Intracranial arteriovenous malformations: natural history, diagnosis and management strategies

Malformações arterio-venosas intracranianas: história natural, diagnóstico e estratégias de tratamento

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ABSTRACT

Objective: The purpose of this report is to review intracranial arteriovenous malformations, present strategies for the evaluation and selection of optimal treatment modalities, and to discuss factors important to formulating a successful treatment plan.

Methods: The authors performed a critical literature review in order to highlight recent and classic studies about intracranial arteriovenous malformations.

Results: Recent advances in diagnostic techniques, microsurgery, endovascular therapy, and stereotactic radiosurgery have significantly improved the treatment outcome of vascular malformations of the central nervous system. In patients who are minimally symptomatic, in normal neurologic condition, or whose treatment risk is high, not recommending any treatment can be an excellent viable option. For the others, microsurgery, endovascular embolization, and stereotactic radiosurgery offer complementary advantages and improve the chances of a lifetime cure.

Conclusion: A thorough knowledge of the natural history of intracranial arteriovenous malformations is fundamental to the treatment decision making process. A multidisciplinary team approach with the neurosurgeon taking a leading role is as well essential for a successful intracranial arteriovenous malformation management.

Key-words: Intracranial Arteriovenous Malformations; Vascular Malformations; Endovascular Embolization; Stereotactic Radiosurgery.

SUMÁRIO

Objetivo: O objetivo deste artigo é revisar e discutir alguns aspectos referentes às malformações arteriovenosas intracranianas, apresentando estratégias para avaliação clínica, diagnóstico e seleção das específicas modalidades de tratamento.

Métodos: Os autores realizaram uma revisão crítica da literatura atual, destacando estudos recentes e estudos clássicos sobre as malformações arteriovenosas intracranianas.

Resultados: Avanços recentes em técnicas diagnósticas, microcirurgia, terapêutica endovascular e radiocirurgia esterotáctica têm melhorado significativamente o manejo das malformações arteriovenosas do sistema nervoso central. Em pacientes oligosintomáticos, em condição neurológica normal ou cujo risco do tratamento é elevado, não indicar tratamento pode ser uma excelente opção. Para os demais casos, microcirurgia, embolização endovascular e radiocirurgia estereotáctica oferecem vantagens e melhoram as chances de cura.

Conclusão: Um conhecimento minucioso sobre a história natural das malformações arteriovenosas é fundamental para o processo de decisão do manejo neurocirúrgico. Além disso, uma equipe multidisciplinar com a presença de um neurocirurgião no comando é essencial para o sucesso terapêutico das malformações arteriovenosas.

Palavras-chave: Malformação Arteriovenosa Intracraniana; Malformações Vascular; Embolização Endovascular; Radiocirurgia Estereotáctica.
INTRODUÇÃO

Recent advances in diagnostic techniques, microsurgery, endovascular therapy, and stereotactic radiosurgery have significantly improved the treatment outcome of vascular malformations of the central nervous system. Better information regarding the natural history of the various types of lesions has allowed us to weigh the natural risk of the untreated disease, versus the morbidity and mortality of different treatment options. The ultimate goal of treatment should be the prevention of future complications from the lesion, while minimizing the therapeutic risk to the patient. In most patients this is best achieved by total elimination of the lesion. In certain instances, however, only palliative treatment or expectant medical management is the least risky alternative for a given patient.

The purpose of this report is to review intracranial arteriovenous malformations, present strategies for the evaluation and selection of optimal treatment modalities, and discuss the factors important to formulating a successful treatment plan.

INTRACRANIAL ARTERIOVENOUS MALFORMATIONS (AVMs)

NATURAL HISTORY

It is not recommended to make treatment decisions regarding AVMs without a comprehensive knowledge of their natural history and long-term outcome. Wilkins analyzed 1,500 cases and showed that intracranial AVMs are associated with a significant morbidity and mortality; a 3% risk of hemorrhage and 1% mortality per year. The best study outlining the natural history of AVMs was published by Ondra in 1990, where 160 patients who presented mostly with hemorrhage were followed conservatively for an average of 24.7 years. The mean patient age at presentation was 33 years. The rehemorrhage rate was 4% per year with an average of 7.7 years for the next hemorrhage to occur (range, 6 weeks to 22 years). The yearly mortality rate was 1.7%, and the mortality rate was 1%. This study emphasized the high morbidity and mortality associated with AVMs regardless of the initial mode of presentation, be it a hemorrhage, headache, or seizure. Older studies have confirmed similar results.

