Neuroophthalmological evaluation after Gamma Knife surgery for cavernous sinus meningiomas

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Object. Treatment options for patients with cavernous sinus meningiomas (CSMs) include microsurgical tumor resection, radiotherapy, and radiosurgery. Gamma Knife surgery (GKS) is increasingly being used because it is associated with lower mortality and morbidity rates than microsurgery. The purpose of this study was to assess the role of GKS in the treatment of CSM and to thoroughly analyze the clinical response to GKS.

Methods. Between January 2001 and December 2005, 123 patients (25 men and 98 women; mean age 62.6 ± 11 years, range 31–86 years) who underwent treatment for CSMs were included in this study. Of these, 41 patients underwent microsurgery before GKS, whereas the remaining 82 had GKS as a first-line therapy after a diagnosis was made based on magnetic resonance imaging findings. Dysfunction in cranial nerves (CNs) II, III, IV, V, and VI was noted in 74 patients at the time of GKS. The mean tumor volume was 7.99 cm³ (0.7–30.5 cm³). The mean prescription dose to the tumor margin was 13.8 ± 1.1 Gy (range 10–20 Gy).

Results. The overall tumor control rate was 98.4% with a median follow-up of 36 months. The actuarial tumor control rate at 5 years was 90.5%. A reduction in tumor volume was observed in 53 patients (43.1%), whereas in 68 patients (55.3%) no volumetric variation was recorded. Of the 74 patients who presented with CN deficits, improvement was noted in 23 (31.1%).

Conclusions. Gamma Knife surgery is a useful treatment for CSM both as a first- or second-line therapy. It is a safe and effective treatment for tumors located close to the optic pathways. (DOI: 10.3171/FOC-07/12/E10)

Key Words • cavernous sinus • Gamma Knife surgery • meningioma • neuroophthalmological evaluation

Meningiomas are usually benign neoplasms arising from the arachnoid cap cells. Meningiomas most frequently become symptomatic because of their mass effect on cerebral structures or induction of seizures. They account for ~ 20% of all primary intracranial tumors and represent the most common tumor affecting the cavernous sinus.

Although microsurgery remains the gold standard for treating intracranial meningiomas, different authors have shown that total resection of CSMs represent a formidable challenge to the neurosurgeon. The commonly reported mortality and morbidity rates range between 2 and 7% and 10 and 65%, respectively. In particular, CN damage is reported to occur in 17–43% of cases. The results of the microsurgical approach have led to the evaluation of a different strategy.

Abbreviations used in this paper: CN = cranial nerve; CSM = cavernous sinus meningioma; MR = magnetic resonance; GKS = Gamma Knife surgery.

Gamma Knife surgery is increasingly being used as both adjuvant and primary treatment for parasellar meningiomas. There is a growing body of literature showing the effectiveness of GKS in achieving long-term tumor control. However, few authors have specifically analyzed the effects of GKS on CSM concerning neuroophthalmological function. We performed this retrospective study to evaluate the neuroophthalmological status in patients with CSM treated with GKS.

Clinical Material and Methods

Patient Population

Between January 2001 and December 2005, 127 patients underwent GKS for CSMs. Of these, 123 patients were available for follow-up (2 patients died of unrelated causes, and 2 patients were lost to follow-up).

The mean patient age was 62.6 ± 11 years (range 31–86 years); 25 were men and 98 were women. Microsurgery was performed in 41 patients before GKS; the remaining
82 underwent GKS as the first-line therapy after a diagnosis based on MR imaging findings. All patients underwent neuroophthalmological evaluation (visual acuity, visual field, and oculomotor examination) the day before GKS. Cranial nerve deficits were noted in 74 patients prior to GKS (Table 1). Of these, 24 had undergone previous microsurgery. Evaluation of CN function before GKS is shown in Table 1.

**Gamma Knife Surgery**

All patients underwent stereotactic radiosurgery with the aid of the Leksell Gamma Knife Unit model C (Elekta Instruments). A Leksell stereotactic head frame (model G) was positioned after mild sedation and a local anesthetic was administered. Magnetic resonance images (1.5-tesla, Magnetom Vision, Siemens) were performed for tumor visualization. The MR imaging sequences used are as follows: T1- and T2-weighted without contrast and T1-weighted with contrast. Slices were obtained every 2 mm in axial and coronal planes. The GammaPlan system (Elekta Instruments) was used for treatment planning and dose calculation.

