Results of surgical treatment after Gamma Knife radiosurgery for cerebral arteriovenous malformations: patient series

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BACKGROUND Gamma Knife radiosurgery (GKRS) is a safe and effective treatment, but it has a risk of bleeding. Herein, the authors describe their experience with some patients who required surgical removal of cerebral arteriovenous malformations (AVMs) located mainly in eloquent areas of the brain after GKRS, and they consider the advantages of surgical removal after GKRS.

OBSERVATIONS Twelve patients who had undergone surgical removal of AVMs after GKRS at Tokyo Women’s Medical University between April 2013 and July 2019 were selected for analysis. All participants underwent GKRS as first-line therapy for AVMs located in an eloquent region or if requested by the patient. Complete obliteration was achieved in 7 patients, and the size of the nidus decreased in 3 patients during the follow-up period. The Spetzler-Martin grade decreased in 11 patients. Three patients experienced symptomatic intracerebral hemorrhage before and after confirmation of complete obliteration of the nidus via GKRS, and 7 patients experienced some neurological deficits because of an encapsulated expanding hematoma. All patients underwent resection of the nidus without complications. The preoperative neurological deficits improved in 6 patients and remained unchanged in 6 patients.

LESSONS This report indicates that performing GKRS before surgery may be useful for future multimodal therapy.

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KEYWORDS cerebral arteriovenous malformation; Gamma Knife radiosurgery; encapsulated expanding hematoma; eloquent area

Gamma Knife radiosurgery (GKRS) is a safe and effective treatment modality for cerebral arteriovenous malformations (AVMs) that reduces the risk of bleeding, seizure, and some neurological deficits caused by stroke. However, there is a risk of bleeding and radiation-induced perifocal edema and seizure before complete resolution of the nidus can be obtained with GKRS. Bleeding secondary to GKRS is usually caused by a residual AVM or recanalization of the organized intraluminal thrombus and hemodynamic changes (e.g., thrombosis or narrowing of the draining vein). Complete obliteration of the nidus after radiosurgery takes 1–3 years. The bleeding and success rates are reported as 54% and 92%, respectively. The persistent risk of hemorrhage is a major disadvantage of radiosurgery compared with complete resection. A small risk of rebleeding persists even if angiography reveals complete obliteration of the nidus after GKRS. Furthermore, the AVM cannot be eliminated without any neurological deficits in every case.

Resection for AVMs located in eloquent areas of the brain is accompanied by a high risk of neurological deficits after surgical treatment. Multimodal therapy, including radiation therapy, staged radiosurgery, endovascular treatment, surgical treatment, and so forth, has recently been instituted for treating cerebral AVMs. Herein, we describe our experience with some patients who required surgical removal of AVMs located mainly in eloquent areas of the brain after GKRS, and we consider the advantages of surgical removal after GKRS.

Study Description Twelve patients who had undergone surgical removal of AVMs after GKRS at Tokyo Women’s Medical University between April 2013 and July 2019 were included in this study. All participants provided informed consent, and the study design was approved by an ethics review board.

ABBREVIATIONS AVM = arteriovenous malformation; GKRS = Gamma Knife radiosurgery; MRI = magnetic resonance imaging.

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All participants underwent GKRS as first-line therapy for AVMs located in an eloquent region or if requested by the patient. Follow-up every 6 months or 1 year included computed tomography, magnetic resonance imaging (MRI), or angiography. GKRS was performed twice in 2 patients because complete obliteration of the AVM was not confirmed on follow-up MRI. On MRI 15–280 months after GKRS, 3 patients had intracerebral hemorrhage, 8 patients had progressive expanding hematomas, and a residual nidus was observed in 1 patient. Patient details, including location of the AVM, Spetzler-Martin grade before the first GKRS, radiation dose, time elapsed after the final GKRS, and presentation of bleeding after GKRS are shown in Table 1.

**Illustrative Cases**

**Case 3**

A 14-year-old girl had experienced numbness in the upper right limb and tongue 4 years before presentation and had been diagnosed with a cerebral AVM around the right central sulcus. Angiography revealed that the nidus was fed by the left precentral and central arteries and drained through a single cortical vein to the superior sagittal sinus. The nidus measured approximately 4 cm. Deep drainage was absent. She had first been treated with GKRS (22 Gy) approximately 3 years before her current presentation because the AVM was located in an eloquent area (in the motor and sensory cortex) (Fig. 1). Follow-up MRI revealed perifocal edema and a wide T2-hyperintense lesion on the deep side of the nidus approximately 6 months after GKRS. However, the nidus appeared to shrink, and the administration of low-dose corticosteroids markedly improved the brain edema temporarily. Unfortunately, intracerebral hemorrhage occurred, with seizures and right-sided hemiparesis, 3 years after GKRS. Angiography revealed that the nidus had shrunk compared with its pre-GKRS size, but the flow velocity of the draining vein had decreased because of stenosis caused by GKRS. She underwent residual nidus removal with the transcortical