There is a slight female preponderance in AVM patients. However, this does not reach statistical significance. The peak age for developing symptoms is between the second and fourth decade of life, where the incidence of hemorrhage is also at its peak. Most AVMs appear to be sporadic lesions which are congenital or develop early in life. The AVM nidus often becomes more compact and may develop angiomatous changes over time. Lesions infrequently “grow” and rarely spontaneously involute. Some AVMs are associated with an inherited and familial predisposition, others are part of complex extracranial and intracranial malformations.

GENERAL EVALUATION

The patient’s age, the location of the AVM, and its angioarchitecture play a major role in the evaluation and treatment of these lesions. The overall morbidity and mortality rates derived from published series suggest that the presence of a symptomatic AVM is sufficient to initiate evaluation and possible treatment. The impact of the AVM on the patient should be closely scrutinized, including duration and severity of symptoms and resulting functional impact on the patient’s quality of life. Prior hemorrhage, while it does not clearly impact the long-term risk of future bleeding, might place the patient at a greater risk of rebleeding in the subsequent months, or year and might convince the patient and clinicians to reconsider management options and to accept treatment risks. Past medical history should be assessed with an eye towards associated clinical conditions which might complicate AVM treatment (renal failure, coagulopathy) or might affect the patient’s life expectancy or natural risk from the lesion. A careful review of systems and general medical examination may reveal a familial history or associated medical conditions relevant to the diagnosis, prognosis, counseling, and treatment. For example, a history of epistaxis or familial disease might suggest the diagnosis of hereditary hemorrhagic telangiectasia (Osler-Weber-Rendu disease) with the consequent consideration of pulmonary AVMs requiring treatment.

Many factors play a role in the decision to treat an intracranial AVM. A 75-year-old man who presents with an initial seizure from an AVM has already beaten the odds (lower actuarial risk of hemorrhage in his remaining lifetime) and carries a risk factor much different than a 35-year-old who presents with the same lesion. Assuming that the risk of hemorrhage from an AVM is 4% per year and the risk of neurologic deficit or death related to the hemorrhage is 30%, a 35-year-old patient with an average life span of 78 years is exposed to an actuarial risk of more than 50% of neurologic disability or death from the lesion during his lifetime. This justifies recommending treatment as long as the therapeutic risk is significantly lower, the recommended treatment efficacious (eliminating the lesion or significantly lowering the hemorrhagic risk), and the patient’s acceptance of an immediate impact and risk of therapeutic intervention. These factors are obviously variable and depend on each unique patient and lesion.
DIAGNOSTIC STUDIES

Computed tomography (CT) scanning is useful in evaluating acute hemorrhage and AVM calcifications. Magnetic resonance imaging (MRI) supplements CT scanning of the brain by providing a three-dimensional anatomical correlation. Functional MRI (fMRI) is valuable in delineating the relationship of the AVM to physiologically functional brain such as the primary sensory, motor, visual, and speech areas. This information, all from noninvasive studies, may be sufficient to discuss treatment options, associated risks, and potential strategies (whether embolization may be advisable, and whether more than one session may be needed, etc.) or to advise against treatment in certain cases (elderly, debilitated patients, nidus clearly involving eloquent brain, etc.). Maximizing information from noninvasive studies has significantly reduced the number (and hence, the risk, inconvenience, and cost) of repeated and often unnecessary diagnostic angiograms, and has allowed combining diagnostic angiography with embolization or with stereotactic radiosurgical treatment.

Cerebral angiography remains the gold standard for comprehensive AVM evaluation. Four vessel angiography including external carotid artery injections in large AVMs is mandatory. Refinements in microcatheterization of cerebral vessels have made superselective angiography possible, thus allowing better visualization of the AVM angioarchitecture and permitting mini Wada testing for more accurate functional brain mapping. Detailed cerebral angiography should reveal the location and true size of the AVM nidus, the feeders to the AVM, including the deep and transventricular arterial supply, the type of shunting from the arterial to the venous side (high versus low flow), and the venous drainage pattern. Cerebral angiography can also alert us to the presence of associated arterial or intranidal aneurysms and venous outflow obstructions or anomalies. In rare exceptional cases of small AVMs (nidus size less than 2-3 cm), and where significant contraindications to angiography exist (infant, renal failure, etc.), surgical excision of an AVM may be undertaken based on noninvasive studies alone, with the consideration of follow-up angiography at a later time to confirm complete lesion obliteration.

