ORIGINAL ARTICLE

Radiosurgery as Treatment for Acoustic Neuroma. Ten Years’ Experience

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Acoustic neuroma; Microsurgery; Radiosurgery; Stereotactic radiotherapy; Gamma Knife; LINAC

Abstract

Introduction and objective: The acoustic neuroma is a benign tumour that usually affects the vestibular portion of the vestibulocochlear nerve. It represents 8% of all intracranial tumours and 80% of those arising at the cerebellopontine angle. There are 3 treatment options: microsurgery (the technique of choice), radiosurgery and observation. The objective of the study was to evaluate the results and side effects obtained using radiosurgery as treatment for acoustic neuroma.

Material and methods: We performed a review of all patients treated with radiosurgery (Gamma Knife and linear accelerator) at doses of 1200–1300 cGy for unilateral acoustic neuroma in our hospital from January 1999 until January 2010. In all patients we evaluated the overall state, tumour growth control rate (tumour smaller or remaining the same size), the involvement of V and VII cranial nerves and central nervous system disorders. We also assessed follow-up time and changes in hearing thresholds after radiosurgery.

Results: From a total of 35 patients studied, with a mean age of 58.29 years and lacking statistically significant differences in gender, the tumour growth control rate was over 90%. The main reason for visit (65.71%) was unilateral and progressive hearing loss. After treatment, 34.28% of patients had hearing loss. The involvement of the cranial nerves (V–VII) was transitory in 100% of cases. Gamma Knife radiosurgery was administered in 82.85% of patients.

Conclusion: Although microsurgery is the treatment of choice for acoustic neuroma, we consider radiosurgery as a valid alternative in selected patients (elderly, comorbidity, small tumour size and sensorineural hearing loss, among others).

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PALABRAS CLAVE
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estereotáctica;
Gamma Knife;
LINAC

Radiocirugía como tratamiento del neurinoma del acústico. Diez años de experiencia

Resumen
Introductión y objetivo: El neurinoma del acústico es un tumor benigno que suele afectar a la porción vestibular del VIII par craneal. Representan el 8% de todos los tumores intracraneales y el 80% de los que surgen a nivel del ángulo pontocerebeloso. Existen 3 opciones terapéuticas: la microcirugía, que es la técnica de elección, la radiocirugía y la observación. El objetivo del estudio ha sido valorar los resultados obtenidos con la radiocirugía en el tratamiento del neurinoma del acústico, así como los efectos secundarios derivados del mismo.

Material y métodos: Hemos realizado en nuestro hospital una revisión de todos los pacientes tratados con radiocirugía (Gamma Knife y LINAC) a dosis de 1.200-1.300 Gy por neurinoma del acústico unilateral, entre enero de 1999 y enero del 2010. En todos los pacientes se valoraron el estado general, la tasa de control de crecimiento tumoral, entendiéndose como tal que no cambia de tamaño o que se reduce, la afectación del VIII par craneal, así como alteraciones del sistema nervioso central. También el tiempo de seguimiento y las variaciones de los umbrales auditivos tras la radiocirugía.

Resultados: De un total de 35 pacientes estudiados, con una edad media de 58,29 años y sin diferencias estadísticamente significativas en cuanto al sexo, la tasa de control de crecimiento tumoral fue mayor al 90%. El principal motivo de consulta fue la hipoacusia unilateral y progresiva. Un 34,28% de los pacientes tratados presentaron empeoramiento en su nivel de audición post-tratamiento. La afectación de los pares craneales (V-VIII) en el 100% de los casos fue transitoria. La radiocirugía tipo Gamma Knife fue administrada en la mayoría de los pacientes (82,85%).

Conclusión: Aunque la microcirugía sigue siendo el tratamiento de elección para los neurinomas del acústico, consideramos la radiocirugía como una alternativa válida en pacientes seleccionados (edad avanzada, comorbilidad asociada, pequeño tamaño e hipoacusia sensorial, entre otros).

