Functional and topographical considerations in the surgical management of cerebral vascular malformations

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Hemorrhage from intracranial cerebral vascular malformations accounts for only approximately 10% to 15% of all intracranial hemorrhages and is eight times less frequent than bleeding from berry aneurysms.[1,2] Cerebrovascular malformations can be classified according to their pathology into arteriovenous, capillary, and venous malformations *(Table I)*. Arteriovenous malformations (AVM) and cavernous malformations (CM) are the most frequent lesions requiring surgical attention due to their propensity to bleed. Dural AVMs account for 10% of hemorrhages from vascular malformations.[3]

Arteriovenous malformations

AVMs are believed to result from faulty maturation of the embryonic vascular system through lack of involution of the primary vascular plexus between the 37th and 40th intrauterine day, thus resulting in an absent capillary bed.[4] They are composed of dilated thin-walled arteriovenous channels devoid of an internal elastic lamina *(Figure 1)*. The structure of an AVM consists of one or several arterial feeders supplying a nidus of varying size, usually conical in shape with the large base at the convexity and the extremity reaching towards the ependymal surface of the ventricular system.[2,4] Most AVMs are located within the distribution territory of the middle cerebral artery (MCA) and therefore affect mostly the frontal, parietal, and temporal lobes; in rarer cases, they affect deeper portions of the brain, such as the corpus

Cerebral vascular malformations with potential surgical consequences mainly consist of arteriovenous malformations (AVM) and cavernous malformations. The standard preoperative workup of these lesions includes basic neuroradiological investigation, such as computed tomography, magnetic resonance imaging (MRI), and magnetic resonance angiography, and conventional angiography, to assess the exact neurotopographical relationships of the nidus, arterial feeding pedicles, and venous drainage. In cases where lesions are located near or within eloquent areas, precise documentation of the anatomy can be obtained using various functional tests including functional MRI, activated positron emission tomography, and magnetoencephalography (MEG), which may then be integrated into a neuronavigational system allowing for selective, image-guided surgery, thus potentially reducing surgical morbidity. Preoperative embolization may in certain cases improve the surgical excision by reducing blood flow through the AVM. Cavernous malformations may also be removed with minimally invasive and highly selective techniques.

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Clinical research
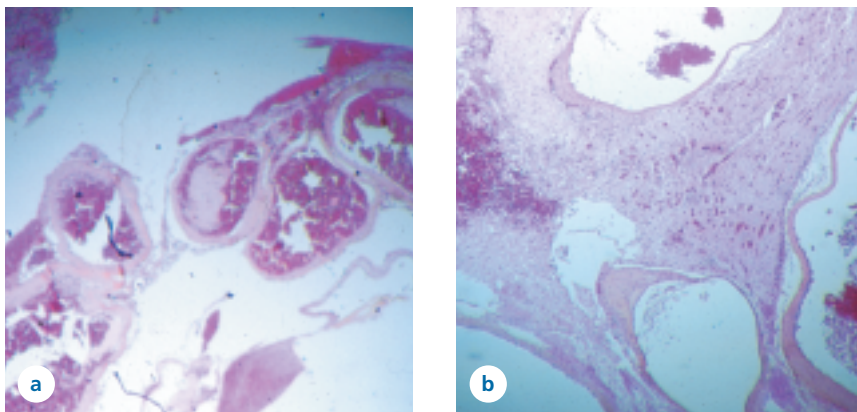
Figure 1. a. Photomicrograph of pathology specimen of arteriovenous malformation nidus showing multiple dilated channels with thick media and some thin peripheral venous structures (hematoxylin and eosin, low magnification ×3). **b.** Same specimen at higher magnification (hematoxylin and eosin, magnification ×10).

1. Arteriovenous malformations (AVM)
2. Cavernous malformations (cavernous angioma)
3. Dural arteriovenous fistula (dural AVM)
4. Capillary telangiectasia
5. Developmental venous anomaly (venous angioma)

Table I. Classification of intracranial vascular malformations.

