial nerve paresis. Two patients had transient vertigo just after the treatment. Another two patients required implantation of a shunt because of developing hydrocephalus.

Hearing acuity was studied in 20 patients after radiosurgery. Eight patients were excluded, six were already deaf at treatment and two underwent subsequent surgical removal of the tumor. Hearing acuity was maintained at the pretreatment levels in 85% (17/20) at 3 months, 80% (16/20) at 6 months, 72% (13/18) at 9 months, 75% (12/16) at 12 months, 67% (8/12) at 15 months, 60% (6/10) at 18 months, and 50% (2/4) at 24 months. Patient T.Y. had a pure

Fig. 3 Change of auditory acuity, original tumor size, and dose rate delivered to the tumor periphery. *Open circles* show patients with early decrease of hearing acuity after radiosurgery. *Asterisks* show those patients with late decrease. *Closed circles* show patients preserving hearing acuity.

tone average of 30 dB and speech discrimination score of 90% before treatment, and 28.8 dB and 85% 2 years after treatment. Patient S.A. had 35 dB and 100% before treatment, and 43.8 dB and 60% after 15 months. Speech tone audiometry detected subtle changes of hearing.

The irradiation dose rate in the periphery was higher in patients with early hearing changes and the tumor was larger in patients with late changes (Fig. 3). A patient with neurofibromatosis type 2 showed late hearing change, although the dose rate was low. The hearing acuity was, however, already below the serviceable level before treatment. There was no definite correlation between the risk of hearing disturbance and the dose delivered to the periphery or center of the tumor. Even 10 Gy at the periphery induced hearing change. There was also no definite correlation with the length of the acoustic nerve irradiated.

Auditory function levels before treatment and during follow-up varied in the six patients with hearing disturbance after treatment (Fig. 4). Two of the six showed rapid decrease of hearing acuity within 3 months, and three showed a gradual decrease after 3 months. Interestingly, patient M.K. achieved recovery of hearing acuity after several months, from 16.3 dB and 100% before treatment, to 60 dB

Fig. 4 Decrease of auditory acuity during follow-up. *Triangles* show patients with early decrease of auditory acuity. *Circles* show patients with late decrease. *Diamonds* show a patient with recovery of auditory acuity after initial decrease.

and 55% after 3 and 6 months, 46.3 dB and 100% after 9 months, 45 dB and 95% after 12 months, and 51.3 dB and 85% after 21 months. Ten patients still suffered from tinnitus after radiosurgery, worsening in some.

III. Histological study

The most prominent features of the tumor specimens were various vascular changes. There were fibrin deposits in the vascular wall and infiltration of macrophages and small lymphoid cells around the

Fig. 5 Photomicrograph showing degradation of the basement membrane and thrombus formation. Periodic acid methenamine silver staining, specific for the basement membrane of the vascular wall, $\times 320$.

Fig. 6 Photomicrograph showing thickening of the vascular wall and endothelial proliferation. Factor VIII-related antigen staining, specific for the endothelium, $\times 320$.

vessels. Degradation of the basement membrane of the vascular wall and formation of thrombosis were present (Fig. 5). However, vascular proliferative changes were also seen as thickening of the vascular wall and endothelial proliferation (Fig. 6).

Discussion

Our study showed that gamma knife radiosurgery is effective for suppressing the growth of acoustic schwannoma with relatively low radiation doses, though the follow-up time was short. Previous reports found that high radiation doses^{6,7,9,10} controlled tumor growth in 90% of cases. Low radiation doses^{11,15} ranging from 10 to 15 Gy achieved arrest of tumor growth in 81% of cases. Previous studies also found the MR signal intensity lowered in 70% of cases, and signs of shrinkage appeared in 30% of cases during the first 24 months after treatment. The MR imaging change rates in our study were slightly lower, but our patients were only followed up for a short time. As the beginning of signal change was within a period equivalent to that of other studies, the rate of change can be expected to increase later. Interestingly, doses ranging from 10 to 17 Gy at the periphery and from 17 to 34 Gy at the center all achieved lowering of the MR signal intensity. Larger tumors showed easier shrinkage and more rapid start of MR signal intensity changes. Our patients were treated with almost the same marginal dose, so these results suggest that the changes in the tumors occurred when the dose exceeded a threshold level rather lower than that previously considered. The histological study of surgical specimens 4 months after radiosurgery suggested that radiosurgery causes

