Aneurysms can occur in patients with brain arteriovenous malformations (AVMs), and this not uncommon association poses important therapeutic challenges. In patients presenting with intracranial hemorrhage, the AVM is responsible for bleeding in 93% of cases, with the remaining 7% related to associated intracranial aneurysms. The incidence of aneurysms in patients with AVMs is higher than expected on the basis of the frequency of each lesion individually. This observation suggests that factors such as increased regional flow (hence hemodynamic stress) may play a causative role in the formation of aneurysms associated with AVMs, although other causative factors such as genetic predisposition cannot be excluded. In this article, we review the various types of aneurysms and aneurysm-like dilations seen in patients with AVMs and discuss their clinical significance and therapeutic implications.

Intracranial aneurysms can occur in patients with brain arteriovenous malformations (AVMs), and this not uncommon association poses important therapeutic challenges. In patients presenting with intracranial hemorrhage, the AVM is responsible for bleeding in 93% of cases, with the remaining 7% related to associated intracranial aneurysms. The incidence of aneurysms in patients with AVMs is higher than expected on the basis of the frequency of each lesion individually. This observation suggests that factors such as increased regional flow (hence hemodynamic stress) may play a causative role in the formation of aneurysms associated with AVMs, although other causative factors such as genetic predisposition cannot be excluded. In this article, we review the various types of aneurysms and aneurysm-like dilations seen in patients with AVMs and discuss their clinical significance and therapeutic implications.

Intracranial aneurysms can occur in patients with brain arteriovenous malformations (AVMs), and this not uncommon association poses important therapeutic challenges. In patients presenting with intracranial hemorrhage, the AVM is responsible for bleeding in 93% of cases, with the remaining 7% related to associated intracranial aneurysms. The incidence of aneurysms in patients with AVMs is higher than expected on the basis of the frequency of each lesion individually. This observation suggests that factors such as increased regional flow (hence hemodynamic stress) may play a causative role in the formation of aneurysms associated with AVMs, although other causative factors such as genetic predisposition cannot be excluded. In this article, we review the various types of aneurysms and aneurysm-like dilations seen in patients with AVMs and discuss their clinical significance and therapeutic implications.

Dr. Gardenghi is Research Fellow, Department of Neurologic Surgery, Mayo Clinic, Rochester, Minnesota; Dr. Bortolotti is Attending Physician, Division of Neurosurgery, IRCCS Institute of Neurological Science, Bologna, Italy; and Dr. Lanzino is Professor, Department of Neurologic Surgery, Mayo Clinic, 200 SW First St, Rochester, MN 55905; E-mail: lanzino.giuseppe@mayo.edu.

All faculty and staff in a position to control the content of this CME activity, and their spouses/life partners (if any), have disclosed that they have no financial relationships with, or financial interests in, any commercial organizations related to this CME activity.

**Learning Objectives:** After participating in this CME activity, the neurosurgeon should be better able to:

1. Assess the various classifications of cerebral aneurysms associated with arteriovenous malformations (AVMs).
2. Compare the various hypotheses about the pathogenesis of the cerebral aneurysms associated with AVMs.
3. Evaluate the role of surgery, endovascular therapy, and radiosurgery in the treatment of intracranial aneurysms associated with AVMs.

**Classification**

A clear understanding of the various types of aneurysms and aneurysm-like dilations that occur in patients with AVMs is paramount to clarify their pathophysiology and clinical significance. These aneurysms can be classified on the basis of location, histopathologic characteristics, and hemodynamic features.

**Location**

Aneurysms associated with AVMs can occur on the arterial side (*arterial aneurysms*) or the venous side (*venous aneurysms*). In relation to the nidus of the AVM, aneurysms and aneurysm-like dilations are categorized as either extranidal (arterial or venous) or intranidal. Intranidal aneurysms are within the nidus and fill “early” during angiography, before substantial venous filling has occurred. Intranidal aneurysms are usually venous aneurysms.

