Gamma Knife Radiosurgery for Atypical and Anaplastic Meningiomas

Wei-Hsin Wang[1,3], Cheng-Chia Lee[1-3], Huai-Che Yang[1,3], Kang-Du Liu[1,3], Hsiu-Mei Wu[3,4], Cheng-Ying Shiau[3,5], Wan-You Guo[3,4], David Hung-Chi Pan[1,3], Wen-Yuh Chung[1,3], Ming-Teh Chen[1,3]

■ BACKGROUND: **Atypical and anaplastic meningiomas have much higher recurrence rates after surgical resection compared with benign meningiomas, but the role of adjuvant radiosurgery remains unclear. This study was undertaken to evaluate the outcomes of gamma knife radiosurgery for patients with atypical and anaplastic meningiomas.**

■ METHODS: **In this retrospective analysis of a prospectively maintained database, 46 patients with histologically proven atypical or anaplastic meningiomas by current World Health Organization (WHO) criteria underwent postoperative Gamma Knife radiosurgery between 1993 and 2013. The median follow-up period was 32.6 months. The median tumor volume and margin dose were 11.7 mL (range, 2–53 mL) and 13.1 Gy (range, 12.0–16.5 Gy), respectively.**

■ RESULTS: **Local control at 3 and 5 years was 50.6% and 32.1%, respectively. Gender ($P = 0.013$) and marginal dose less than or equal to 13Gy ($P = 0.049$) were associated with the local control. The 3- and 5-year overall survival for patients with WHO grade II was 97.1% and 88.3%, respectively, compared with 66.7% and 66.7% for patients with WHO grade III meningiomas. Radiation therapy before Gamma Knife radiosurgery (GKRS; $P = 0.018$) and tumor grade ($P = 0.019$) were the factors associated with a worse overall survival rate. Fourteen patients (30.4%) developed adverse radiation effects after GKRS treatment, and all were Radiation Therapy Oncology Group grade I.**

■ CONCLUSIONS: **Postoperative GKRS treatment for patients with atypical and anaplastic meningioma is challenging. More aggressive treatment, including of safely maximizing the extent of surgical resection and using a higher margin dose (>13Gy), should be applied to achieve better local control.**

INTRODUCTION

The World Health Organization (WHO) grade II atypical and WHO grade III anaplastic meningiomas have much higher rates of recurrence and poor overall survival rates compared with WHO grade I meningiomas.[1-6] According to the revisions of the WHO grading system in 2000 and 2007,[7,8] the percentage of WHO grade II atypical meningiomas increased from 5% to 20%–35%, and it remained approximately 1%–2% for WHO grade III anaplastic meningiomas.[9,10] Despite the primary treatment of atypical and anaplastic meningiomas being aggressive surgical resection, surgery alone is insufficient for good prognosis. Adjuvant treatments to primary surgical resections were usually used to reduce the incidence of tumor recurrence. During the last 2 decades, stereotactic radiosurgery (SRS) has proved to be an effective treatment for WHO grade I benign meningioma.[11,12] However, the efficacy of SRS in the treatment of Grade II atypical and WHO grade III anaplastic meningiomas is still unclear. To create a better understanding of the role of radiosurgery in the management of these aggressive tumors, we present a single-institution retrospective review of using Gamma Knife radiosurgery (GKRS) in this study.

Key words
- Atypical meningioma
- Anaplastic meningioma
- Gamma Knife radiosurgery

Abbreviations and Acronyms
EBRT: External beam radiation therapy
GKRS: Gamma Knife radiosurgery
MRI: Magnetic resonance imaging
PFS: Progression-free survival
SRS: Stereotactic radiosurgery
WHO: World Health Organization

From the [1]Department of Neurosurgery, Neurological Institute, Taipei Veterans General Hospital, Taipei; [2]Department of Surgery, Hsinchu Branch, Taipei Veterans General Hospital, Hsinchu; [3]School of Medicine, National Yang-Ming University, Taipei; [4]Department of Radiology, Taipei Veterans General Hospital, Taipei; and [5]Cancer Center, Taipei Veterans General Hospital, Taipei, Taiwan

