American Association of Neurological Surgeons

Arteriovenous Malformations

Patient Information

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Arteriovenous malformations (AVMs) are defects in the vascular system, consisting of tangles of abnormal blood vessels (nidus) in which the feeding arteries are directly connected to a venous drainage network without interposition of a capillary bed. Arteries carry oxygen-rich blood away from the heart to the rest of the body's tissues and cells. Veins return oxygen-depleted blood to the lungs and heart. Capillaries connect the arteries and veins. The presence of an AVM disrupts this vital cyclical process, causing a snarled tangle of arteries and veins that are connected to one another without the presence of any capillaries(19).

An AVM can occur anywhere in the body, but brain and spinal AVMs present substantial risks when they bleed. Because the brain and its blood vessels are formed together during embryological development, abnormal blood-vessel formation is often associated with abnormal brain tissue. Little is known about the etiology of brain AVMs. The cause of brain AVMs is debated, although it is likely multifactorial, with both genetic manipulation and angiogenic stimulation (the physiological process through which new blood vessels form from pre-existing vessels) appearing to play roles during AVM development. Some believe that AVMs develop in utero, while others advocate an angiopathic reaction, following either a cerebral ischemic or hemorrhagic event (sub-types of stroke) as a primary factor in their development (1).

Incidence and Prevalence

- The incidence of AVM is estimated at one in 100,000.
- The prevalence of AVM is estimated at 18 in 100,000.
- An estimated two-thirds of AVMs occur before age 40.
- Every year, about four out of every 100 people with an AVM will experience a hemorrhage.
- Each hemorrhage poses a 15 to 20 percent risk of death or stroke, 30 percent neurological morbidity, and 10 percent mortality.
- When hemorrhage occurs, it affects the following regions statistically: intracerebral (41 percent), subarachnoid (24 percent), intraventricular location (12 percent) and various combinations (23 percent).
- AVMs are the second most identifiable cause of subarachnoid hemorrhage after cerebral aneurysms, accounting for 10 percent of all cases of subarachnoid hemorrhage.
- About one percent of people with AVMs will develop epileptic seizures for the first time.

Symptoms

Approximately 50 percent of patients present initially with a bleed; often patients with an AVM experience no symptoms, and their AVMs are discovered only incidentally, usually either during an autopsy or during treatment for an unrelated disorder. The proportion of patients being diagnosed with un-ruptured AVMs has almost doubled in the past three decades, with improved non-invasive imaging (2). About 12 percent of people with AVMs will experience symptoms, varying in severity. AVMs can irritate the surrounding brain tissue and cause seizures or headaches. Any of the following symptoms may occur:

- Seizures, new onset
- Muscle weakness or paralysis
- Loss of coordination
- Difficulties carrying out organizational tasks
- Dizziness
- Headaches
- Visual disturbances
- Language problems
- Abnormal sensations such as numbness, tingling or spontaneous pain
- Memory deficits
- Mental confusion
- Hallucinations
- Dementia

Traditionally, the annual rupture rate of four percent has been cited for brain AVMs, based on a study on natural history of symptomatic AVMs; this study also included the AVMs that had previously ruptured (3). A recent randomized trial of unruptured brain arteriovenous malformations (ARUBA) reported a low spontaneous rupture rate of 2.2 percent per year (4). Other recent prospective studies have also reported lower bleeding rates of about one percent per year for unruptured AVMs (5, 6). The bleeding risk increases after the rupture, achieving 6-8 percent during the first year, and then it drops to the aforementioned initial values (7).

AVM characteristics associated with a relatively higher risk of hemorrhage/re-hemorrhage include (6, 8):

- When the brain AVM presents with hemorrhage
- When it has a deep venous drainage
- When it is associated with aneurysms or
- When it is in a deep location.

Diagnosis

AVMs are usually diagnosed through a combination of magnetic resonance imaging (MRI) and angiography. These tests may need to be repeated to analyze a change in the size of the AVM, recent bleeding or the appearance of new lesions. Left untreated, AVMs can enlarge and rupture, causing intracerebral hemorrhage or subarachnoid hemorrhage, resulting in permanent brain damage. Deep bleeding is usually referred to as an intracerebral or intraparenchymal hemorrhage; bleeding within the membranes or on the surface of the brain is known as subdural hemorrhage or subarachnoid hemorrhage.

