Treatment Results of Gamma Knife Radiosurgery for Central Neurocytoma: Report of a Japanese Multi-Institutional Cooperative Study

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OBJECTIVE: **Central neurocytoma (CN) is a rare benign neuronal tumor, and a limited number of reports have described the usefulness of radiosurgery for a relatively large group of patients. We evaluated the effectiveness and outcomes of Gamma Knife radiosurgery (GKS) for CN in a Japanese multi-institutional study.**

METHODS: **We performed retrospective analysis of 36 patients with CN who were treated with GKS in 12 institutes in Japan. All patients underwent surgery before GKS. The median tumor volume at GKS was 4.9 mL (range, 0.07–23.4 mL), and the median radiation dose prescribed to the tumor margin was 15 Gy (range, 10–20 Gy). The median follow-up period was 54.5 months (range, 3–180 months).**

RESULTS: **The local tumor progression-free survival rates at 5 and 10 years were 94% and 86%, respectively. Three patients developed distant dissemination 16–90 months later. Overall progression-free survival was unrelated to the prescribed dose (<15 Gy vs. ≥15 Gy, $P = 0.62$), tumor size (<6 mL vs. ≥6 mL, $P = 0.46$), gender ($P = 0.36$), age (<30 vs. ≥30 years, $P = 0.37$), target of GKS (residual vs. recurrence, $P = 0.90$), and type of enhancement (homogeneous vs. inhomogeneous, $P = 0.19$). Two permanent complications occurred with 1 intratumoral hemorrhage and 1 radiation injury.**

CONCLUSIONS: **GKS is effective for CN because of its high rate of long-term local tumor control. GKS may have a potential role as a primary treatment for asymptomatic, relatively small tumors in the absence of hydrocephalus without surgical resection.**

INTRODUCTION

Central neurocytoma (CN) is a rare benign neuronal tumor that was first described by Hassoun et al. in 1982; its incidence is 0.1%–0.5% of all brain tumors.[1,2] CNs tend to be located in the lateral ventricle and are classified as World Health Organization (WHO) grade 2. Although surgical removal is the standard treatment, complete removal of the tumor is often difficult because of its location. Although the recurrence rate after incomplete removal is reduced with adjuvant radiation therapy,[3-5] problems that are related to delayed complications due to radiation therapy are seen in some cases.[6-9] A limited number of reports have been published about the usefulness of radiosurgery for CN.[3,4,10-18] We evaluated the treatment results of Gamma Knife radiosurgery (GKS) for CN in multiple Japanese institutes.

MATERIAL AND METHODS

We collected the records of 44 patients who underwent GKS for CNs in multiple Japanese institutes between January 1990 and December 2011. Eight patients were excluded because no follow-up data were available in 5 patients, no histologic diagnosis was available in 1, boost GKS after radiation therapy was performed in 1, and fractionated treatment was performed in 1. Finally, we reviewed 36 patients with histologically verified CN. The numbers of treated patients was 7 at Yokohama Rosai Hospital, 6 at Komaki

Key words
- Central neurocytoma
- Gamma Knife radiosurgery
- Stereotactic radiosurgery
- Tumor control

Abbreviations and Acronyms
CN: Central neurocytoma
GKS: Gamma Knife radiosurgery
KPS: Karnofsky performance scale
MRI: Magnetic resonance imaging

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City Hospital, 5 at Kitanihon Neurosurgical Hospital, 5 at Osaka City General Hospital, 3 at Tokyo Women's Medical University, 3 at Shin-Suma Hospital, and 7 at 6 other institutes in Japan. As the number of all treated patients with CN in 12 institutes was 61 during the same period, about 60% of the CN patients underwent GKS. Informed consent was obtained from the patients when possible, and approval of the study was granted by the ethics committees of all participating institutions.

The patients included 17 men and 19 women, and their mean age at GKS was 35 years (range, 9–73 years) (Table 1). The initial symptoms were headache in 20 patients, hemiparesis in 4, gait disturbance in 3, consciousness disturbance in 2, and others in 3. Four patients were diagnosed incidentally. All patients underwent surgery before GKS, and the degree of resection was total in 4 patients, subtotal in 5, partial removal in 24, and 3 patients underwent only a biopsy. The histologic diagnosis was CN in all patients, and no atypical findings were noted. A ventriculo-peritoneal shunt was also performed for hydrocephalus in 6 patients. After surgery, conventional local radiation therapy was added in 1 patient, and stereotactic radiosurgery with a linear accelerator was added in 1 patient.

