Radiosurgery for Cerebral Arteriovenous Malformations with Associated Arterial Aneurysms

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■ OBJECTIVE: **The radiosurgical outcomes for cerebral arteriovenous malformations (AVM) with AVM-associated arterial aneurysms (AAA) are poorly understood, because many AAAs are embolized before nidal intervention. The aim of this retrospective case-control study is to determine the effect of AAAs on AVM radiosurgery outcomes.**

■ METHODS: **We evaluated an institutional AVM radiosurgery database from 1989 to 2013. AAAs were classified as intranidal (type I) or prenidal (type II). The case cohort comprised AVMs with patent type I or II AAAs. The control cohort comprised AVMs without AAAs and matched 2:1 to the case cohort.**

■ RESULTS: **The case cohort comprised 51 AVMs, including 23 with type I and 28 with type II AAAs. The control cohort comprised 102 AVMs without AAAs. The cumulative AVM obliteration, annual postradiosurgery hemorrhage, and radiologically evident radiation-induced changes rates were 67%, 3.3%, and 28%, respectively, for the case cohort, compared with 70%, 2.0%, and 35%, respectively, for the control cohort. The presence of an AAA was not significantly associated with obliteration ($P = 0.293$), postradiosurgery hemorrhage ($P = 0.209$), or radiation-induced changes ($P = 0.323$). The rates of type II AAA occlusion at 3, 5, and 10 years were 46%, 77%, and 95%, respectively. The type II AAA occlusion rate was significantly higher in obliterated AVMs ($P = 0.002$).**

■ CONCLUSIONS: **Patent intranidal or prenidal AAAs do not significantly affect AVM radiosurgical outcomes. Occlusion of distal prenidal AAAs commonly occurs after radiosurgery. These findings may support a more conservative stance for embolization before radiosurgery for AVMs with AAAs.**

INTRODUCTION

Cerebral arteriovenous malformations (AVMs) are associated with intranidal or prenidal arterial aneurysms in approximately 10%–30% of cases, although a wide variation exists in the range of reported incidences.[1-8] The presence of AVM-associated arterial aneurysms (AAAs) has been shown to significantly increase a patient's risk of hemorrhage.[7,9] Radiosurgery is an effective management option for patients harboring AVMs, and it is an especially attractive treatment alternative to resection for nidi associated with a relatively high operative morbidity.[10-31] However, because AAAs are considered high-risk angioarchitectural features, they are frequently occluded by endovascular embolization before radiosurgical treatment of the nidus.[6,32-34] Previous studies have reported the presence of patent AAAs to increase the risk of latency period hemorrhage after radiosurgery, although these analyses excluded intranidal AAAs and were limited by relatively few AVMs with AAAs.[35,36]

Thus, the radiosurgery outcomes for AVMs with AAAs are incompletely understood. Given the typical latency interval of 2–3 years that exists between radiosurgery and, when successful, AVM obliteration and the potentially increased risk of hemorrhage accompanied by AAAs, AVMs with AAAs may be predisposed to relatively poorer radiosurgery outcomes. In this retrospective

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- Gamma knife
- Intracranial aneurysm
- Intracranial arteriovenous malformation
- Intracranial hemorrhages
- Radiosurgery
- Stroke
- Vascular malformations

Abbreviations and Acronyms
AAA: AVM-associated arterial aneurysm
AVM: Arteriovenous malformation
CT: Computed tomography
IQR: Interquartile range
MRI: Magnetic resonance imaging
RIC: Radiation-induced changes
VRAS: Virginia Radiosurgery AVM Scale

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case-control study, our aims are to 1) analyze the outcomes after radiosurgery for the treatment of AVMs with AAAs, 2) define the predictors of AVM obliteration, prenidal AAA occlusion, latency period hemorrhage, and radiosurgery-induced complications after radiosurgery for AVMs with AAAs, and 3) determine the effect of patent AAAs on AVM radiosurgery outcomes.

METHODS

AVM-Associated Aneurysm Classification and Cohort Composition

We performed a retrospective evaluation of a prospective database, approved by the institutional review board, comprising approximately 1400 patients with AVM who underwent treatment with Gamma Knife (Elekta AB, Stockholm, Sweden) radiosurgery, from 1989 to 2013, at the University of Virginia. AAAs were categorized based on the classification system previously described by Redekop et al.,[7] as follows: intranidal AAAs were located within the boundaries of the AVM nidus and filled early during angiography before substantial venous filling (type I); prenidal (i.e., flow-related) AAAs were located on feeding arteries supplying AVM (type II); prenidal AAAs were subclassified as proximal (type IIa) if they were located on the supraclinoid internal carotid artery, vertebrobasilar trunk, circle of Willis, middle cerebral artery, including the middle cerebral artery bifurcation or trifurcation, or anterior cerebral artery up to the anterior communicating artery; prenidal AAAs were subclassified as distal (type IIb) if they were located beyond the aforementioned proximal arterial systems. Unrelated aneurysms were located on arteries that did not supply the AVM (type III).