The mean tumor volume was 7.99 cm³ (0.7–30.5 cm³), and the mean prescription dose to the tumor margin was 13.8 ± 1.1 Gy (range 10–20 Gy). To obtain more conformal planning, multiple small isocenters were used. The isodose line for the tumor margin varied from 40 to 54%; the 50% isodose line was used in the majority of the patients.

The radiation dose to the optic pathways and the highest dose to the optic apparatus were measured by the computer dose plan (GammaPlan). The optic pathways received a maximum dose of 10 Gy.

All patients were discharged the day after treatment, and none experienced acute radiation injury such as vomiting or nausea.

**Follow-Up Protocol**

Clinical evaluation was performed in our outpatient service for patients living near the hospital and by phone interview for the others. Magnetic resonance imaging and neuroophthalmological examination were performed at 6 and 12 months after GKS and every year thereafter. Tumor reduction was calculated by volumetric examination with OsiriX (version 2.7.5).

**Statistical Analysis**

Statistical analysis was performed using StatView 5.0 (SAS Institute Inc.). A probability value < 0.05 was considered significant. The survival data were calculated using the nonparametric Kaplan–Meier method.

The prognostic value of the individual covariates was obtained by using the Cox proportional hazards model. The following data were entered: age, sex, dose, and tumor volume, and whether pre-GKS microsurgery was performed.

**Results**

At the end of the observation period (March 2007), the median follow-up period was 36 months (range 7–71 months).

**Tumor Growth Control**

Overall tumor growth control was achieved in 121 patients (98.4%). The tumor growth control rate was 99.9% in patients who had not undergone microsurgery before GKS, whereas it was 97.6% in patients who had had microsurgery before GKS. The actuarial tumor control rate at 5 years was 90.5% (Fig. 1).

Tumor reduction (Fig. 2) was observed in 53 patients (43.1%), whereas the tumor remained unchanged in 68 patients (55.3%). Tumor recurrence was observed in 2 patients only (1.6%); one of them underwent further microsurgery and the other refused it.

Statistical analysis failed to show a significant difference in tumor growth control rate between patients who had undergone microsurgery before GKS and patients in whom GKS was the first-line treatment.

**Clinical Response**

Of the 74 patients with a CN dysfunction before GKS,

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**TABLE 1**

*Cranial nerve function in patients with CSMs treated by GKS*

<table>
<thead>
<tr>
<th>Neurological Deficit (affected CN)</th>
<th>Pre-GKS</th>
<th>Post-GKS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Improved</td>
<td>Unchanged</td>
</tr>
<tr>
<td>II</td>
<td>42 (12)</td>
<td>6 (0)</td>
</tr>
<tr>
<td>III</td>
<td>28 (12)</td>
<td>8 (4)</td>
</tr>
<tr>
<td>IV</td>
<td>11 (2)</td>
<td>2 (0)</td>
</tr>
<tr>
<td>V</td>
<td>13 (10)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>VI</td>
<td>31 (18)</td>
<td>12 (9)</td>
</tr>
</tbody>
</table>

* Numbers in parentheses indicate CNs in patients treated by GKS only.

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**Fig. 1.** Graph showing the progression-free survival rate in 123 patients affected by CSMs treated using GKS. The actuarial tumor control rate at 5 years was 90.5%.
23 (31.1%) experienced an improvement after radiosurgery. Of these, 13 underwent GKS as a first-line treatment, whereas 10 underwent GKS as an adjuvant therapy (Table 1). The acuity and visual field defects improved in 6 cases, trochlear nerve function improved in 1 case, trigeminal nerve symptoms improved in 1 case, oculomotor nerve deficit improved in 8 cases, and abducens nerve deficit improved in 12 cases. Interestingly, patients who had undergone radiosurgery as a first option showed better improvement in CN function. This happened especially for oculomotor and abducens nerve function. We did not find any significant correlation between CN function after GKS and the examined variables (age, sex, dose, tumor volume, and pre-GKS cranial nerve function).

