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Failure in Radiosurgery Treatment of Cerebral Arteriovenous Malformations

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OBJECTIVE: The aim of this study was to retrospectively analyze the reasons for the failure of radiosurgical treatment of cerebral arteriovenous malformations (AVMs).

METHODS: Seventeen cases of noncured AVMs were reviewed 3 years after radiosurgical treatment. Follow-up ranged from 33 to 54 months (mean, 44.3 mo). Lesion dimensions varied from 9 to 55 mm (mean, 29.2 mm). The lesions were located in critical or near-critical brain regions. Angiography was performed under Talairach's stereotactic conditions. Two large AVMs bled 36 and 39 months after receiving irradiation, respectively. These two AVMs had been incompletely irradiated.

RESULTS: Retrospectively, in four cases (23.5%) we observed errors in determining AVM target shape and size because of inaccurate definition of the nidus and/or because of stereoangiographic incompleteness (absence of external carotid artery injections). In five large and/or irregularly shaped AVMs (29.4%), a strategy of partial volume irradiation had been used. In one patient (5.8%), we observed the recanalization of previously embolized AVMs. In another case (5.8%), the target had been partially missed. The AVMs in one case (5.8%) had been treated with an ineffective peripheral dose. In one (5.8%), the failure occurred because of the lesion angio-architecture. In four cases (23.5%), no evident reasons for failure were determined.

CONCLUSION: The results of this study suggest the necessity of complete irradiation of the nidus. The strategy of partial volume irradiation might be avoided, even if it necessitates lowering the doses to treat large AVMs. Accuracy in the target determination is required, and complete stereoangiography is necessary. (Neurosurgery 42:996-1004, 1998)

Key words: Arteriovenous malformations, Failure, Radiosurgery, Retrospective analysis

Partial obliteration in radiosurgically treated cerebral arteriovenous malformations (AVMs) is considered to be a failure of the therapy, independent of the percentage of obliterated volume. The survival rates in incompletely cured AVMs resemble the natural history of untreated lesions, and the risk of hemorrhage remains. For this reason, the absolute goal of the treatment is the complete angiographically proven obliteration of the AVMs and the normalization of the cerebral vascular anatomy. Radiosurgery is currently considered to be an effective method of treatment for selected patients affected by cerebral AVMs. A 70 to 95% rate of complete obliteration is reported in the radiosurgical literature (2, 7, 8, 11, 21, 33, 34, 41). Retrospective analyses of noncured AVMs are the means for investigating the factors

associated with the failure of radiosurgery. Understanding these factors can provide further improvement of the results, enable the avoidance of mistakes, and permit a better selection of patients. With this aim, we reviewed the clinical, angiographic, and dosimetric data of 17 cases in which radiosurgery did not achieve, after 3 years, the cure of the AVMs.

PATIENTS AND METHODS

A previous analysis of 120 patients affected by cerebral AVMs that were radiosurgically treated with a linear accelerator by our group (named SALT from the names of our institutions, Ste Anne, Lariboisière and Tenon University Hospitals), between January 1990 and July 1992, showed a

complete cure of the AVMs in 86 patients (71.6%). In this study, we reviewed the data of 17 patients (14.2%), who underwent follow-up angiography 3 years after radiosurgery and whose angiograms did not show the AVMs to be cured according to the criteria presented by Lindquist and Steiner (20), which are normal circulation time, absence of former nidus vessels, and disappearance or normalization of draining veins. The remaining 17 patients (14.2%) were not included in this study because they had only 2 years of angiographic follow-up. Angiographic evaluation performed 24 months after irradiation was considered to be only one interval assessment at a time when obliteration may still progress (17).

Patient population

This series includes 5 female and 12 male patients whose ages at the time of the radiosurgery varied from 11 to 67 years (mean, 31.9 yr). Hemorrhage was the symptom at the time of presentation for 10 patients. In one patient, the AVMs presented with headaches, and in three patients, the AVMs presented with seizures. A combination of seizures and a neurological deterioration was the presentation sign in one patient, a combination of seizures and headache was the presentation sign in another patient, and a progressive neurological deficit was the presentation symptom in a third patient. At the time of radiosurgery, nine patients presented with neurological deficits. Before radiosurgery, 13 patients had been previously treated (12 with incomplete AVM embolization and 1 with a combination of surgery and embolization). Eleven patients harbored hemispheric AVMs in cortical and/or subcortical regions (frontal region, five cases; temporal region, three cases; parietal region, two cases; temporo-occipital region, one case). Four occurrences of AVMs were deep-seated in the basal ganglia. One occurrence of AVMs was localized in the callosal region and one in the cingulo-occipital region.

