

Gamma Knife surgery–induced meningioma

Report of two cases and review of the literature

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Gamma Knife surgery (GKS) is a minimally invasive neurosurgical technique. During the past 30 years, radiosurgery has been performed for a number of intracranial disorders with a generally low incidence of side effects. Although radiation-induced neoplasia following radiotherapy is well documented, there are few reports of this complication following radiosurgery.

The authors are engaged in an ongoing project in which they are studying the delayed adverse effects of radiosurgical changes in 2500 patients with arteriovenous malformations (AVMs) treated within a 30-year period. The cases of 1333 patients treated by the senior author (L.S.) have been reviewed thus far. A subset of 288 patients in this group underwent neuroimaging and participated in clinical follow up for at least 10 years.

The authors report two cases of radiosurgically induced neoplasia. In both cases the patient was treated with GKS for an AVM. Longer than 10 years after GKS, each of the patients was found to have an incidental, uniformly enhancing, dura-based mass lesion near the site of the AVM. These lesions displayed the imaging characteristics of a meningioma. Because in both cases the lesion has displayed no evidence of a mass effect, they continue to be followed using serial neuroimaging. These are the fifth and sixth cases meeting the criteria for radiation-induced neoplasms defined by Cahan, et al., in 1998.

Although radiosurgery is generally considered quite safe, the incidence of radiation-induced neoplasms is not known. These cases and the few others detailed in the literature emphasize the need for long-term neurological follow-up review in patients after radiosurgery.

KEY WORDS • meningioma • radiation-induced tumor • Gamma Knife

SINCE April 1970, the Gamma Knife has become an increasingly important neurosurgical tool in the treatment of AVMs. Because of its minimally invasive nature and its precision, radiosurgery is associated with a low morbidity rate and essentially a 0% mortality rate. Rare instances of a serious complication, however, do occur. An attempt to contact 2500 patients with AVMs that were treated with GKS by the senior author (L.S.) has thus far yielded follow-up data on 1333 patients. During a retrospective examination of cases in which there was long-term follow-up review, we discovered two cases of radiosurgically induced masses. We provide a detailed description of these cases and a summary of the related literature.

Case Report

Case 1

History. At the age of 7 years, this boy collapsed and had a seizure while playing football. He was taken to a hospital in Italy where a CT scan revealed an acute hemorrhage in the right thalamus and ventricles. A subsequent cerebral angiogram demonstrated a 32 × 20 × 16-mm AVM nidus in the region of the right basal ganglia with feeding vessels from the lenticulostriate branches of the middle cerebral artery and drainage into the internal cerebral veins. The patient underwent placement of a ventriculoperitoneal shunt and made a favorable recovery. His only neurological deficit was mild left hemiparesis.

Radiosurgery. The 7-year-old patient underwent GKS at the University of Virginia in May 1990. His lesion was treated with GKS by the senior author (L.S.) has thus far yielded follow-up data on 1333 patients. During a retrospective examination of cases in which there was long-term follow-up review, we discovered two cases of radiosurgically induced masses. We provide a detailed description of these cases and a summary of the related literature.

Follow-Up Review. Magnetic resonance images obtained in 1996 (Fig. 1 left) and 1997 (Fig. 1 right) demonstrated the persistence of the AVM but no evidence of any other intracranial lesion. In 2002, the presence of a dura-based enhancing mass in the right lateral middle cranial fossa was

Abbreviations used in this paper: AVM = arteriovenous malformation; CT = computed tomography; GBM = glioblastoma multiforme; GKS = Gamma Knife surgery; MR = magnetic resonance.
observed on MR images (Fig. 2 left). A subsequent MR imaging study performed in 2004 revealed slight growth of this lesion but no significant mass effect or peritumoral edema (Fig. 2 right). On neuroimaging, this lesion appears most consistent with a meningioma. Because the mass is asymptomatic, no histopathological testing has been performed. The area of brain tissue in which the lesion appeared received approximately 0.6 Gy during GKS in 1990 and 0.25 Gy in 1995. The patient, who is now 22 years old, will be monitored closely using serial MR imaging to detect any further growth of this lesion.

