JBNC Brazilian Journal of Neurosurgery
Jornal Brasileiro de Neurocirurgia

Revisão

Cerebral Arteriovenous Malformations. Integrated Global Management and Therapeutic

Malformações Arteriovenosas Cerebrais. Manejo Global Integrado e Terapêutica

Paulo Henrique Aguiar[1]
Marco Antonio Stefani[1,2]
Gustavo Rassier Isolan[1]
Carlos Alexandre Zicarelli[4,3]
Apio Claudio Martins Antunes[1,2]

RESUMO

Melhora significativa dos resultados do tratamento das Malformações Arteriovenosas (MAV) do sistema nervoso central tem sido observada, associada a avanços das modalidades de diagnóstico e tratamento. Os autores relatam esses avanços no diagnóstico e tratamento global integrado das MAV.

Palavras Chave: *Malformação Arteriovenosa, Tratamento Cirúrgico, radiocirurgia, embolização*

ABSTRACT

A significant improvement of central nervous system arteriovenous vascular malformations (AVM) outcome has been observed due to the advances in all modalities of diagnosis and treatment. The authors report the advances in diagnosis and integrated global treatment of AVM`s.

Keywords: *Arteriovenous Malformation, Surgical Treatment, radiosurgery. embolization*

[1]Post Graduation Course in Surgical Sciences, Universidade Federal do Rio Grande do Sul- Porto Alegre, Brazil
[2]Neurosurgery Unit, Hospital de Clinicas de Porto Alegre, Brazil, Associate Professor, Faculdade de Medicina, UFRGS
[3]Department of Neurosurgery, Santa Casa de Londrina, Londrina, Brazil
[4]Post Graduation in Health Technology of Catholic University (PUC/PR) of Paraná, Brazil

Recebido em 12 de junho de 2012, aceito em 14 de setembro de 2012

JBNC Brazilian Journal of Neurosurgery
Jornal Brasileiro de Neurocirurgia

Introduction

A significant improvement of central nervous system arteriovenous vascular malformations (AVM) outcome has been observed due to the advances in all modalities of diagnosis and treatment.

A better knowledge of the natural history of the various types of lesions [4,19] allow us to estimate the risk of untreated disease versus the morbidity and mortality of different treatment options in individual patients.

The target of treatment must be the prevention of complications of the lesion, while minimizing the therapeutic risks to the patient. In our opinion, this is best achieved in most cases by total exclusion of the lesion, however in certain circumstances, only conservative management or palliative procedures are less aggressive for the patient outcome.

Regarding to the treatable lesions, we prefer the procedure that provides the highest rate of cure with the least risk, with individualization for each specific case.

Natural History of AVMs and evaluation

Due to advances in neuroradiologic imaging, incidental AVMs have been diagnosed with greater frequency.

Truly asymptomatic AVMs, however, are rarely discovered at autopsy as opposed to aneurysms, where the incidence has been reported to be between 3 to 5% of the population [3]. Although we believe that the majority of AVMs will eventually remain symptomatic, the natural history of asymptomatic AVMs has not been documented.

The natural history and long-term outcome must be analyzed before choosing any type of management: a significant morbidity and mortality of 3% risk of hemorrhage and 1% mortality rate per year have been observed in patients with AVM [25]. There is a slight female preponderance in AVM patients, but without statistical significance [9].

The peak age for developing symptoms is between the second and fourth decade of life, whereas the incidence of hemorrhage is also at its peak [9]. Most AVMs appear to be sporadic lesions that are congenital or develop early in life. The AVM nidus often becomes more compact and may develop angiomatous changes over time.

Higher rates of annualized hemorrhage have been found by others [20]. Ondra et al [18] outlined the natural history of 160 patients who presented mostly with hemorrhage and 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 morbidity 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. Other studies [18,20] showed similar results.

After diagnosis, AVMs rarely " grow", and unusually decrease spontaneously their volume. Some AVMs are associated with an inherited and familial predisposition, and some are part of complex extracranial and intracranial malformations. The patient's age, the location of the AVM, its size, and its venous and arterial angioarchitecture play a major role in the evaluation and treatment of these lesions. The overall morbidity and mortality rates derived from published series [3, 4, 18] suggest that the presence of a symptomatic AVM is sufficient to initiate evaluation and possible treatment.

Certainly AVM impact regarding to duration and severity of symptoms, as well as resulting functional impact on the quality of life should be closely scrutinized.

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, so we should clearly note the treatment alternatives and risks with the patient.

Beyond any doubt, past medical records should be assessed looking for associated clinical conditions that might complicate AVM treatment (renal failure, coagulopathy, cardiac failure, cancer) or might affect the patient's life expectancy or natural risk of the lesion.

A careful analysis of systems and general medical examination may reveal familial history or associated medical conditions relevant to the diagnosis, prognosis, counseling, or treatment.

JBNC Brazilian Journal of Neurosurgery
Jornal Brasileiro de Neurocirurgia

IMAGE DIAGNOSIS

Non-invasive studies

Computed tomography (CT) scan is useful in evaluating acute hemorrhage and AVM calcifications. Magnetic resonance imaging (MRI) supplements CT scan of the brain by providing a 3 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 non-invasive studies, may be sufficient to analyse 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 non-invasive studies has significantly reduced the number (and hence the risk, inconvenience, and cost) of repeated and often unnecessary diagnostic angiograms, and allowed combining diagnostic angiography with embolization or with stereotactic radiosurgical treatment.

Angio MRI does not provide complete specific and sensitive information for the complete diagnosis, so it should be used as a complimentary way of diagnosis.

Angio CT scan probably will improve the diagnosis and management planning in a near future, however an invasive study like angiography is still the option for the therapeutic decision.

Invasive studies

Cerebral angiography is still the gold standard exam for comprehensive AVM evaluation. Four-vessel cerebral angiography including external carotid artery injections in large AVM is necessary.

Refinements in microcatheterization of cerebral vessels has made superselective angiography possible, thus allowing better visualization of the AVM angioarchitecture, and permiting 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 of the AVM, including the deep and transventricular arterial supply, the type of shunting from the arterial to the venous side (high vs. low flow), and the venous drainage pattern.

Digital cerebral angiography can also show the presence of associated arterial or intranidal aneurysms, and venous outflow obstructions or anomalies [9]

Only in exceptional cases of small AVMs (nidus size less than 2-3 centimeters), and where significant contraindications to angiography exist (infants, renal failure, etc.), surgical excision of an AVM may be undertaken based on non-invasive studies alone, with the reconsideration of follow-up angiography at a later time to confirm complete lesion obliteration.

As part of the evaluation process, cerebral angiography should be considered in asymptomatic AVMs to define any associated aneurysms, venous outflow obstruction or ectasias, which may warn of a greater risk of impending hemorrhage. An AVM with a single draining vein poses a greater risk of hemorrhage than one with multiple draining veins. In such cases, prophylactic treatment may be warranted.

In AVMs close to physiologically functional brain, mini Wada testing using superselective sodium amital injections can define our margin of safety better.