various changes in the vascular wall of the tumor, both destructive and proliferative. Acoustic schwannoma demonstrates various changes in vessels, such as ongoing thrombosis, hemorrhage, and angiogenesis,¹⁴ so it is not clear which changes occurred as a result of radiosurgery. Nevertheless, the changes of the vascular wall in the tumor may be related to the MR signal intensity change or shrinkage of the tumor after radiosurgery. The radiobiological behavior of acoustic schwannoma *in vivo* is not well known,⁸ so further study is needed to clarify the mechanism and the minimum dose for suppressing tumor growth.¹

Hearing preservation² has become the major target of treatment of acoustic schwannoma by both gamma knife radiosurgery and microsurgery.^{3,4} In our study, 70–85% of patients maintained hearing at the pretreatment levels for 1 year, and about 50–60% beyond 1 year. Loss of useful hearing acuity began after 1 week to 12 months.⁷ Comparison of hearing acuity at about 1 and 5 years showed the percentage of patients with unchanged hearing was about the same.¹¹ Therefore, our series shows that hearing acuity can be maintained for more than 2 years after treatment. Hearing disturbance was not significantly correlated with the marginal dose, central dose, or the length of acoustic nerve irradiated. The minimum dose delivered to the periphery, 10 Gy, caused hearing disturbance. Therefore, the dose¹⁶ or the length of cranial nerves irradiated,⁵ suggested risk factors for peripheral nerve injury, were not significant predictors of cochlear nerve injury in this study. Tumor size and especially marginal dose rate might be correlated with hearing disturbance. The latter was higher in patients with hearing disturbance after treatment. This is also observed in patients with trigeminal neuropathy. As our patients were treated within the last 2 years and received almost the same marginal dose, a combination of collimators might be a primary factor. A combination of larger collimators used to plan the dosimetry results in a higher marginal dose rate. Therefore, our study reemphasizes the importance of precise dose planning to preserve hearing. For small schwannomas, especially those located in the internal auditory meatus, the collimator selection for the dose planning is very limited. More attention should be given to dose planning when treating very small schwannomas with the gamma knife. Classification of the auditory function before treatment and how to define serviceable hearing are also significant problems.^{2,4,12}

Cranial nerve injury, except for the cochlear nerve, was infrequent in our series. There was only one case each of trigeminal and facial neuropathy,

and both were temporary. No patient showed lower cranial nerve paresis. This might be ascribed to the low marginal radiation dose or to precise dose planning. We always planned dosimetry on both MR images and CT scans three-dimensionally. The MR image provided a clear anatomical correlation between the tumor and critical structures such as the brainstem or cranial nerves, but distortion of the images was unavoidable. Comparing the dosimetry on both MR images and CT scans, especially at the porus of the internal auditory meatus, allowed correction of the distortion of MR images.

Hydrocephalus developed in two patients. The intratumoral cyst enlarged after treatment in another two patients. The mechanisms of hydrocephalus and cyst enlargement are unknown. Treatment of cyst enlargement remains difficult. We must beware of hydrocephalus and enlargement of intratumoral cyst after radiosurgery.^{7,11)}

Relatively low dose gamma knife radiosurgery was effective in suppressing growth of acoustic schwannoma with preservation of hearing and low rates of complication. We can expect to obtain better treatment results with precise dose planning using CT and MR imaging, using an optimum dose and dose rate delivered to the periphery of the tumor.

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