Gamma Knife Surgery for Cavernous Sinus Meningiomas

Radiocirurgia Gamma Knife em Meningiomas do Seio Cavernoso

Julio C. Antico

ABSTRACT

Introduction: Patients with cavernous sinus meningiomas (CSM) have an elevated risk of surgical morbidity and mortality. Recurrence is often observed after partial resection. Stereotactic radiosurgery (SRS), either alone or combined with surgery, represents an important advance in CSM management, but long-term results are still lacking. Methods and Materials: A total of 98 CSM patients, treated from January 2000 to December 2013, were retrospectively reviewed. The mean follow-up was 86.8 months (range = 17.1–179.4 months). Among the patients, 15 were followed for more than 10 years. There was a female predominance (75.46%). The age varied from 24 to 79 years (mean = 49.6). From all, 98 patients, 57 (53.4%) received SRS alone, and 41 patients (46.6%) had undergone surgery before Gamma-knife surgery (GKS). A dose of 14 Gy was prescribed to isodose curves from 50% to 90%. In 25 patients (28.4%), as a result of the proximity to organs at risk, the prescribed dose did not completely cover the target. Results: After GKS, 53 (51.9%) patients presented with tumor volume reduction; 36 (35.2%) remained stable, and 9 (8.8%) had tumor progression. The progression-free survival was 87.23% at 5 years, and 79.5% at 10 years. Age, sex, maximal diameter of the treated tumor, previous surgery, and complete target stereotactic radiosurgery can control tumor growth if the whole mass can be irradiated by dosages of more than 14 Gy. When optimal radiosurgical planning is not feasible because of large size, irregular shape, or proximity of the tumor to visual pathways, the use of limited surgical resection before radiosurgery is the best option, and should provide sufficient long-term tumor control with minimal complications.

Key words: Gamma-knife; Radiosurgery; Meningioma; Cavernous sinus

RESUMO

Introdução: Pacientes com meningiomas do seio cavernoso (MSC) apresentam risco elevado de mortalidade e morbidade cirúrgica. Após ressecção parcial frequentemente é observada recorrência. A Radiocirurgia estereotáxica (SRS), sozinha ou combinada a cirurgia, representa um importante avanço na gestão do MSC, mas os resultados em longo prazo ainda são escassos. Materiais e Métodos: Foi analisado retrospectivamente, um total de 98 pacientes tratados por MSC, no período de janeiro de 2000 a dezembro de 2013. O follow-up médio foi de 86,8 meses (intervalo de 17,1 – 179,4 meses). Dentre os pacientes, 15 foram acompanhados por mais de 10 anos. Houve predominância feminina (75,46%). A idade variou de 24 a 79 anos (média = 49,6). Dos 98 pacientes, (53,4%) receberam somente SRS, e 41 pacientes (46,6%) realizaram cirurgia antes da radiocirurgia (GKS). Uma dose de 14 Gy foi prescrita para curvas de isodose de 50% a 90%. Em 25 pacientes (28,4%), devido à proximidade de órgãos em risco, a dose prescrita não atingiu completamente o alvo. Resultados: Após GKS, 53 (51,9%) pacientes apresentaram redução de volume tumoral; 36 (35,2%) permaneceram estáveis, e 9 (8,8%) apresentaram progressão do tumor. A taxa de sobrevida livre de progressão foi 87,23% em 5 anos, e 79,5% em 10 anos. Fatores como idade, sexo, diâmetro máximo do tumor tratado, cirurgia prévia e cobertura total do alvo não mostraram associações significativas com prognóstico. Dentre os 98 pacientes tratados, 17 apresentaram morbidade relacionada à SRS e 6 desses pacientes se recuperaram espontaneamente. Conclusões: Os dados indicam que a radiocirurgia estereotáxica pode controlar crescimento tumoral, se toda a massa puder ser irradiada com doses de mais de 14 Gy. Quando o planejamento radiocirúrgico ideal não for viável por causa de tamanho excessivo do tumor, forma irregular ou proximidade do tumor com sistemas visuais, o uso de ressecção cirúrgica limitada antes de radiocirurgia é a melhor opção e deve fornecer controle de tumor em longo prazo suficiente com mínimas complicações.

Palavras-Chave: Gamma-knife; Radiosurgery; Meningioma; Seio Cavernoso

INTRODUCTION

Despite improvements achieved in neurosurgery for cavernous sinus meningiomas, there is still high morbidity and mortality relating to cranial nerve injuries1-3.

The usefulness of radiosurgery for cavernous sinus meningiomas was recently reported4,5. It is possible to achieve a significant tumor growth control rate with low morbidity. Nevertheless, cavernous sinus meningiomas often compress the optic apparatus, and surgical resection is recommended in these cases. Radiation doses to the optic apparatus are limited and result in a reduced dose for tumors, which has been reported to correlate with lower tumor growth control rates4. Surgical resection is sometimes difficult, even in cases of partial or subtotal removal of tumors that are situated entirely in the cavernous sinus7. We planned to treat these lesions primarily by using low-dose radiosurgery, even for tumors compressing...
the optic apparatus. In our experience this strategy is helpful for cavernous sinus meningiomas.

