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Combined Embolization and Stereotactic Radiosurgery for the Treatment of Large-Volume, High-Risk Arteriovenous Malformations

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The treatment of choice for most of the cerebral arteriovenous malformations (AVMs) is surgical resection or endovascular embolization followed by surgical resection. However, in spite of contemporary microsurgical techniques, operative removal is still associated with considerable risk for those AVMs located in deep or eloquent cerebral regions with multiple arterial feeders and deep venous drainage [1–4]. The unacceptable rates of surgical morbidity and mortality have stimulated the evaluation of therapeutic alternatives [5], such as stereotactic radiosurgery which carries an 87% of cure and 3% complication rates, respectively, in properly selected small volume AVMs [6, 7]. Modern endovascular embolization may completely obliterate small AVMs, but partial obliteration of large lesions to a size manageable by radiosurgery can often be achieved. As there is an increasing risk of complications associated with large target volumes, combined partial embolization of AVMs with raidosurgery of the remaining nidus seems to be a promising therapeutic strategy for patients harboring large lesions that otherwise would not have a possibility of treatment [8–15]. We have evaluated retrospectively our experience with 53 patients treated with the combined approach, staged endovascular embolization followed by stereotactic radiosurgery.

Patients and Methods

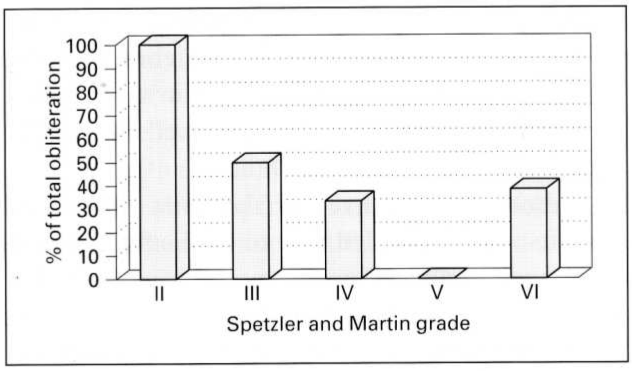
From November 1990 to May 1998, 53 patients harboring a brain AVM were treated at UCLA with endovascular embolization followed by stereotactic radiosurgery. This combined approach was used mainly because of the large volume and either deep or critical location of the nidus, or because the patients were not good candidates for open surgery because of their clinical condition or because they had refused surgery. The clinical records of these 53 patients were retrospectively studied. Fifty-seven percent of the patients were male and 43% were female. Their ages ranged from 5 to 68 years, mean 30.6 years, standard deviation 14.0 years.

The AVMs' location were: motor and sensory strips: 30%, frontal, thalamus and temporal lobe: 11.5% each one, basal ganglia and cerebellum in 9% each one, parietal: 8%, brainstem and occipital: 4%, respectively, and vein of Galen AVM in 2%, most of them located in the dominant hemisphere and proximal to pial and or ependymal surfaces. The AVMs ranged from grade II to VI of the Spetzler and Martin classification. Grades IV–VI reached 64% of the cases. All patients except 1 had a compact nidus. This series does not include isolated direct AV fistulae. The size of the nidus was measured angiographically. The mean nidus diameter and volume were 4.43 cm and 37.80 cm^3, respectively. Multiple feeders (four or more) were present in 94% of the AVMs.

Embolizations were staged in order to decrease the risk of normal pressure perfusion breakthrough and to achieve a better tolerance by the patients. The embolizations were stopped at a point where a proper position of the microcatheter tip for embolization was not reached, or the nidus volume was decreased to a volume suitable for radiosurgery. Electrically detachable platinum microcoils were used to obliterate associated proximal aneurysms and intranidal fistulae. The patients received corticosteroids for 48 h in the intensive care neurosurgical unit and were discharged if there were no complications. Volume of the nidus before and after embolization was measured on the angiograms. Relative changes in volume were calculated.

Radiosurgery was performed at our institution in all 53 cases using a linear accelerator system and a BRW stereotactic frame (Radionics, Burlington, Mass.). Multiple converging noncoplanar arcs of radiation delivery were used. The beam diameter varied from 7 to 52.5 mm (mean 26.62 mm). One to five isocenters were used (mean 1.38) to cover each lesion and four to eight arcs were applied to each isocenter (mean 5.04 arcs). A mean marginal dose of 1,490 cGy (range 1,200–2,000 cGy) was delivered to a mean prescribed line of 80.52% (range 50–90%) obtaining a mean maximum dose of 1,890.33 cGy (range 1,333–4,000 cGy).