THERAPEUTIC OPTIONS

Microsurgery, endovascular embolization, and stereotactic radiosurgery are the main treatment options for AVM. These can be used individually or in combination.

A multidisciplinary approach consisting of neurosurgeon, stroke neurologist, interventional rediologist and neuropsychologist is fundamental in the initial management and decision making process.

The therapeutic decision should be individually formulated and recommended to each patient's AVM.

Endovascular Embolization

Recent advances in microcatheters and endovascular embolizaton techniques have improved the rate of success to catheterize smaller and more tortuous arterial feeders, resulting in better intranidal deposition of embolic agents and more comprehensive devascularization of AVMs.

Embolization with n-butylcyanoacrylate (NBCA) may be employed and rarely recanalization of the embolized portion is noted [15]. Also, particle embolization may be useful by means of polyvinyl alcohol (PVA), however with a higher incidence

of recanalization [15, 16] Ethylene-vinyl alcohol copolymer (Onyx) has been recently introduced as another promising embolization agent [15, 16].

In order to minimize hyperperfusion hemodynamic complications, it is recommended staged endovascular embolization, especially in large AVMs with multiple arterial feeders [15]. 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.

Endovascular embolization is rarely curative and therefore is used mainly as an adjunct to surgery or stereotactic radiosurgery.

Endovascular embolization achieves an immediate reduction in blood flow to the AVM. This significantly reduces the chance of intraoperative normal perfusion pressure breakthrough [11,12] and decreases operative time and blood loss [15]. The disadvantages of endovascular embolization include a 5% risk of hemorrhage, errant embolization causing stroke, catheter gluing intravascularly, and decreased "compressibility" of the AVM during surgery [15].

For larger lesions, embolization is invaluable in decreasing decreasing posible 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

Rationale for Surgical Treatment

Advances in microscopic visualization, microsurgical techniques, stereotactic guidance, intraoperative electrophysiological monitoring, neuroanesthetic techniques, postoperative critical care management, a better understanding of microsurgical anatomy of encephalic arteries and angiography have significantly improved the surgical outcome in AVM treatment.

Surgical resection is the main 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 [7, 14]. The Spetzler -Martin grading system [23] is useful in evaluating the operative risk and is a good predictor of postoperative complications. This grading system relies on three parameters: AVM size, presence of a deep venous component, and the involvement of physiologically functional ("eloquent") brain.

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.

Postoperative is essencial for confirmation of total excision. Postsurgically, AVMs rarely recur after complete angiographic confirmation of cure, except in pediatric cases where ther may be a higher recurrence rate.

The natural history of partially treated or residual AVMs matches that of untreated lesions, which means that no demonstrable protection is given. Residual or recurrent AVMs require the consideration of additional treatment based on the individualized risk assessment.

Timing of surgery

Surgery for arteriovenous malformation should ideally be performed electively. Occasionally, an intraparenchymal hemorrhage (IPH) should be removed in an emergency basis, if its mass effect threatens patient's life. In this situation, some prefer to perform an operation as much conservative as possible, but avoiding removing much of the hemorrhagic content with minimal approach to venous malformations. After edema regression, one can return for definitive therapy. In most cases, AVM may be treated conservatively for 3 to 4 weeks after the initial bleeding, with late surgical approach for complete excisionexcision: the existing hematoma progressively liquefies, making surgery easier. During this awaiting period, it is important to evaluate all possible forms of therapy forms of therapy, and an angiogram should be repeated before any definitive therapy is attained.

When the clot is fully reabsorbed, the AVM has frequently changed; also, there may be some further angiographic changes, such as thrombosis of feeding arteries or visualization of vessels not initially displayed.

The use of steroids in the preoperative and perioperative stages may be justified by the fact that during surgery a significant brain retraction may be needed. Moreover, prophylactic antibiotics should be prescribed preoperatively and, in the case of supratentorial lesions, anticonvulsants are also prescribed. Lumbar drainage or intravenous mannitol may help to achieve brain relaxation. For intracranial cases, anesthesia should

JBNC Brazilian Journal of Neurosurgery
Jornal Brasileiro de Neurocirurgia

include fentanyl and pentobarbital joined with a neuromuscular blocking agent for induction. Hyperventilation to approximately a pCO2 of 25 to 30 mmHg is indicated. Anesthesia with 30 percent of nitric oxide and an inhalation agent, such as isoflurane combined with intermittent doses of fentanyl, is also required. Most prefer not to use hypotensive (HTR) agents to control bleeding, except in very rare circunstances where patient' s blood pressure goes under normal.

Positioning and Craniotomy

Positioning is a critical factor while planning arteriovenous malformation surgery. Position may change for different types and localizations of lesions but, generally speaking, patient's head must be positioned in such a manner that does not cause neck veins compression which could significantly impede venous drainage. Also, placement must be such that brain retraction during resection is minimal, and, whenever possible, be aided by the force of gravity. In most cases, the head should be rigidly attached to a fixing equipment, with a cortical representation of the lesion positioned parallel to the ground, in such way that the supplying arteries stay as perpendicular as possible.

A large incision should be used, particularly with wide and moderately sized malformations. A large portion of the brain tissue around the AVM may be exposed, so one can have a better orientation regarding the feeding arteries, venous drainage and other cortical points of reference. Frequently, the abnormality is not completely visible at the cortical surface, and recognition depends on proper identification of supplying arteries or draining veins. In addition, a large craniotomy allows a greater freedom to adjust the angle of the microscope and may help to deal with an unexpected hemorrhage. Also it may provide a slightly different approach in case of a different operative finding (figure 1 a,1b,1c,1d,1e).

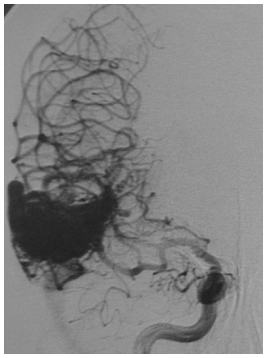


Figure 1a: Digital angiography (coronal view): Spetzler-Martin II temporal AVM, in a 25 year old male patient with partial seizures

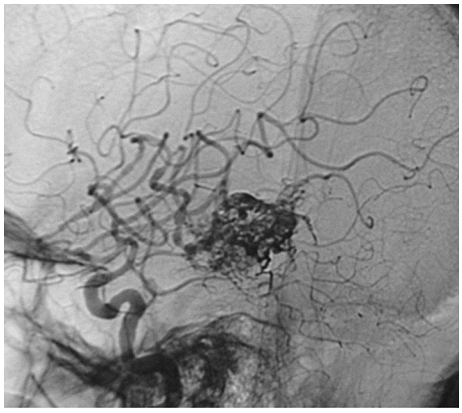


Figure 1b: Digital Angiography (sagital view): temporal AVM fed by branches of middle cerebral artery

