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Clinical Study

Stereotactic radiosurgery of meningiomas following resection: Predictors of progression

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ABSTRACT

Residual or recurrent meningiomas after initial surgical resection are commonly treated with stereotactic radiosurgery (SRS), but progression of these tumors following radiosurgery is difficult to predict. We performed a retrospective review of 60 consecutive patients who underwent resection and subsequent Gamma Knife (Elekta AB, Stockholm, Sweden) radiosurgery for residual or recurrent meningiomas at our institution from 2001–2012. Patients were subdivided by Simpson resection grade and World Health Organization (WHO) grade. Cox multivariate regression and Kaplan–Meier analyses were performed to assess risk of tumor progression. There were 45 men (75%) and 15 women (25%) with a median age of 56.8 years (range 26.5–82 years). The median follow-up period was 34.9 months (range 6–108.4 months). Simpson grade 1–3 resection was achieved in 17 patients (28.3%) and grade 4 resection in 43 patients (71.7%). Thirty-four tumors (56.7%) were WHO grade 1, and 22 (36.7%) were WHO grade 2–3. Time from resection to SRS was significantly shorter in patients with Simpson grade 4 resection compared to grade 1–3 resection ($p < 0.01$), but did not differ by WHO grade ($p = 0.17$). Post-SRS complications occurred in five patients (8.3%). Overall, 19 patients (31.7%) experienced progression at a median of 15.3 months (range 1.2–61.4 months). Maximum tumor diameter >2.5 cm at the time of SRS ($p = 0.02$) and increasing WHO grade ($p < 0.01$) were predictive of progression in multivariate analysis. Simpson resection grade did not affect progression-free survival ($p = 0.90$). The mortality rate over the study period was 8.3%. SRS offers effective tumor control for residual or recurrent meningiomas following resection, especially for small benign tumors.

1. Introduction

Complete or near-complete resection of meningiomas is often not possible, and even when gross total resection (GTR) is achieved, tumors may still recur. Recurrence of intracranial meningiomas after resection approaches 20% with long-term follow-up [1]. Stereotactic radiosurgery (SRS) has gained favor as a minimally invasive approach to treat residual or recurrent meningiomas after initial surgical resection. While the combination of microsurgery and SRS has proven efficacious for tumor control [2–5], few series have analyzed for factors predictive of progression following SRS. Identifying factors associated with future progression is important for optimal long-term management of these patients and also may guide neurosurgeons to achieve specific goals during resection.

In order to evaluate the efficacy of SRS to treat residual or recurrent meningiomas, we analyzed rates and predictors of tumor progression in patients who underwent SRS after initial surgical resection. Evaluations were made between patients with Simpson grade 1–3 *versus* grade 4 resection and between World Health Organization (WHO) grade 1 *versus* grade 2–3 tumors.

2. Patients and methods

2.1. Patient population

We performed a retrospective review of an Institutional Review Board approved database containing 518 consecutive patients treated with Gamma Knife radiosurgery (Elekta AB, Stockholm, Sweden) for intracranial meningiomas at the University of Virginia from 2001–2012. Patients were excluded from analysis if they did not undergo previous resection at our institution or had less than 6 months of follow-up data.

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2.2. Operative classification

Resection grade was classified according to the Simpson grading system through retrospective review of operative notes by a neurosurgeon blinded to outcome as follows: grade 1 = GTR including resection of underlying bone and associated dura; grade 2 = GTR including coagulation of dural attachment; grade 3 = GTR without removal or coagulation of dural attachment; and grade 4 = subtotal resection [6]. The 2007 WHO criteria were utilized for histopathologic diagnosis for patients who underwent surgery since 2007 [7]. The 2000 WHO criteria was utilized for patients who underwent surgery from 2001–2006 [8]. Skull base location included the following tumor sites: olfactory groove, planum sphenoidale, cerebellopontine (CP) angle, Meckel's cave, clinoidal, petroclival, suprasellar, and cavernous sinus.

2.3. SRS

Our radiosurgical technique has been previously described [9,10]. Patients underwent placement of a Leksell model G stereotactic frame (Elekta Instruments, Norcross, GA, USA) in the operating room under monitored anesthetic care. Pre- and post-contrast thin-slice (1 mm) volume acquisition axial and coronal MRI sequences were then obtained for treatment planning. Thin-slice stereotactic CT scan was obtained with and without contrast for patients with medical contraindications to MRI. Radiosurgical dose plans were constructed by a neurosurgeon, medical physicist and radiation oncologist. Elekta's Gamma Plan software was used for dose planning. Since 2007, we have used the Gamma Knife Perfexion system. Prior to that, we used the Leksell Gamma Unit Model U until July 2001 when the C Model (Elekta Instruments) replaced it. All patients in this series were treated with single session radiosurgery.