Arterial aneurysms can be localized on vessels that do not contribute to the vascular supply of the AVM (*unrelated aneurysms*, Figure 1A) or arise from vessels that participate in the vascular supply of the AVM (Figures 1A–C) and are such are related to flow dynamics (*flow-related aneurysms*).

**Category:** Cerebrovascular

**Key Words:** Intracranial aneurysms, Cerebral arteriovenous malformations, Risk of hemorrhage, Multidisciplinary treatment

Lippincott Continuing Medical Education Institute, Inc. is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

Lippincott Continuing Medical Education Institute, Inc. designates this enduring material for a maximum of 1.5 AMA PRA Category 1 Credits™. Physicians should only claim credit commensurate with the extent of their participation in the activity. To earn CME credit, you must read the CME article and complete the quiz and evaluation on the enclosed form, answering at least 70% of the quiz questions correctly. This activity expires on October 31, 2015.
Flow-related arterial aneurysms can occur away from the nidus (proximal flow-related aneurysms, Figures 1A–C) or originate from feeding vessels adjacent to the nidus (distal flow-related aneurysms). Although proximal flow-related aneurysms usually occur at bifurcation points (a result of the combined effects of hemodynamic stress and intrinsic weakness of the vessel wall at bifurcation points), distal flow-related aneurysms often occur along the feeding pedicle not related to branching points.

A different subcategory of arterial aneurysm-like dilation is the arterial pseudoaneurysm, which is thought to be the result of rupture of thin-walled small perforating arteries that supply the AVM. A pseudoaneurysm results from the uncloaked portion of the hematoma still in communication with vessel lumen and as such can show rapid interval growth on subsequent imaging studies. Pseudoaneurysms usually are close to the nidus, with irregular shape. They often originate from small or perforating arteries, very close to the ependymal surfaces. Definitive diagnosis can be made on histologic analysis, but their nature is often implied by progressive growth on serial early angiograms.

The term venous aneurysm is a misnomer, because the venous aneurysm does not contain the typical wall components of the aneurysm wall, but this term is established in the terminology of aneurysms associated with AVMs and will be maintained in this article. Intranidal aneurysms are a subtype of venous aneurysms. Venous pseudoaneurysms can be seen at the periphery of the nidus and can be identified if surgery is performed shortly after a parenchymal bleed as areas of venous dilation at the periphery of the nidus partially filled with clotted blood. The draining veins of the AVM often present dilations and varices (Table 1).

Figure 1. A 57-year-old woman had undergone fractioned radiotherapy for a left frontal AVM at another institution 20 years previously. She was referred for evaluation of multiple aneurysms. A, Catheter angiography, right internal carotid artery (ICA) injection, anteroposterior view showing multiple proximal flow-related aneurysms (white arrows) and an unrelated middle cerebral artery aneurysm (red arrow). B, Anteroposterior view and C, lateral view of left ICA injection showing multiple proximal flow-related aneurysms (arrows) and the persistent large AVM.
**Histopathologic Characteristics**

Based on the composition of the wall, aneurysms associated with AVMs can be categorized as arterial aneurysms, venous aneurysms, and pseudoaneurysms.

**Epidemiology**

The reported incidence of aneurysms associated with AVMs varies among various studies depending on factors such as type of aneurysm considered and imaging modality used (whether superselective angiography was performed). In the first cooperative study of intracranial aneurysms, multiple aneurysms were found in 8 of 34 patients (24%) who had AVM-associated hemorrhage. Similarly, a recent report from the Scottish AVM study group reported 34 aneurysms in 114 patients with unruptured brain AVMs, although the type of aneurysm considered was not specified in this study.

*Unrelated arterial aneurysms* (ie, on vessels that do not participate in the supply of the AVM) have an incidence comparable to the incidence of berry aneurysms in the general population, and they follow the same anatomic distribution.