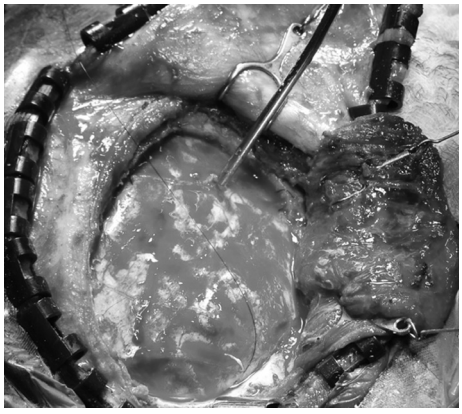
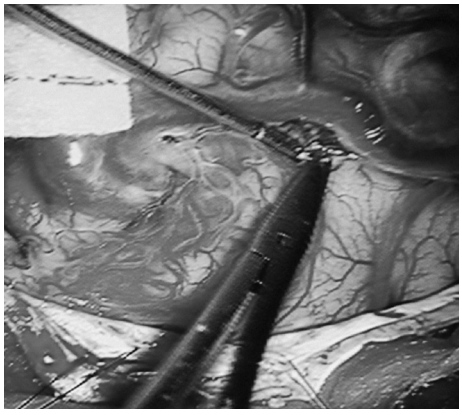


Figure 1c: Large temporal and subtemporal craniotomy facilitates the surgical view and exposes the borders of temporal AVM



Figures 1d: Surgical view shows sharp dissection of main feeders that should be done in circumferencial fashion.

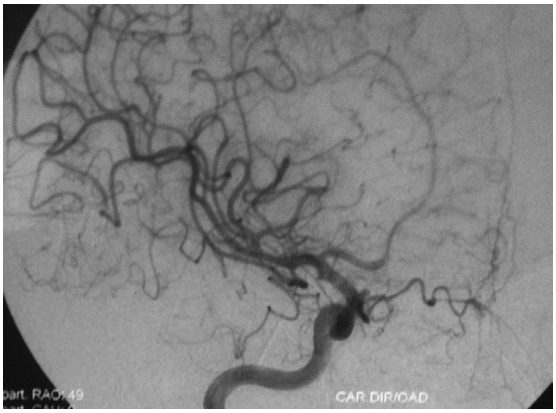


Figure 1e: Digital angiography (coronal view) final control after total removal of AVM

MICROSURGICAL PITFALLS

Excision of the AVM can be divided into five stages: identification and exclusion of the superficial feeding vessels, circumferential dissection, dissection of the apex, final vascular pedicle division with its complete excision and complete hemostasis. The surgical steps can be visualized in figure 2a to figure 2i.

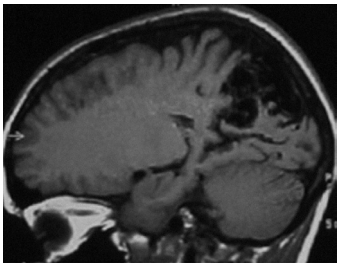


Figure 2a: MRI (sagital view): flow void compatible with occipito parietal AVM in a 49 year-old patient who refused to be treated initially

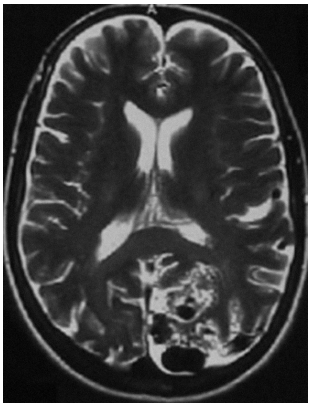


Figure 2b: MRI(axial T2 images): Spetzler-Martin II AVM, in occipito-parietal region near the left ventricle carrefour

1) Identification and exclusion of feeding arteries

If the malformation is not visible on the cortical surface after a large bone flap and a wide dural opening, one has to decide the entry point. Any feeding artery covered by arachnoid should be identified with the microscope, especially the point of penetration to the malformation: the vessel should not feed any adjacent area of the brain, particularly found in arteries of perisylvian lesions and also those found in the corpus callosum. When the main lesion abnormality is not visible on the surface, ultrasound may be useful for identification.

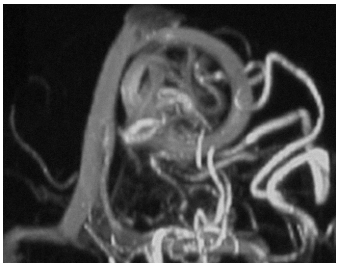
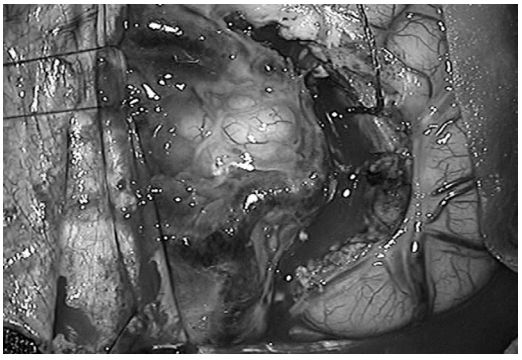


Figure 2c: Angio MRI: left parieto-occipital AVM, with superficial drainage, fed by parieto-occipital artery and calcarine artery.

As regards the identification of feeding superficial vessels, it is extremely important not to misidentify a reddish draining vein as an artery, which usually must be preserved until the end of the surgical procedure. An exception would be a malformation draining to one or more deep veins, with only a small superficial drainage. Premature obliteration of a major venous drainage can lead to extensive swelling and intraoperative bleeding. With experience and wide magnification, it is quite easy to differentiate those veins from the arteries: the veins have a thinner wall and are less turgid than same size arteries. Also, the veins tend to have a larger diameter than the majority of the feeding arteries. If identification is doubtful, applying a temporary clip will clearly indicate if we are dealing with an artery or vein. Moreover, veins and arteries can often be identified by tactile sensation of a slight compression between the ends of the bipolar forceps. Finally, during vessel coagulation, applying a short intensity current with bipolar forceps can immediately distinguish one artery from a vein: the vein shrinks more quickly.



Figures 2d: Surgical view: typical circumferencial disection of main feeders and nidus of AVM.

JBNC Brazilian Journal of Neurosurgery
Jornal Brasileiro de Neurocirurgia

During dissection of feeding arteries, besides bipolar coagulation, one may use microhemoclips for vessels larger than 1 mm in diameter.

