Gamma Knife Radiosurgery in Cerebral Arteriovenous Malformations: Report of Three Patients Treated Twice

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Summary: We report three patients with cerebral arteriovenous malformations (AVMs) treated twice each by means of gamma knife radiosurgery: Case 1; 16 year old girl with an AVM located in the splenium of the corpus callosum, Case 2; 9 year old boy with a pontine AVM and case 3; 14 year old boy with an AVM located in the left middle temporal gyrus. In cases 1 and 2, three- or two-year angiography demonstrated small persistent residual nidi and sequential angiographic studies showed no nidus shrinkage over the two year period following these examinations. In case 3, however, three year angiographic examination disclosed a residual nidus which was located outside the previously irradiated region. At the time of reirradiation, in cases 1 and 3, more than 20 Gy was delivered at the periphery because the target volumes were very small and the residual nidi were located in non-critical brain structures. In case 2, however, because of the nidus location (within the pons), we...
selected the same dose (16 Gy) as that used in the initial treatment, although this dose was not considered to be optimal. Relatively little information is available on the doses used for reirradiation: What is the safest, optimal dose for achieving AVM obliteration? Further study of many such cases is necessary to resolve these issues.

Although follow-up angiography has not yet been performed in these patients, in cases 1 and 2, magnetic resonance (MR) angiography showed no vascular abnormalities and MR images suggested nidus obliteration 29 and 20 months, respectively, after reirradiation. The three patients have experienced neither rebleeding nor complications related to irradiation for, respectively, nine, six and six years since the initial gamma knife radiosurgery.

Based on these three cases, as well as our long-term follow-up experience with AVM patients treated by gamma knife radiosurgery, we have tentatively concluded that: 1) If the initial treatment was optimal, the patient should be followed without reirradiation as long as diminution of the nidus size is angiographically verified to be ongoing, regardless of the results of examination at three years. 2) If the initial treatment was less than optimal, the second course of gamma knife treatment should be done three years after the initial irradiation.

Introduction

In radiosurgery for an arteriovenous malformation (AVM), it is widely accepted that angiographically confirmed disappearance of the nidus is the primary goal of treatment. Only complete obliteration can eliminate the risk of hemorrhage. Using a gamma knife or a recently developed linear accelerator system, overall angiographic obliteration rates for patients with AVMs undergoing radiosurgery indicate that approximately 80% of AVMs have been obliterated two or three years after radiosurgery. Therefore, the next issue is how to treat the approximately 20% of patients whose nidus remains angiographically visible. Relatively little information has been published, to date, regarding the second course of irradiation using a gamma knife. Herein, we present three patients who underwent a second course of gamma knife treatment for a residual nidus demonstrated by three-, four- or five-year angiography, respectively. The timing and dose planning of reirradiation are also briefly discussed.

Backgrounds of the Three Cases

Since 1978, we experienced 39 patients with AVMs treated by means of gamma knife radiosurgery. One of these patients has thus far refused follow-up angiography, for seven years, eight have not yet undergone angiography because of post-radiosurgical intervals of two years or less, and 30 patients have undergone periodic angiographic examinations. Among the 30 patients, complete nidus obliteration has thus far been angiographically demonstrated in 20 (67%) between one and five years after radiosurgery and significant decreases in nidus volume have been observed in eight, while the nidus was essentially unchanged in the two remaining cases. Of the eight patients in whom a decreased, though not obliterated, nidus was demonstrated on repeat angiography, further follow-up examinations are awaited in two and have thus far been refused by three, while the other three did eventually undergo a second course of gamma knife treatment.

In all 39 cases, none had rebleeding although we did experience two cases of radiation-induced morbidity and one of angiography-related mortality.

Case Presentation

Case 1: A 16-year-old female underwent gamma knife radiosurgery, for a ruptured AVM located in the splenium of the corpus callosum, on December 10, 1985. Coverage of the 22 × 12 × 11-mm nidus was planned with a 50% isodose volume administered with two 14-mm collimators (Fig. 1A). A central dose of 50 Gy, considered necessary to obtain a marginal dose of 25 Gy, was used. Although angiography showed that the AVM had gradually decreased in size over the three years following treatment (Fig. 1B), no significant diminution in the size of the residual nidus could be seen between the three and five year angiographies (Figs. 1, B and C). Retrospective investigation of the dose planning data using a modern computer technique disclosed that the area of the residual nidus was irradiated with a dose of less than 14 Gy (Wan Yuo Guo, M.D., Department of Neuroradiology, Karolinska Hospital, personal communication, 1991). Thus, she received a second course of gamma knife irradiation on November 21, 1991. The residual nidus, the volume of which was about
4% of the initial volume, was covered with a 90% isodose volume administered with one 14-mm collimator (Fig. 1D). A central dose of 24.4 Gy was used to obtain a marginal dose of 22.0 Gy. Magnetic resonance (MR) angiography showed no vascular abnormalities, and MR images demonstrated significant, homogenous nidus enhancement by gadolinium (Fig. 2) and absence of any signal void 29 months after reirradiation; taken together, these findings strongly suggested nidus obliteration.19) This patient
has experienced neither rebleeding nor complications related to irradiation over the nine year period since her initial gamma knife radiosurgery.