Stereotactic neuroradiology

The angiographic study of the AVMs was performed under Talairach's stereotactic conditions (39, 40). Two images per second were obtained. The AVM images were transposed onto Talairach's proportional grid system that permitted correct localization of the lesion in its anatomophysiological environment (37, 38). All of the AVMs resulted as localized in eloquent or near-eloquent areas of the brain. Table 1 shows the angiographic characteristics of the AVMs for which radiosurgery failed.

The spatial conformation of the AVMs was defined as having three possible shapes: four cases had a spherical shape, eight cases had an elliptical shape, and five cases presented irregular spherical forms. In four of these cases (three of which had previously been embolized), the AVMs presented as having two or more separate nodules.

TABLE 1. Angiographic Characteristics of 17 Arteriovenous Malformations That Were Not Cured by Radiosurgery^a

Characteristics	No. of Patients
AVM size (mm)	≤10 2
	11–20 6
	21–40 7
	41–60 2
External carotid artery supply	4
Venous drainage	Superficial 6
	Deep 5
	Both 6
Aneurysms	None
High blood flow	8

^a AVM, arteriovenous malformation.

Strategy, dosimetry, and method of irradiation

The strategy practiced by our group was to include all the nidus as well as the origin of the draining veins in the target volume. The target was defined by stereotactic angiography in stereoscopic conditions by a neurosurgeon experienced in radiosurgery. Magnetic resonance (MR) imaging was used as a help in the spatial definition of the nidus. The dosimetry planning was obtained with the three-dimensional treatment planning software system ARTEMIS-3D working on a VAX Station (Model 3200; Digital Equipment Corp., Maynard, MA). The target volume varied between 0.31 and 18.44 cc (mean, 5.09 cc). In seven cases, one irradiation isocenter was used, whereas in the remaining cases, two to four isocenters were used. The additional collimator diameter varied between 8 and 20 mm. The radiation dose at the margins of the target was 25 Gy in 15 cases, 18 Gy in 1 case, and 15 Gy in the remaining case. The margins of the target were encompassed by isodoses of 70% in 13 cases and of 60 or 50% in 4 cases. The irradiation was performed in a single session, with the patient seated in the Betti arm chair and the head secured in the Talairach stereotactic frame (1, 3). One occurrence of AVMs (34 mm in maximum diameter) that was localized in the basal ganglia and was formed by two compartments was irradiated in two different sessions (each treating only one of the compartments), distanced by 27 months. Patients were irradiated with an isocentric linear accelerator (15-MV x-rays) with a 1-mm isocenter position precision for a 130-degree arc.

RESULTS

Follow-up ranged from 33 to 54 months (mean, 44.3 mo). In two cases, the AVMs bled. Table 2 shows the clinical and angiographic data of these two AVMs. The nonfatal hemorrhage took place 36 and 39 months after treatment, respectively. Angiograms showed changes in blood flow, reduction in the number and in the caliber of the draining veins, and an increase in tortuosity. These AVMs had received partial volume irradiation. More precisely, the origin of the draining

TABLE 2. Characteristics of Two Noncured Arteriovenous Malformations That Bled after Radiosurgery

Patient No.	Age (yr)	Symptom at Presentation	Previous Treatment	Site	Size (mm)	Venous Drainage
2	27	Hemorrhage	Embolization	Central region	40	Deep
13	23	Seizure	Embolization	Basal ganglia	40	Superficial

veins was out of the radiation field in one case. A radiation dose of 25 Gy in one case and of 18 Gy in the other case was delivered at the margins of the target.

The angiographic controls were performed in nonstereotactic conditions. Each of 16 patients underwent at least two angiographic controls. Angiograms were separately submitted to two neuroradiologists. The lecturers analyzed qualitatively the changes in nidus size in the anteroposterior and lateral views and in nidus opacification, as well as the slowing of the blood flow in relation to the pretreatment aspect of the AVMs.

In relation to their initial dimensions in 14 patients, angiography showed reduction in the nidus volume, slowing of blood flow, and reduction of the number and/or the caliber of the draining veins. In each of two cases, the nidus had disappeared but a dilated draining vein was observed early. One patient obtained complete obliteration of the AVMs, but signs of venous blush were present, corresponding to the region previously occupied by the nidus.