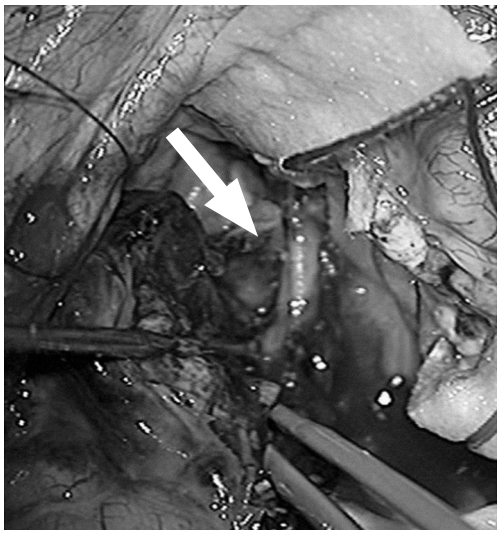


Figure 2e: Surgical view: parieto-occipital artery exposed; occlusion performed by means of bipolar coagulation or clipping (red arrow)

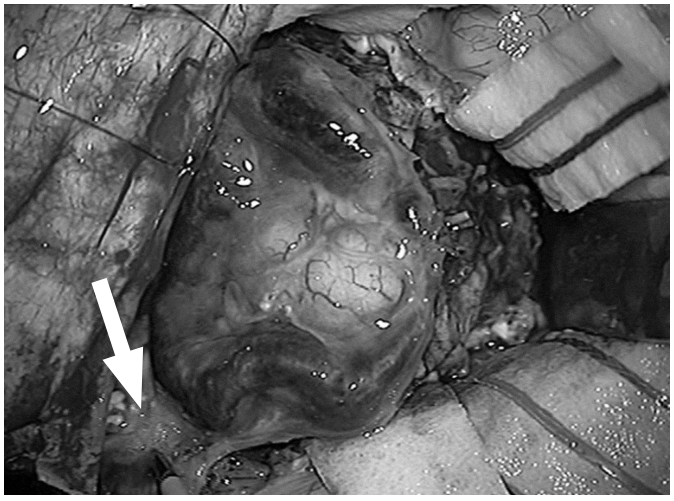


Figure 2f: Surgical view: last step, with occlusion of main venous drainage with bipolar coagulation

2) Circumferential dissection

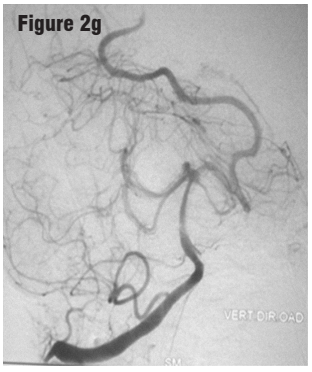
After angiographic identification, to make sure that all superficial feeding vessels were identified and isolated, one should start a circumferential dissection of the malformation. It is imperative that the dissection is performed as close as possible to the margin of the lesion to prevent any damage to the adjacent brain tissue. The plane of dissection may be slightly more peripheral, only when malformations are located far from neurologically critical areas. Contrary to reports from contemporary literature about the existence of an avascular plan surrounding a malformation, rarely one can find such plan encircling the entire lesion. If the dissection plan becomes very avascular, it may be that the surgeon is dissecting far awy from the malformation. Any eventual bleeding around the margins should be controled: blood may descend along AVM margins, with late intraparenchymal or intraventricular hemorrhage, only recognized until the occurrence of a catastrophic swelling. In cerebral convexity lesions, the initial circumferential corticectomy should continue until approximately 2.5 cm which is the maximum depth of the groove sulcus. The reason is that the superficial arterial supply penetrates the malformation along the sulcus and may not be visible on the surface. Usually after exposing the sulcal feeding arteries, no large feeding vessels will be found until the AVM apex is reached.

3) Dissection of the apex

The circumferential dissection continues in a conical shape until reaches the resection step, which is the hardest of all. It is at this stage that the final feeding vessels are found. The most difficult to deal with are the small and friable subependymal vessels that resist to any attempt of coagulation. This stage of the resection is often frustrating and time consuming, because the vessels resist to coagulation, are difficult to identify and bleeding persists. Some find difficult to use hemoclips and small aneurysm clips at this depth and, sometimes, the vessels continue to bleed, besides cliping. With persistence and patience, the surgeon eventually achieve hemostasis. Again, one should avoid the accumulation of blood in the white matter, which which may cause vessel retraction and difficult coagulation. Some surgeons feel that arterial hypotension is valid to control bleeding at this stage but if it is used, it is advisable to keep the patient sedated and hypotensive for 2 or 3 days after surgery.

4) Final removal of vascular pedicle.

After circumferential dissection and control of the apex, the malformation must literally be "hung" by its pedicle. Frequently, at this stage, the veins are still somehow arterialized due to small feeding arteries right below or adjacent to the draining veins. One must pay careful attention to this possibility, even if the veins are clipped and separated.



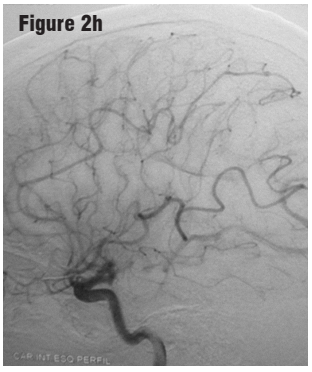


Figure 2g: Posterior circulation digital angiograpghy: complete occlusion of AVM and feeders from posterior cerebral artery. **Figure 2h:** Anterior circulation angiography (sagital view): complete occlusion of parieto-occipital artery feeders and AVM.

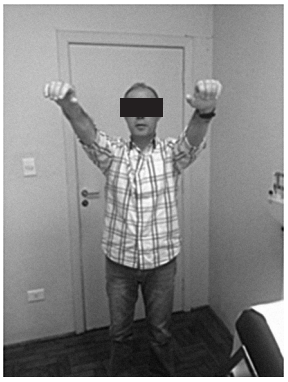


Figure 2i: Patients 2 months after the surgery without any neurological deficit

5) Complete hemostasis

At this point, the resection cavity must be carefully inspected, checking for the presence of any residual bleeding or malformation. One should carefully remove any material used during ressection, like hemostatics, in order to avoid aditional bleeding. The resection cavity wall must be inspected under microscopic magnification. Special attention should be given to this part of the procedure, since it can mean the difference between a quiet postoperative course and a catastrophic hemorrhage.

In case a residual malformation is found, a careful removal takes place at this stage. After the surgeon is sure that all the malformation was removed and all bleeding was controlled throughout the entire cavity, it is lined with a layer of hemostatic film. The anesthetist is then required to gently raise the blood pressure 15 to 20 mm Hg above the resting pressure to check the occurrence of any bleeding: in this case, new bipolar coagulation, compression and hemostatic film and then after the cavity inspected once again with the blood pressure raised. Ten to 15 minutes later, with microscope inspection, the anesthetist allows blood pressure to return to anesthesia levels, with mantainance up to the end of the procedure.

COMPLICATIONS OF SURGICAL TREATMENT

The types of complications occurring in the surgical treatment of malformations involve all aspects of patient's preoperative evaluation, the intraoperative period and postoperative course.