Gamma knife surgery–related adverse effects occurred in 5 patients (4.1%). None of the patients experienced deterioration of visual acuity and visual field. Only 1 patient developed a new abducens nerve palsy 8 months after GKS. Two patients developed facial pain 3 and 4 months after GKS; the conditions in both resolved spontaneously in the follow-up.

Two patients experienced generalized convulsion and focal seizure 3 and 6 months after radiosurgical treatment. A T2-weighted MR image showed edema that disappeared 24 months after GKS.

Discussion

Cavernous sinus meningiomas commonly envelop major blood vessels and CNs. To minimize mortality and major morbidity, total resection is not always feasible. Knosp and colleagues reported on 29 patients with CSMs. Cranial nerve function improved in 7 to 50% of patients and worsened in 14 to 58% (depending on the CN evaluated). DeMonte et al. achieved total tumor removal in 76% of patients. They reported that CN function improved in 14%, remained unchanged in 80%, and deteriorated in 6%. Sekhar and associates achieved a 78% rate of total removal in 114 patients and a 43% rate of preserved postoperative extraocular muscles function. Thus, GKS has been proposed for cranial base meningiomas as an adjuvant treatment or as an alternative therapy.

Tumor Growth Control

The overall tumor control rate was 98.4% with a median follow-up of 36 months. Similar results have been found by various authors who have reported tumor control rates of 82 to 100% in a period ranging from 15 to 82 months. Tumor reduction has been observed in 43.1%, whereas 55.3% of meningiomas have remained stable. Zachenofer and coworkers reported a reduction in tumor size in 33%
of patients. Nicolato and colleagues26 reported a tumor shrinkage rate in 43.5% of patients with an average follow-up of < 30 months and in 80% of patients with a longer follow-up. Kondziolka and coauthors12 also reported a reduction in meningioma volume after long-term observation.

In our study, the tumor control rates in patients who underwent GKS as the first treatment and in patients who had previously undergone microsurgical removal before GKS were 99.9 and 97.6%, respectively. The difference between these 2 subgroups does not appear to be statistically significant. These findings are, however, similar to those reported in the aforementioned reports. In a series of parasagittal meningiomas, Lee et al.35 reported a higher tumor control rate in patients undergoing radiosurgery only compared with patients who had undergone previous surgical treatment. Residual tumors may in fact be more difficult to delineate on GammaPlan due to postoperative meningeal enhancement.

Clinical Response

Cranial nerve radiation tolerance has been well known since the first evidence reported by Tishler and colleagues13 who observed no complications in patients treated with < 25 Gy to the cavernous sinus region. No visual complications occurred in patients in whom the dose to the optic pathways was kept at < 10 Gy. These observations have been later confirmed by the reports of Morita et al.,10 and Leber et al.14 None of our patients suffered visual field deterioration or visual acuity loss. Instead, in the present study we report a clinical improvement in CN function in 31.1% of the patients presenting with a deficit at the time of GKS.

Our data do not support any significant statistical correlation between the rate of clinical improvement and the aforementioned variables (age, sex, dose, tumor volume, and pre-GKS microsurgery). Nonetheless we noticed a trend toward a better improvement for CNs III and VI (Table 1). Our data are in line with the results reported in the literature.26

Furthermore, we noticed a slightly higher percentage of clinical improvement in those patients who underwent GKS as a first-line therapy. In this subgroup, the functional deficit might reflect a reversible damage due to either tumoral compression or infiltration. On the other hand, as suggested by Nicolato and associates,20 the pretreatment neurological deficit in patients previously undergoing microsurgery might be the consequence of irreversible surgical injury to the nervous structure.

The incidence of adverse effects in our study is low (4.1%). This value is comparable with what is reported in the literature,26 where it has been reported to vary between 3 and 7%.17

In our series, 2 patients experienced seizure. The rate of post-GKS seizures has been reported to be between 1.3 and 5.8%.26 Some authors hypothesize that postradiosurgery seizure might be due to a radiation-related injury; seizure resolution after corticosteroid therapy has been reported.9,15

Conclusions

Gamma Knife surgery is an effective treatment for CSMs. Good tumor control can be achieved with a very low incidence of adverse effects. Cranial nerve function can improve after the treatment.

References

21. O’Sullivan MG, van Loveren HR, Tew JM Jr: The surgical re-
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