Retrospective analysis of factors associated with radiosurgery failure (Table 3)

For each of four patients (23.5%), we discovered an error in determining the target. This was the consequence of an inaccurate definition of the nidus and of the origin of the draining veins and/or of incomplete stereotactic angiography. Of these four occurrences of AVMs, despite that the target at the time of irradiation was judged to have covered the entire nidus, three were determined to have been incompletely irradiated because of an error in the angiographic definition of the target volume. These three occurrences of AVMs (previously embolized) had a mean of 32 mm. One had an irregular shape produced by multiple compartments resulting from previous embolizations. In the fourth case (AVMs presenting a meningeal vascular supply), we discovered errors in the target determination because of incompleteness of stereotactic angiography, caused by absence of external carotid artery injections.

Five patients (29.4%) were intentionally selected for subtotal irradiation (the target did not comprise the nidus in its totality as well as the origin of the draining veins). The largest diameter of these five occurrences of AVMs ranged between 16 and 55 mm (mean, 31 mm), and they were situated in the basal ganglia in two cases, in the central region in two cases, and in the callosal region in the remaining case. Three had irregularly shaped spatial conformation, and, in particular, two of them were of multinodular form.

In one case (5.8%), recanalization of part of the AVMs that was previously embolized was observed. This part of the AVMs was outside the target because it was not visible at the time the stereotactic angiography was performed. In one case

TABLE 3. Factors Associated with Radiosurgery Failure in 17 Cases of Arteriovenous Malformations^a

Inaccurate target determination: three cases of AVMs (17.6%)
Largest diameter, 20–40 mm
Shape:
Spherical, 1
Irregularly spherical, 1
Irregularly spherical with separate nodules, 1
Origin of veins not covered by the target, 1
Incomplete stereotactic angiography: one case of AVMs (5.8%)
Largest diameter, 34 mm
Shape: irregularly spherical, 1
Origin of draining veins not covered by the target
Strategical choice: five cases of AVMs (29.4%)
Largest diameter, 16–55 mm
Shape:
Spherical, 1
Elliptical, 1
Irregularly spherical, 1
Elliptical with separate nodules, 2
Origin of the draining veins not covered by the target, 2
Revascularisation of part of the nidus: one case of AVMs (5.8%)
Largest diameter, 20 mm
Shape: spherical
Origin of the draining veins covered by the target
Missed target: one case of AVMs (5.8%)
Largest diameter, 26 mm
Shape: elliptical
Origin of the draining veins covered by the target
Lesion angioarchitecture: one arteriovenous fistula (5.8%)
Largest diameter, 9 mm
Shape: spherical
Low dose delivered at the margin of the lesion: one case of AVMs (5.8%)
Largest diameter, 47 mm
Shape: irregularly spherical
No evident reasons found: four cases of AVMs (23.5%)

^a AVMs, arteriovenous malformations.

(5.8%), we detected a target that had been missed because of an error in the superposition of the drawing of the target on the angiographic films at the moment the stereotactic angiography was performed. In one case (5.8%), large AVMs (47 mm in diameter) located in the central region were treated with an ineffective radiation dose (<15 Gy at the periphery of the lesion). In one case (5.8%), the failure was attributed to angioarchitecture of the malformations, an arteriovenous fistula that was not very sensitive to radiosurgery.

In four cases (23.5%), no evident reasons associated with the failure of the radiosurgery were determined. (One of these four cases of AVMs was completely obliterated, but we considered it noncured because of the presence of venous blush corresponding to the region of the nidus. In this case, we think that no technical or strategical errors were made).

DISCUSSION

Postradiosurgical hemorrhage in noncured AVMs

The complete obliteration of the AVMs is the absolute goal of the radiosurgery. No cases of bleeding in AVMs that are cured as confirmed by angiography have been observed. Controversy exists regarding a possible role of protection by radiosurgery from bleeding in nonobliterated AVMs. According to Kjellberg (16) the risk decreases statistically after a period of 2 years. Steiner et al. (35) support a delayed protection from bleeding (after 5 yr) in these cases. Forster (8) observed no hemorrhages in 15% of the 615 patients who, 2 years after undergoing radiosurgery, had only partial reduction in the AVM nidus flow with the persistence of an abnormal venous drainage. On the other hand, many reports assert that partial obliteration produces no protection against hemorrhage. Kondziolka et al. (17) observed no difference between the hemorrhage rates in patients with nonobliterated AVMs and the expected natural history of untreated AVMs. Steinberg et al. (33) observed 10 cases of bleeding, two of them occurring during the 3rd year after irradiation in nonobliterated AVMs. Friedman et al. (10), recently, in a detailed analysis of 201 patients, did not observe a statistically significant departure from the natural hemorrhage rate at any time period after radiosurgery in those cases in which total cure was not achieved. Pollock et al. (28) observed no protective effect against bleeding for AVMs that were incompletely obliterated 5 years after radiosurgery.