To whom correspondence should be addressed: Ming-Teh Chen, M.D. [E-mail: weihsin0103@gmail.com]

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Table 1. Clinical Characteristics of Intracranial Atypical and Malignant Meningioma in 46 Patients

Characteristics	Value	Percentage or Range
Sex (Male:Female)	12:34	
Median age (years)	60.1	15.8–81.2
Tumor size (mL)	11.7	2–53
Accompanied lesion number		
1 (single lesion)	35	76.1%
2	6	13.0%
3	4	8.7%
>3	1	2.2%
Location		
Convexity	15	32.6%
Falx	17	37.0%
Parasellar	4	8.7%
Tentorial	3	6.5%
Cerebellopontine angle	5	10.9%
Petroclival	2	4.3%
Intratumoral hemorrhage	1	2.2%
Extracranial metastasis		
Yes	1	2.2%
No	45	97.8%
Pre-GKRS surgical resection	46	100%
GTR		
Simpson grade I	0	0%
Simpson grade II	2	4.3%
Simpson geade III	4	8.7%
STR		
Simpson grade IV	40	87%
Simpson grade V	0	0%
Pre-GKS radiation therapy	4	8.7%
Pre-GKS chemotherapy	0	
Histologic classification		
WHO grade II (atypical)	37	80.4%
WHO grade III (anaplastic)	9	19.6%
Radiosurgery parameters (median)		
Radiation volume (mL)	17.8	3.3–65.9
Margin dose (Gy)	12.5	12.0–16.5
Isodose level (%)	57.0	50–62
Maximum dose (Gy)	21.9	20–32
Number of isocenters	17.0	4–29
Median clinical follow-up (months)	32.6	6.2–177.5
Median image follow-up (months)	29.5	5.2–167.5
Mortality (n)	6	13.0%

GKRS, Gamma Knife radiosurgery; GTR, Gross total resection; STR, Subtotal resection.

METHODS

Patient Population

This is a retrospective analysis using a prospectively maintained, institutional review board–approved database. Forty-six patients with histologically confirmed atypical (WHO grade II, n = 37) or anaplastic (WHO grade III, n = 9) meningioma according current WHO criteria underwent GKRS at the Taipei Veterans General Hospital between 1993 and 2013. The median age at the time of radiosurgery was 60.1 years (range, 15.8–81.2 years). Thirty-five patients (76.1%) had a single tumor, 6 patients (13%) had 2 tumors, 4 patients (8.7%) had 3 tumors, and 1 patient (2.2%) had 7 tumors. There were total 66 tumors treated in these 46 patients. Four patients (8.7%) had accepted previous conventional external beam radiation therapy (EBRT). The patient characteristics and tumor locations are presented in Table 1.

Radiosurgery and Dosimetry

At Taipei Veterans General Hospital, the Leksell frame was placed for all adult patients under local anesthesia. Stereotactic magnetic resonance imaging (MRI) was then performed for treatment planning. If the patient could not tolerate MRI because of incompatible implants, computed tomography (CT) was used to define the target. Multiple isocenters (median, 17.0) were used to irradiate the tumors. In this series, the median margin dose of 12.5 Gy (range, 12.0–16.5 Gy) was delivered to a median isodose line of 57.0% (range, 50%–62%). The median maximum dose was 21.9 Gy (range, 20.0–32.0 Gy).

Patient Follow-Up

Patients were followed after GKRS by the neurosurgeon clinically, and serial MRI was arranged 3 months after GKRS, every 6 months for the first 2 years, and annually thereafter. Tumor recurrences were divided into infield and outfield recurrences. An infield recurrence was defined as occurring within the radiation volume. New tumor formation outside the radiation volume was defined as outfield recurrence. Effect was coded as regression, stable, and progression according to the tumor volume decreasing greater than 10%, changing less than 10%, and increasing greater than 10%, respectively.

Statistics

Kaplan-Meier analysis was used to estimate local tumor control (progression of irradiated tumor, infield recurrence), progression-free survival (infield or outfield recurrence) and overall survival. Univariate analysis was performed using the log-rank test. All factors with a P value ≤ 0.05 on univariate analysis were entered into multivariate analysis using Cox proportional hazards model.