Microsurgical Resection for Persistent Arteriovenous Malformations Following Gamma Knife Radiosurgery: A Case-Control Study

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■ OBJECTIVE: **To explore outcomes after microsurgery of brain arteriovenous malformations (AVMs) that failed to be obliterated by Gamma Knife radiosurgery (GKRS).**

■ METHODS: **From January 2000 to January 2014, 42 consecutive patients underwent surgical resection of persistent AVMs after GKRS. These 42 patients with AVMs who underwent radiosurgery (radiosurgery group) were individually matched with 42 patients with AVMs who did not undergo radiosurgery (no radiosurgery group) based on patient and AVM characteristics. The modified Rankin Scale was used to assess neurologic status of patients. The effects of GKRS on AVM resection and surgical outcomes were analyzed.**

■ RESULTS: **After GKRS, the mean AVM volume was significantly reduced by 76.8% ($P < 0.01$), the size was reduced by 41% ($P < 0.01$), and the Spetzler-Martin grade was reduced in 61.9% of the patients ($P < 0.01$). During the time interval from radiosurgery to surgical resection, subsequent hemorrhages led to significant neurologic deterioration ($P = 0.046$). Compared with the control group, the frequency of preoperative embolization, operative time, and blood loss were significantly lower in the radiosurgery group (all $P < 0.05$). The no radiosurgery group had a significantly higher rate of worsening in mRS scores at 6 months after surgery (40.5% vs. 16.7%, $P = 0.029$). Good neurologic status (mRS score <3) was achieved in 81% of the radiosurgery group and 83% of the no radiosurgery group at the final follow-up evaluation.**

■ CONCLUSIONS: **GKRS performed several years before microsurgical resection can facilitate resectability of AVMs and decrease the rate of postoperative neurologic deterioration. For patients with persistent AVMs several years after GKRS, microsurgical resection is recommended to achieve good clinical outcomes.**

INTRODUCTION

Surgical resection of brain arteriovenous malformations (AVMs) is challenging in regard to postoperative neurologic deficits, especially for large and complex AVMs in eloquent locations. There are no clear guidelines for choosing the optimal treatment modality for each individual patient with an AVM. Gamma Knife radiosurgery (GKRS) is mainly applied as a single treatment for AVMs that are small (<3 cm diameter), unruptured, or poorly accessible. GKRS may also be recommended as part of multimodal therapy in combination with microsurgical resection and embolization to reduce the size of high-volume AVMs.[1,2] In the literature, 5-year obliteration rates after GKRS range from 23% to 94%.[3-9] However, there are still a large proportion of incompletely obliterated or persistent AVMs following GKRS. Controversy exists regarding the risk of hemorrhage in persistent AVMs.[7,10,11] However, most studies in the literature state that the hemorrhage risk exists as long as the AVM nidus persists.[9-15]

Treatment options for persistent AVMs after radiosurgery include repeat radiosurgery, surgical resection, endovascular embolization, and observation.[3,9,16-18] However, there is no

Key words
- Gamma Knife radiosurgery
- Microsurgical resection
- Persistent arteriovenous malformations

Abbreviations and Acronyms
AVM: Arteriovenous malformation
DSA: Digital subtraction angiography
GKRS: Gamma Knife radiosurgery
mRS: Modified Rankin Scale
RS−: No radiosurgery
RS+: Radiosurgery
S-M: Spetzler-Martin

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current consensus on the optimal management of persistent AVMs after radiosurgery. The decision to pursue a given modality of retreatment must be based on the characteristics of the AVM after radiosurgery, the patient's clinical symptoms, the perceived hemorrhage risk, the obliteration rate, and treatment-related complications.[3] In a recent review of the literature by Awad et al.,[3] repeat radiosurgery obliterated 61% of persistent AVMs. The most common complications included hemorrhage during the latency period in 7.6% and radiation-induced changes in 7.4%. Compared with repeat radiosurgery, surgical resection of persistent AVMs is less frequently reported,[19-25] and only 3 studies reported >20 cases.[21,23,24]

Biologic changes in the arteries induced by radiosurgery include intimal hyperplasia, medial hyalinization, wall thickening, and subsequent lumen narrowing or obliteration.[23,26] These biologic changes brought about by radiosurgery can facilitate AVM resection during surgery.[20,23-25] After radiosurgery, AVMs may become less vascular.[20,23,24] Preoperative embolization may be used less.[23] Radiosurgery effects may create gliotic planes adjacent to the AVMs to improve dissection during resection. Blood loss, operative time, and hospital stay may decrease significantly.[23] However, in the literature, only 1 study by Sanchez-Mejia et al.[23] quantified the surgical advantages of radiated AVMs. Conflicts also exist regarding the surgical advantages offered by AVM radiosurgery. In 2009, Asgari et al.[19] found that AVMs incompletely obliterated by radiosurgery bear an increased surgical risk. A more complicated AVM morphology was revealed by angiographic studies. The authors also found that microsurgical resection was extremely challenging and led to unfavorable outcomes in many patients.[19]