In our series, two patients suffered nonfatal hemorrhage. The diameter of these two occurrences of AVMs was significantly larger (40 mm), compared to the mean diameter of the other 15 lesions that did not bleed (25.8 mm). This finding is in accordance with other reports (10, 14) that suggest an increased risk of hemorrhage with increasing AVM size. We retrospectively determined that these two occurrences of AVMs had received partial volume irradiation. The angiograms at the time of the bleeding showed changes in blood flow, reduction of the number and of the caliber of the draining veins, and increase in tortuosity. Similar findings were revealed by angiographic studies of partially obliterated AVMs that had bled. These signs were related to the increased pressure gradient through the malformations (6). Colombo et al. (7), in a review of 180 patients, observed a higher tendency for bleeding in incompletely irradiated AVMs. The authors emphasized the importance of a homogeneous radiation dose to the whole nidus to avoid partial irradiation and, consequently, increased risk of hemorrhage. Considering the time of bleeding, Colombo et al. (7) did not once observe hemorrhages in partially irradiated cases after 24 months. Contrary to this observation, our two occurrences of AVMs bled after 3 years.

The criteria of cure, as defined by Lindquist and Steiner (20), include not only the complete obliteration of the AVMs but also the normalization of the cerebrovascular anatomy. For this reason, we considered as a failure a case of AVMs for which the control angiography showed only a venous blush corresponding to the region of the nidus. The angiographic results for this patient did not correspond to the criteria of cure, but it seemed reasonable to consider that in this case, the risk of hemorrhage practically did not exist because of the absence of shunt.

Factors associated with AVM noncure

In 11 patients (64.7%) of this series, we retrospectively observed that, for different reasons, the AVMs were partially irradiated. The influence of incomplete coverage by the irradiation field on the failure of the radiosurgery has already been noted. Steinberg (33) observed that in 43 cases of AVMs treated with irradiation focused on the earliest component of the arterial phase, only the irradiated part of the AVMs was obliterated. Yamamoto et al. (41) reported that the analysis of the dose plan in cases of nonobliterated AVMs often revealed that a part of the nidus was not covered by the prescribed treatment volume. Merienne et al. (23), in a previous report, observed better response to radiosurgery in cases in which all of the nidus and the origin of the draining veins were in the target.

Our results confirm the implication of the partial volume irradiation in the failures of the treatment. The partial volume irradiation of the malformations was the consequence of the following.

1) Error in target shape and size evaluation

Many articles have already reported the difficulty involving the spatial representation of AVMs (2, 16, 31, 41). Stereotactic biplanar angiography alone was determined not to be an optimal database for an accurate evaluation of the nidus size and shape. Other reports have discussed the accuracy and usefulness of different imaging databases (5, 25–27, 31). Blatt et al. (4) observed that the nidus isocenter and diameter, as identified by stereotactic angiography, often differed from that identified by stereotactic enhanced computed tomography. Smith et al. (30), who studied the MR images, computed tomographic scans, and angiograms of 15 patients with AVMs, observed that the MR images and computed tomographic scans were superior to the angiograms in defining the different structures of the malformations. Kondziolka et al. (18) studied the accuracy and usefulness of stereotactic MR angiography (sMRA) in 28 patients in comparison with stereotactic angiography. In 24 cases, the sMRA information was identical to that of angiography, and in 3 cases, sMRA was superior. In one case, angiography was better because it detected a second separate nidus of small size (10 mm) that was not revealed by sMRA. Kondziolka et al. (18) concluded that it can be used as the sole database for medium-sized AVMs. Stein et al. (32) observed that small or other difficult-to-see vascular anomalies may not be detected on sMRA images. More recently, Pollock et al. (29), in a retrospective

analysis of 45 cases of incompletely obliterated AVMs, determined that for 21 patients, an error in the biplanar angiographic determination of the nidus had occurred. They suggest the use of stereotactic angiography coupled with contrast-enhanced stereotactic MR imaging and MR angiography.