Preoperative

An erroneous to some author's evaluation, an erroneous judgment about the surgical procedure is the most common cause of surgical complications. The most common error is miscalculation of the exact topography of a lesion that involves speech, primary motor-sensory or capsular areas or brainstem. Misconceptions of spacial localization are less frequent nowadays, since high resolution MRI can delineate the exact extension of a given lesion and its proximity to the motor track, the internal capsule or brainstem. The experience of some surgeons demonstrates. There are several occasions in which surgery is recommended based solely on angiography, but after MRI, motor cortex or brainstem involvement is detected. If the lesion involves a critical area, one may expect some postoperative deficit: some patients' accceptance to deficits depends on patient's age, occupation and willingness to live with the threat of an uncertain future hemorrhage. There is evidence that cortical mapping can help in some cases, however the resection technique will not be changed: in case preoperative mapping with functional MRI shows involvement of critical areas, surgical decision may be modified. Another decision-making mistake involves patients with significant clinical comorbidities, and therefore at high surgical risk: the patient must be able to withstand a prolonged period under anesthesia, with significant hemodynamic changes and often large blood loss. A complete evaluation of pulmonary and cardiovascular systems in every patient should be performed. Sometimes we may underestimate patients' ability to recover from an initial hemorrhage. In a patient presenting with significant deficit, early surgery might be contemplated, figuring that the deficit will not be made worse by surgery. While this may be true, a potentially reversible deficit may be made permanent, if surgery is undertaken in the acute phase, taking into all difficulties created by operating with hemorrhage and increased intracranial pressure. Waiting a few weeks often allows the patient to recover significantly, with minimal additional risks, since the chances of another bleeding

JBNC Brazilian Journal of Neurosurgery
Jornal Brasileiro de Neurocirurgia

are small. Furthermore, while waiting, a new angiographic study may show different AVM findings, including complete thrombosis.

Intraoperative

Parenchymal damage: The second most common cause of complications is damage to the parenchyma, although sometimes it can be difficult to separate from errors caused by poor spatial concept or resection too close to eloquent areas. Damage to the parenchyma may be caused an enlarged surgical margin, with the purpose of finding a bloodless dissection plane. In addition, working in a dry field often means that one is too far away from the edges of the malformation, with penetration of adjacent white matter. As mentioned before, a relatively avascular gliotic plan surrounding arteriovenous malformations is often incomplete or even nonexistent in most non –ruptured malformations. A temporal or frontal pole AVM may be dissected a little bit far away from the malformation, in case the dissection plane is not too clear. Ischemia and infarction may develop when AVM feeding vessels are coagulated before any parenchymal branch is preserved. This can be a problem with AVM supplied by so called "transitional vessels ", i.e., those that supply both the malformation and the adjacent brain tissue. In the case of superficial feeding vessels, the arachnoid must be opened and the vessel followed to the depth of the sulcus. Anterior Sylvian and anterior callosal AVM, in particular, are often supplied by middle cerebral artery and anterior cerebral artery branches, which must be carefully skeletonized during its passage through the lesion, in order not to obstruct the main trunks, which ultimately supply normal brain tissue.

The damage to the AVM surrounding tissue is due to shrinkage and consequent edema as the cause of most transient postoperative deficits. Certainly, major retraction of the frontal, temporal or occipital lobe can result in significant edema and infarct due to occlusion of large draining veins. Therefore, some surgeons prefer approaches involving resection of non-eloquent areas, in order to prevent vigorous retractions, like retraction of the temporal lobe and potential damage to Labbé's vein in a subtemporal approach to medial temporal lesions. This can be avoided by an operation through the inferior temporal gyrus. Excessive frontal retraction (with potential damage to any large draining veins) or a transcallosal interhemispheric approach with injury to the head of the caudate nucleus can be avoided with a transcortical surgery in the presence of ventriculomegaly. Occipital lobe damage due to an interhemispheric approach to a lesion in the medial paratrigonal area can be minimized by means of a posterior parietal transcortical approach. Due to its long course through the temporal and occipital lobes, one should pay special attention to the optic radiation fibers during resection of any temporal or occipital paratrigonal AVM. Also, careful consideration should be taken in addressing the geniculo-calcarine fibers. There is evidence that a sylvian fissure approach to the anteromedial temporal lobe does not generate visual field defects.

Bleeding: Intraoperative hemorrhage may result from a premature venous occlusion generating hyperemia and engorgement of the brain and remaining malformation. As previously noted, one lesion, unless more than one substantial vein drain the malformation. It is proper to leave intact any arterialized vein until the lesion has been circumferentially dissected. After AVM excision, any bleeding inside the residual cavity, most likely, represents retained malformation. Bleeding coming from the deepest perforating branches can be problematic as there may be substantial damage to the parenchyma during attempts to coagulate these fragile white matter vessels.

Postoperative

Hemorrhage: The most common cause of bleeding in the postoperative period is leaving AVM remnants. For this reason, it is absolutely required a careful inspection of the resection wall: it is advisable elevating the blood pressure and inspecting the resection bed for at least 15 minutes. Intraoperative angiography can be extremely helpful in revealing malformation remnants. Bleeding due to rupture under normal perfusion pressure is a rare occurrence, but it can be cause of postoperative hemorrhage.

The majority of patients who suffer from such complication present with large congenital lesions with high flow abnormalities. Treatment includes draining the hematoma, careful control of blood pressure, institution of barbiturate coma and anti-edema therapy.

Vascular thrombosis: After excision of high flow lesions with sudden interruption of large draining veins, there is a risk of retrograde venous thrombosis, likely to be accompanied by venous infarct and hemorrhage. There is also a hypothetical possibility of a retrograde arterial thrombosis after resection,

JBNC Brazilian Journal of Neurosurgery
Jornal Brasileiro de Neurocirurgia

particularly if long and tortuous supplying arteries are interrupted near the main entrance of the malformation.

Although vasospasm may be seen in postoperative angiograms, after surgical excision of arteriovenous malformations it is rarely responsible for ischemic deficits, which not rarely happen after aneurismal subarachnoid hemorrhage

Epilepsy: Epileptic seizures develop in 6 to 22 % of patients epilepsy-free pre-operatively, depending upon MAV localization and on the follow-up. In one study, 15 % of patients had onset of seizures, but only half of them had one or two seizures over the immediate postoperative period. If a patient with an arteriovenous malformation presents with refractory seizures while in medical treatment, intraoperative electrocorticography can help guide resection of the epileptogenic tissue around the lesion.

Stereotactic Radiosurgery

AVM obliteration rate in small AVMs (less than 3 cm diameter) is reasonably high (more than 80%) [17, 24], but less than half of the larger lesions are effectively cured. Stereotatic radiosurgery seems to be less aggressive than surgery, by avoidance of an open craniotomy and general anesthesia, and allowing treatment of surgically inaccessible deep seated AVMs, however obliteration occurs two or more years after the procedure. During this time, the patient is subject to the hemorrhagic risk of an untreated AVM, and in fact 8-10% of patients suffer a hemorrhage while waiting for the therapeutic benefit of a stereotactic radiosurgery procedure (consistent with a 4% per year AVM hemorrhage rate). A previously irradiated AVM can be retreated by irradiation, albeit with a higher complication rate [18].