Case 2

History. At the age of 12 years, this girl presented to a hospital in Italy with onset of an acute right-sided headache, nausea, vomiting, fatigue, diaphoresis, and left-sided weakness and numbness. A CT scan revealed a right temporal intracerebral hemorrhage, and a cerebral angiogram demonstrated that the underlying lesion was an AVM. The patient underwent craniotomy and extirpation of the malformation. A routine follow-up angiogram obtained 4 years later revealed a residual right-sided AVM with feeding vessels from the posterior cerebral artery branches and with drainage into the infratentorial venous system.

Radiosurgery. The patient was subsequently referred to our institution for GKS. At the time of her presentation in 1992, the patient had no neurological deficits. She underwent GKS on November 9, 1992. Stereotactic angiography was performed, and the GKS plan was devised by the senior author. One 14-mm isocenter was used. The maximum dose administered was 28 Gy, and the peripheral dose was 25 Gy. The AVM nidus volume was 1.2 cm³. The patient tolerated radiosurgery well.

Follow-Up Review. A follow-up MR image obtained 6 months post-GKS revealed a signal change and encephalomalacia in the right temporal region, which was unchanged from that documented preradiosurgery. A significant decrease in the volume of the AVM nidus was noted, however. In 1994, angiography performed 21 months after GKS revealed no evidence of any residual malformation or tumor blush.

As part of the continued long-term neuroimaging follow-up review of this patient, she underwent MR imaging 10 years after GKS. The MR images were significant for a new, rounded homogeneously enhancing 12-mm extraaxial mass adjacent to the superior surface of the right tentorium (Figs. 3 left and right). The mass was located in the area of the previous AVM and had the neuroimaging appearance of a meningioma. This lesion had not been seen on any of the patient’s previous MR or CT images, and no evidence of a tumor blush was observed on the angiogram obtained in 1994. Moreover, the mass was clearly located in the irradiation field of the obliterated AVM; this area of brain tissue received a radiation dose of approximately 25 Gy. The presumed meningioma does not appear to exert any mass effect. As such, we have chosen to follow it with serial MR imaging. No specimen has been obtained for a histopathological study. During the past 3 years, there has been no evidence of an increased size of the mass on serial MR images.

Discussion

Mechanisms and Criteria for Radiation-Induced Tumor Formation

Radiation is carcinogenic and can cause damage to DNA. It can cause overexpression of oncogenes and inactivation of tumor suppressor genes even at low doses.

Despite the fact that radiosurgery has been performed in more than 250,000 patients during an epoch longer than 30 years, the precise incidence of radiosurgery-induced neoplasms is difficult to estimate because of the delayed fashion in which such lesions may develop and their apparently low rate of occurrence. For a tumor to be considered the result of radiosurgery, the following criteria must be met: 1) the tumor must occur in the irradiation field; 2) it cannot be present prior to irradiation; 3) any primary tumor must diff-
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cases exist, and the true incidence may be greater Published in peer-reviewed journals in which the authors de-

Based on the literature, the incidence of stereotactic radiosurgery-induced neoplasia has been reported to range between zero and three per 200,000 patients. If this is true, the incidence is very low. However, the true incidence of radiosurgery-induced neoplasms following GKS is likely to be higher than that reported by Ganz. The denominator of the ratio reported by Ganz would appear to be the approximate number of patients treated with the Gamma Knife through the year 2001. However, few of these 200,000 patients have participated in as long a follow-up review as the 10-year follow up of our patients. It was only because MR images were obtained 10 years after GKS that our patients were discovered to harbor asymptomatic mass lesions consistent with a meningioma. In fact, many centers do not rou-

Estimated Incidence of Tumor Formation Following Radiosurgery

It is our contention that radiation-induced neoplasia must be considered in broad terms when evaluating patients who have undergone radiosurgery. With GKS, radiation passes through the head along as many as 201 different trajectories, and, therefore, even distant areas of the brain are exposed to low doses of radiation. Even areas relatively remote from the treatment area can receive doses greater than 1 Gy during radiosurgery, and this procedure could cause tumors to arise remote from the targeted lesion. Low doses of radi-

Cases of Radiation-Induced Tumor Formation

In children who were treated for tinea capitis with radio-
therapy in Israel, the risks of benign and malignant tumors were increased in the presence of radiation doses as low as 1 to 2 Gy. A review of 25 cases in which gliomas were induced after radiotherapy illustrated that these tumors can develop following the delivery of doses ranging from 1.5 to 60 Gy, and the latency period can range from 4 to 26 years. Following radiation therapy, Brada has demonstrated that radiation-induced neoplasms (GBMs or meningiomas) de-