We think that conventional biplanar angiography may have limitation as a stereotactic database because of the difficulty of representing a volume using only two planes of space. For this reason, the methodology that we use implies that the dimensions of the nidus, its spatial conformation, and the relationships with the surrounding structures be studied using teleangiography and stereoscopy. This allows a reliable image of the AVMs with very low magnification and minimum deformation (23, 36, 39, 40). In cases of hemorrhage, the stereoangiography was always performed after the complete reabsorption of the hematomas to avoid an incomplete nidus recognition caused by compression of the vessels. However, we retrospectively determined that even in satisfactory conditions, a skilled radiosurgery neurosurgeon failed to determine the target in three cases. The volume target of the 17 cases of AVMs was redetermined blindly by the same neurosurgeon who defined the target at the time of the stereotactic angiography. For 3 of the 17 cases of AVMs, the new and original targets differed. Retrospective analysis of the radiosurgical plans of these cases showed that part of the nidus and the origin of the draining veins in one case was outside the treatment isodose. This observation emphasizes that there are some difficulties in understanding the shape and size of the nidus and that there is even more difficulty in understanding the origin of the draining veins. This difficulty is, in our experience, greater for medium and large lesions, and it is correlated with subjectivity in defining the structure of the malformations. At present, we use MR imaging to help in the three-dimensional target volume definition (24, 37, 38). Difficulties in nidus shape and size evaluation are more often observed in previously partially embolized AVMs. One of the goals of embolization in the multidisciplinary treatment of the AVMs is to reduce the volume of the lesion to a size that facilitates successful stereotactic radiosurgery (12). Unfortunately, the endovascular treatment often leaves the shape of the AVMs irregular and fragmented. Moreover, in embolized AVMs, the presence of embolic material often makes the appreciation of the structures difficult. For this reason, stereotactic angiography in cases of embolized AVMs always needs subtractions.

Another factor responsible for errors is, as previously reported (29), inadequate or incomplete cerebral angiography with partial visualization of the nidus and of the origin of the draining veins. In one case in this series, we determined that the incompleteness of the stereotactic angiography (absence of external carotid artery injections) was responsible for a partial visualization of the AVMs and thus for incomplete irradiation. Pollock et al. (29) reported that in 11% of their series, radiosurgery failed for the same reason, and they stressed the importance of complete angiography (including superselective and external carotid artery injection).

2) Strategic choice

In five cases, we deliberately used a strategy of partial volume irradiation in AVMs located in eloquent regions of the brain, often of large size and of irregular shape or multinodular form. The aim of this approach was to decrease the risk of radiation-induced complications in patients without, or with minor, neurological deficits. This strategy did not further deteriorate the neurological status of the patients but did not produce satisfying results from the viewpoint of obliteration. Alternatively, in one case of large AVMs bearing two distinct compartments, we preferred to irradiate the two nodules separately in two different sessions instead of performing a partial volume irradiation. We did not observe radiation-induced complications, and the patient's deficit partially improved, but AVM cure was not achieved.

3) Repermeabilization of part of the AVMs

In one patient, the partial volume irradiation was the consequence of the repermeabilization of part of the previously embolized AVMs. This part was not visible at the moment that stereotactic angiography was performed, and, consequently, it was not included in the target volume. Thus, an incomplete irradiation resulted. The nonobliterated part of the AVMs corresponded to this nonirradiated component. Gobin et al. (12), who analyzed the results of the combined treatment of AVMs by embolization and radiosurgery, reported a less favorable response to irradiation of embolized AVMs compared to the native AVMs of the same size. They determined that this difference could be explained by the revascularization of embolized parts of the AVMs. Pollock et al. (29) reported three cases of AVM recanalization among 19 patients who underwent irradiation and previous embolization.

4) Missed target

We retrospectively observed a missed target in one case (because of an error in the transposition of the drawing of the target on the angiographic films at the moment of the stereotactic study), with the consequent displacement by 15 mm in the anteroposterior direction of the isocenter with respect to the target center. Consequently, at least half of the AVMs did not receive an effective radiation dose. In this case, a human error was made.

AVM size, radiation dose, and response to radiosurgery

Different opinions exist regarding the influence of AVM size on the response to radiosurgery. Betti and Munari (2) reported a correlation between smaller dimension and better AVM obliteration. According to Lunsford (21), the volume is the only strategical factor implicated in AVM cure. Colombo et al. (7) observed 2-year AVM obliteration rates of 96.5% for AVMs smaller than 15 mm, 73.9% for AVMs between 15 and 25 mm, and 33.3% for AVMs larger than 25 mm. Kondziolka et al. (17) reported that for malformations 0 to 4 cc in volume, the obliteration rate was 82%, whereas for lesions larger than 4 cc, the obliteration rate lessened as the volume increased. Steinberg et al. (33) observed that malformations smaller than 4 cc (2 cm in diameter) had obliteration rates of 94% after

2 years and 100% after 3 years. AVMs 4 to 25 cc in volume had obliteration rates of 75% after 2 years and 95% after 3 years, whereas lesions larger than 25 cc had obliteration rates of 42% after 2 years and 73% after 3 years. On the other hand, Kemeny et al. (15) did not observe differences in obliteration rates between AVMs that were smaller than or larger than 2 cc in volume. Friedman and Bova (9) noted that the obliteration rate at 2 years was independent of the AVM volume. Yamamoto et al. (41), who analyzed the radiosurgical results in 121 patients, did not observe a statistical difference in the obliteration rate between AVMs smaller than or greater than 10 cc in volume.