In this study, we performed a retrospective analysis of 42 patients who were surgically treated for AVMs several years after GKRS. The patients were matched individually with 42 patients who were surgically treated for AVMs without prior radiosurgery. The radiosurgical effects on AVM features, surgical resection, and neurologic outcomes were analyzed and discussed. In this case-control study, we hypothesized that good clinical outcomes can be achieved by surgical resection of persistent AVMs several years after GKRS.

MATERIALS AND METHODS

Patients

This study was approved by the institutional review board of Beijing Tiantan Hospital Affiliated to Capital Medical University. The prospectively maintained AVM database at Beijing Tiantan Hospital was searched to identify patients who underwent microsurgery to treat incompletely obliterated brain AVMs after GKRS between January 2000 and January 2014.

Patients meeting the following criteria were included: 1) patients treated with microsurgical resection for persistent brain AVMs after GKRS; 2) patients with a definite diagnosis of persistent AVMs after GKRS confirmed by preoperative digital subtraction angiography (DSA) and postoperative pathologic examination; and 3) patients with sufficient clinical, radiologic, radiosurgical, and follow-up data. The following patients were excluded: 1) patients treated with microsurgical resection for persistent brain AVMs after other types of radiotherapy (e.g., helium ion, proton beam, linear accelerator); 2) patients with other types of vascular malformations, such as cavernous malformations, revealed by postoperative pathology; 3) patients with insufficient clinical, radiologic, and radiosurgical data; and 4) patients lost to follow-up after microsurgical treatment.

Of the 1726 patients with AVMs surgically treated during the period 2000–2014, 42 consecutive patients with sufficient data were included in the study. The baseline patient characteristics (sex, age, history) and AVM features (size, side, location, angioarchitecture, Spetzler-Martin [S-M] grade) were collected. The time span between GKRS and surgical resection was recorded.

For this case-control study, the matching was performed independently by an observer blinded to postoperative neurologic outcomes. We used a case-matching method similar to the one described by Sanchez-Mejia et al.[23] in their study of AVM surgical outcome after radiosurgery. The 42 patients with prior radiosurgery (RS+) were individually matched with 42 patients with no radiosurgery (RS−) based on the following criteria: patient age, AVM size, location, diffuseness, deep venous drainage, S-M grade, hemorrhagic presentation, and modified Rankin Scale (mRS) scores at diagnosis (Table 1). All these criteria may affect the neurologic outcomes after AVM resection.

Gamma Knife Radiosurgery Treatment

GKRS was chosen based on the following factors: clinical presentation, AVM characteristics, functional status, and patient preference. Generally, GKRS is indicated as a single treatment for AVMs that are small (<3 cm diameter), unruptured, or poorly accessible. For high-volume AVMs, GKRS is also indicated as part of multimodal therapy in combination with microsurgical resection and embolization to reduce the AVM size. GKRS is also indicated for AVMs that are located in eloquent regions associated with high surgical risks. The patients were treated with the Leksell Gamma Knife (Elekta AB, Stockholm, Sweden) at the Radiosurgical Center of our institution. The mean irradiated AVM volume was 40,000 mm^3 (range, 1000–83,100 mm^3). The mean maximum dose was 38 Gy (range, 28–50 Gy). The mean marginal dose at the 50% isodose line was 20 Gy (range, 16–25 Gy). The mean radiation time was 36 minutes (range, 20–80 minutes). The patients were followed clinically at least every 6 months after radiosurgery. After GKRS, magnetic resonance imaging was performed at 3-month intervals in the first year, at 6-month intervals in the following 2 years, and then on a yearly basis. Follow-up DSA was performed to confirm AVM obliteration 3–4 years after GKRS. The patient's neurologic status was assessed with mRS. Subsequent AVM hemorrhages and complications after radiosurgery were recorded.

Microsurgical Treatment

Preoperative embolization was considered to facilitate surgical resection in 10 cases in RS+ group. Microsurgical AVM resection was performed in RS+ patients at the following times after GKRS: 1 year (3 patients), 2 years (5 patients), 3 years (4 patients), 4 years (8 patients), 5 years (3 patients), 6 years (6 patients), 7 years (4 patients), 8 years (4 patients), 9 years (2 patients), 10 years (1 patient), 11 years (1 patient), and 13 years (1 patient). The reasons for surgical resection were subsequent hemorrhages and