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Clinical Study

Gamma Knife radiosurgery for intracranial hemangioblastoma

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ABSTRACT

Gamma knife radiosurgery (GKRS) has become a treatment option for intracranial hemangioblastomas, especially in patients with poor clinical status and also high-risk surgical candidates. The objective of this study was to analyze clinical outcome and tumor control rates. Retrospective chart review revealed 12 patients with a total of 20 intracranial hemangioblastomas treated with GKRS from May 1998 until December 2014. Kaplan-Meier plots were used to calculate the actuarial local tumor control rates and rate of recurrence following GKRS. Univariate analysis, including log rank test and Wilcoxon test were used on the Kaplan-Meier plots to evaluate the predictors of tumor progression. Two-tailed p value of <0.05 was considered as significant. Median follow-up was 64 months (2-184). Median tumor volume pre-GKRS was 946 mm^3 (79-15970), while median tumor volume post-GKRS was 356 mm^3 (30-5404). Complications were seen in two patients. Tumor control rates were 100% at 1 year, 90% at 3 years, and 85% at 5 years, using the Kaplan-Meier method. There were no statistically significant univariate predictors of progression identified, although there was a trend towards successful tumor control in solid tumors (p = 0.07). GKRS is an effective and safe option for treating intracranial hemangioblastoma with favorable tumor control rates.

1. Introduction

Hemangioblastomas (HB) are benign vascular tumors classified as grade I by the World Health Organization (WHO) [1,2] and they comprise around 1 to 3% of all central nervous system (CNS) tumors [3–5]. There is male sex predominance with a peak incidence around the third to fifth decade of life [6]. They are most often sporadic, but approximately 25% of HB can be part of the multiple neoplasia syndrome known as von Hippel-Lindau (VHL) disease, an autosomal dominant condition caused by a mutation of the VHL tumor suppressor gene located on the short arm of chromosome 3 [3]. Both sporadic and VHL-associated intracranial HB are frequently located in the posterior fossa, mainly in the cerebellum, accounting for around 7.5% of all posterior fossa tumors in the adult population [3]. Despite being highly vascular tumors, hemorrhage is rare [7]. Clinical presentation most commonly involves cerebellar symptomatology (gait disturbances, ataxia, dizziness) from tumor edema and/or cyst formation or symptoms due to obstructive hydrocephalus [6,8–10].

Standard treatment for recently diagnosed and symptomatic intracranial HB has been surgical resection, with good outcomes reported in the neurosurgical literature [4,8,9] Although surgical treatment remains the gold standard for intracranial HB, patients with multiple lesions, recurrent and/or residual tumors, tumors in inaccessible locations, patients with poor clinical status who are not good candidates for surgery, as well as those wishing a minimally invasive approach can benefit from alternative therapies. Furthermore, the management of spinal HB has increasingly come under study utilizing less invasive treatment modalities. During the last two decades, there has been increasing interest in different modalities of radiotherapy and stereotactic radiosurgery (SRS) as treatment options for both intracranial and spinal HB [5,6,10–21]. Recent literature has shown that SRS can offer good tumor control rates associated with good clinical outcomes, in a minimally invasive fashion [5,6,11–21]. However, limited data is available regarding the outcome of intracranial HB treated with SRS as most studies have a short term follow-up. The objective of this study was to analyze our experience with Gamma Knife radiosurgery (GKRS – Elekta AB, Stockholm, Sweden) for intracranial HB and report the clinical outcomes and tumor control rates at our institution. Secondarily, we also sought to identify factors predictive of successful or failed treatment to serve as a guide for patient selection.

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2. Material and methods

2.1. Patient population

This study was approved by the local Institutional Review Board. We conducted a retrospective chart review of 12 patients with a total of 20 intracranial HB treated at Cleveland Clinic Gamma Knife Center from May 1998 until December 2014. Median follow-up was 64 months (range, 2–184 months). Data regarding patient characteristics, clinical outcome and radiosurgery parameters were analyzed. Histopathological confirmation of HB was present in eight patients. Four patients were diagnosed on the basis of neuroimaging characteristics of the lesions. Four patients had multiple lesions, of whom three had a positive diagnosis of VHL disease. A total of four patients had VHL disease, with a combined total of 11 tumors. The majority of tumors were solid (n = 18) and located in the cerebellum (n = 19). SRS was employed as the primary treatment in nine lesions, and utilized to treat recurrence after surgical resection in the remaining 11 tumors. Of the nine patients who underwent suboccipital craniotomy for tumor resection prior to GKRS, four of them had multiple surgeries before proceeding with radiosurgery $\widehat{T}$.