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Introduction

Acoustic neuroma (AN) is a benign tumour which affects the statoacoustic nerve, which is also known as the eighth cranial or cochleovestibular nerve, and generally affects the vestibular portion of the nerve. Perhaps the most correct name for it would be "vestibular neuroma" or "schwannoma vestibular". The nerve comprises a multitude of nerve fibres which are prolongations of the neurones and cells which surround them to protect them and enable the conduction of nerve impulses, the Schwann cells, and it is in these cells where the schwannoma or neuroma originates.

These represent 8% of all intracranial tumours and around 80% of those which arise at the level of the cerebellopontine angle.1,2 They tend to appear in the inner ear canal, and as they grow they occupy the cerebellopontine angle. If they are diagnosed late they can be found to compromise the brain stem.

There is the sporadic AN, which generally affects one ear; this is the most common form with an incidence lower than 0.07%.3 It is usually diagnosed between the ages of 20 and 50, generally with a slight female predominance (55%).1 It is included in the group of rare diseases by the European Union and by the U.S.A.’s National Organization for Rare Disorders.4 And there is the hereditary AN, which is usually bilateral, appears in patients with neurofibromatosis type II and is diagnosed at younger ages.

Its basic symptom is unilateral sensorineural hearing loss of variable progression; although this does not always present and other accompanying symptoms can be found: vertigo, tinnitus, earache, headache and even facial hyperesthesia. Larger tumours can cause facial weakness, dysarthria, dysphagia and even hydrocephaly.5 The diagnostic technique of choice is magnetic resonance with contrast medium,6 which has enabled an increase in the number of diagnosed AN, either with minimal symptoms or asymptomatic, and also allows us to monitor cases for whom conservative treatment has been decided. These tumours are slow growing, around 2 mm per year, although everything indicates that they are very random and that the tumour growth, rather than following a geometric line, seems to grow in unpredictable spurts.7-9

There are 3 currently accepted therapeutic options: microsurgery, which is the technique of choice, radiosurgery (RS) and observation.

The objective of microsurgery is the complete excision of the tumour and it has a high complication rate (59.5%), surgical (28.2%), neurological (26.2%) and medical (5.1%).10 The mortality rate of the procedure is 0.2% and complete resection of the tumour is not achieved in 11.7% of the cases undergoing microsurgery, which means other therapeutic options need to be considered. No significant changes have been seen over the past 15 years. Being a non-Caucasian female, the presence of comorbidities and the practice of
this surgery in hospitals with a low volume of patients are the main risk factors for the presentation of complications.\textsuperscript{11}

Unlike microsurgery, the objective of RS is to halt the growth of the tumour by causing avascular necrosis with subsequent depositing of collagen.\textsuperscript{12} Gamma-Knife Radio Surgery was described by Lars Leksell in 1951 and consists of focussing multiple radiations on an intracranial target using a cobalt source (\textsuperscript{60}Co telecobaltotherapy).\textsuperscript{5,13} The first treatment for AN was applied by Leksell\textsuperscript{14,15} in 1971. RS might involve complications such as, hearing loss, weakness and loss of facial sensitivity, tinnitus, loss of balance, headache, dysarthria, dysphagia, cystic necrosis and hydrocephaly.\textsuperscript{16} Although it is true that these complication rates are not high, since a balance is sought between the dose administered to appropriately control the growth of the tumour and to prevent the side effects of radiation; hearing loss is the main bone of contention with RS. The traditional indications for RS according to Karpinos et al.\textsuperscript{10} are a tumour measuring less than 3 cm and at least one of the following concurrent criteria: progressive symptoms in patients over 40, associated comorbidity, tumour in the only ear with useful hearing, bilateral AN, post-surgical recurrence or rejection of surgery.

Finally, observation or therapeutic abstention might be a useful alternative in selected cases, avoiding side effects and retaining the possibility of opting at any time for the other therapeutic options. Observation takes into account that the growth of the AN, rather than being constant, takes place in spurts\textsuperscript{17-19} and that there is no clinicoradiological correlation, which means that we find small ANs which cause symptoms and medium ANs which are asymptomatic and found incidentally on X-ray examination.

In the following article, we present our experience after 10 years, in 35 patients diagnosed with unilateral and sporadic AN treated with RS, where we assess the results obtained and the side effects which occurred with this treatment.

