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Clinical commentary

Gamma knife radiosurgery for residual or recurrent intracranial hemangiopericytomas

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ABSTRACT

Residual or recurrent hemangiopericytoma (HPC) has been treated with radiosurgery; however, its long-term outcome is not well known. This study is to investigate the long-term outcome of gamma knife radiosurgery (GKS) for residual or recurrent HPCs. We conducted a retrospective analysis of 18 patients who underwent gamma knife radiosurgery for residual or recurrent HPCs. Of the 18 patients, 10 patients had high-grade HPCs (27 tumors) and 8 had low-grade HPCs (13 tumors). Median overall survival (OS) after the first GKS was 134.7 months and actuarial survival rate at 1, 5, and 10 years was 85.6%, 85.6%, and 37.4%, respectively. At the last follow-up, local tumor control was achieved in 32 (80.0%) of the 40 GKS-treated tumors. New lesions developed out of initial GKS target in 8 patients (44.4%). They were also treated with additional GKS. The actuarial local control rate of 40 tumors at 1-, 3-, and 5-years was 89.3%, 60.9%, and 37.5%, respectively. The median local recurrence-free interval of 40 tumors after initial GKS for each lesion was 86.1 months for low-grade and 40.5 months for high-grade tumors ($p = 0.010$). Extracranial metastases developed in 7 (38.9%) patients with high-grade pathology and became a cause of death in 3 patients. Intracranial tumor control can be achieved over the long term, though additional GKS is frequently necessary. Extracranial metastasis is common in HPC of high-grade pathology. Close surveillance and aggressive treatment is recommended not only for intracranial tumor but also for possible extracranial metastases.

1. Introduction

Hemangiopericytomas (HPCs) are rare, highly cellular, and vascularized mesenchymal tumors arising from the pericytes of Zimmerman, cells surrounding the capillary and postcapillary venules [1]. These tumors account for 0.4% of all primary central nervous system (CNS) tumors and constitute 2.5% of all meningeal tumors [2,3]. HPCs have slight male predominance [2,4,5] and the mean age of presentation is between 38 and 42 years [6,7]. For many years, there have been controversies about whether HPCs should be included in a distinct entity in the classification of CNS tumors. Only in 1993, World Health Organization (WHO) distinguished HPC from meningioma as a distinct clinicopathological entity on the basis of their tendency to recur locally and metastasize outside the CNS, as well as their immunohistochemical, ultrastructural, and genetic characteristics [5,8–13].

Subsequently, HPCs were divided into 2 pathological subclasses i.e., WHO grade II and III (anaplastic variant) [4]. Recently, solitary fibrous tumor (SFT) is considered to form a spectrum of disease with CNS HPCs. They share some histopathological features and have an overlapping immunophenotype [14]. Aggressive surgical resection is the standard treatment. However, frequently long-term tumor control is not possible with surgical resection alone and postoperative adjuvant radiotherapy was suggested to be beneficial in reducing local recurrence rate [2]. Meanwhile, the debates for the efficacy of postoperative radiotherapy for residual or recurrent lesion exist [2,15–17]. Gamma knife radiosurgery (GKS) has been proposed as an alternative option with some advantages over fractionated radiotherapy.

However, long-term follow-up is lacking in most of the study and there are only a few reports that analyzed the outcome of GKS according to the histologic grade of HPCs [18]. We reviewed long-term clinical course in 18 patients who had undergone GKS for HPCs and investigated outcome in different histological grades.

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2. Materials and methods

2.1. Patient population

Medical records of 18 patients who underwent GKS from September 2002 to April 2014 for residual or recurrent HPCs were reviewed retrospectively. All patients were histologically proven as HPC. An Institutional Review Board approved the study protocol. There were 10 male and 8 female patients, with a median age of 38 years (range, 22–71) at the first GKS. All patients had initially undergone surgical resection and 6 of them had received postoperative adjuvant radiotherapy. In this study, the neuropathologist reviewed the histopathological specimen of all patients and graded them according to the WHO classification of brain tumors [4].

2.2. GKS technique

GKS was performed for residual or recurrent tumors that can be delineated in brain MRI. After application of Leksell stereotactic frame type G under local anesthesia, stereotactic MR imaging with T2-weighted and post-contrast FLASH (Fast Low Angle SHot) sequences was obtained. Post-contrast FLASH images (1-mm-thick slices with no gap, 512 × 512 pixels) were obtained after administration of double dose contrast medium. Images were transferred to the planning workstation for GKS. The 3-dimensional-treatment plan was individualized to each patient using Leksell GammaPlan version 5.31, 5.32, 5.34, or 9.0 (Elekta Instruments, Stockholm, Sweden). Leksell gamma knife model B, C and Perfexion (Elekta Instrument, Stockholm, Sweden) were used for irradiation.