Edema induced by symptomatic radiation may be a severe complication, which is associated with the location and radiation-dose delivered. Edema after irradiation in AVM patients occurs in about 10% of cases [8], more frequently in larger irradiated lesions and in eloquent and near eloquent encephalic structures [8]. Frequently actinic edema causes focal neurologic deficits or seizures, but often complete recover happens after several weeks to months. In few cases, high doses of corticosteroids are necessary for treatment of edema. Serious and permanent neurologic deficits can occur in 3% of cases.

Integrated Global Management and Therapeutics

Whenever the risk of surgery is prohibitive due to AVM location, or due to patient's poor medical condition, stereotactic radiosurgery either alone or in conjunction with embolization can be an effective alternative. Embolization serves as a useful adjunct to surgery but is rarely successful as the sole mode of therapy. 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 rarely 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 preoperative 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 may be helpful. The brain adjacent to an AVM can also be mapped intraoperatively with cortical stimulation and evoked potentials to avoid lesioning primary functional areas.

Many AVMs located in deeper brain locations, including those in the diencephalon, basal ganglia, internal capsule or brainstem are treated with radiosurgery, with or without embolization. Endovascular embolization can be used as an adjunct to decrease AVM size and increase the curative rate of successful radiosurgery (likelihood of AVM obliteration).

JBNC Brazilian Journal of Neurosurgery
Jornal Brasileiro de Neurocirurgia

Larger AVMs (Spetzler-Martin grades IV and V) are difficult to treat and carry a higher complication rate of treatment [23]. 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.

SPECIAL TOPICS

Aneurysms Associated with AVMs

Fifteen percent of AVMs are associated with aneurysms. Unfortunately, the literature does not differentiate between intranidal, flow related, or aneurysms on vessels not directly related to the AVM. Redekop et al. [19] reviewed their experience with 632 angiographically proven AVM cases and found a 5.5% incidence of intranidal aneurysms, an 11.2% incidence of flow related aneurysms, and an 0.8% incidence of unrelated aneurysms.

Whenever an AVM is associated with an aneurysm, it is recommended treating the aneurysm first (2). Following AVM obliteration, there is a theoretical change of an increased risk of aneurysmal rupture due to a temporary rise in the pressure in the feeding artery.

Nidal and venous aneurysms have also been associated with hemorrhagic presentations of an AVM, but it is not clear if such features influence prospective hemorrhagic risks in the long term: in this case it is recommend treating the symptomatic lesion first.

AVMs and Acute Recent Hemorrhage

It is important to consider that an AVM that has recently bled is at a greater risk of a recurrent hemorrhage for the subsequent several months, although the risk of an imminent rebleed is nowhere as great as that of an aneurysmal subarachnoid hemorrhage.

As a rule, paraventricular AVMs or those associated with an intranidal aneurysm are included in this category. These are evaluated during angiography and may dictate more urgent therapeutic intervention. Otherwise, a non-life threatening hemorrhage is not a reason for emergent AVM therapy. It is not necessary to unduly delay treatment until full recovery from a hemorrhage occurs, and combined with rehabilitation, initiating treatment when the patient has stabilized may result in a substantially shorter convalescence.

Life-threatening hemorrhages often call for emergent hematoma evacuation, and critical care management of intracranial hypertension and ventricular obstruction. The decision to evacuate a hematoma in the setting of an AVM must be deliberate, taking the time to define,what almost always can be done by contrast enhanced CT study, or better , by digital angiography[15].

The craniotomy flap should be generous enough to allow tackling of the AVM at the same or at a subsequent setting, the primary aim of surgery is to drain and remove life-threatening hematomas and to relieve the mass effect. Overjudicious hematoma drainage or manipulation of the nidus might precipitate a serious hemorrhage. The AVM itself should only be resected if complete angiographic evaluation has been performed, the brain relatively slack with good access to the AVM, and the surgical and neuroanesthetic teams prepared for a lengthy and technically demanding procedure dictated by lesion size and angioarchitecture. Otherwise, it is best to drain the hematoma, achieve hemostasis and postpone the surgical excision of the AVM (perhaps after preoperative embolization). An exception to the above is post-embolization hemorrhage, where conjoint evacuation of the hematoma and excision of the AVM might be entertained.

AVMs and Epilepsy

Seizures are frequently associated with intracranial AVMs, and may be the sole presenting symptom. Most seizure disorders associated with AVMs can be well controlled with anticonvulsant therapy. Seizures might improve, remain unchanged, or worsen after any therapeutic intervention for an AVM. De novo seizures might also ensue after treatment [15].

Intractable seizures often become easier to control after AVM excision and not infrequently anticonvulsants may be discontinued altogether after a seizure-free period. There is no evidence that extensive monitoring, mapping, and excision of epileptogenic brain is necessary, cost-effective, or achieves a better overall outcome relative to seizure control than the primary treatment of AVMs. In cases of persistent intractable seizures after AVM excision, formal mapping and excision of epileptogenic zones can achieve seizure control [15, 16].

JBNC Brazilian Journal of Neurosurgery
Jornal Brasileiro de Neurocirurgia

NORMAL PRESSURE BREAKTHROUGH

Frequency

Drake reported the occurrence of NPPB in 4/166 (2%) patients undergoing surgery for AVMs, and all four patients died [7]. Heros reported the occurrence of NBBP in only 4/300 (1.3%) patients in his surgical series; good outcomes were observed in 3 of them [13]. Day et al successfully treated NPPB that began intraoperatively in 3 patients with 3 to 5 days of management mentioned above, including return to operating room for evacuation of delayed hematomas [5].

Physiopathology

Hemodynamic changes are of importance while removing large and high-flow arteriovenous malformations (AVM), because excision of AVMs can be complicated by postoperative edema and hemorrhage in adjacent brain tissue, despite the complete excision of the malformation. Various theories have purported to explain the hemodynamic basis for this predisposition, including disordered autoregulation causing "normal perfusion pressure breakthrough" and obstruction of venous drainage leading to "occlusive hyperemia [21].

Two main hypotheses, normal perfusion pressure breakthrough (NPPB) and occlusive hyperemia, are placed in the literature regarding the development of haemorrhage and oedema following AVM surgery. NPPB hypothesis was introduced in 1978. Since the occlusive hyperemia hypothesis was first postulated in 1993, however, a debate has persisted within the cerebrovascular societies, concerning which hypothesis better explains the complications of edema and hemorrhage observed after AVM resection [29].

There is an association between increases in global cerebral blood flow(CBF) from pre- to post-resection and NPPB-type complications, but there is no relationship of these CBF changes to preoperative regional arterial hypotension [27]. These data do not support a uniquely hemodynamic mechanism that explains cerebral hyperemia as a consequence of repressurization in hypotensive vascular beds [28].

Yamada et al [26] evaluated hemodynamic changes in 14 cases of high-flow AVM with cerebral angiogram and intraoperative monitoring of cortical-surface blood flow. The criteria they used for high-flow AVM are: nidus larger than 4 cm, a few large feeders, high-flow shunt in the nidus, and reduced circulation or dilated arteries in the adjacent brain tissue. Nine of these were operated on for total removal of AVM. Of those, 2 cases evolved with postoperative local edema and hemorrhage and was thought to be due to NPPB. Intraoperative monitoring of cortical-surface blood flow was useful to predict occurrence of "perfusion breakthrough", because blood flow in the adjacent brain tissue increased markedly with feeder clipping. Intraoperative barbiturate protection and postoperative controlled hypotension were thought to be useful for prevention of NPPB, though the details of mechanisms are unknown [26].

