Brain Metastases in Renal Cell Carcinoma: Management with Gamma Knife Radiosurgery

Beatriz E. Amendola, MD, FACR, a Aizik L. Wolf, MD, a Sammie R. Coy, PhD, a Coral Gables, Florida, Marco Amendola, MD, Miami, Florida, a Laurie Bloch RN, a Miami, Florida

PURPOSE

The purpose of this study was to evaluate survival and local control of brain metastases in patients with renal cell carcinoma.

METHODS AND MATERIALS

From November 1993 through March 1999, 38 radiosurgical treatments using the Leksell gamma knife unit were performed on 22 patients with renal cell carcinoma. The indications for treatment were failure after whole-brain radiation therapy or de novo treatment. All radiosurgical treatments were given on an outpatient basis. The workup included computed tomography and magnetic resonance imaging. The age of the patients ranged from 38 to 80 years (median age, 60 years). The mean minimum tumor dose was 18 Gy, and the mean volume was 3.9 cc. Previous whole-brain radiation therapy was used in 11/22 (50%) patients. Four of 22 patients presented with single metastasis. Thirteen patients were treated once, one patient was treated four times and one patient seven times for new lesions. The number of lesions treated ranged from one to 21.

RESULTS

One patient is alive at 63 months of follow-up. Twenty-one patients died, with a median survival of 8 months (range, 1–38 months). Eighteen of 21 patients died of nonneurologic causes. Overall local control was 98.5%. One patient developed radiation necrosis.

CONCLUSIONS

The long-term survival achieved in patients with renal cell carcinoma requires aggressive management, even in the presence of multiple brain metastases. Gamma knife radiosurgery for renal cell carcinoma is an effective noninvasive modality of treatment. It offers high local control rate and improved quality of life and survival. (Cancer J 2000;6:372–376)

KEY WORDS

Renal cell cancer, brain metastases, gamma knife radiosurgery

Metastatic disease to the brain is a deadly and debilitating condition that develops in 20% to 40% of the general cancer population. Systemic steroids, whole-brain radiation therapy (WBRT), and surgery for single accessible metastasis have established value in reversing neurologic dysfunctions and increasing survival. However, even after the use of these modalities, the median survival remains short. Intracranial metastases represent more than 50% of all malignant brain tumors. Renal cell carcinoma (RCC) accounted for 30,000 new cases and 12,000 deaths in the United States in 1998, making up 2% of all cancer-related deaths. Its incidence is increasing in the United States. This is due not only to improved detection of asymptomatic tumors by computed tomography, ultrasound, and magnetic resonance imaging but also to a real upward trend reflected in higher incidence of more advanced tumors and a corresponding increase in mortality. RCC is generally considered a radioresistant tumor, and the results of conventional radiotherapy for RCC metastases to the brain are disappointing. Brain metastases from RCC are uncommon and are usually reported as single, surgical removal is associated with prolonged survival. Gamma knife radiosurgery offers an alternative to the open surgical method, delivering a high dose of focused radiation to the tumor area and sparing adjacent normal tissues. Longer survival times with improved local control have been documented with radiosurgery in grouped histologies. These facts form the rationale for the hypothesis that gamma knife radiosurgery may offer significant advantages in the treatment of RCC that is metastatic to the brain.
PURPOSE
The purpose of the study is to evaluate the efficacy of radiosurgery for patients with RCC that is metastatic to the brain who are treated at a single center and to determine adverse risk factors.

MATERIALS AND METHODS
From November 1993 to March 1999, 38 radiosurgery treatments were performed using the Leksell gamma knife unit model U on 22 RCC patients (eight females and 14 males) with metastatic tumors to the brain. The indications of treatment were failure after WBRT and de novo treatment. Patients' ages ranged from 38 to 80 years (median age, 60 years). Doses ranged from 15 to 22 Gy (mean dose, 18 Gy). Tumor volume ranged from 0.1 to 75.5 cc (mean, 3.9 cc). Previous WBRT had been used in 11 of 22 patients. Four patients were treated for single metastasis and 18 patients for multiple lesions. The number of lesions treated ranged from one to 21 sites with an average of six sites per patient and 3.5 sites per treatment. Survival time was measured from the date of radiosurgery to the date of death. Freedom from relapse was measured from radiosurgery to the first imaging study performed. Patient characteristics are included in Table 1.

Statistical analysis was performed using the SAS software package (SAS Institute, Cary, NC). Survival curves were calculated using actuarial techniques and were compared using the log-rank statistic. Follow-up time was calculated from the date of the gamma knife treatment.