Table 1. Characteristics of Patients with Central Neurocytomas Treated with Gamma Knife Radiosurgery

Age (years)	Mean 35 (range, 9–73)
Sex	
Male	17
Female	19
KPS score	Median, 100 (range, 50–100)
Previous treatment	
Op	34
Op + RT	1
Op + SRS	1
Surgery	
Total removal	4
Subtotal removal	5
Partial removal	24
Biopsy	3
Lesion	
Recurrence	10
Residual tumor	23
Primary tumor	3
Location	
Lateral ventricle	32
Third ventricle	4
Period between Op & GKS	Median, 6.9 months (range, 0.75–191 months)
Tumor volume at GKS	Median, 4.9 mL (range, 0.04–23.4 mL)
Prescribed dose	Median, 15Gy (range, 10–20 Gy)
% isodose	Median, 50 (range, 40%–55%)
Follow-up period	Median, 54.5 months (range, 3–179 months)

KPS, Karnofsky performance scale; Op, operation; RT, radiation therapy; SRS, stereotactic radiosurgery; GKS, Gamma Knife radiosurgery.

The procedure for GKS was as follows: A Leksell G stereotactic frame was attached to the patient's head under local anesthesia, and stereotactic magnetic resonance imaging (MRI) was performed. MRI sequences including gadolinium enhancement images with 1- to 3-mm slice thickness were obtained. Treatments were planned with the Leksell gamma plan. After confirming the tumor margin, an isodose curve fit to the tumor margin was made using 4 sizes of collimators. Finally, the prescribed dose to the tumor margin was determined. Treatments were carried out according to the dose plan with the Leksell gamma knife model B, model C, and model 4C.

The median period between surgery and GKS was 6.9 months (range, 0.75–191 months), and GKS was performed for 23 residual tumors, 10 recurrent tumors, and 3 primary tumors after biopsy. Although no neurologic signs were noted in 24 patients, 4 patients showed hemiparesis, 2 showed cognitive dysfunction, and 6 showed other neurologic deficits at the time of GKS. The median Karnofsky performance scale (KPS) score was 100 (range, 50–100). The median tumor volume was 4.8 mL (range, 0.07–23.4 mL), and the median prescribed dose at GKS was 15 Gy (range, 10–20 Gy). After GKS, we checked the neurologic findings, KPS score, tumor control on images, and complications every 6 months. The median follow-up period was 54.5 months (range, 3–179 months) after GKS. We defined the change in the tumor size according to response evaluation criteria in solid tumors (RECIST): complete response—disappearance of targeted lesion; partial response—at least a 30% decrease of the longest diameter of lesion; progressive disease—at least a 20% increase of diameter of lesion; stable disease—neither sufficient shrinkage to qualify for partial response nor sufficient increase to qualify for progressive disease.[19]

The local tumor progression-free survival rate, overall progression-free survival rate, and overall survival rate were analyzed with the Kaplan-Meier method. Univariate analysis was carried out using the log-rank test method. Statistical analyses were performed with EZR (Saitama Medical Center, Jichi Medical University, http://www.jichi.ac.jp/saitama-sct/SaitamaHP.files/statmedEN.html), which is a graphical user interface for R (The R Foundation for Statistical Computing, version 1.29).[20]

RESULTS

Tumor Control

Tumors were controlled locally in 34 lesions including 7 with a complete response, 15 with a partial response, and 12 with no change. The median rate of decrease in tumor volume was 74% (range, 15%–100%). Two patients developed local recurrences after initial partial response. After GKS, the local tumor progression-free survival rates at 5 and 10 years were 95% and 86%, respectively (Figure 1). The local tumor progression-free survival rate was unrelated to the prescribed dose (<15 Gy vs. ≥15 Gy, P = 0.14) and tumor size (<6 mL vs. ≥6 mL, P = 0.12). Three