Flow-related arterial aneurysms are much more frequent in patients with AVMs than their incidence in the general population would indicate, suggesting a causative role of the AVM in their development. These aneurysms often arise from the wall of feeding arteries without any relationship to major bifurcations. Unlike berry aneurysms not associated with AVMs (which have a definite female preponderance), there is no difference in the distribution of flow-related aneurysms between males and females. As these aneurysms are probably related to flow dynamics, they are more commonly observed in association with high-flow (often larger) AVMs rather than slower-flow (often smaller) AVMs. The incidence of AVM-associated aneurysms seems to increase with age.

**Pathogenesis**

The incidence of arterial aneurysms in patients harboring an AVM is higher than the incidence of aneurysms in the general population, and this observation suggests a causal relationship. The most valid theory to explain this association is the hemodynamic theory (ie, the genesis of aneurysms in patients with AVMs is most likely related to hemodynamic factors attributable to the AVM). This theory is supported by the following observations:

- The vast majority of aneurysms seen in association with AVMs are located on vessels hemodynamically connected to the AVM or within the nidus;
- In many cases, excision of the AVM leads to a complete or partial reduction of the associated aneurysms, especially those closer to the nidus (flow-related distal arterial aneurysms); and
- Arterial aneurysms are more frequent in patients with high-grade (and often higher-flow) AVMs and in elderly patients rather than in children, suggesting that their formation is acquired, and that time was required for the effects of increased flow to form them.

**Risk of Bleeding**

The presence of associated arterial aneurysms increases the risk of hemorrhage from an unruptured AVM. In a classic study of patients with unruptured AVMs seen at the Mayo Clinic between 1974 and 1985, the risk of intracranial hemorrhage among patients with a coexisting, originally unruptured AVM and aneurysm was 7% at 1 year compared with 3% among those with an AVM alone. In a recent study of patients with Spetzler-Martin grade 1 and 2 AVMs treated with gamma knife radiosurgery, the presence of an associated aneurysm was identified as an independent risk factor for bleeding after radiosurgery. The rate of bleeding after stereotactic radiosurgery in patients with associated aneurysms was 28% at 5 years versus 2.6% in patients without associated aneurysms. These observations underscore the importance of considering treatment of aneurysms associated with AVMs in patients undergoing gamma knife radiosurgery.

**Treatment**

Management of aneurysms associated with AVMs depends on several factors, the most important being rupture status. In patients with ruptured AVMs that harbor an aneurysm, it is critical to understand whether the source of the hemorrhage is the associated aneurysm or the AVM. The initial head CT scan obtained after presentation is of paramount importance, as it often provides important clues about the source of bleeding.

The presence of pure subarachnoid hemorrhage (SAH) without associated intraparenchymal hemorrhage often implicates the aneurysm as the potential source of hemorrhage. If the aneurysm is the source of the bleeding, there is often more focal clot in the area of the aneurysm with secondary spread to the surrounding subarachnoid space. In patients with intraparenchymal hemorrhage with or without associated SAH, the epicenter of the hemorrhage may give clues as to the potential source. Of course, the information obtained from the presentation CT scan must be interpreted in relation to high-definition catheter angiography with 3D reconstructions, which remains the gold standard for detailed depiction of the AVM angioarchitecture and associated aneurysms. From the angiogram, the shape, size, and exact location of associated aneurysms can help in determining whether the aneurysm may be the offending source.

If the aneurysm is suspected to be the source of hemorrhage, it should be treated as early as safely possible in accordance
with treatment protocols for any ruptured arterial aneurysm. If the source of bleeding is a pseudoaneurysm arising from a small perforating branch, this should also be treated early, as pseudoaneurysms lack a true wall and are at risk for early expansion and rupture. In such cases, the AVM can be treated at a later time, once the source of bleeding has been secured and the patient has recovered from the acute effects of the hemorrhage. If the suspected source of bleeding is an intranidal aneurysm, treatment may not need to be urgent, as the risk of early rerupture is relatively low if no significant outflow obstruction is identified on the angiogram. In recent years, with evolution of endovascular techniques, some authors have advocated superselective catheterization, with embolization of the portion of the nidus/feeding pedicle supplying that portion of the AVM harboring the intranidal aneurysms. At present, however, it is unknown whether this strategy protects the patient from recurrent hemorrhage.