**Patients and Methods**

We treated 98 consecutive patients with cavernous sinus meningiomas between January 2000 and December 2013. Patients underwent gamma knife radiosurgery (GKS) with a 201-source cobalt-60 gamma knife (Elekta Instruments Inc.). The age range was 18 to 81 years (mean = 55 yr). Thirty-six patients (34.3%) underwent surgery before GKS, including 9 patients who were subjected to surgery more than twice because of tumor regrowth. The other 62 patients (60.76%) were diagnosed only by magnetic resonance imaging (MRI) before radiosurgery. None of the patients had previously received external-beam radiotherapy.

Preradiosurgical neurological deficits are shown in Table 1. Neurological deficits occurred in 21% of patients who underwent surgical resections. Seven patients were diagnosed asymptotically before radiosurgery; their cavernous sinus meningiomas were diagnosed incidentally at screening for other intracranial lesions. Among them, one patient experienced diplopia and facial numbness secondary to left trigeminal and abducens nerve palsy two years later, during the period before radiosurgery. Tumor extension was classified according to classification proposed by Sekhar (Table 2).

The relationship between the optic apparatus and the tumor was examined on magnetic resonance images (MRI) obtained at radiosurgery. The findings were 21 patients (20.58%) with tumors compressing the optic apparatus, and 11 patients (10.78%) with tumors attached to the optic apparatus. There was some distance (mean = 3.4 mm; range 1–16 mm) between the optic apparatus and the tumor in 28 patients (27.44%). The mean tumor diameter ranged from 11 to 37.0 mm (mean = 27.9 mm); tumor volume ranged from 0.9 to 26.6 cm³ (mean = 4.3 cm³). In tumors compressing or adhering to the optic apparatus, the tumor marginal dose was reduced to 8 Gy. All patients were treated with a 50% isodose, and discharged the day after GKS without acute radiation injury, such as nausea and vomiting. Follow-up imaging was requested at 4-month intervals during the first year, at 6-months intervals on the second year, and after once a year. Tumor reduction was calculated as any measurable reduction, anteroposterior or mediolateral.

**Table 1**

<table>
<thead>
<tr>
<th>Feature</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>no. of patients</td>
<td>98</td>
</tr>
<tr>
<td>tumor volume (cm³)</td>
<td>0.9 - 26.6; median 4.3</td>
</tr>
<tr>
<td>tumor diameter (lx y z/3; cm)</td>
<td>1.1 - 3.7; median 2</td>
</tr>
<tr>
<td>extension outside CS (33 patients)</td>
<td></td>
</tr>
<tr>
<td>middle cranial fossa</td>
<td>88</td>
</tr>
<tr>
<td>petrous or petroclival region</td>
<td>17</td>
</tr>
<tr>
<td>tentorium</td>
<td>13</td>
</tr>
<tr>
<td>orbit</td>
<td>9</td>
</tr>
<tr>
<td>suprasellar region</td>
<td>12</td>
</tr>
<tr>
<td>radiosurgical dosimetry (Gy)</td>
<td></td>
</tr>
<tr>
<td>maximum dose</td>
<td>24 - 36; median 32</td>
</tr>
<tr>
<td>dose to margin</td>
<td>12 - 16; median 14</td>
</tr>
<tr>
<td>Number of isocenter</td>
<td>6 - 18; median 12</td>
</tr>
<tr>
<td>dose to brainstem (Gy)</td>
<td>1 - 10; median 4</td>
</tr>
<tr>
<td>dose to optic nerve (Gy)</td>
<td>0.3 - 7; median 5</td>
</tr>
</tbody>
</table>

**Table 2**

<table>
<thead>
<tr>
<th>Cranial Nerve</th>
<th>At Radiosurgery</th>
<th>Improved</th>
<th>Worsened</th>
</tr>
</thead>
<tbody>
<tr>
<td>II</td>
<td>8 (5)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>III</td>
<td>18 (6)</td>
<td>0</td>
<td>2 (0)</td>
</tr>
<tr>
<td>IV</td>
<td>8 (5)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>V</td>
<td>31 (9)</td>
<td>5 (1)</td>
<td>6 (1)</td>
</tr>
<tr>
<td>VI</td>
<td>24 (9)</td>
<td>5 (0)</td>
<td>0</td>
</tr>
<tr>
<td>VII</td>
<td>3 (3)</td>
<td>1 (1)</td>
<td>0</td>
</tr>
<tr>
<td>VIII</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

* Values in parentheses reflect the number of deficits caused by previous surgery.

**Results**

The tumor control rate observed after 5 years was 87.22%. Using Kaplan-Meir survival analysis, this control rate remained the same for up to 8 years. In nine patients (8.92%), MRI showed evidence of progressive tumor growth. These patients were defined as a failing radiosurgery procedure. No recurrence was observed when the entire tumor received a minimum dose of 15 Gy. In cases in which the tumor received between 9 and 11 Gy, a 20% recurrence rate was observed. Adverse radiation effects occurred in 6 patients (5.88%). Two patients suffered a third and fourth cranial nerve palsy...
and four patients experienced a new trigeminal dysfunction (V and V3 paresthesias). These adverse effects were defined as the presence of clinical or neurological deterioration in the absence of tumor growth, confirmed on MRI.

