Radiosurgery for Cavernous Malformations: Theory and Practice

Bruce E. Pollock, M.D.

Stereotactic radiosurgery is the precise delivery of a therapeutically effective radiation dose to an imaging-defined target. Over the past 5 decades, stereotactic radiosurgery has undergone significant advances that have improved patient outcomes and made it a critical part of modern neurosurgical practice and training. A review of the history of radiosurgery clearly shows a parallel between the development of new imaging technologies and indications for this technique. The first patients treated with radiosurgery had their dose planning based on cerebral angiography or skull radiographs, so the majority of patients in this first phase had arteriovenous malformations (AVMs), tumors adjacent to cranial base landmarks such as the sella, or trigeminal neuralgia with the gasserian ganglion being the target. With the advent of computed tomography and magnetic resonance imaging (MRI), the potential use of radiosurgery for both intra- and extra-axial tumors expanded greatly since they could be stereotactically defined.

Cavernous malformations (CMs) are vascular lesions that comprise the majority of angiographically occult vascular malformations diagnosed in the modern neuroimaging era. Although seen on cerebral angiography, CMs have a typical appearance on MRI that has permitted a better understanding of their incidence and natural history. Cavernous malformations may present with bleeding, seizures, or as incidental findings. Surgical resection of CMs is the preferred management for patients with symptomatic lesions. Radiosurgery has been performed as an option for a select group of patients with CMs. The traditional indication for CM radiosurgery is a patient with a history of multiple ICHs from a surgically inaccessible lesion. The goal of performing CM radiosurgery is the same as AVM radiosurgery: to protect the patient from the future risk of ICH. Undoubtedly, the positive results noted after AVM radiosurgery lead to the radiosurgical treatment of a small number of patients with CMs. As discussed earlier, patients having CM radiosurgery typically had deeply located malformations and a documented history of multiple bleeds. The effect that radiosurgery has on the endothelial lined channels is poorly understood as a result of the small number of analyzed lesions. Gewirtz et al. examined 11 occult vascular malformations that were resected 1 to 10 years after either radiation therapy or radiosurgery and compared them histopathologically with a group of nonirradiated control subjects. Fibrinoid necrosis was the only pathological finding unique to the irradiated lesions; all the irradiated lesions had patent vascular channels. Importantly, 10 of these patients had recurrent bleeding after radiosurgery and were considered failures, so they may not be representative of the “successful” patients with CM after radiosurgery. Karlsson et al. presented a patient having CM radiosurgery and the lesion was unchanged on MRI 5 years later. Histological study revealed that more than 75% of the lesion was obliterated. More recently, Nyáry et al. analyzed a CM from a patient who had undergone fractionated radiation therapy (40 Gy) 1 year earlier. This CM exhibited endothelial cell destruction, marked fibrosis with hyaline degeneration, and scar tissue formation.

Copyright © 2008 by The Congress of Neurological Surgeons
0148-703/08/5501-0097
Several vessels were obliterated; however, there was a large number of newly formed thin-walled channels. Overall, it appears that radiosurgery induces a similar response in CMs that has been observed in subtotally obliterated AVMs, although the number of specimens examined to date remains small.

**Results of Cavernous Malformation Radiosurgery**

A number of studies have outlined the effect of CM radiosurgery on hemorrhage rates and the risk of radiation-related complications. Hasegawa et al. from the University of Pittsburgh reported 82 patients having CM radiosurgery from 1987 to 2000. The mean follow-up after radiosurgery was 5 years. The annual hemorrhage rate was 12.3% for the first 2 years after radiosurgery and then 0.8% thereafter. Kida and Hasegawa reported outcomes for 152 patients undergoing CM radiosurgery. Bleeding after radiosurgery occurred in 20 patients (13%). The hemorrhage rate was 8% the first year after radiosurgery, 5% the second year, reducing to 0% by Year 7. Other smaller series have documented annual hemorrhage rates from 4.5 to 9.4% for the first several years after radiosurgery, then lower bleeding rates in later years of follow-up.

An important issue associated with CM radiosurgery is the risk of radiation-related complications. Hasegawa et al. from the University of Pittsburgh reported 82 patients having CM radiosurgery from 1987 to 2000. The mean follow-up after radiosurgery was 5 years. The annual hemorrhage rate was 12.3% for the first 2 years after radiosurgery and then 0.8% thereafter. Kida and Hasegawa reported outcomes for 152 patients undergoing CM radiosurgery. Bleeding after radiosurgery occurred in 20 patients (13%). The hemorrhage rate was 8% the first year after radiosurgery, 5% the second year, reducing to 0% by Year 7. Other smaller series have documented annual hemorrhage rates from 4.5 to 9.4% for the first several years after radiosurgery, then lower bleeding rates in later years of follow-up.

An important issue associated with CM radiosurgery is the risk of radiation-related complications. Hasegawa et al. from the University of Pittsburgh reported 82 patients having CM radiosurgery from 1987 to 2000. The mean follow-up after radiosurgery was 5 years. The annual hemorrhage rate was 12.3% for the first 2 years after radiosurgery and then 0.8% thereafter. Kida and Hasegawa reported outcomes for 152 patients undergoing CM radiosurgery. Bleeding after radiosurgery occurred in 20 patients (13%). The hemorrhage rate was 8% the first year after radiosurgery, 5% the second year, reducing to 0% by Year 7. Other smaller series have documented annual hemorrhage rates from 4.5 to 9.4% for the first several years after radiosurgery, then lower bleeding rates in later years of follow-up.