THERAPEUTIC OPTIONS

The primary goal of AVM treatment is to prevent hemorrhage, control seizures, and arrest or reverse any progressive neurologic deficits while minimizing the risk related to the treatment. All of these objectives have been shown to be optimally achieved by complete elimination of the AVM. Treatment modalities which provide less than complete obliteration of the lesion have not been shown to provide a lasting therapeutic benefit. Microsurgery, endovascular embolization, and stereotactic radiosurgery constitute the mainstay of AVM treatment. These can be used individually or in combination. A team approach consisting of neurosurgeons, stroke neurologists, neurointerventional radiologists and neuropsychologists is essential in the initial evaluation and decision making process. Each patient’s AVM should be individually assessed and treatment options are formulated and recommended to the patient.

ENDOVASCULAR EMBOLIZATION

Advances in microcatheters and endovascular embolization techniques have improved the ability to catheterize smaller and more tortuous arterial feeders, resulting in better intranidal deposition of embolic agents and more comprehensive devascularization of AVMs.

In order to minimize hyperperfusion hemodynamic complications, staged endovascular embolization is preferred in large AVMs with multiple arterial feeders. It is technically easier to embolize the large arterial feeders. However, this may cause recruitment of blood supply to the AVM through deep perforating vessels which in turn increase the difficulty of surgery. Therefore, if at all possible, our endovascular embolization is also tailored toward occluding the least surgically accessible feeders. On occasion, when the deep feeders cannot be embolized, we have refrained from embolizing large surface feeders which are easily accessible surgically. Endovascular embolization is rarely curative and therefore is used mainly as an adjunct to surgery or stereotactic radiosurgery. In AVMs close to physiologically functional brain, mini Wada testing using superselective sodium amytal injections can define our margin of safety better.

Endovascular embolization achieves immediate reduction in blood flow to the AVM. This significantly reduces the chance of intraoperative normal perfusion pressure breakthrough and decreases operative time and blood loss. The disadvantages of endovascular embolization include a 5% risk of hemorrhage, errant embolization causing stroke, catheter gluing intra- vascularity, and decreased compressibility of the AVM during surgery. The risks of embolization (additive risk in staged cases) must be integrated into the overall management risk assessment when choosing a therapeutic plan. For larger lesions, embolization is invaluable in decreasing subsequent surgical catastrophic sequelae. For smaller lesions, the decision to embolize must be highly individualized, considering the skills, experience and demonstrated results of the team, and the particular features of the lesion.

MICROSURGICAL RESECTION

Advances in microscopic visualization, stereotactic guidance, intraoperative electrophysiologic monitoring and angiography...
have significantly improved the surgical outcome in AVM treatment. Surgical resection is the preferred method of treatment. It provides an immediate and permanent elimination of the risk of hemorrhage, improvement in neurologic function, and a decrease in the incidence of seizures\textsuperscript{3,6}. The Spetzler and Martin grading system\textsuperscript{11} is useful in evaluating the operative risk and is a good predictor of postoperative complications. This grading system relies on three parameters: the size of the AVM, the presence of a deep vascular component, and the involvement of physiologically functional ("eloquent") brain. The higher the grade, the greater the treatment risk.

Disadvantages of surgery include the inherent risks of a craniotomy, general anesthesia, neurologic deficit related to the surgery, and longer hospitalization compared to embolization or stereotactic radiosurgery.

A postoperative arteriogram is recommended to verify total excision. Postsurgically, AVMs rarely recur after complete angiographic confirmation of a cure, except in pediatric cases where there might be a higher frequency of recurrence. The natural history of partially treated or residual AVMs matches that of untreated lesions, which means that no demonstrable protection is confirmed. Residual, or recurrent, AVMs require the consideration of additional treatment based on the individualized risk assessment.

