Editorial

Stereotactic radiosurgery for arteriovenous malformations

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Arteriovenous malformations (AVMs) continue to be uniquely challenging lesions because of their extreme heterogeneity in terms of arterial supply, venous drainage, location, and presence or absence of intranidal aneurysms. The treatment of choice for AVMs remains controversial as technological advancements continue to provide alternative options for management and as long-term follow-up studies become increasingly available. Tools such as stereotactic radiosurgery (SRS) and endovascular embolic agents are viable adjuncts and, in many cases, replace traditional treatment via resection, which itself in recent years has also benefited from technological improvements, including intraoperative monitoring, stereotactic computer-assisted localization, and enhanced imaging capabilities with microscopy videoangiography.

In the group of papers by Kano and colleagues from the University of Pittsburgh, published in the Journal of Neurosurgery: Pediatrics and the Journal of Neurosurgery: Pediatrics, the authors have collected their combined 18 years of experience in the treatment of AVMs with Gamma Knife surgery. Such a large series provides important data regarding the long-term efficacy and results of treatment, but the findings must be carefully interpreted for providing guidance in treatment recommendations.

Common to this series of papers is its retrospective nature and methodology. An area of criticism of the data is related to the definition of “complete obliteration” used by the authors. The authors use a combination of MR imaging and angiography to determine complete obliteration and treatment success. Although angiography is considered a gold standard for determining obliteration following radiosurgery, even patients with a lack of findings on angiography after SRS may subsequently present with hemorrhage. The authors assume that serial MR imaging is predictive of total obliteration in 84% of patients and (with additional observational intervals) may be predictive in up to 97%. It is important to remember that these predictive values, although thoughtfully calculated, are assumptions for treatment success, which is particularly important considering that up to 60% of patients in the series underwent MR imaging alone to document complete AVM obliteration. Also important is the assumption that all patients lost to follow-up do not contribute to treatment failures. If the papers instead represented a prospective clinical trial, such patients could not simply be omitted from the analysis and results. In the entire series, up to 20% of patients were lost to follow-up. Although it may be reasonable to assume that these patients can be omitted from the analysis without negatively impacting the treatment success rate, it seems more likely that this is not entirely accurate and introduces an important source of bias. These considerations are important when comparing obliteration and complication rates to surgical treatment series in which adverse events and treatment success are usually ascertainable in the immediate postoperative period.

In Part 1, the authors review their experience in treating Spetzler-Martin Grade I and II AVMs. The series is large, encompassing 217 patients. The overall rate of complete obliteration is 90% at 5 years and 93% at 10 years. Interestingly, although the median time to complete obliteration is reported as occurring at 30 months, only 58% of patients had lesions that were treated with SRS and achieved a cure at 3 years. Also of significance is the hemorrhage rate of 6% during the latency period, during which time 6 patients died. As discussed in other reports in the literature, obliteration is more likely with smaller lesions and with higher radiation doses. The data in this series are of importance in counseling patients with respect to treatment options. In experienced hands, the surgical morbidity of resection for Grade I and II AVMs is quite low. This low morbidity is particularly true for lesions that are not located in eloquent cortex, which, in our opinion as well as the opinion of others, should always be treated with excision as the first-line treatment except in special circumstances. For Grade I and II AVMs located in eloquent regions, SRS is a reasonable alternative to surgical treatment, particularly in older or medically ill patients. Of interest, the authors do not provide a separate series highlighting their experience in treating Grade III AVMs as these lesions have proven to be the most difficult in terms of predicting morbidity after resection due to their heterogeneity.
In Part 2, the authors provide a review of their experience in the treatment of pediatric patients. This paper confirms the initial results in Part 1 that incompletely obliterated AVMs represent a risk of bleeding during their latency period and that total obliteration may not occur for 5–10 years. Such sobering results must be weighed against the surgical treatment risks of higher neurological morbidity taken upfront at the time of surgery but with an immediate cure rate of nearly 100% and lifelong immediate protection from rebleeding. There is evidence that children have superior outcomes compared with adults after resection and that children can recover from immediate postoperative deficits despite severe initial disability. Nevertheless, we believe that the authors’ conclusion that SRS is an acceptable treatment option in pediatric patients with small-volume AVMs in critical brain regions is a reasonable one.