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**TABLE 1. Characteristics of 12 patients with AVM after GKRS**

| Case No. | Age (yrs)/Sex | Onset | Location of AVM | Spetzler-Martin G* | Radiation Dose (GKRS) | Duration After Final GKRS (mos) | Manifestation After GKRS |
|----------|---------------|-------|-----------------|-------------------|-----------------------|-------------------------------|-------------------------|
| 1        | 45/F          | Epilepsy | Lt temporal     | G 3 (2.1.0)       | 22 Gy 50% isodose   | 24                            | Intracerebral hemorrhage  |
| 2        | 26/F          | Hemorrhage | Lt medial frontal | G 3 (2.0.1)       | 22 Gy & 24 Gy 50% isodose | 84                            | Encapsulated expanding hematoma |
| 3        | 13/F          | Epilepsy | Lt motor cortex | G 2 (1.1.0)       | 22 Gy 50% isodose   | 34                            | Intracerebral hemorrhage  |
| 4        | 40/M          | Unknown | Lt frontotemporal | G 5 (3.1.1)       | Unknown               | Unknown                       | Intracerebral hemorrhage  |
| 5        | 45/F          | Hemorrhage | Rt occipital     | G 2 (1.1.0)       | 24 Gy 80% isodose   | 218                           | Encapsulated expanding hematoma |
| 6        | 35/M          | Incidental | Lt motor & sensory cortex | G 4 (3.1.0)       | 24 Gy 50% isodose ×2 | 15                            | Encapsulated expanding hematoma |
| 7        | 40/F          | Hemorrhage | Lt temporal      | G 1 (1.0.0)       | 22 Gy 55% isodose   | 40                            | Residual nidus            |
| 8        | 49/F          | Epilepsy | Rt temporooccipital | G 3 (2.1.0)       | Unknown               | 280                           | Encapsulated expanding hematoma |
| 9        | 44/M          | Headache | Rt motor & sensory cortex | G 3 (1.1.1)       | Unknown               | 260                           | Encapsulated expanding hematoma |
| 10       | 53/M          | Headache | Rt occipital     | G 4 (2.1.1)       | 18 Gy 50% isodose   | 150                           | Encapsulated expanding hematoma |
| 11       | 62/F          | Hemorrhage | Lt posterior horn of ventricle | G 3 (2.1.0)       | 20 Gy 60% isodose   | 200                           | Encapsulated expanding hematoma |
| 12       | 41/M          | Headache | Lt occipital     | G 2 (1.1.0)       | 22 Gy 50% isodose   | 130                           | Encapsulated expanding hematoma |

G = grade.
* Numbers in parentheses represent the scores for each of the three categories that make up the grade.
approach via the hematoma cavity. The nidus shrunk in size, and partial obliteration was observed deep within the nidus. The primary motor cortex was posterior to the nidus; thus, we stimulated the posterior wall of the excavated nidus directly during surgery to confirm the motor function of the right finger. She experienced complete right upper limb paresis for 3 days after direct surgery, which resolved completely within 1 week. MRI and angiography revealed complete resection of the AVM after direct surgery.

Case 2
The patient was a 26-year-old woman who presented with intracerebral hemorrhage in the left frontal lobe at 15 years of age and was diagnosed with a left frontal base AVM. The patient underwent GKRS (22 and 24 Gy) twice, first in December 2003, followed by a second procedure in September 2007 because complete obliteration was not confirmed on MRI and cerebral angiography after the first GKRS. Follow-up cerebral angiography revealed a small residual nidus after the second GKRS, but the patient did not wish to undergo surgery and was followed up with MRI, which revealed a small T2-hyperintense lesion around the nidus that appeared to be increasing in size. The patient experienced severe headaches approximately 7 years after the second GKRS. MRI revealed an encapsulated expanding hematoma with severe cerebral edema in the left frontal lobe. MRI also revealed exacerbation of cerebral edema, and a small residual nidus (diameter <1 cm) with a single deep draining vein was observed on angiography. The encapsulated expanding hematoma gradually increased in size because of repeated small bleeding in the hematoma cavity, and the patient’s consciousness worsened. The patient underwent resection via the hematoma cavity with complications. The lesion was covered with a cavernous angioma-like wall, with small feeding arteries and a draining vein in the posterior region, which were removed en bloc. The boundary between the lesion and surrounding brain tissue was clear, and hemostasis was achieved easily. The brain edema disappeared completely after surgery, and the patient’s disturbance of consciousness improved (Supplementary Fig. 1).