STUDY CRITERIA
All patients with newly diagnosed or recurrent brain metastasis from RCC were included in the study, independent of primary status and/or extracranial disease,

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Abbreviations: BMR, cause of death related to brain metastasis; KPS, Karnofsky performance score; METS, metastasis; WBRT, whole-brain radiation therapy.
*Indicates more than one treatment.
*Indicates one site retreated.
with a Karnofsky performance score of 40% or above. Follow-up included triple-contrast magnetic resonance imaging 1 month after treatment and every 3 months thereafter.

Failure was defined as the appearance of new lesions (relapse-free survival) from remote areas of previous treatment or failure in a treated site (local failure).

**RESULTS**

Overall actuarial survival for the entire group was 56% at 6 months and 19% at 24 months. Median survival was 8.4 months (range, 0.8 to >63 months). Local con-

**FIGURE 1** Overall survival for all patients.

**FIGURE 2** Initial treatment magnetic resonance imaging (MRI) examinations in a 56-year-old female treated with whole-brain radiation therapy and gamma knife for brain metastases from renal cell carcinoma with follow-up MRI at 34 months. Currently, the patient is without evidence of disease at 63 months.
trol was achieved in 20 of 22 patients (91%). Retreatment was performed in eight of 22 (36%) patients for new lesions. One patient developed radiation necrosis. Three of 22 (14%) patients experienced brain-related death. The remaining patients died of non-neurological causes. For all patients, overall survival was 55% at 6 months, 36% at 12 months, and 18% at 24 months (Fig. 1). Patients who were younger than 60 years had a statistically significant improved survival compared with patients aged 60 years or older. At 1 year, the survival for those 60 or older was 24%, versus 54% for those younger than 60 (P = 0.002). The number of metastatic sites, the history of prior external-beam radiation therapy and the Karnofsky performance score status did not have a statistically significant effect on survival. One patient is alive 63 months after the first radiosurgical procedure (Fig. 2).

**Discussion**

Although RCC metastatic to the brain is generally considered a radioresistant tumor, it is clear that high doses of WBRT can palliate local symptoms.6 Maor et al8 treated 46 patients at M.D. Anderson Cancer Center between 1968 and 1985, achieving an overall median survival rate of 2 months. In a subgroup of 10 patients in whom shrinkage of the brain metastases occurred, median survival was 4.2 months. In a larger retrospective study from the same institution, a median survival rate of 3.3 months was reported for 119 patients treated with WBRT alone.13 Of interest is the fact that 78% of these patients died of progression of the brain disease.

Aggressive surgical management improves survival, as indicated by the results of Wronska et al in 50 patients operated on between 1974 and 1993.7 A postoperative mortality rate of 10% (five patients) was reported.2 Overall median survival from the time of craniotomy was 12.6 months. In the absence of effective chemotherapy regimens, the authors suggested that patients with brain metastases from RCC be considered for operative resection for treatment and palliation. They pointed out that most brain metastases from RCC are well circumscribed and relatively firm, making them suitable for complete surgical resection en bloc.

Recently, there have been several reports of gamma knife radiosurgery for the management of brain metastases from RCC.14-18 In a selected population of 14 patients, 10 of whom had either only one lesion (five patients) or two brain metastases (five patients) and with a median Karnofsky performance score of 90, Dave et al14 reported a median survival rate of 14.1 months.

In a series of 21 consecutive patients with 37 metastatic lesions and a Karnofsky performance score of 80 or greater at the time of gamma knife radiosurgery, a median survival of 8 months was achieved by Payne et al.15 The median survival time for the 13 patients with active extracranial disease at the time of initial gamma knife radiosurgery was 4 months, and that for the seven patients without extracranial disease was 19 months.15 Our results in a similar, largely unselected group of patients are comparable, with a median survival of 8.4 months. In our group, 18 of 21 patients died of nonneurological causes, and one patient is alive at 63 months' follow-up. In our series and despite the relatively high number of patients retreated for new lesions, only one experienced radiation necrosis. This toxicity compares well with the morbidity associated with WBRT and surgery for this indication.50

**Conclusion**

The long-term survival and excellent local control achieved in our experience with RCC metastatic to the brain treated with gamma knife radiosurgery shows that this group of patients deserves aggressive management, even in the presence of disseminated disease or multiple brain metastases. Gamma knife radiosurgery for RCC is an effective and noninvasive modality of treatment. It offers high local control rate and improved survival with excellent quality of life and minimal complications.

**References**