2.3. Patient evaluation

The patients underwent follow-up MRI scan at 3 months, 6 months and then every 1-year after GKS. Assessments of tumor responses after GKS were made in comparison with radiosurgical images. Tumor volumes were measured by manually contouring the area of contrast enhancement in each image slices and using Leksell Gammaplan software version 9.0. The tumor volume response was classified in following manner: 'decrease' (⩾20% decrease in tumor volume), 'stable' (between <20% decreased and >20% increase in tumor volume), and 'increase' (⩾20% increase in tumor volume). Local tumor control was defined as either 'decrease' or 'stable' volume of the treated lesion on the last follow-up MR images. Local recurrence was defined as tumor growth or reappearance of tumor within the previous GKS volume. Tumor that developed outside the previous GKS volume was considered as new lesion progression. Overall survival (OS) after initial diagnosis was calculated from the time of the initial surgery and OS after initial GKS from the time of the first GKS. Local recurrence-free interval was calculated from the time between the first GKS for each lesion and local recurrence of that lesion. Brain progression-free survival (PFS) was calculated from the time between the first GKS and local recurrence or new lesion progression. Metastasis-free survival was defined as the time between the initial surgery and identification of extracranial HPC.

2.4. Statistical analysis

Statistical analysis was performed using SPSS version 23.0 (SPSS Inc., Chicago, IL, USA). We used Kaplan–Meier plot for OS and PFS. Univariate analysis was performed on the Kaplan–Meier curves using log-rank test. Statistical significance was set at $p < 0.05$.

3. Results

Twenty-three tumors from 18 patients were treated in the first GKS and locally progressive tumor or new lesions that developed after the first GKS required additional treatment. Therefore, a total of 40 tumors were treated in 44 GKS procedures. Repeat GKS was performed in 8 (44.4%) of 18 patients (twice in 2, 3 times in 2, 5 times in 2, 6 times in 1, and 8 times in 1) [Table 2]. The mean and median follow-up time after the initial diagnosis were 119.6 and 97.8 months (range, 7.1–326.2 months), respectively. The mean and median follow-up time after the first GKS were 76.6 and 71.8 months (range, 3.3–153.3 months), respectively. Of the 18 patients, 10 (55.6%) had high-grade pathology (Anaplastic, WHO Grade III) and 8 (44.4%) had low-grade pathology (WHO Grade II in 7, SFT in 1). The median cumulative tumor volume at the time of the first GKS was 1.2 cm^3 (range, 0.4–7.4 cm^3). The median marginal dose was 16.0 Gy (range, 13–30). On a per tumor basis, the median tumor volume of 40 lesions at the time of the initial GKS for each lesion was 1.2 cm^3 (range, 0.04–9.9 cm^3). The

Table 1
Patients characteristics and radiosurgical parameters according to pathologic grade.

Characteristics	Low-grade	High-grade	Total
No. of patients (%)	8 (44.4)	10 (55.6)	18 (100.0)
No. of tumors (%)	13 (32.5)	27 (67.5)	40 (100.0)
Age (years)			
Median (range)	39 (27–71)	37 (22–57)	38 (22–71)
Sex			
Male	1 (12.5)	9 (90.0)	10 (55.6)
Female	7 (87.5)	1 (10.0)	8 (44.4)
FU duration after Dx (months)			
Median (range)	64.2 (7.1–148.7)	130.2 (72.2–326.2)	97.8 (7.1–326.2)
FU duration after the first GKS (months)			
Median (range)	46.9 (3.3–137.7)	87.1 (5.4–153.3)	71.8 (3.3–153.3)
Previous radiotherapy (%)	1 (12.5)	5 (50.0)	6 (33.3)
Tumor volume (cm^3)			
Median (range)	1.1 (0.4–3.5)	1.8 (0.4–7.4)	1.2 (0.4–7.4)
Marginal dose (Gy)			
Median (range)	17 (13–25)	16 (13–30)	16 (13–30)
Patients presenting new lesion			
After the first GKS (%)	3 (37.5)	5 (50.0)	8 (44.4)
Patients presenting extracranial			
Metastasis (%)	0 (0)	7 (100.0)	7 (100.0)
No. of expired patients (%)	0 (0)	6 (100.0)	6 (100.0)

*No, number; FU, follow-up.