Case 6
The patient was a 35-year-old man whose cerebral AVM was discovered incidentally in 2011. MRI and angiography revealed a left parietal AVM (Fig. 2) in an eloquent area, with a Spetzler-Martin grade of 4. The first GKRS (24 Gy) was performed in 2011. The nidus decreased in size gradually. However, a second GKRS was performed in 2014 because MRI revealed a residual nidus. A small hemorrhage and perifocal edema (T2-hyperintense lesion) were observed on MRI 1 year after the second GKRS, but angiography did not reveal a residual nidus or early venous drainage (i.e., complete obliteration of the nidus after GKRS, according to angiography). However, the initially small hematoma expanded gradually and was accompanied by severe perifocal edema. Resection was performed via the transcortical approach (Fig. 3). Intraoperative findings included complete thrombotic occlusion of the main draining vein, a nearly occluded nidus, and residual small feeding arteries around the wall of the hematoma. Hemostasis was achieved easily, and the cleavage between the nidus and surrounding brain tissue was clear because of GKRS. Thus, the nidus was removed completely with the thrombosed main draining vein, without postoperative neurological deficits. MRI revealed complete elimination of the expanding hematoma and brain edema after resection.
Case 10

The patient was a 53-year-old man who presented with severe headache in July 1999 and was diagnosed with a right occipital AVM located in an eloquent area of the brain. Thus, treatment was conservative with follow-up for several years. The patient was treated with GKRS (18 Gy) in February 2005 at another hospital. Complete obliteration of the nidus was confirmed in 2009 with cerebral angiography and MRI. However, subsequent follow-up MRI revealed cyst formation in the right occipital lobe, and the patient experienced hemianopsia in 2015. The patient was administered corticosteroids, which proved ineffective. The cyst increased in size, and brain edema occurred in the adjacent tissue. The cyst was excised surgically without neurological complications. The contents of the cyst included sequential by-products of the hematoma. The findings were almost similar to those of case 6, and

FIG. 2. Case 6. A: Pre-GKRS T2-weighted MRI showing the nidus located in the left motor and sensory cortex. B–D: Pre-GKRS angiograms demonstrating the AVM. E: T2-weighted MRI scan obtained after the first GKRS, showing a residual nidus. F and G: T2-weighted MRI scans obtained after the second GKRS, demonstrating severe brain edema with an encapsulated expanding hematoma. H: Angiogram obtained after the second GKRS, showing complete nidus obliteration.

FIG. 3. Case 6. A–D: Intraoperative photographs showing complete thrombosis of the draining vein, small residual feeding arteries around the hematoma wall, and clear cleavage between the nidus and brain tissue. E and F: Postoperative T2-weighted MRI showing the absence of the expanding hematoma and disappearance of the brain edema.
### TABLE 2. Characteristics of angiographic findings before surgery and the change in neurological findings after surgery

| Case No. | Spetzler-Martin G Before GKRS | Spetzler-Martin G After GKRS | Complete Obliteration | Reduction of Nidus | Stenosis of Drainer | Neurological Deficit | Change in Neurological Deficit After Surgery |
|----------|-------------------------------|-------------------------------|----------------------|-------------------|-------------------|---------------------|-------------------------------------------|
| 1        | G 3 (2.1.0)                   | G 3 (2.1.0)                   | −                    | +                 | +                 | Dyslexia           | None                                       |
| 2        | G 3 (2.0.1)                   | G 2 (1.0.1)                   | −                    | +                 | −                 | Disturbance of consciousness | Improved                                   |
| 3        | G 3 (2.1.0)                   | G 2 (1.1.0)                   | −                    | +                 | −                 | Rt hemiparesis     | Improved                                   |
| 4        | G 5 (3.1.1)                   | G 4 (2.1.1)                   | −                    | +                 | −                 | Rt hemiparesis; disturbance of consciousness | Improved                                   |
| 5        | G 2 (1.1.0)                   | No nidus                      | +                    | +                 | −                 | Rt hemianopsia     | None                                       |
| 6        | G 4 (3.1.0)                   | No nidus                      | +                    | +                 | −                 | Sensory disturbance | Improved                                   |
| 7        | G 1 (1.0.0)                   | G 1 (1.0.0)                   | −                    | +                 | −                 | None               | None                                       |
| 8        | G 3 (2.1.0)                   | No nidus                      | +                    | +                 | −                 | Lt hemianopsia     | Improved                                   |
| 9        | G 3 (1.1.1)                   | No nidus                      | +                    | +                 | −                 | Sensory disturbance | Improved                                   |
| 10       | G 4 (2.1.1)                   | G 4 (1.1.1)                   | −                    | +                 | −                 | Hemianopsia        | None                                       |
| 11       | G 2 (1.1.0)                   | No nidus                      | +                    | +                 | −                 | Hemianopsia        | None                                       |
| 12       | G 2 (1.1.0)                   | No nidus                      | +                    | +                 | −                 | None               | None                                       |

+= partial disappearance; ++ = more than half disappeared; +++ = almost disappeared; G = grade.