Size	Small (less than 3 cm)	1
	Medium (3-6 cm)	2
	Large (greater than 6 cm)	3
Eloquence of involved brain	Noneloquent	0
	Eloquent	1
Type of venous drainage	Superficial	0
	Deep	1

Table II. Spetzler-Martin grading system for arteriovenous malformations.

callosum, basal ganglia, cerebellum, and brainstem. The nidus is a plexiform structure composed of arterioles, venules, and dilated vascular channels that drain into larger veins. The Spetzler-Martin classification of AVMs[5] into six grades according to their size, deep venous drainage, and relationship to eloquent brain lesions has introduced a means of standardizing the predictability of technical difficulty and morbidity *(Table II)*.

It is estimated that 30% to 40% of AVMs will bleed during an individual's lifetime, but the exact natural history is still controversial: while some authors estimate the mortality rate at 15% to 20% over a 15-year period of observation,[1,6,7] the current cumulative risk of hemorrhage of an unruptured AVM is estimated at 2% per year, and at 6% per year for a previously ruptured AVM.[8] Besides hemorrhage, AVMs may present with chronic headaches,

seizures, and, in rarer cases (mainly large AVMs), with progressive cognitive changes due to the hemodynamic steal depriving surrounding brain parenchyma.

Present day treatment of cerebral AVMs includes surgery, endovascular embolization, and stereotactic radiosurgery, which may be used in combination as part of a multimodality treatment or alone in selected cases. The aim of AVM therapy is to exclude the nidus completely, either by excision or thrombosis, in order to eliminate the source of bleeding and to spare the surrounding brain tissue by preserving the transit vessels that may participate in the feeding of the nidus but are responsible for blood supply to normal surrounding brain.

Cavernous malformations (cavernous angioma, cavernoma)

These lesions are congenital vascular hamartomas consisting of a collection of dilated sinusoidal vascular spaces (caverns) separated by thin walls devoid of muscle and elastic fibers, lined by a single layer of endothelial cells, without any intervening cerebral parenchyma, which distinguish them from AVMs and capillary telangiectasias *(Figure 2)*. They are most frequently located in the cerebral hemispheres (85%) and are associated with seizures as the presenting symptom in 50% of the cases. The introduction of magnetic resonance imaging (MRI) means they are more frequently diagnosed based on the typical mixed signal characteristics with high T1 and low T2 signals ("salt and pepper" or "popcorn" appearance) due to the presence of hemosiderin within the caverns producing hyper-T1 signals and calcifications and mural fibrosis producing hypo-T2 signals.[9,10] The natural history of cavernous

Figure 2. a. Pathology of cavernous malformation: presence of multiple clustered venous structures with thin wall and blood at various stages (hematoxylin and eosin, magnification ×3). **b.** Higher magnification of same specimen showing recent blood clot in the left superior quadrant, fibrous tissue in the left lower quadrant, and an organizing clot in the right lower quadrant (hematoxylin and eosin, magnification ×10).
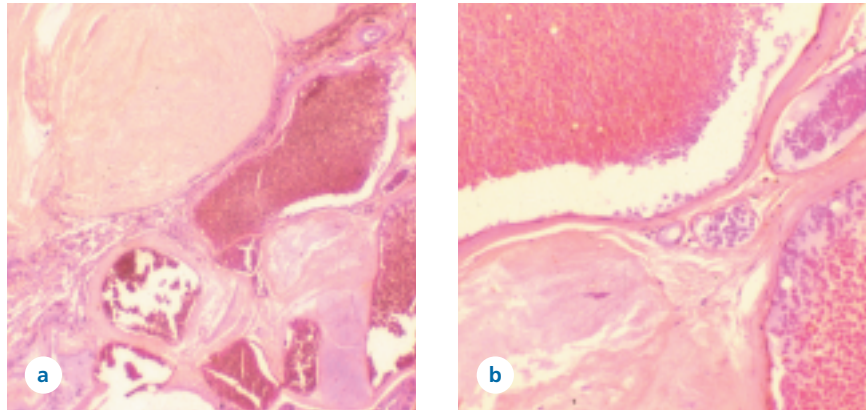
angiomas involves a risk of rupture that varies between 2% and 3% per year.[11] Symptomatic lesions presenting with epilepsy or with MRI signs of perilesional hemorrhage are considered candidates for surgical removal. In spite of some reports of beneficial results with radiation therapy, CMs are not usually candidates for stereotactic radiosurgery.[10,12]

Illustrative case histories

Three relevant case histories are presented in order to illustrate some of the surgical management strategies and problems.