Clinical and magnetic resonance imaging (MRI) follow-ups were obtained in 40 cases. More than 18 months' follow-up angiography was available in 22 cases (mean 29.57 months). MR scans were obtained annually. Once the MRI showed evidence of complete obliteration, angiography was performed to confirm complete treatment. After 3 years' follow-up an angiogram was indicated regardless of the MRI result. If angiography showed a significant nidus volume remaining or if residual AVM was seen after 3 years, a second radiosurgery was prescribed.



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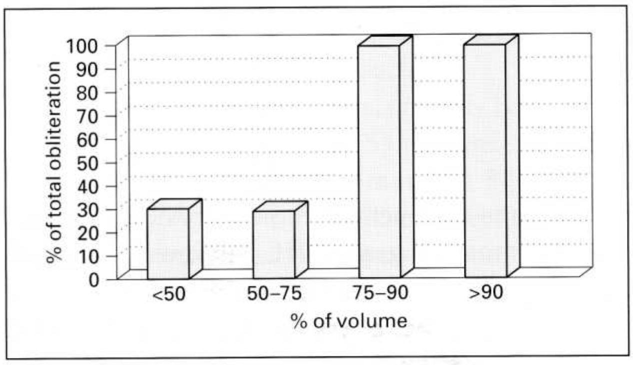

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Fig. 1. Results of the angiographic obliteration second to Spetzler and Martin AVM grade.

Fig. 2. Angiographic obliteration results second to percentage of the AVM nidus embolized.

Results

Patients were treated in a stable clinical condition. In cases of previous intracranial bleeding, most of the patients had experienced significant neurological recovery at the time of radiosurgery. Prior to radiosurgery, 105 sessions of embolization were performed in 53 patients (mean 1.98 per patient). After the last embolization, radiosurgery was performed within 1 month or less in 24 cases (45%), within 2–6 months in 20 (38%) and in more than 6 months in 9 (17%). Five patients (9.43% underwent a second radiosurgery).

A mean postembolization AVM volume reduction of 53.65% and endovascular embolization followed by stereotactic radiosurgery obliteration rates of 50% ($<10\ cm^3$), 33% ($10–50\ cm^3$) and 50% ($>50\ cm^3$) were achieved. The embolization plus radiosurgery results are presented according to the Spetzler and Martin grading scale (fig. 1). The higher percentage of nidus volume embolized the higher cure rate. The cure rate reached 100% for lesions with more than 75% of embolization reduction of the original volume (fig. 2).

Long-term clinical and angiographic evaluations 18 months or longer were available in 22 patients. Three of them experienced intracerebral bleeding at some point, resulting in 2 neurological deficits (9%) and in one fatality (4.5%). Recanalization after NBCA embolization was observed in 2 of 22 patients (9%), both of which resulted in radiosurgical failures.

Complications related to embolization occurred in 5 patients (9.45%), all were transient neurological deficits and responded well to medical treatment. One of them was an asymptomatic cerebral bleeding discovered in a control CT scan. There was no mortality in this series. Radiosurgery-related complications occurred in 2 cases (3.77%) and consisted in the first one in a fixed hemisensory loss while in the second in a motor deficit. Complications related to a second radiosurgery are not included in this analysis.

Discussion

Microsurgical excision remains the treatment of choice for AVMs Spetzler and Martin grades I and II and most of grades III. However, in grades IV and V the surgical treatment is associated with significant risks [1–4]. Embolization itself may cure only small and low-grade lesions but in most of the cases it can achieve significant reduction of the nidus volume [16]. On the other hand, stereotactic radiosurgery is indicated for definitive treatment of small, critically located AVMs [17–20], mainly because of the volume restrictions of the technique. For AVMs with diameters of less than 2.5 cm, a 2-year obliteration rate of 80% has been reported [17, 21]. For lesions greater than 2.5 cm in diameter the obliteration rate falls down to 10–56% [17–19, 21]. Traditionally, for larger volume AVMs the marginal dose to the target has to be decreased in order to reduce the risk of radiation injury to the surrounding brain. By reducing the dose to the nidus, the chance of cure becomes smaller.