An important issue associated with CM radiosurgery is the risk of radiation-related complications. Hasegawa et al. from the University of Pittsburgh reported 82 patients having CM radiosurgery from 1987 to 2000. The mean follow-up after radiosurgery was 5 years. The annual hemorrhage rate was 12.3% for the first 2 years after radiosurgery and then 0.8% thereafter. Kida and Hasegawa reported outcomes for 152 patients undergoing CM radiosurgery. Bleeding after radiosurgery occurred in 20 patients (13%). The hemorrhage rate was 8% the first year after radiosurgery, 5% the second year, reducing to 0% by Year 7. Other smaller series have documented annual hemorrhage rates from 4.5 to 9.4% for the first several years after radiosurgery, then lower bleeding rates in later years of follow-up.

An important issue associated with CM radiosurgery is the risk of radiation-related complications. Hasegawa et al. from the University of Pittsburgh reported 82 patients having CM radiosurgery from 1987 to 2000. The mean follow-up after radiosurgery was 5 years. The annual hemorrhage rate was 12.3% for the first 2 years after radiosurgery and then 0.8% thereafter. Kida and Hasegawa reported outcomes for 152 patients undergoing CM radiosurgery. Bleeding after radiosurgery occurred in 20 patients (13%). The hemorrhage rate was 8% the first year after radiosurgery, 5% the second year, reducing to 0% by Year 7. Other smaller series have documented annual hemorrhage rates from 4.5 to 9.4% for the first several years after radiosurgery, then lower bleeding rates in later years of follow-up.

An important issue associated with CM radiosurgery is the risk of radiation-related complications. Hasegawa et al. from the University of Pittsburgh reported 82 patients having CM radiosurgery from 1987 to 2000. The mean follow-up after radiosurgery was 5 years. The annual hemorrhage rate was 12.3% for the first 2 years after radiosurgery and then 0.8% thereafter. Kida and Hasegawa reported outcomes for 152 patients undergoing CM radiosurgery. Bleeding after radiosurgery occurred in 20 patients (13%). The hemorrhage rate was 8% the first year after radiosurgery, 5% the second year, reducing to 0% by Year 7. Other smaller series have documented annual hemorrhage rates from 4.5 to 9.4% for the first several years after radiosurgery, then lower bleeding rates in later years of follow-up.
lesions remains poorly understood.\textsuperscript{2,16,22} The most typical statistical method used to determine the effect that radiosurgery has had on bleeding risk is to compare the hemorrhage rate for patients in the period leading up to radiosurgery with the hemorrhage rate observed after radiosurgery. However, because patients tend to be treated shortly after they have bled, this methodology may artificially inflate the annual risk of bleeding. Moreover, observations that untreated CMs tend to bleed in “clusters” followed by more quiescent periods creates doubt that radiosurgery has any effect on hemorrhage risk for these patients.\textsuperscript{2} As stated by Karlsson et al.,\textsuperscript{9} “The 32 percent incidence of hemorrhage before radiosurgery reported in another paper is more a reflection of the timing of the treatment than the natural course of the disease.” To reconcile this issue, a prospective, randomized trial comparing radiosurgery against conservative therapy for patients with hemorrhagic, surgically high-risk CMs is needed to accurately determine the true effect that CM radiosurgery has on hemorrhage risk for these patients. Such a study was once proposed but was not completed as a result of methodological considerations.

Seizure Protection

One of the early observations made on CM radiosurgery was that treated patients appeared to have fewer seizures after the procedure. Régis et al. retrospectively reviewed the experience of five centers to evaluate the efficacy of CM radiosurgery on epilepsy control.\textsuperscript{24} A total of 49 patients were identified with long-lasting (mean duration of seizures before radiosurgery, 7.5 yr) drug-resistant epilepsy. The mean CM margin dose was 19.2 Gy. At a mean follow-up of 24 months, 26 patients (53\%) were seizure-free. The medial temporal region was associated with the greatest risk of failure. They concluded that seizure control can be achieved when there is a clear electroclinical correlation between the CM location and the epileptogenic zone. Two studies have compared seizure control for patients with CM having radiosurgery or surgical excision. Shih and Pan compared 46 patients with solitary supratentorial CMs having craniotomy and excision (n = 16) with patients having radiosurgery (n = 30).\textsuperscript{26} Seventy-nine percent (11 of 14 patients) of the craniotomy group remained seizure-free compared with 25\% (four of 16 patients) in the radiosurgery group (P < 0.01). Likewise, Hsu et al. found that 13 of 15 patients (87\%) were seizure-free after CM resection compared with nine of 14 patients (64\%) treated with linear accelerator-based radiosurgery.\textsuperscript{7} Consequently, whenever technically possible, surgical resection should be considered the first option for patients with CM having epilepsy associated with their lesion.

CONCLUSION

Our limited knowledge on the natural history of untreated CMs combined with the relative high risk associated with CM radiosurgery precludes one from recommending its use except for very highly selected patients. Surgical resection of CMs should continue to be the primary management strategy whenever this can be accomplished with acceptable morbidity.

Disclosure

The authors did not receive financial support in conjunction with the generation of this article. The authors have no personal or institutional financial interest in drugs, materials, or devices described in this article.

REFERENCES