In a study of survivors of the atomic bomb explosions in Hiroshima and Nagasaki, the incidence of meningiomas ranged from 2.3 to 6 per 100,000 person-years and the overall incidence of brain tumors was 14 per 100,000 person-years. The incidence of meningiomas in Hiroshima survivors varied de-

Both the radiation dose and the time elapses correlated with an increase in the incidence of meningiomas in survivors of the atomic bomb explosion in Hiroshima. Shibata, et al., reported that in 1994 the incidence of meningiomas in survivors of an atomic bomb explosion increased significantly 36 years after the explosion. This finding highlights the latency period of radiation-in-

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![Fig. 3. Case 2. Axial (left) and coronal (right) contrast-enhanced T_1-weighted MR images obtained in a patient 10 years postradiosurgery. The encephalomalacia in the temporal region is unchanged from that shown in previous MR images. This image does not reveal any evidence of abnormal vessels or cyst formation. However, there is a rounded, homogeneously enhancing extraaxial 12-mm mass adjacent to the superior surface of the right tentorium. It is located in the area where the previous AVM was situated and has the imaging characteristics of a meningioma.](image-url)
ed the cases of 1333 patients with AVMs treated using the Gamma Knife, and follow-up imaging was performed over a period of at least 10 years in 288 of these patients. If we conservatively estimate that radiosurgery-induced lesions would be evident within a 10-year time interval, then our incidence of radiosurgery-induced neoplasia is 2 in 2880 person-years or 69 in 100,000 person-years. Thus, there is a 0.7% chance that a radiation-induced tumor may develop within 10 years following GKS. This is less than the 1.9% risk detailed by Brada, et al., but our results encompass a follow-up period of only 10 years, compared with the 20 years that those investigators reported. The annual incidence of primary brain tumors ranges from 10.97 to 15.5 per 100,000 person-years and, for meningiomas, it varies from 0.6 to 7 per 100,000 person-years. The long latency and relative rarity of these lesions following radiosurgery may defy a conclusive determination of the true incidence. Malis and others have shown that the latency of radiation-induced tumors can be as long as 30 to 40 years. Very few patients have participated in a 30-year follow-up review following radiosurgery.

Risk/Benefit Profile of Radiosurgery

The risk of radiosurgically induced neoplasia must be weighed in the treatment of pediatric patients and in patients with benign tumors and a long life expectancy. Alternative treatments if available can also have appreciable risks and sometimes there are no viable options other than radiosurgery. Although time will reveal the true incidence of radiosurgically induced neoplasms, the substantial body of information presently available would suggest that its overall side-effect profile is acceptable.

Treatment of Radiation-Induced Tumors With Radiosurgery

Radiation-induced neoplasms have at times been treated effectively by performing radiosurgery. Investigators at the Mayo Clinic recently reported a 100% 5-year local tumor control rate in 16 patients with radiation-induced tumors. The median follow-up period in the Mayo Clinic report was only 40.2 months. At our center, we have used the Gamma Knife to treat a few patients with radiation-induced meningiomas. The follow-up period of these patients is too short to draw any meaningful conclusion. Studies with longer follow-up periods are necessary to assess the local control rates of radiation-induced benign tumors following radiosurgery. If radiosurgery can be used to treat radiosurgically induced tumors, this result would have interesting neuro oncological implications.

Conclusions

Based on available reports, it would appear that the incidence of radiosurgically induced neoplasms is low. However, few of the large GKS series have sufficiently long follow-up review periods to establish the true incidence of radiosurgically induced neoplasia. Both physicians and patients need to be aware of this possibility. Serial neuroimaging after radiosurgery can lead to early detection. A neurosurgeon must determine the appropriate course of action (such as resection, radiosurgery, or serial imaging) for each of these cases.

Acknowledgments

The authors thank Dr. Mark R. Conaway, director of the Division of Biostatistics and Epidemiology at the University of Virginia, for his guidance. Dr. David Schlesinger and Dr. Harold Berk provided assistance with the dosimetry calculations.

References


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Manuscript received September 27, 2005. Accepted in final form February 23, 2006.
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