Case 2: A 9-year-old boy underwent gamma knife radiosurgery, for a ruptured AVM located in the pons, on June 28, 1988. The $21 \times 18 \times 16$-mm nidus was covered with a 50% isodose volume administered with two 14-mm collimators (Fig. 3A). A central dose of 32.0 Gy was used to obtain a marginal dose of 16.0 Gy. Although angiography showed that the AVM had gradually decreased in size over the two years following treatment (Fig. 3B), no significant diminution in the residual nidus could be seen between the two year and four year angiographies (Figs. 3, B and C). Thus, he received a second course of gamma knife irradiation on January 7, 1993. The residual nidus, the volume of which constituted about 30% of the initial volume, was covered with a 70% isodose volume administered with one 14-mm collimator (Fig. 3D). A central dose of 22.9 Gy was used to obtain a marginal dose of 16.0 Gy. At 20 months after reirradiation, MR angiography demonstrated no vascular abnormalities, MR images showed neither a flow signal void nor any areas of abnormal intensity (Fig 4), and there was no contrast enhancement on computed tomography (CT); these findings strongly suggested nidus obliteration.19) This patient has experienced neither rebleeding nor complications related to irradiation over the six year period following the initial gamma knife radiosurgery.

Case 3: A 14-year-old boy underwent gamma knife radiosurgery, for a ruptured AVM located in the left middle temporal gyrus, on September 20, 1988 (Figs. 5, A and B). The nidus was considered to have been covered with a 50% isodose volume administered with one 14-mm collimator (Fig. 5C). A central dose of 40 Gy, expected to obtain a marginal dose of 20 Gy, was used. Three-year angiography demonstrated nidus obliteration within the area covered by the 50% isodose volume (Figs. 5, D and E). However, the anterior part of the nidus, which was not irradiated with an optimal dose, was still visible. This patient

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Fig. 3 Sequential angiograms obtained in Case 2 at the time of radiosurgery (A), two years (B) and four years (C) after radiosurgery, and at the time of the second radiosurgical treatment (D). Although a significant decrease in nidus size was angiographically apparent two years after radiosurgery, the angiograms taken two and four years after radiosurgery demonstrated no significant decrease in the residual nidus volume.
received a second course of gamma knife treatment on March 17, 1992. The residual nidus, the volume of which was about 40% of the initial volume, was covered with a 90% isodose volume administered with one 14-mm collimator (Fig. 5F). A central dose of 26.7 Gy was used to obtain a marginal dose of 24.0 Gy. Although no neurodiagnostic imaging studies have yet been performed following reirradiation, this patient has experienced neither rebleeding nor complications related to irradiation in the six years since the initial gamma knife radiosurgery.

Discussion

Gamma knife radiosurgery is now a well-established treatment alternative for small AVMs that are considered to be inoperable because of their location in critical brain regions and for patients who have concurrent medical risk factors. Although approximately 80% of patients show complete angiographic obliteration within a latency interval of two to three years, at which point the risk of subsequent hemorrhage is eliminated. However, debate persists as to whether a very small residual nidus which is angiographically demonstrated two or three years after gamma knife radiosurgery retains the potential to bleed, it is generally believed that the AVM must be reirradiated using a gamma knife so long as any vascular abnormalities can be angiographically observed. Guo et al. reported an AVM patient who experienced further bleeding from a small residual nidus 59 months after gamma knife radiosurgery.

Lindquist et al. recommended that reirradiation be considered when the AVM is still present on angiograms obtained two or three years after radiosurgery. Kawamoto, as well as Colombo et al., concur with this opinion. As is well known, the most marked nidus changes induced by irradiation using a gamma knife are evident by the end of the second postoperative year. However, radiosurgery-induced changes in the nidus continue for several years after treatment, as we reported elsewhere. We did, in fact, experience a case of complete obliteration confirmed five years after irradiation despite only partial obliteration at the time of three-year angiography. Therefore, we tentatively conclude that: 1) If, at the initial treatment, the nidus was totally covered and an optimal dose was delivered (“an optimal treatment”, as described by Steiner), the patient should be followed without reirradiation as long as a diminution in the nidus size is angiographically verified to be ongoing, regardless of the results of examination at three years. 2) If the initial treatment was not “optimal”, the second course of gamma knife treatment should be done at the point of three years after the initial irradiation.

Relatively little information is available on the dose given at the time of reirradiation: What is the safest, optimal dose for achieving AVM obliteration? Dose-volume relations in gamma knife radiosurgery for a vascular malformation have been discussed by Flickinger et al. and by Kondziolka et al. and are widely used for safe radiosurgical treatment at present. However, these criteria can be applied only for the first treatment. Steiner et al. reported that the radiation induced changes observed on CT scanning or MR imaging were more frequently seen in AVMs treated twice (10%) than in those treated once (6.7%). In addition, 5.0% of patients in the former group developed a neurological deficit, whereas only
In cases 1 and 3 presented here, doses of more than 20 Gy could be given because the target volumes were very small and the residual nidi were located in non-critical brain structures. In case 2, however, because of the nidus location (within the pons), we selected the same dose (16 Gy) as that used for the initial treatment, although this dose was less than optimal for achieving AVM obliteration. Further study of many such cases is necessary to resolve this issue.

**Fig. 5** Sequential angiograms obtained in Case 3 before radiosurgery (A: arterial phase, B: capillary phase), at the time of radiosurgery (C), 33 months after radiosurgery (D: arterial phase, E: capillary phase) and at the time of the second radiosurgical treatment (F). Although the portion of the nidus which had been irradiated with an optimal dose was angiographically shown to be obliterated 33 months after radiosurgery, the anterior part of the nidus located outside the previously irradiated region was still visible (arrows).

**Acknowledgment**

In our previous paper,16) we partially reported two of the three cases presented here. Therefore, Figs. 1A, 1C, 5A, 5C and 5D, which have already been published, are presented again for the readers' convenience.

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