**Materials and Methods**

We undertook a 10 year revision (January 1999 to January 2010) in our hospital of all the patients diagnosed with unilateral AN who were treated with RS.

During this period we saw a total of 62 AN in our centre, of which 35 (56.5\%) underwent stereotactic RS, either with Gamma Knife telecobaltotherapy or with linear accelerator (LINAC), administering a maximum marginal dose of between 1200 and 1300 cGy, already described in detail in previous publications.\textsuperscript{17-19} The remaining AN, 27 (43.5\%), were subjected to observation or therapeutic abstention, either because of the size of the AN (5-16 mm), because of the age of the patients, because there were associated comorbidities which contraindicated RS or because this was the express decision of the patient. None of the ANs diagnosed in this period were operated.

The general condition of all the patients was assessed, the tumour size calculated with its largest diameter in magnetic resonance imaging and the tumour growth control rate, which is understood to mean that the AN reduces or does not change in size after RS. The follow-up time and the variations in hearing thresholds after RS were also assessed, according to the Gardner–Robertson scale.\textsuperscript{20} The degree of facial paralysis post treatment was classified according to the House and Brackmann scale\textsuperscript{21} and post-treatment trigeminal involvement was assessed using a 3-item subjective scale: normal sensitivity, altered sensitivity or absence of sensitivity.\textsuperscript{3}

All the patients underwent audiometric control and magnetic resonance imaging every 6 months for the first 2 years and then annually.

The SPSS\textsuperscript{9} programme was used for statistical data management. The statistical test chosen was the Student’s t test and the significance level selected was 0.05.

**Results**

A total of 35 patients were studied treated with stereotactic RS after diagnosis of unilateral (14 right-sided and 21 left-sided) and sporadic AN, of whom 17 were male (49\%) and 18 women (51\%), with no statistically significant differences in terms of gender (P= .072). The mean age was 58.29 with an age range of between 31 and 76 years of age. None of the patients had been treated beforehand with microsurgery and none had a personal clinical history of interest, we should mention that 4 patients (11.42\%) were diabetic and one patient (2.85\%) was hypertensive, all were well controlled with their medical treatment. The reason for consultation for more than half of the cases, 65.71\% (24 patients), was unilateral, progressive hearing loss. Sudden deafness was highlighted in 11.42\% of the cases (4 patients). The mean follow-up time varied between 3 and 10 years, with a mean of 4.7 years.

In our series there are no statistically significant differences (P=.098) with regard to intra and extra canalicual AN in the results obtained.

The type of RS administered was distributed as follows: 29 patients (82.85\%) underwent Gamma-Knife treatment (Leksell Gamma Knife) and 6 patients (17.14\%) linear accelerator (LINAC).

The initial size of the tumour, calculated with its greater diameter on magnetic resonance imaging, was 15.17 mm, reducing to 12.69 mm after RS (Fig. 1). The reduction in the volume of the tumour or mean growth control rate in our series was 2.48\%, with a statistically significant P of .041.

Before treatment, the distribution of hearing according to the Gardner and Robertson scale\textsuperscript{26} was: 15 patients had grade I, 17 grade II, 2 grade III and one patient had grade IV, none of the patients presented a grade V. After treatment, the distribution was: 9 patients with grade I, 15 with grade II, 7 with grade III and 4 patients with grade IV, none of the patients presented grade V (Fig. 2). Therefore, hearing preservation after the 10 years of the study was 65.71\%. And 3 patients (8.57\%) were affected by facial paralysis after RS but only transitorily.

**Discussion**

According to the series of Table 1,\textsuperscript{16,22-27} in the majority the tumour growth control rate (this being understood as the AN presenting the same or smaller tumour size after RS) exceeds 90\%. Currently efforts are concentrated on more exact dosing and planning using
the advances achieved in high resolution resonance, on fractioning the doses administered and on reducing the marginal dose to achieve fewer collateral side effects and to increase the extent of hearing preservation.