**Figure 1.** A. April 30, 2009. B. May 16, 2011.

**Figure 2.** A. October 15, 2003. B. November 1, 2011.

**Figure 3.** A. August 01, 2001. B. June 03, 2011.

**Figure 4.** A. June 03, 2002. B. September 21, 2011.

**Figure 5.** Effects of Gamma Knife Surgery in extensions outside CS

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**DISCUSSION**

The results of surgery as a treatment for cavernous sinus meningiomas have improved with the use of modern microsurgical techniques, but surgery is still accompanied by some morbidity. Sekhar et al. operated on 114 patients and achieved a 78% rate of total removal and a 43% rate of preserving the same or better postoperative extraocular muscle functions. One hundred eight patients (95%) could return to their previous occupations but still had high rates of postoperative ocular dysfunction. They also experienced 20% regrowth after incomplete resection at 3.9 years of follow-up.

Radiosurgery may be considered less invasive than conventional radiation therapy from the standpoint of radiation effects on surrounding structures. Also, long-term malignant transformation is likely to occur much less frequently with radiosurgery than with radiotherapy because of the smaller volume of normal tissue irradiated. If radiosurgery has the

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same results as conventional radiation therapy for tumor growth control and preservation of cranial nerve function, radiosurgery is indicated instead of conventional radiation therapy.

The usefulness of radiosurgery for meningiomas has been reported\(^1,16\). There have been several reports of cavernous sinus meningiomas treated by GKS. All patients achieved tumor growth control with a mean of 39 months of follow-up. They also recommended partial or subtotal resection for preserving postoperative cranial nerve function when surgical resection of these tumors was performed. Liscak et al.\(^14\) reported 67 patients who received a mean marginal dose of 12 Gy. None of the patients experienced tumor growth, and there was a transient morbidity of 3.8% during a mean of 19 months of follow-up. They recommended that tumors close to the optic nerve also could be treated with radiosurgery by use of a new neuroradiological and radiation dose plan. Chen et al.\(^2\) reported 69 patients with cavernous sinus lesions, including 35 meningiomas. Only one patient (1.5%) remained with permanent deficits, whereas 6 patients (9%) improved clinically, a dose of 15 Gy to the tumor margin was used.

The radiation dose for the optic apparatus is very important for the radiosurgical treatment of cavernous sinus meningiomas because these tumors often are adjacent to or compressing the optic apparatus. Tishler et al.\(^25\) reported that the cranial nerves in the cavernous sinus could tolerate approximately 40 Gy, but there was a 24% incidence of visual disturbances when the optic apparatus received radiation of more than 8 Gy during radiosurgery. Leber et al.\(^13\) reported that the optic nerve could be irradiated with less than 10 Gy with no complication. However, a radiation dose of 10 to 15 Gy had a 26.5% risk of optic neuropathy, and doses greater than 15 Gy had a 77.8% risk of optic neuropathy. Also, cranial nerves in the cavernous sinus could be irradiated with a mean of 14.1 Gy and the trigeminal nerve with a mean of 12.9 Gy without any new deficits. Depending on an optimal dose for the tumor margin, the tumors close to or adhering to the optic nerve would have to be resected before radiosurgery to prevent optic neuropathy. In these situations, the most suitable approach may include decompression of the tumor mass to increase the distance between the optic apparatus and the tumor. However, surgical resection carries the possibility of some morbidity.

In our series tumor marginal dose was reduced to 8 to 10 Gy in tumors adhering to or compressing the optic apparatus. Also, radiation doses to the optic apparatus were planned to not exceed 8 Gy. If the tumor compressed the optic apparatus, we did not use a beam-blocking pattern, and the marginal dose was kept a small distance away from the optic apparatus. In these cases, the tumor close to the optic apparatus could be irradiated with less than 8 Gy without allowing regrowth of the tumor. Perhaps if most of the tumor receives a sufficient dose, the entire tumor does not require the same dose. We still consider the optimal dose for the meningioma to be 12 Gy to the tumor margin, but from our experience, a reduced radiation dose of 8 to 10 Gy may be acceptable for cavernous sinus meningiomas close to the optic apparatus. Our actual tumor growth control at 5 years was 87.22%. Our study will also require further long-term follow-up.

Patients who develop neurological deficits during the observation period experience a decrease in quality of life with the deterioration of the cranial neuropathy. In our conception a patient with an asymptomatic cavernous sinus meningioma may also be a candidate for radiosurgery if the tumor is growing. Our treatment data post-radiosurgery show very low rates of radiation injury, high rates of tumor growth control, and preservation of cranial nerve function.

**Conclusions**

Gamma knife radiosurgery seems to be a safe and effective option for a subgroup of patients harboring a cavernous sinus meningioma. In a significant number of patients, oculomotor functional restoration can be observed. The treatment appears to be an alternative to surgical removal of confined enclosed cavernous sinus meningiomas and should be proposed as an adjuvant to surgery in case of extensive meningiomas.

**References**


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