Case history 1

A 40-year-old lady with no previous medical history was admitted following an acute headache and loss of consciousness with decreased sensorium and mild right hemiparesis. A computed tomography (CT) scan *(Figure 3a)* revealed a significant left intracerebral frontal hematoma. Following insertion of a ventriculostomy, her level of consciousness improved and she gradually recovered from all neurologic deficits. MRI confirmed a large AVM in the left fronto-opercular region *(Figure 3b)*, and a four-vessel conventional angiogram confirmed a 4-cm AVM nidus that was fed via the MCA, dilated branches of the anterior cerebral artery, and lenticulostriate vessels with venous drainage mostly via a dilated basal vein of Rosenthal, thus accounting for a Spetzler-Martin grade IV *(Figures 3c and 3d)*. The patient refused preoperative embolization, and, using a left frontotemporal craniotomy, the AVM was resected completely using standard microsurgical techniques. The patient did well postoperatively and had no speech disturbances in spite of the location close to or within the dominant Broca's area. An angiogram peformed 1 week postoperatively confirmed the complete resection and persistence of moderate vasospasm *(Figures 3e and 3f)*.

Case history 2

A 23-year-old previously healthy student was admitted to the emergency room following a severe headache accompanied by drowsiness and left hemiparesis. A CT scan revealed a significant intraparenchymal hematoma in the right parietal region *(Figure 4a)*. Angiography revealed a high-flow AVM with a 4.5 × 5 cm nidus, a large intranidal aneurysm draining into the basal vein of Rosenthal, and arterial feeders from a large distal MCA branch and accessorily from the anterior choroidal artery *(Figures 4b and 4c)*. After stabilization of the patient who recovered completely from his deficit, a preoperative embolization was performed (10 days after the initial hemorrhage) using a mixture of bucrylate and lipiodol, which allowed for substantial reduction of the nidus *(Figures 4d, 4e, and 4f)*.