According to the theory of edema surrounding the surgical bed of excised AVM, arteries supplying cerebral AVMs become dilated and lose their capacity to dilate or constrict according to autoregulation. Acutely after removal of a cerebral AVM, excessive blood pressure in these arterial feeders can cause normal brain tissue to bleed [1].

Experimental Normal Pressure Breakthrough

Sekhon et al [21] examined the capillaries in adjacent brain parenchyma for any structural deficiencies that would predispose the brain to the postoperative formation of edema and hemorrhage. In their study, arteriovenous fistulas (AVFs) were created surgically in the neck of 10 male Sprague-Dawley rats, which caused chronic cerebral hypoperfusion with a reduction in cerebral blood flow of between 25% and 50%. Ten age-matched animals were used as controls. Twenty-six weeks after AVF formation, the animals were killed and perfusion fixed [21]. Their brain tissue was prepared for light microscopic studies by staining for glial fibrillary acidic protein or for transmission electron microscopy. In the CA1 pyramidal cell region of the hippocampus, it was found that in the animals with AVFs there was increased capillary density and absent astrocytic foot processes in some of these vessels. It was concluded that these vessels had developed as a result of neovascularization, in response to chronic cerebral ischemia and that their anatomical configuration made them prone to mechanical weakness and instability following the increase in perfusion pressure that occurs in adjacent brain parenchyma after AVM excision. The authors believe that this study pinpoints a structural accompaniment to the hemodynamic changes that occur in brain tissue in the vicinity of cerebral AVMs that predispose these areas to the formation of edema and hemorrhage after AVM excision [21].

Hai et al, [12] studied 24 Sprague-Dawley rats randomly assigned to either a sham-operated group, an arteriovenous fistula

JBNC Brazilian Journal of Neurosurgery
Jornal Brasileiro de Neurocirurgia

(AVF) group, or a model group (eight rats each). The animal model was prepared by creating a fistula through an end-to-side anastomosis between the right distal external jugular vein (EJV) and the ipsilateral common carotid artery (CCA), followed by ligation of the left vein draining the transverse sinus and bilateral external carotid arteries. Systemic mean arterial pressure (MAP), draining vein pressure (DVP), and CPP were monitored and compared among the three groups preoperatively, immediately postoperatively, and again 90 days later. Following occlusion of the fistula after a 90-day interval, blood-brain barrier (BBB) disruption and water content in the right cortical tissues of the middle cerebral artery territory were confirmed and also quantified with transmission electron microscopy. Formation of a fistula resulted in significant decreases in MAP and CPP, and a significant increase in DVP in the AVF and model groups. Ninety days later, there were still significant increases in DVP and decreases in CPP in the model group compared with the other groups ($p < 0.05$). Damage to the BBB and brain edema were noted in animals in the model group during restoration of normal perfusion pressure by occlusion of the fistula. Electron microscopy studies revealed cerebral vasogenic edema and/or hemorrhage in various amounts, which correlated with absent astrocytic foot processes surrounding some cerebral capillaries. The results demonstrated that an end-to-side anastomosis between the distal EJV and CCA can induce a decrease in CPP, whereas a further chronic state of cerebral hypoperfusion may be caused by venous outflow restriction, which was associated with perfusion pressure breakthrough. This animal model conformed to the basic hemodynamic characteristics of human cerebral arteriovenous malformations [30].

In similar study, Hai et al [11] randomly divided male Sprague-Dawley rats into either a sham-operated group, a control group, or a model group with reperfusion assessed at 1, 12, 24 and 72 h after restoration of normal perfusion pressure. BBB disruption was judged by extravasation of Evans blue (EB) dye. They observed that EB and water content in rat brains of the model group with reperfusion were significantly increased compared with the other groups. The most predominant increase occurred at 1 h after reperfusion, and the next at 24 h after reperfusion, representing biphasic changes which are similar to the pathological processes of acute cerebral ischemia/reperfusion injury. There was no difference of the percentage of apoptotic cells in rat brains between the sham-operated group and the control group using flow cytometry. No prominent apoptotic cells were found in the model group with reperfusion at 1 h. However, the percentage of apoptotic cells increased significantly in rat brains of the model group with reperfusion at 12 h, peaked at 24 h, and decreased at 72 h after reperfusion. Apoptotic cells were confirmed with electron microscopy and terminal deoxynuleotidyl transferase-mediated dUTP-biotin nick end labeling (TUNEL). A significant enhancement of MPO activity in combination with reduction of SOD activity was observed at 12, 24 and 72 h in rat brains of the model group with reperfusion. Our data indicates that reperfusion after restoration of normal perfusion pressure with chronic cerebral hypoperfusion lead to secondary neuronal damage which may associate with cerebral ischemia/reperfusion injury [11].

Prevention

Prevention of NPPB is the best form of treatment. High fistula flow with a paucity of flow entering the immediately adjacent brain is the angiographic hallmark predicting this condition. Staging AVM treatment with repeat operative approaches and /or endovascular embolization techniques can be effective prophylaxis. This approach theoretically allows autoregulation to be restored at a gradual step, as the high flow shunting is methodically diminished.

Management

When NPPB occurs intraoperatively, it usually appears toward the end of the resection when the high flow shunt has been removed.

Recent advances in cerebrovascular imaging and hemodynamic analysis have allowed a better evaluation of intracerebral changes following AVM resection. It is likely that these 2 hypotheses are not mutually exclusive and perhaps exist in a spectrum of hemodynamic alteration following AVM resection [29].

Gutiérrez-González et al demonstrate that not only autoregulation impairment in the ipsilateral hemisphere occurs but also contralateral remote vessels response does. Such findings may be observed at 2-4 weeks and may resolve after 1-3 months [10].

Treatment consists of immediate brain protection from elevated cerebral perfusion pressure (CPP) by EEG burst suppressive anesthesia with pentobarbital and systemic arterial blood pressure reduction (Systolic 80-90 mm Hg) with sodium

nitroprussside or nicardipine [5]. This approach usually arrests the spread of cerebral edema, allowing for duramater closure. Eventually, in order to finish the surgery and craniotomy, hemorrhagic brain tissue may need to be resected. ICP monitoring should be placed and patient should be taken for immediate cerebral angiogram to find out complete AVM resection.

ICP should be lowered by administration of anti hypertensive drugs and anti edema drugs over the next 24 hours under barbiturate coma, and head CT scans should be performed for any unexplained alteration. If the surveillance CT scans demonstrate no progression, the patient can be weaned off from the anti-hypertensive agent over the next 12 to 24 hours provided that ICP remains controlled and systemic blood pressure does not rise inappropriately. Also, barbiturate should be progressively taken out over the following 24 hours, although it may take a few days to metabolize and clear systemically.