We noted that AVM size in the whole population, including the 120 patients who were treated (mean diameter, 22 mm), was smaller than the mean AVM dimension of the 17 noncured AVMs in this study (mean diameter, 29.2 mm). However, more detailed analysis showed that 50% of our noncured AVMs were 20 mm or less in diameter. Lesions of this size usually have an excellent response to radiosurgery (2). Moreover, two occurrences of AVMs had diameters of less than 10 mm. The reasons for the failure of one of these small malformations remain unknown. For the other one, the failure was attributed to the angioarchitectural structure of the lesion. These malformations consisted of a single arteriovenous channel (arteriovenous fistula according to the Houdart classification) (13). Meder et al. (22), in a previous report, studied the value of radiological parameters in predicting response to irradiation. They determined that this type of malformation is less sensitive to irradiation. Our case confirms that radiosurgery does not represent an ideal approach for this type of lesion, even those of small size.

The question of the radiosurgery dose is still open. Kondziolka et al. (17) determined that the best results are achieved when doses between 22 and 25 Gy are delivered at the periphery of the lesion. Steinberg et al. (33) reported a high complete obliteration rate in AVMs treated with higher doses (30–45 Gy) or intermediate doses (24–28 Gy), whereas lesions treated with doses of 15 Gy or less had a low complete obliteration rate. On the other hand, Yamamoto et al. (41) reported that the obliteration rate for larger malformations treated with a dose of 16 to 18 Gy is similar to that for smaller malformations treated with 18 to 20 Gy and that a radiosurgical dose of 16 Gy to the margins of the nidus could be effective. Friedman and Bova (9) reported an obliteration rate between 69 and 89% (according to the volume), with a mean irradiation dose of 15.6 Gy at the periphery.

In our radiosurgical strategy, using knowledge derived from previous experience, we delivered a dose of 25 Gy at the margins of the lesion (19, 23). In one case in our series of noncured AVMs, we delivered a dose of 15 Gy at the margins of the malformations. We think that this dose was ineffective and probably responsible for the failure of the radiosurgery in this case. No more significant conclusions concerning the dose could be reached by this study because we try to treat all of the AVMs in the most homogeneous way and we did not observe significant difference between the radiosurgical dose delivered in cured or in noncured AVMs. Thus, the dose did not represent a true variable in our irradiated patients.

CONCLUSION

The results of this study suggest the necessity of complete irradiation of the nidus and of the origin of the draining veins to obtain AVM cure. AVMs of small or medium sizes, as well, might not be cured if optimal irradiation is not performed. The strategy of partial volume irradiation might be avoided, even if it necessitates lowering the radiation doses for large AVMs located in critical regions. Accuracy in the three-dimensional volume target determination is required, and complete stereotactic angiography is necessary.

In 13 cases (76.4%) of these noncured AVMs, we retrospectively determined that a strategic or technical error was responsible for the radiosurgery failure. Other recent studies support these conclusions. These errors are independent of methodology and of equipment. Currently, thanks to knowledge derived from experience and retrospective analyses of results, it will be possible to avoid such errors. We think that the results of radiosurgery in the treatment of selected cerebral AVMs may be further improved.

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REFERENCES

1. Betti OO, Derechinsky VE: Irradiations stéréotaxiques multifaisceaux. *Neurochirurgie* 28:53–56, 1982.
2. Betti OO, Munari C: Radiosurgical treatment of minor intracranial arteriovenous malformations by using a linear accelerator [in French]. *Neurochirurgie* 38:27–34, 1992.
3. Betti OO, Munari C, Rosler R: Stereotactic radiosurgery with the linear accelerator: Treatment of the arteriovenous malformations. *Neurosurgery* 24:311–321, 1989.
4. Blatt DR, Friedman WA, Bova FJ: Modifications based on computed tomographic imaging in planning the radiosurgical treatment of arteriovenous malformations. *Neurosurgery* 33:588–596, 1993.
5. Bova FJ, Friedman WA: Stereotactic angiography: An inadequate database for radiosurgery? *Int J Radiat Oncol Biol Phys* 20:891–895, 1991.
6. Colombo F: Linear accelerator radiosurgery of cerebral arteriovenous malformations: Technique and results, in Steiner L, Lindquist C, Forster D, Backlund EO (eds): *Radiosurgery Baseline and Trends*. New York, Raven Press, 1992, pp 189–194.
7. Colombo F, Pozza F, Chierago G, Casentini L, De Luca G, Francescon P: Linear accelerator radiosurgery of cerebral arteriovenous malformations: An update. *Neurosurgery* 34:14–21, 1994.
8. Forster DE: The Sheffield "gamma knife" experience: Results in arteriovenous malformations radiosurgery in 507 patients, in Lunsford LD (ed): *Stereotactic Radiosurgery Update*. New York, Elsevier, 1992, pp 113–115.