In patients with unruptured AVMs, the treatment strategy of the associated aneurysm(s) follows the criteria applied to the treatment of unruptured incidental aneurysms in general, with the caveat that some aneurysms hemodynamically connected to the AVM may decrease in size or even disappear after treatment of the AVM. In one study, which analyzed the fate of untreated aneurysms associated with AVMs after treatment of the AVM, 4 of the 5 (80%) distal flow-related aneurysms disappeared after complete excision of the AVM, and only 1 (20%) was unchanged. There were no instances of SAH from a flow-related aneurysm after AVM cure during the follow-up period (7.4 years). Instead, of the 23 proximal aneurysms, 18 (78.3%) were unchanged, 4 (17.4%) were smaller, and only 1 (4.3%) regressed completely after treatment of the AVM. Because distal flow-related arterial aneurysms more often resolve or decrease in size after effective AVM treatment compared with other types of aneurysms, conservative management of small distal aneurysms may be indicated if the AVM is treated.

Conclusions

Intracranial aneurysms can be associated with cerebral AVMs. The incidence of aneurysms in patients harboring an AVM is higher than the incidence of aneurysms in the general population. The presence of an aneurysm associated with an AVM may increase the risk of hemorrhage and poses therapeutic challenges. The most important factor, which also dictates therapeutic strategy, is rupture status. In patients presenting with intracranial hemorrhage, it is mandatory to understand the source of bleeding. If the aneurysm is suspected to be the cause of hemorrhage, then treatment of this lesion should be prompt. If the source of the hemorrhage is suspected to be within the nidus, however, treatment can be delayed, as the risk of early rebleeding from a ruptured AVM is relatively low as long as there is no severe outflow obstruction to the AVM drainage.

In most patients with unruptured AVMs, the treatment strategy for associated aneurysms follows the same criteria applied to isolated unruptured aneurysms in the general population. Distal flow-related aneurysms may decrease in size or even disappear after AVM treatment. Thus, conservative management of a small distal aneurysm can be considered if the AVM is treated.

Readings


Visit www.contempneurosurg.com

Your online subscription to Contemporary Neurosurgery offers:

• Most popular articles feature
• Access to the archive of published issues
• e-Pub downloads to access articles on your e-reader device
• e-Table of Contents delivered to your inbox
• Personalization features, such as saved search results and article collections
• CME access

To activate your online access, click “Register” at the top right corner of the website.
1. Distal flow-related aneurysms may not be related to arterial branching points.
   True or False?

2. Pseudoaneurysms have an irregular shape and are thought to be related to rupture of thin-walled perforating vessels feeding the AVM.
   True or False?

3. Unrelated aneurysms follow the same anatomic distribution as berry aneurysms in the general population.
   True or False?

4. Flow-related aneurysms in patients with AVMs are as frequent as aneurysms in the general population.
   True or False?

5. Flow-related aneurysms are more often associated with high-flow AVMs.
   True or False?

6. The most valid explanation of the association of aneurysms and AVMs is the hemodynamic theory.
   True or False?

7. The presence of associated aneurysms in a patient with an AVM increases the risk of bleeding.
   True or False?

8. If an aneurysm is suspected to be a source of hemorrhage, treatment of the bleeding source can be delayed and is not urgent.
   True or False?

9. In a patient who presents with hemorrhage and is found to have an AVM associated with aneurysms, head CT at admission may provide invaluable information regarding the potential source of the hemorrhage.
   True or False?

10. In a patient with unruptured AVMs, treatment considerations with regard to the one or more associated aneurysms follow the same general criteria applied to the treatment of incidental unruptured aneurysms.
    True or False?