Conclusion

A thorough knowledge of the natural history of AVMs is mandatory to the treatment decision-making process. A multidisciplinary team approach is essential. Minimally symptomatic or asymptomatic patients, in normal neurologic status, 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 should be employed in order to improve the chances of a lifetime cure, sometimes in a complimentary fashion. Microsurgery is the main method of treatment of AVM patients. Embolization serves as a useful adjunct to surgery but is rarely successful as the sole mode of therapy

References

1. Alexander MD, Connolly ES, Meyers PM. Revisiting normal perfusion pressure breakthrough in light of hemorrhage-induced vasospasm. World J Radiol. 2010; 28;2 (6):230-2.

2. Batjer H, Suss RA, Samson D: Intracranial arteriovenous malformations associated with aneurysms. Neurosurgery 1986; 18:29-35.

3. Brown RD, Jr., Wiebers DO, Forbes G, O'Fallon WM, Piepgras DG, Marsh WR, et al. The natural history of unruptured intracranial arteriovenous malformations. J Neurosurg 1988; 68:352-357.

4. Crawford PM, West CR, Chadwick DW, Shaw MD: Arteriovenous malformations of the brain: natural history in unoperated patients. J Neurol Neurosurg Psychiatry 1986; 49:1-10.

5. Day AL, Friedman WA, Sypert GW, Mickle JP. Successful treatment of the normal perfusion pressure breakthrough syndrome. Neurosurgery. 1982;11(5):625-30

6. Del Curling O, Jr., Kelly DL, Jr., Elster AD, Craven TE: An analysis of the natural history of cavernous angiomas. J Neurosurg 1991; 75:702-8.

7. Drake CG: Cerebral arteriovenous malformations: considerations for and experience with surgical treatment in 166 cases. Clin Neurosurg 1979; 26:145-208.

8. Flickinger JC, Kondziolka D, Maitz AH, Lunsford LD: Analysis of neurological sequelae from radiosurgery of arteriovenous malformations: how location affects outcome. Int J Radiat Oncol Biol Phys 1998; 40:273-8.

9. Graf CJ, Perret GE, Torner JC: Bleeding from cerebral arteriovenous malformations as part of their natural history. J Neurosurg 1983; 58:331-7.

10. Gutiérrez-González R, Gil A, Serna C, López-Ibor L, Boto GR. Normal perfusion pressure breakthrough phenomenon: what still remains unknown. Br J Neurosurg. 2012;26(3): 403-5.

11. Hai J, Lin Q, Li ST, Pan QG.Chronic cerebral hypoperfusion and reperfusion injury of restoration of normal perfusion pressure contributes to the neuropathological changes in rat brain. Brain Res Mol Brain Res. 2004; 26;126 (2):137-45.

12. Hai J, Ding M, Guo Z, Wang BA. New rat model of chronic cerebral hypoperfusion associated with arteriovenous malformations. J Neurosurg. 2002 ;97(5):1198-202.

13. Heros RC, Korosue K. Deep parenchymous lesions. In: Apuzzo MLJ, ed. Brain Surgery. Complication avoidance and Management. New York: Churchill Livingstone, 1990: 1175-1193

14. Houser OW, Campbell JK, Campbell RJ, Sundt TM, Jr.: Arteriovenous malformation affecting the transverse dural venous sinus--an acquired lesion. Mayo Clin Proc 1979; 54:651-61.

15. Jafar JJ, Davis AJ, Berenstein A, Choi IS, Kupersmith MJ: The effect of embolization with N-butyl cyanoacrylate prior to surgical resection of cerebral arteriovenous malformations. J Neurosurg 1993; 78:60-9.

16. Jafar JJ, Huang P. Cerebral Arteriovenous Malformations: Clinical Decisions and Multimodality Management Strategies. In: Aguiar PH, Simm R, Antunes AC, Lehmann MF, Damasio R (Eds). Tratado de Neurologia Vascular, Rocca, São Paulo, 2012, Chapter 31, pp 267-274

17. Kondziolka D, Lunsford LD, Flickinger JC: Gamma knife stereotactic radiosurgery for cerebral vascular malformations, in: Alexander E, Loeffler JS, Lunsford LD (eds): Stereotactic Radiosurgery. New York, McGraw-Hill, 1993, pp 147-155.

18. Ondra SL, Troupp H, George ED, Schwab K: The natural history of symptomatic arteriovenous malformations of the brain: a 24-year follow-up assessment. J Neurosurg 1990; 73:387-91.

19. Redekop G, TerBrugge K, Montanera W, Willinsky R: Arterial aneurysms associated with cerebral arteriovenous malformations: classification, incidence, and risk of hemorrhage. J Neurosurg 1998; 89:539-46.

20. Sekhar LN, Heros RC: Origin, growth, and rupture of saccular aneurysms: a review. Neurosurgery 1981; 8:248-60.

21. Sekhon LH, Morgan MK, Spence I. Normal perfusion pressure breakthrough: the role of capillaries. J Neurosurg. 1997; 86(3):519-24.

22. Spetzler RF, Wilson CB, Weinstein P, Mehdorn M, Townsend J, Telles D: Normal perfusion pressure breakthrough theory. Clin Neurosurg 1978; 25:651-72.

23. Spetzler RF, Martin NA: A proposed grading system for arteriovenous malformations. J Neurosurg 1986; 65:476-83.

24. Steinberg GK, Chang SD, Levy RP, Marks MP, Frankel K, Marcellus M: Surgical resection of large incompletely treated intracranial arteriovenous malformations following stereotactic radiosurgery. J Neurosurg 1996; 84:920-8.

25. Wilkins RH: Natural history of intracranial vascular malformations: a review. Neurosurgery 1985; 16:421-30.

26. Yamada K, Hayakawa T, Yoshimine T, Nakao K, Ushio Y, Mogami H. Surgery of high-flow arteriovenous malformation: with special reference to normal perfusion pressure breakthrough phenomenon. No Shinkei Geka. 1986 ;14 (6):741-8.

27. Young WL, Kader A, Ornstein E, Baker KZ, Ostapkovich N, Pile-Spellman J, et al. Cerebral hyperemia after arteriovenous malformation resection is related to "breakthrough" complications but not to feeding artery pressure. The Columbia University Arteriovenous Malformation Study Project. Neurosurgery 1996 ;38(6):1085-93.

28. Young WL, Kader A, Prohovnik I, Ornstein E, Fleischer LH, Ostapkovich N, et al. Pressure autoregulation is intact after arteriovenous malformation resection. Neurosurgery. 1993 ;32 (4):491-6.

29. Zacharia BE, Bruce S, Appelboom G, Connolly ES Jr.Occlusive hyperemia versus normal perfusion pressure breakthrough after treatment of cranial arteriovenous malformations. Neurosurg Clin N Am. 2012; 23(1):147-51

Corresponding author

Carlos Zicarelli
e-mail: carloszicarelli@gmail.com