9. Friedman WA, Bova FJ: Linear accelerator radiosurgery for arteriovenous malformations. *J Neurosurg* 77:832-841, 1992.
10. Friedman WA, Blatt DL, Bova FJ, Buatti JM, Mendenhall WM, Kubilis PS: The risk of hemorrhage after radiosurgery for arteriovenous malformations. *J Neurosurg* 84:912-919, 1996.
11. Friedman WA, Bova FJ, Mendenhall WM: Linear accelerator radiosurgery for arteriovenous malformations: The relationship of size to outcome. *J Neurosurg* 82:180-189, 1995.
12. Gobin YP, Laurent A, Merienne L, Schlienger M, Aymard A, Houdart E, Casasco A, Lefkopoulos D, George B, Merland JJ: Treatment of brain arteriovenous malformations by embolization and radiosurgery. *J Neurosurg* 85:19-28, 1996.
13. Houdart E, Gobin YP, Casasco A, Aymard A, Herbreteau D, Merland JJ: A proposed angiographic classification of intracranial arteriovenous fistulae and malformations. *Neuroradiology* 35:381-385, 1993.
14. Karlsson B, Lindquist C, Kihlstrom L, Steiner L: Gamma knife surgery for AVM offers partial protection from hemorrhage prior to obliteration. *J Neurosurg* 82:345A, 1995 (abstr).
15. Kemeny AA, Dias PS, Forster DM: Results of stereotactic radiosurgery for arteriovenous malformations: An analysis of 52 cases. *J Neurol Neurosurg Psychiatry* 52:554-558, 1989.
16. Kjellberg RN: Proton beam therapy for arteriovenous malformations of the brain, in Schmidek HH, Sweet WH (eds): *Operative Neurosurgical Techniques*. New York, Grune & Stratton, 1988, pp 911-915.
17. Kondziolka D, Lunsford LD, Flickinger JC: Gamma knife stereotactic radiosurgery for cerebral vascular malformations, in Alexander E III, Loeffler JS, Lunsford LD (eds): *Stereotactic Radiosurgery*. New York, McGraw-Hill, 1993, pp 136-146.
18. Kondziolka D, Lunsford LD, Kanal E, Talagala L: Stereotactic magnetic resonance angiography for targeting in arteriovenous malformations radiosurgery. *Neurosurgery* 35:585-591, 1994.
19. Lefkopoulos D, Schlienger M, Touboul E: A 3D radiosurgical methodology for complex arteriovenous malformations. *Radiation Oncol* 28:233-240, 1993.
20. Lindquist C, Steiner L: Stereotactic radiosurgical treatment of malformations of the brain, in Lunsford LD (ed): *Modern Stereotactic Neurosurgery*. Boston, Martinus Nijhoff, 1988, pp 491-505.
21. Lunsford LD: The role of stereotactic radiosurgery in the management of brain vascular malformations, in Alexander E III, Loeffler JS, Lunsford LD (eds): *Stereotactic Radiosurgery*. New York, McGraw-Hill, 1993, pp 111-121.
22. Meder JF, Oppenheim C, Blustajn J, Nataf F, Merienne L, Lefkopoulos D, Laurent A, Merland JJ, Schlienger M, Fredy D: Cerebral arteriovenous malformations: The value of radiologic parameters in predicting response to radiosurgery. *AJNR Am J Neuroradiol* 18:1473-1483, 1997.
23. Merienne L, Laurent A, Meder JF, Lefkopoulos D: Stereotactic radiation of 46 cerebral angiomas: Analysis of the angiographic results 2 and a half years after treatment [in French]. *Neurochirurgie* 37:185-195, 1991.
24. Musolino A, Talairach J, Tournoux P, Missir O: Comparative study between stereotactic angiography and magnetic resonance imaging (MRI) data on spatial organization of sulci and convolutions in man. *Boll Lega It Epil* 62/63:51-56, 1988.
25. Noorbehesht B, Fabrikant JI, Enzmann DR: Size determination of supratentorial arteriovenous malformations by MR, CT and angio. *Neuroradiology* 29:512-518, 1987.