**STEREOTACTIC RADIOSURGERY**

Focused beam stereotactic radiosurgery avoids an open craniotomy and general anesthesia, and allows treatment of AVMs even in deep or inaccessible locations with relatively low morbidity. There is little immediate risk or discomfort with the procedure, but also no immediate effect on the AVM. In general, lesion obliteration occurs over two or more years following the procedure. The AVM obliteration rate in small AVMs (less than 3 cm diameter) is reasonably high (more than 70%)\textsuperscript{9,13}, but less than half of the larger lesions are effectively cured. More recently, retreatment of previously irradiated lesions has been promising, albeit with a higher complication rate\textsuperscript{8}.

Disadvantages of stereotactic radiosurgery include a 2-3-year latent period for any curative effects of radiation to set in. During this time, the patient is subject to the hemorrhagic risk of untreated AVMs, and in fact 8-10% of patients suffer a hemorrhage while waiting for the therapeutic benefit of stereotactic radiosurgery to take effect (consistent with a 4% per year AVM hemorrhage rate). Symptomatic radiation induced edema is another significant complication which is related to the location and radiation dose delivered, and occurs in about 10% of cases\textsuperscript{4}. It happens more frequently in larger radiated volumes and near eloquent brain structures\textsuperscript{4}. This can result in focal neurologic deficits or seizures, but often recovers without any lasting sequelae after periods of several weeks to months.

**TREATMENT DECISION PLANNING**

In summary, total microsurgical excision of an AVM is the preferred method of treatment. Embolization serves as a useful adjunct to surgery but is rarely successful as the sole mode of therapy. If the risk of surgery is prohibitive because of the location of the AVM, or if the patient’s general medical condition is poor, stereotactic radiosurgery either alone or in conjunction with embolization can be an effective alternative. Radiosurgery is also helpful in treating postsurgical residual AVMs, especially those located in deep regions of the brain.

A cerebrovascular team approach is utilized in reaching a consensus regarding the best treatment modality. The neurosurgeon should take a leading role in that decision-making process as he or she is most familiar with the range of treatment options, their limitations and risks, and the potential clinical behavior of the lesion. As discussed previously, the size, location, and unique angioarchitecture of each AVM is essential in evaluating the treatment risks. The final recommendation should also take into consideration the patient’s age, medical condition, neurologic status, and profession, with the goal of treatment being total AVM elimination with the least risk to the patient.

Small symptomatic AVMs (less than 3 cm in diameter) located in non-physiologically functional brain are best treated with surgery. Preoperative embolization is optional in these cases and might not justify the added risk of the procedure. Nevertheless, AVMs with a single feeding vessel may occasionally be cured by embolization alone, and an attempt at total endovascular obliteration may be considered.

Cortical AVMs larger than 3 cm in diameter are usually treated with preparatory embolization followed by surgical excision. This approach can be advocated even if the AVM is located close to physiologically functional areas. In these specific cases, preoperative fMRI of the brain can be helpful. The brain adjacent to an AVM can also be mapped intraoperatively with cortical stimulation and evoked potentials to avoid corticectomies in primary functional areas.

Many AVMs located in deeper brain locations, including those in the diencephalon, basal ganglia, internal capsule or brain stem are treated with radiosurgery with or without embolization. Endovascular embolization can be used as an adjunct to decrease the AVM size and increase the curative rate of successful radiosurgery (likelihood of AVM obliteration). We have reserved palliative endovascular treatment in inoperable AVMs to cases where the patient suffered from severe debilitating headaches, or to occlude a perinidal hemorrhagic aneurysm.

Larger AVMs (Spetzler-Martin grades IV and V) are difficult
to treat and carry a higher complication rate of treatment\(^1\). In many cases, the risk of treatment is possibly equal to or worse than the risk associated with the natural history of these lesions. The experience and results of the cerebrovascular team must be considered when deciding on a course of action for these difficult AVMs. In general, we have refrained from treating patients whose treatment risk has been estimated to be more than 20% unless they were already severely disabled by the lesion.

**CONCLUSION**

In conclusion, a thorough knowledge of the natural history of AVMs is fundamental to the treatment decision making process. A multidisciplinary team approach with the neurosurgeon taking a leading role is essential. In patients who are minimally symptomatic, in normal neurologic condition, or whose treatment risk is high, not recommending any treatment can be an excellent viable option. For the others, microsurgery, endovascular embolization, and stereotactic radiosurgery offer complementary advantages and improve the chances of a lifetime cure.

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