The damaging effects and the extent of damage in the neurological status of patients from a hemorrhage are related to lesion location. Bleeding from AVMs located deep inside the interior tissues, or parenchyma of the brain, generally causes more severe neurological damage than does bleeding from lesions located in the dural or pial membranes or on the surface of the brain or spinal cord. AVM location is an important factor to consider when weighing the relative risks of surgical versus nonsurgical treatment. Preventing the rupture or re-rupture of vascular malformations is one of the major reasons that early neurosurgical treatment is recommended for AVMs.

A commonly used grading scale to predict the risk of surgical morbidity and mortality with brain AVMs is the Spetzler-Martin Grade (SMG) scale, which is a composite score of nidus size (<3 cm, 3-6 cm, >6 cm; 1-3 points), eloquence of adjacent brain (1 point if located in brainstem, thalamus, hypothalamus, cerebellar peduncles or sensorimotor, language, or primary visual cortex) and presence of deep venous drainage (1 point if any or all drainage is through deep veins, such as internal cerebral veins, basal veins or precentral cerebellar veins). The higher the score, the higher is the surgical morbidity and mortality risk (9).

Treatment

The goal of brain AVM treatment is typically the prevention of new or recurrent hemorrhage from rupture. However, seizure control or stabilization of progressive neurological deficits are occasionally treatment goals. Interventional treatment of ruptured brain AVMs is generally advisable, considering a higher subsequent hemorrhage risk (4.5 to 34%percent) than previously un-ruptured ones (0.9 to 8 percent) (10).

The management options for brain AVMs (ruptured or un-ruptured) include observation or various treatment techniques, such as microsurgical techniques, endovascular embolization and stereotactic radiotherapy used alone or in combination with varying degrees of treatment-associated morbidity and mortality. A treatment plan is devised to offer the lowest risk, yet highest chance of obliterating the lesion.

Although microsurgical treatment affords the opportunity for immediate removal of the AVM, some AVMs may be best dealt with using a multi-modality treatment. In some patients, the AVM is monitored on a regular basis with the understanding that there may be some risk of hemorrhage or other neurological symptoms including seizures or focal deficit. In the most recent study (ARUBA) on 223 patients with unruptured brain AVMs, the risk of death or stroke was significantly lower in the medical management group (the patients were symptomatically treated in the medical management group) than in the interventional therapy group, after a mean follow-up of about 33 months (4). It is a prospective, multicentre, parallel design, non-blinded, randomized controlled trial in which the patients were enrolled from 39 active clinical sites in nine different countries (4).

Microsurgery

Because the nature of AVM may be congenital (although there can be other reasons why AVMs develop), and therefore associated in most cases with a focal abnormality of brain tissue, it may be removed with minimal disruption of normal brain tissue. This constitutes the rationale and strategy for microsurgical removal. The recommendation for surgery is typically elective, except in the case of large, life-threatening blood accumulations (hematomas) caused by bleeding of the AVM. In such cases, only superficial AVMs that are readily controllable are removed along with the hematoma. When the hematoma is caused by a complicated AVM, the blood clot can be removed, and the patient given time to recover until further details are known regarding the exact nature of the AVM. Surgery may be part of a multimodal treatment involving a preliminary endovascular intervention to reduce nidus volume and curing or mitigating eventual additional vascular anomalies, such as aneurysms.

For surgical resection, the neurosurgeon will perform a craniotomy (surgical window in the skull) and use microsurgical techniques to gain access to the AVM. The use of an operating microscope and image-guided surgical navigation (also known as computer-assisted or frameless stereotaxy) helps enable safer surgery with as little disruption to normal brain tissue as possible. Once the skull is opened, the AVM feeders are cauterized or closed off with special clips, and ultimately removed. The skull bone is then secured back in place with miniplates, and the incision in the scalp is closed.

The gold-standard in AVM management is surgery whenever safely feasible with angiographic cure in about 94 to 100 percent of cases with low morbidity rates (from 1-10 percent) in small (nidus < 3cm) AVMs in experienced hands. A meta-analysis on the microsurgical AVM management reported permanent neurological deficits or death in a mean of 7.4 percent (range, 0–40%) patients after microsurgery; successful brain AVM obliteration was achieved in 96 percent (range, 0–100%) patients (11).