On the following day, a right temporal parietal craniotomy was performed and the lesion was entirely removed using the operating microscope *(Figure 4g)*. Postoperative angiography confirmed complete resection of the AVM *(Figures 4h and 4i)*. The patient recovered well from the surgery apart from a generalized convulsion 48 hours postoperatively and a temporary left inferior homonymous quadrantanopia.
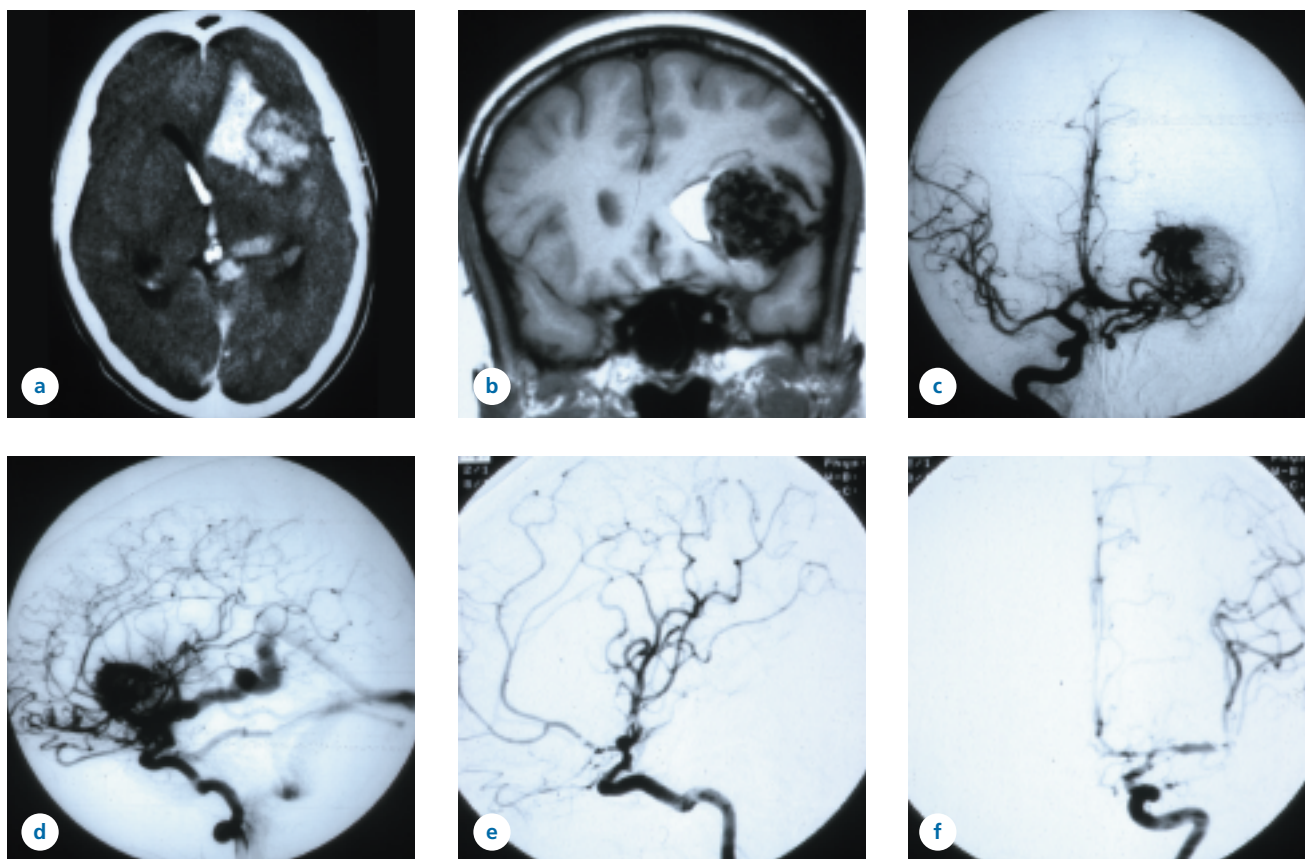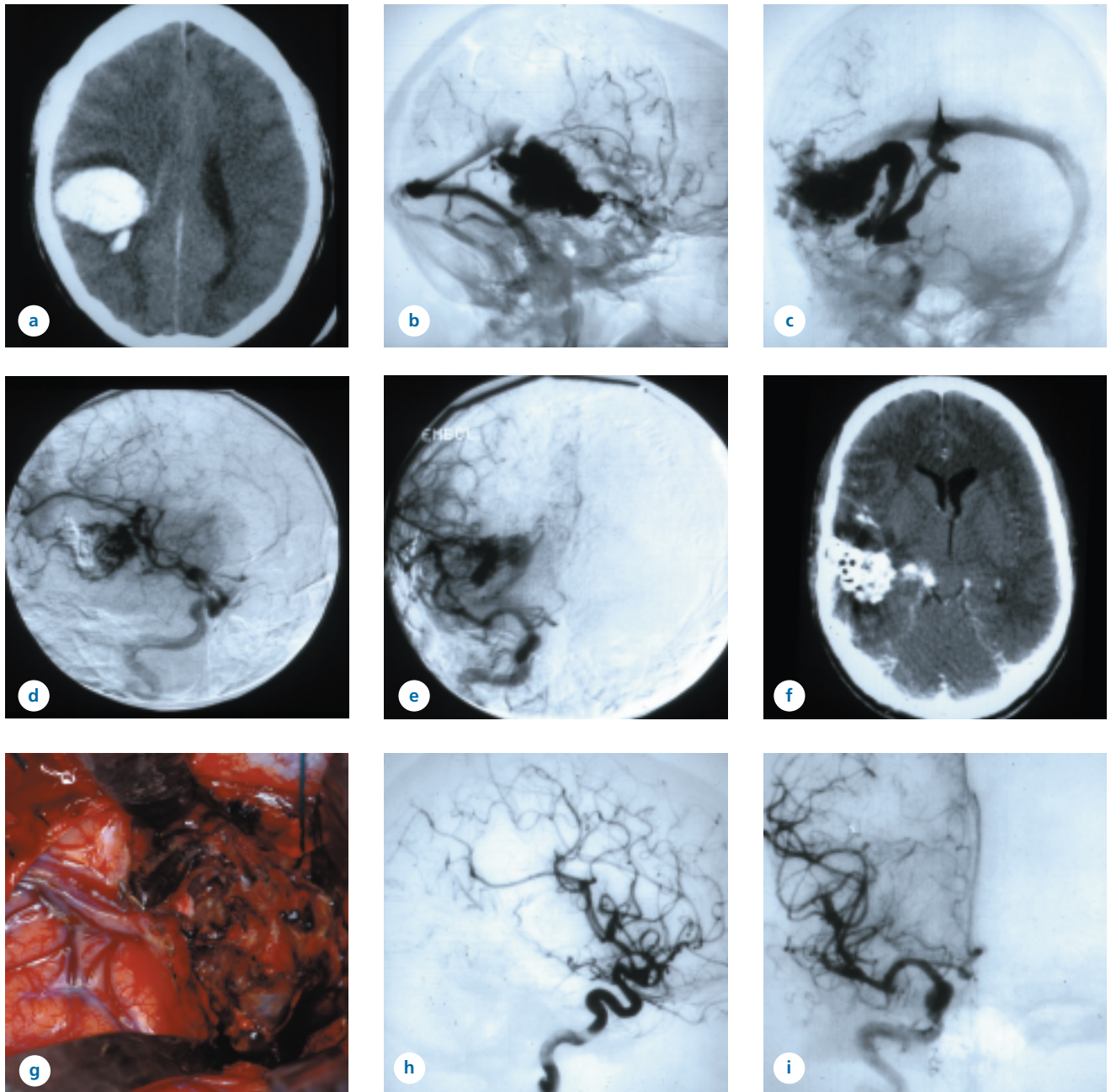
Figure 3. a. Axial computed tomography scan showing right frontal hemorrhage and left fronto-opercular arteriovenous malformation (AVM) (case 1). **B.** Magnetic resonance imaging scan done 3 weeks later showing large AVM and resolving blood clot. **c.** and **d.** Right carotid angiogram showing opacification of AVM nidus via left anterial cerebral artery branches and early filling of basal vein of Rosenthal. **e.** and **f.** Postoperative angiogram 1 week after surgery showing complete removal of lesion and mild residual vasospasm.