26. Phillips MH, Frankel KA, Lyman JT, Fabrikant JI, Levy RP: Heavy charged-particle stereotactic radiosurgery: Cerebral angiography and CT in the treatment of intracranial vascular malformations. *Int J Radiat Oncol Biol Phys* 17:419-426, 1989.
27. Phillips MH, Kessler M, Chuang FY, Frankel KA, Lyman JT, Fabrikant JI, Levy RP: Image correlation of MRI and CT in treatment planning for radiosurgery of intracranial vascular malformations. *Int J Radiat Oncol Biol Phys* 20:881-889, 1991.
28. Pollock BE, Flickinger JC, Lunsford LD, Bissonette DJ, Kondziolka D: Hemorrhage risk after stereotactic radiosurgery of cerebral arteriovenous malformations. *Neurosurgery* 38:652-661, 1996.
29. Pollock BE, Kondziolka D, Lunsford LD, Bissonette D, Flickinger JC: Repeat stereotactic radiosurgery of arteriovenous malformations: Factors associated with incomplete obliteration. *Neurosurgery* 38:318-324, 1996.
30. Smith HJ, Strother CM, Kikuchi Y, Duff T, Ramirez L, Merless A, Toutan S: MR imaging in the management of supratentorial intracranial AVMs. *AJR Am J Roentgenol* 150:1143-1153, 1988.
31. Spiegelmann R, Friedman WA, Bova FJ: Limitations of angiographic target localization in planning radiosurgical treatment. *Neurosurgery* 30:619-624, 1992.
32. Stein BM, Sisti MB, Goodman RR: Stereotactic magnetic resonance angiography for targeting in arteriovenous malformations radiosurgery. *Neurosurgery* 35:590, 1994 (comment).
33. Steinberg GK, Levy RP, Marks MP, Fabrikant JI: Charged-particle radiosurgery, in Alexander E III, Loeffler JS, Lunsford LD (eds): *Stereotactic Radiosurgery*. New York, McGraw-Hill, Inc., 1993, pp 122-135.
34. Steiner L: Treatment of arteriovenous malformations by radiosurgery, in Wilson CB, Stein BM (eds): *Intracranial Arteriovenous Malformations*. Baltimore, Williams & Wilkins, 1984, pp 295-313.
35. Steiner L, Lindquist C, Adler JR, Torner JC, Alves W, Steiner M: Clinical outcome of radiosurgery for cerebral arteriovenous malformations. *J Neurosurg* 77:1-8, 1992.
36. Szikla G: *Angiography of the Human Brain Cortex*. New York, Springer-Verlag, 1977.
37. Talairach J, Tournoux P: *Co-Planar Stereotactic Atlas of the Human Brain 3 Dimensional Proportional System: An Approach to Cerebral Imaging*. New York, Thieme Medical Publishers, 1988.
38. Talairach J, Tournoux P: *Referentially Oriented Cerebral MRI Anatomy: Atlas of Stereotactic Anatomical Correlation for Gray and White Matter*. New York, Thieme Medical Publishers, 1994.
39. Talairach J, David M, Tournoux P, Corredor H, Kvasina T: *Atlas d'Anatomie Stéréotaxique*. Paris, Masson, 1967.
40. Talairach J, Szikla G, Tournoux P, Prossalantis A, Bordas Ferrer M, Covello L, Jacob M, Mempel E: *Atlas d'Anatomie Stéréotaxique du Télencéphale*. Paris, Masson, 1957.
41. Yamamoto Y, Coffey RJ, Nichols DA, Shaw EG: Interim report on the radiosurgical treatment of cerebral arteriovenous malformations. *J Neurosurg* 83:832-837, 1995.

COMMENTS

Gallina et al. provide a thoughtful review of 17 patients harboring arteriovenous malformations (AVMs) in whom stereotactic radiosurgery failed to completely obliterate the vascular malformations after more than 3 years of follow-up. These 17 cases were taken from an analysis of 120 patients with cerebral AVMs treated using a linear accelerator by their group of separate institutions in Paris, France, between January 1990 and July 1992. They had documented complete angiographic obliteration in 86 patients (71.6%). The other 17 patients treated were not included, because they had only 2 years of follow-up angiograms available.