All patients underwent follow-up MRI following treatment. Tumor progression or regression was defined as an increase or decrease in 15% of the tumor volume, respectively, compared to the tumor volume on MRI performed on the day of GKRS [6]. Tumor progression following GKR on MRI was considered as failure and the endpoint of the study. All tumor volumes were measured using the last follow-up brain MRI with the iPlan 3.0 Cranial™ software (Brainlab AG, Feldkirchen, Germany).

2.2. Radiosurgery technique

During the study period, the radiosurgical procedures were performed using different Gamma Knife models represented by Model B, C, 4C and, since July 2007, the Perfexion Model (Elekta AB). At our institution, either pre- or post-frame planning MRI images were obtained based on physician preferences. The stereotactic Leksell G-Frame (Elekta AB) was used in all procedures. The frame was applied with local anesthesia to the pin sites and intravenous neuroleptic sedation. High resolution, 1 mm cut, three-dimensional gadolinium contrast enhanced MPRAGE (magnetization prepared rapid acquisition gradient echo) sequence brain MRI was used for stereotactic planning with the Gamma Plan software (Elekta AB). The contrast enhancing tumor was used as the target volume in all cases. The treatment plan was approved by a multidisciplinary team composed of a neurosurgeon, radiation oncologist and medical physicist.

2.3. Statistical analysis

Statistical analysis was carried out using Microsoft Excel and JMP, version 12 (SAS institute, Cary, NC, USA). The descriptive data was expressed as median and range. Kaplan–Meier plots were used to calculate the actuarial local tumor control rates, rate of recurrence following GKRS or surgical resection. Univariate analysis such as log-rank test and Wilcoxon test were used on the Kaplan–Meier plots to evaluate the predictors of tumor progression. Two-tailed p value of <0.05 was considered significant.

3. Results

3.1. Patient demographics

Twelve (n = 12) patients underwent GKRS for twenty tumors (n = 20) over a period of 6 years. Median age at the time of SRS was 51.7 years (range: 34–80 years) with an equal sex distribution. The majority of patients had a single lesion (n = 8) and the number of lesions was 2–5 in those with multiple tumors. SRS was considered for recurrence following surgical resection in the majority of lesions (11 tumors) and one patient underwent surgical resection after SRS. The median follow-up was 64 months. The median time to clinical and radiographic progression was 21.5 and 20.4 months respectively (Table 1).

Nine patients were clinically asymptomatic at the time of radiographic tumor progression, while three presented with classic signs and symptoms of cerebellar dysfunction attributed to HB growth. All patients had demonstrable radiographic progression on MR imaging prior to treatment. Patients with newly diagnosed HB were all asymptomatic, with incidentally diagnosed tumors. Clinical presentation prior to radiosurgical treatment was related to radiological progression on follow-up imaging, present in all 12 patients, rather than the classical cerebellar signs and symptoms related to HB, which were present in three patients (imbalance, dysarthria, ataxia). No patients received other forms of radiation or chemotherapy prior to GKRS treatment.

3.2. Tumor characteristics, radiosurgery parameters and control rates

The majority of tumors were solid (90%) in consistency and located in the cerebellar hemisphere (90%). The median tumor volume pre-GKRS was 946 mm^3 (range: 79–15970 mm^3) and post-GKRS was 356 mm^3 (range: 30–5404 mm^3) at median follow-up of 64 months. The median maximum dimension pre-GKRS was 15 mm (range: 6.7–43.7 mm) and post-GKRS at last follow-up was 10.2 mm (range: 3–31 mm). This equated to a median percentage reduction in tumor volume of 46%, with 17 tumors (85%) being stable or decreased in size, while the remaining three tumors (15%) showed evidence of radiographic progression at median follow-up of 64 months. The median prescription margin dose was 24 Gy (range: 14–25 Gy) with median isodose line of 54.5% as per Radiation Therapy Oncology Group (RTOG) 90–05 guidelines (24). The median maximum dose was 39 Gy (range: 26.1–48 Gy)

Table 1
Patient demographics, complications and follow up after SRS for intracranial hemangioblastoma

	N (range)
Number of patients	12
Male patients	6
Median age at time of SRS, years (range)	51.7 (34–80)
Patients with >1 lesion	4
Range of lesions per patient for patient with multiple lesions	2–5
Total tumors	20
History of von Hippel-Lindau	11
GKRS as initial treatment	9
GKRS for recurrence after surgery	11
Surgery after GKRS	1
Complications	3
Infection	0
Hemorrhage	0
Hydrocephalus	1
Seizures	0
Radiation necrosis	1
Edema	2
Headaches	2
All cause mortality	1
Median follow-up, months	64 (2–184)
Median time to radiographic progression, months	20.4 (14.4–58.8)
Median time to clinical progression, months	21.5 (21.5–21.5)
Median percentage change in volume	−46% (−93% to 48%)

GKRS = Gamma knife radiosurgery, SRS = stereotactic radiosurgery, VHL = von Hippel Lindau disease.