The inclusion criteria for the case cohort were 1) AVMs with patent type I, IIa, or IIb AAAs at the time of radiosurgery, 2) sufficient data regarding nidus angioarchitectural features, baseline patient characteristics, and outcomes after radiosurgery, and 3) minimum of 2 years radiologic follow-up after radiosurgery, with the exception of completely obliterated AVMs as documented by angiography or magnetic resonance imaging (MRI), which were included even if the radiologic follow-up duration was less than 2 years. The inclusion criteria for the control cohort were the same as those for the case cohort, except only AVMs without patent type I, IIa, or IIb AAAs at the time of radiosurgery were selected. AVMs with type III aneurysms and patients treated with volume- or dose-staged radiosurgery were excluded from both the case and the control cohorts. Selecting a minimum of 2 years of follow-up accounts in part for the delayed beneficial as well as adverse effects after stereotactic radiosurgery. With such a retrospective study on a relatively rare vascular malformation (AAA), selection of inclusion and exclusion criteria for the study requires a blending of factors to achieve a meaningful and statistically sound study.

Data and Variables

The following baseline data were extracted from directed chart and neuroimaging review: 1) AVM angioarchitectural features, 2) patient characteristics, and 3) radiosurgery parameters. AVM variables were presence and classification of AAAs, previous hemorrhage, previous interventions (embolization or surgical resection), size (maximum diameter and volume), location (eloquent vs. noneloquent, superficial vs. deep), and venous anatomy (number of draining veins, superficial only vs. deep component). The following locations were defined as eloquent: sensorimotor, language, and visual cortex, hypothalamus and thalamus, internal capsule, brainstem, cerebellar peduncles, and deep cerebellar nuclei.[37] The following locations were defined as deep: basal ganglia, thalamus, and brainstem.[38] AAA classification was based on angiography performed before radiosurgery or for radiosurgery planning. Patient variables were gender and age. Based on the AVM and patient variables, the Spetzler-Martin grade, modified radiosurgery-based AVM score, and Virginia Radiosurgery AVM Scale (VRAS) were determined for each patient.[37-39]

Our Gamma Knife radiosurgery procedure has been previously described.[40] Before 1991, MRI was not routinely used in addition to angiography for radiosurgical planning. After 1991, both MRI and angiography, and, on occasion, computed tomography (CT) were used to improve the spatial accuracy of treatment planning. Dose planning was performed with the Kula software (Elekta AB) from 1989 to June 1994, and then with the Gamma Plan (Elekta AB) software thereafter. The radiosurgery variables were margin dose and number of isocenters.

Radiologic and Clinical Follow-Up

Standard radiologic follow-up consisted of MRI every 6 months for the first 2 years after radiosurgery, and then MRI annually thereafter. Additional neuroimaging, either CT or MRI, was performed for postradiosurgery neurologic deterioration. All follow-up neuroimaging was reviewed by a neurosurgeon and neuroradiologist at our institution, regardless of where it was performed. AVM obliteration was defined as a lack of flow voids on MRI or as a lack of abnormal arteriovenous shunting on angiography. Angiography was typically performed to confirm obliteration determined by MRI or to plan additional intervention(s) for a residual AVM. AAA patency was defined by follow-up angiography, when available, and categorized as occluded or patent. Patent AAAs that were occluded by embolization between multiple radiosurgical procedures were categorized as patent, and the angiographic follow-up duration for these AAAs was calculated based on the date of the embolization procedure. If the AVM remained patent 3 to 4 years after the initial radiosurgery, repeat radiosurgery was usually performed to treat the residual nidus.

Radiation-induced changes (RIC) were defined as perinidal T2-weighted hyperintensities on follow-up MRI. The time interval between radiosurgery and the first radiologic documentation of RIC and the radiologic duration of RIC were noted. Radiologically evident RIC was further categorized as symptomatic, if there was RIC associated with new or worsening neurologic symptoms, or permanent, if there was symptomatic RIC that was unresolved by the most recent clinical follow-up. Latency period hemorrhage was defined as any AVM- or AAA-related intracranial hemorrhage after radiosurgery on CT or MRI, regardless of the patient's neurologic status. Postradiosurgery cyst formation was defined as the development of a cystic cavity on CT or MRI, within or adjacent to the brain territory occupied by the nidus at the time of radiosurgery.

Clinical follow-up consisted of hospital and clinical records from our institution and outside referring institutions as well as correspondence from patients' local physicians. Clinical status after radiosurgery was categorized as neurologically improved, unchanged, or deteriorated by comparing a patient's neurologic