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**Observations**

In the present study, complete obliteration was achieved in 7 patients, and the size of the nidus decreased in 3 patients during the follow-up period. Three patients experienced symptomatic intraoperative hemorrhage before complete obliteration of the nidus. Two patients experienced symptomatic intraoperative hemorrhage before complete obliteration of the nidus, and 7 patients experienced some neurological deterioration because of incomplete nidus obliteration after radiosurgery for AVMs is reported as approximately 2%–3% per year with interventional therapy for the prevention of death or stroke in patients with unruptured brain AVMs after a 33-month follow-up period. The Spetzler-Martin grade decreased in 11 patients, and the incidence of bleeding or expanding hematomas decreased significantly in the latency period after radiosurgery. Although radiosurgery is highly effective for treating AVMs, the hematoma capsule is difficult to achieve with interventional therapy for the prevention of death or stroke in patients with unruptured brain AVMs after GKRS. Hence, interventional therapy, comprising combinations of stereotactic radiosurgery, interventional treatment, and direct surgical treatment, has recently been initiated for unruptured AVMS. Complete obliteration of the nidus and after obliteration of the nidus is thought to cause postoperative bleeding or neurological deficits secondary to vascular malformations. Symptomatic encapsulated expanding hematomas were observed in 4 patients during the latency period after radiosurgery. Therefore, complete obliteration of the nidus is thought to be the baseline for treatment of unruptured AVMS. Although radiosurgery is highly effective for treating AVMs, the hematoma capsule is difficult to achieve with interventional therapy for the prevention of death or stroke in patients with unruptured brain AVMs after GKRS. Hence, interventional therapy, comprising combinations of stereotactic radiosurgery, interventional treatment, and direct surgical treatment, has recently been initiated for unruptured AVMS. The progressive obliteration of the nidus has been achieved in 6 patients, and 7 patients experienced some neurological deterioration because of incomplete nidus obliteration after radiosurgery. Therefore, interventional therapy for unruptured AVMS must be selected.
Presurgical angiography revealed a residual nidus behind the hematoma cavity in case 3, but the nidus on the deep side had disappeared (Fig. 1 shows the shrunken nidus). MRI revealed the absence of an encapsulated intracerebral hematoma. The residual nidus was confirmed as located on the brain surface intraoperatively, and we identified the main feeding artery and draining vein easily. The cleavage was very clear, and an encapsulated hematoma with a tough wall was located deep within the nidus. This part was almost thrombosed and not visualized on angiography. Several anomalous arteries that fed the hematoma capsule were coagulated and excised. The cleavage was very well demarcated because of GKRS, and the nidus had shrunk, which facilitated removal of the lesion with minimal motor cortex damage.

The nidus appeared completely obliterated on angiography, but MRI depicted an expanding encapsulated hematoma and severe brain edema in case 6. The residual nidus and main draining vein were easily confirmed as located on the brain surface intraoperatively, and the encapsulated hematoma was located anteriorly. The main drainer was completely thrombosed, and several small feeding arteries were observed at the inferior aspect of the encapsulated hematoma. We coagulated and cut these vessels easily so that the hematoma could be removed. (The clear cleavage between the nidus and surrounding brain tissue was attributed to GKRS.) The encapsulated hematoma and residual nidus were removed completely without any neurological deficits.

The residual nidus and encapsulated expanding hematoma were removed without deterioration of neurological findings in all patients. All resections performed in this study were safe and effective because hemostasis was achieved easily and the cleavage between the nidus and normal brain tissue was demarcated very clearly. Conversion of an AVM to an encapsulated expanding hematoma by GKRS may have been advantageous for the subsequent direct surgery, especially for AVMs in eloquent areas. Franzin et al. reported that volume-staged fractionated GKRS was a safe and effective treatment strategy for large, complex AVMs.7 First-line treatment with GKRS for AVMs in eloquent areas should aim to preferentially remove the nidus. We concluded that percutaneous angiography performed as located on the brain surface intraoperatively, and the encapsulated hematoma was located anteriorly.

Lessons

GKRS is a safe and effective treatment modality for AVMs but is accompanied by a risk of intracranial hemorrhage or an encapsulated expanding hematoma, even if angiography confirms complete nidus obliteration after GKRS. The effects of GKRS may facilitate surgery and may therefore minimize complications such as postoperative neurological deficits in cases of eloquent AVMs. We conclude that performing GKRS before surgery will be useful for multimodal therapy in the future.

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