Few publications considering the combined approach of embolization plus radiosurgery for AVMs have appeared in the literature [8–15]. Dawson et al. [8] treated 7 patients. At 2 years' follow-up, 2 of the 7 AVMs were cured, another 2 showed volume reductions greater than 98% and the remaining 3 showed minimal changes. The average greatest diameter of the preradiosurgery nidus for the cured AVMs and for the AVMs with significant volume reduction was 29 mm (range 24–32 mm). The average greatest diameter of the nidus before radiosurgery for those AVMs that showed minimal change was 40 mm (range 34–50 mm).

Mathis et al. [12] treated 24 patients with AVMs larger than 10 cm^3 by particulate embolization and radiosurgery, obtaining cure in 50% of the cases at 2 years, comparing favorably with a 58% obliteration rate in a group of AVMs having 4–10 cm^3 treated by radiosurgery alone. The complication rate was 8% for embolization and 4% for radiosurgery. They demonstrated an enhanced effect of embolization in reducing large nidus to a manageable size, improving the final outcome after radiosurgery. Guo et al. [10] reported on 46 patients who underwent embolization followed by radiosurgery. Of 12 grade III–V AVMs, 5 achieved total obliteration after at least a 2-year angiographic follow-up with an embolization-related morbidity of 17.4% and radiosurgical morbidity of 4.34%. Killer et al. [14] treated 45 patients with staged radiosurgery after endovascular and/or surgical treatment, most of them grades III or more. Embolization-related complications occurred in 8.3% and radiosurgical morbidity was 8.8% without mortality. The authors did not separately analyze the different combined approaches.

Our series is heterogeneous mainly because we have included a wide range of AVM volumes. From the 53 patients treated only 22 had an angiographic follow-up after 18 months or more (41.5%). Microcatheters and embolic materials are rapidly evolving as well as the embolization techniques and capabilities. As in other series, we have moved from the wire microcatheters to the very supple flow-guided ones, from PVA particles and isobutyl cyanoacrylate to n-butyl cyanoacrylate. Additionally, high resolution biplane digital subtraction angiography decreased the time of the procedures and improved the success rate. Radiosurgical technology and techniques also experienced a continuous refinement during the last decade.

None of the AVMs was cured only by endovascular therapy because almost all had more than 3 feeders and the size of the AVMs was unusually high. The mean diameter (4.43 cm) and volume (37.80 cm^3) were well above the optimum range for primary radiosurgical treatment. However, NBCA embolization resulted in a significant mean obliteration rate of 53.65% (range 0–99%). One AVM was considered to be reduced in 0% after effective embolization because a compartment located in the central core of the nidus was obliterated affecting the net volume and density of the AVM but not the target volume irradiated or the marginal dose.

Recanalization after NBCA embolization was seen in 2 cases (9.09%) and both cases resulted in radiosurgical failures, perhaps because the recanalized compartment was not included in the target delineation at the time of radiosurgical planning [15, 16].

As described in the radiosurgical literature, our results confirmed that the larger the AVM, the lower the chance of cure [22]. Even with this combined approach, AVMs grade V had a 0% obliteration rate (fig. 1). However, in the case of grade VI AVMs, deep and located in very eloquent areas, some of them were reduced after embolization to a size suitable for radiosurgery, achieving a 37.5% cure rate. Regardless of the original size of the AVM, the higher the percentage of nidus volume embolized, the higher the cure rate, which reached 100% for lesions with more than 75% of reduction of the original volume, despite the absolute pretreatment nidus size (fig. 2).

Complications were present for both treatment techniques. The complication rate compared favorably with the contemporary limits expected for embolization, 9.45% rate [16, 23] and for Linac radiosurgery (2–5%) with 3.77% [24–26]. There were no fatalities related to the treatments but there was one fatal rebleeding.

Conclusion

When a high degree of endovascular obliteration was feasible, there was an enhanced cure rate after stereotactic radiosurgery, suggesting that further improvement of embolization and radiosurgery techniques will lead to better control of large and complex AVMs. These AVMs until recently were not amenable to any form of treatment.

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