2.4. Clinical and radiological follow-up

Patients were routinely followed with clinical and radiological follow-up every 6 months for WHO grade 1 meningiomas and every 3 months for WHO grade 2–3 meningiomas. Follow-up was performed preferentially at the University of Virginia. If patients were unable to travel to our institution, follow-up imaging and neurologic status were obtained in correspondence with outside referring hospitals and patients' local primary care physicians. All imaging studies were reviewed by a University of Virginia neurosurgeon and neuroradiologist. Radiological progression was defined as a $\geqslant$15% increase in tumor volume as compared to the volume at the time of SRS [11]. Overall progression was defined as patients with neurological deterioration in relation to their tumors or tumors with radiological progression requiring further treatment, including surgical resection, SRS or chemotherapy. Peritumoral edema was defined as the presence of post-SRS T2-weighted hyperintensity changes around the tumor. Clinical correlation in patients experiencing headaches, seizures and/or focal neurological deficits established symptomatic peritumoral edema.

2.5. Statistical analysis

Statistical analyses of categorical variables were carried out using chi-squared and Fisher's exact tests. Statistics of means were carried out using unpaired Student's *t*-test and Wilcoxon rank sum tests when variables were not normally distributed. Kaplan–Meier analysis was performed for risk of tumor progression. Factors predictive of tumor progression ($p < 0.15$) [12] were entered into Cox regression analysis to assess hazard ratios. The covariates analyzed included sex, tumor location, proliferative index, history of previous resection, history of previous radiotherapy, tumor diameter, Simpson grade, WHO grade, SRS margin dose and number of isocenters. Clinically significant variables and interaction expansion covariates were further assessed in both Cox and logistic multivariable analysis as deemed relevant. *p*-values of $\leqslant$0.05 were considered statistically significant.

3. Results

3.1. Patient and tumor characteristics

We identified 60 patients who underwent surgical resection at our institution and subsequently received SRS for residual or recurrent meningiomas. Preoperative patient and tumor characteristics are summarized in Table 1. There were 45 women (75%) and 15 men (25%) with a median age of 56.8 years (range 26.5–82 years) at the time of resection. Prior to surgical resection at our institution, 18 patients (30%) had undergone previous resection and 10 patients (16.7%) had undergone previous radiotherapy. Of these 10 patients with previous radiotherapy, eight had been previously diagnosed with WHO grade 2 tumors and two had been previously diagnosed with WHO grade 3 tumors. The most common tumor locations were parasagittal (n = 13; 21.7%) and CP angle (n = 9; 15.0%). The median maximum tumor diameter prior to resection was 4.2 cm (range 1.3–7.9 cm).

Operative findings are summarized in Table 2. Simpson grade 1–3 resection was achieved in 17 patients (28.3%) and grade 4 resection in 43 patients (71.7%). Thirty-four tumors (56.7%) were

Table 1
Preoperative patient and tumor characteristics

Characteristic	Number (%)
Female	45 (75.0)
Age at surgery, years[a]	56.8 (26.5–82)
Previous resection	18 (30.0)
Previous radiotherapy	10 (16.7)
Location	
Parasagittal	13 (21.7)
CP angle	9 (15.0)
Suprasellar	6 (10.0)
Sphenoid wing	6 (10.0)
Convexity	6 (10.0)
Petroclival	4 (6.7)
Clinoid	4 (6.7)
Planum sphenoidale	4 (6.7)
Olfactory groove	4 (6.7)
Posterior fossa	2 (3.3)
Middle cranial fossa	1 (1.7)
Cavernous sinus	1 (1.7)
Maximum diameter, cm[a]	4.2 (1.3–7.9)

CP = cerebellopontine.
[a] Median (range).

Table 2
Operative findings

Characteristic	Number (%)
Simpson grade	
Grade 1	1 (1.7)
Grade 2	12 (20.0)
Grade 3	4 (6.7)
Grade 4	43 (71.7)
WHO grade	
Grade 1	34 (56.7)
Grade 2	19 (31.7)
Grade 3	3 (5.0)
Unknown	4 (6.7)

WHO = World Health Organization.