The remaining parameters to be assessed were the preservation of hearing and facial and trigeminal nerve involvement. With regard to hearing thresholds, after RS, 12 patients (34.28%) presented a reduction according to the Gardner–Robertson scale, and therefore we find 65.71% preservation of hearing after 10 years of the study. Hearing preservation is still a bone of contention with RS; recent studies\textsuperscript{16,22-27} place it between 71% and 75%. Advances in RS will involve finding the ideal point between the administration of a dose which is sufficiently strong to reduce the AN and achieve good tumour control, while reducing the marginal dose as much as possible to prevent adverse neuropathic side effects. Likewise, involvement of the V and VII cranial nerve in our series affected 3 patients (8.57%), this being transitory involvement, as 100% of the cases recovered.

In our series, we achieved a growth control rate of 91%, hearing preservation of 65.71% post treatment, and involvement of the V and VII cranial nerve, which was transitory in 100% of cases. These results do not show a statistically significant difference ($P=.065$, $P=.072$ and $P=.056$, respectively) compared to the rest in medical literature (Table 1).

\begin{table}
\centering
\caption{Table Summary by Author.}
\begin{tabular}{|l|c|c|c|c|c|}
\hline
Author & (n) & Year & Control rate (%) & Hearing preservation (%) & Lesion VII cn (%) & Lesion V cn (%) \\
\hline
Flickinger et al.\textsuperscript{22} & 190 & 2001 & 97.1 & $71 \pm 4.7$ & 1.1 ± 0.8 & 2.6 ± 1.2 \\
Petit et al.\textsuperscript{23} & 47 & 2001 & 96 & 87 & 0 & 0 \\
Karpino et al.\textsuperscript{16} & 96 & 2002 & 91 & 57 & 6 & 12 \\
Rowe et al.\textsuperscript{24} & 234 & 2003 & 92 & 75 & 4.5 & 5 \\
Chang et al.\textsuperscript{25} & 61 & 2005 & 98 & 74 & 0 & 0 \\
Tamura et al.\textsuperscript{26} & 2053 & 2009 & 93 & 78.4 & 0 & 0 \\
Hayashi et al.\textsuperscript{27} & 182 & 2013 & 87.4 & 63.2 & 5.1 & 2.7 \\
\hline
\end{tabular}
\end{table}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{tumour_size.png}
\caption{Tumour size pre and post RS (calculating the size in millimetres according to the largest diameter in magnetic resonance imaging).}
\end{figure}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{hearing_preservation.png}
\caption{Hearing preservation, results before and after treatment with RS. Gardner–Robertson scale I: 0–30 dB (good hearing); II: 31–50 dB (useful hearing); III: 51–90 dB (non-useful hearing); IV: >91 dB (poor hearing); V: not testable (cophosis).}
\end{figure}
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What we sought to achieve with this study are longer term results than those published to date nationally, obtaining a tumour growth control after RS greater than 90%, and similar to broader foreign series. However, as we mentioned in the introduction, it is true that RS does not eliminate the tumour, and therefore will not remove the need for us to periodically follow-up our patients.

With regard to the possibility of secondary neoplasms occurring in the long term after treatment with RS, especially epidermoid carcinomas and sarcomas\(^2^\); none of our patients presented with these.

Furthermore, we should highlight that out of the 62 AN seen during the course of the study, none was operated, since possible candidates for surgery either presented associated comorbidities, elevated surgical risk, were elderly, and some were even unwilling to subject themselves to the procedure and opted for observation.

Finally, in selected cases of small-sized AN and in patients of advanced age or with comorbidities, the conservative option of observation and strict monitoring with RM is an alternative which should be taken into consideration as, in general, neither clinical morbidity nor radiological imaging showed significant changes. And moreover, there is always time for surgical intervention.

Conclusions

Although microsurgery continues to be the treatment of choice for AN, we consider RS to be a valid and effective alternative in selected patients as it is a less invasive technique with lower associated comorbidity, good tumour growth control rate, better hearing preservation and good control in cranial nerve function. Therefore, RS is best indicated for small-sized AN where there is an obvious surgical risk.

Conflict of Interest

The authors have no conflict of interest to declare.

References