Part 3 reports the findings for patients in whom initial SRS treatment failed and who subsequently underwent re-resection. It is interesting to note that more than 10% of patients in the series required repeat SRS (105 patients in the series of 996 patients). Although the rates of complete obliteration appear to be higher following re-resection, the rate of adverse radiation effects (AREs) approached 10% (10 of 105 patients). It is unclear why resection after initial SRS failure did not seem to be a consideration. In 14 cases of repeat SRS failure, a third session of SRS was pursued in 12 cases with resection in only 2 cases. We have found resection after AVM treatment to be a reasonable therapeutic option, and there is evidence that radiosurgery before treatment may facilitate AVM microsurgery and operative morbidity. The authors omitted follow-up from patients who underwent a third radiosurgery procedure. The efficacy of subsequent treatments would be of interest.

Part 4 (the basal ganglia and thalamus) and Part 5 (brainstem) review SRS treatment for AVMs located in surgically challenging regions of the brain. Arteriovenous malformations in these regions are notoriously difficult to treat and often require multimodality therapy. Resection after embolization is a reasonable treatment option in younger patients with lesions located superficially in the brainstem or thalamus. The devastating neurological sequelae of AVM hemorrhage in these eloquent locations results in a poor natural history for untreated lesions, and treatment of asymptomatic lesions is less controversial than treatment of AVMs in other locations. Given the evidence from this series that total obliteration rates are reported to be 70%–72% at 5 years after SRS, primary treatment with SRS in previously asymptomatic lesions is a reasonable recommendation. Nevertheless, the rate of AREs after treatment of brainstem lesions was 10% in terms of permanent neurological morbidity. Additionally, in basal ganglia and thalamus AVMs, the annual rate of post-SRS hemorrhage approached 4% in this series, which is nearly equivalent to natural history estimations of annual bleeding rates in untreated lesions. This rate was reduced to 2.7% only after omitting patients with early (< 6 months) rebleeding episodes. For these reasons, multimodality treatment with resection of brainstem or thalamic/basal ganglia AVMs in experienced hands remains a primary consideration for therapy, particularly in patients presenting with a symptomatic lesion.

Of the entire series presented in these reports, Part 6 (management of large AVMs) contains the most intriguing results regarding treatment options and alternatives. The authors describe the management of large-volume (> 10 cm³) lesions, which would include Grade IV and V AVMs as well as some Grade III AVMs. Such lesions have been associated with high rates of surgical morbidity and mortality, so much so that treatment generally is reserved for lesions with progressive hemorrhage or treatment of specific high-risk features, such as associated aneurysms. Large Grade III AVMs that are located adjacent to eloquent cortex have a risk of morbidity approaching that of Grade IV and V lesions and are best treated in a similarly conservative manner. In cases in which surgical treatment is considered, multimodality treatment with staged embolization is usually required. Subtotal resection can be followed by subsequent SRS of residual AVMs if the size is acceptable. In past reports, it has become apparent that single-session SRS with or without preradiosurgical embolization has not been shown to result in significant rates of obliteration but does result in significant radiation-related morbidity.

In the current series, the authors report on their use of staged SRS in 47 patients with large AVMs. Over the course of the study, 17% of patients suffered from AVM-related hemorrhages, and 5 patients died. The overall cumulative rate of AVM bleeding at the 3-year follow-up was 28.2% with an annual hemorrhage of 6.5% during the latency period while AREs were reported in 6 patients. Over the course of the study, 13 patients suffered from AVM-related hemorrhages, and 8 patients died. Based on Kaplan-Meier analysis (excluding a second hemorrhage in a patient who had 2 hemorrhages), the overall rate of AVM hemorrhage at 3 years after SRS was 28.2%, and the annual rate of hemorrhage during the latency period was 5.3%. Adverse radiation effects were reported in 6 patients. Using the criteria of this study and the previous studies, the maximum obliteration rate achieved is reported as 55% at 10 years of follow-up. However, these patients were treated with at least 3 sessions of SRS. In those patients treated with the original study protocol of 2 staged SRS sessions, the obliteration rates were reported as 36% after 10 years and only 7% after 3 years. Such sobering results indicate that a great deal of further work is required not only to determine which patients should be aggressively treated but what treatment they should receive.

The authors should be congratulated on a large body of work that has greatly increased our knowledge regarding the risks of SRS and potential outcomes of SRS treatment for AVMs. Such data are critical in counseling our patients regarding the best possible treatments available to deal with these challenging lesions. Readers should note that while continued technological advancements in radiosurgery and endovascular therapy increase therapeutic options, microsurgical techniques also continue to evolve, and resection remains an important therapeutic tool for primary treatment of many of these lesions.