Stereotactic Radiosurgery

Stereotactic radiosurgery (SRS) is a minimally invasive treatment that uses computer guidance to concentrate radiation to the malformed vessels of the brain. This radiation causes abnormal vessels to close off. Radiosurgery is typically recommended for AVMs that are small (< 2–3 cm diameter), unruptured, and surgically inaccessible, but may also be recommended to reduce the size of large AVMs otherwise associated with significant surgical morbidity. For larger lesions, the complete radiosurgical treatment may be delivered either by splitting the dose by fractionated SRS or stereotactic radiotherapy or splitting the volume of the nidus. The full treatment dose is delivered over multiple sessions.

The basic steps of SRS are the following:

1. Attachment of the stereotactic frame, under local anesthesia.
2. Image acquisition, with fiducial markers to allow the 3D reconstruction of the brain and target.
3. Treatment planning: The margin of the AVM nidus (target volume) is contoured in order to obtain a 3D reconstruction of the AVM. Multiple radiation beams are focused to the isocenter of the target where a high dose is delivered with a sharp dose fall-off at the adjacent normal brain.

This plan is executed by a multidisciplinary team consisting of a neurosurgeon, physicist and radiation oncologist. Unfortunately, stereotactic radiosurgery may take up to two to three years (latency period) to completely obliterate the lesion. For this reason, it is not ideally suited to AVMs that have already bled, unless they are surgically inaccessible.

Microsurgical resection is recommended for radiated AVMs that are not completely obliterated after the three-year latency period, but have become more suited to surgical resection, even in asymptomatic patients. Surgery resection, if planned, is timed to allow the AVM to respond fully to radiation and is performed close to or after the three-year latency period (12). Because ionizing radiation is harmful to normal tissue, as well as AVM vessels, it must be used judiciously. It is unavoidable to expose normal brain tissue to ionizing radiation during treatment, as it must be traversed by the beam, independently of how accurately the AVM is targeted. Complete obliteration is observed in 50–90 percent of the cases over a latency period of two to four years, and its rate is inversely proportional to the size of the nidus (13).

A hemorrhagic event may occur in less than 1 percent of patients after curative treatment with radiosurgery (14). Complications after radiosurgery leading to permanent neurological deficits or death can be seen in 5.1 percent (range, 0–21%) of the cases.

Embolization

The endovascular management for AVM may include interventions to obliterate the small malformations or making the AVM nidus smaller in a pre-surgical setting to make the resection safer, reduction prior to radiosurgery or elimination of certain, often associated, vascular anomalies, such as aneurysms, venous varices and fistulas. Endovascular embolization uses specially designed microcatheters, which are guided directly into the AVM via angiography. The lesion is blocked from the inside using the process of embolization, which occludes the abnormal blood vessels in the AVM. Once the catheter reaches the core of the AVM, liquid glue or particles can be injected to close off portions of the AVM or its feeding arteries. Materials used include fast-drying biologically inert glues, polyvinyl alcohol particles and fibered titanium coils.

Neuroendovascular therapy can make subsequent surgical removal of an AVM safer or can reduce the size of an AVM to a size that may inevitably improve the outcome of stereotactic radiosurgery. This procedure is also associated with substantial risk, since the path taken by such embolic materials can be difficult to predict, and blockage of normal vessels or of the outflow of the AVM may occur. The former may result in stroke, and the latter in bleeding from the AVM. These procedures are therefore also used judiciously and with ample clinical judgment. The morbidity rate related to endovascular embolization ranges from 3.8 to 50 percent, with a mortality rate ranging from 1 to 4 percent (16).

Outcome

Patient outcome depends on the location of the AVM and severity of the bleeding, as well as the extent of neurological symptoms. Many patients undergoing microsurgery make an excellent and quick recovery after several days of hospitalization. Following or during surgery, an angiogram is performed to assure complete removal of the AVM. If the AVM is completely removed, the patient is considered cured. About 5 to 10 percent of AVMs (small AVMs) can be obliterated (cured) using endovascular techniques alone. In the first randomized trial of unruptured AVMs, ARUBA, medically managed patients had a significantly lower risk of death or stroke and had better outcomes than those treated with intervention at follow-up of 33 months. However, the trial has been controversial because of significant limitations inherent to the study design. The follow-up was too short to demonstrate the benefits of AVM treatment, which is well-understood to be protective over a lifetime.

Like other major stroke trials, there was a big gap between the screened and the enrolled patients, suggesting selection bias (17). Some studies showed that results in ARUBA-eligible patients managed outside that trial led to an entirely different conclusion about AVM intervention, due to the primary role of surgery, judicious surgical selection with established outcome predictors, and technical expertise developed at high-volume AVM centers (18).

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