Case history 3

A 28-year-old technician in a cardiac hemodynamic laboratory was admitted 48 hours after a generalized convulsion. A CT scan showed a 1.5-cm hemorrhagic lesion in the left parietal lobe *(Figure 5a)*. MRI confirmed the presence of a 1.5-cm CM located within the white matter just below the dominant supramarginal gyrus with signs of a recent perilesional bleed *(Figures 5b and 5c)*. Preoperatively, an activated positron emission tomography (PET) scan was performed using intra-arterial injection of an ^{15}O–loaded saline bolus. Using several functional tests of language including synonym generation and calculation, it was possible to detect increased cerebral blood flow (CBF) in the left superior parietal lobule quite remote from the lesion *(Figure 5d)*. Additional tasks of reading and synonym generation in response to visual presentation showed a CBF increase in the left parietal region close to the area previously lighting up for calculation *(Figures 5e and 5f)*.

Using integration of PET scanning and MRI data, a left parietal mini-craniotomy was performed using neuronavigational frameless stereotaxy guidance (Allegro-Viewing Wand System ISG, Toronto, Canada). After selecting the most appropriate cortical landmark *(Figures 5g and 5h)*, the cortex was incised, the lesion appropriately identified *(Figures 5i and 5j)*, and resected using the operating microscope. The postoperative course was very satisfactory and the patient was discharged home on the fifth postoperative day without any deficits.

Figure 4. a. Computed tomography (CT) scan showing right temporoparietal intraparenchymal hemorrhage in a 23-year-old patient (case 2). **b.** and **c.** Right carotid angiogram showing high-flow arteriovenous malformation (AVM) draining into Rosenthal vein (Spetzler-Martin grade IV). **d.** and **e.** Right carotid angiogram immediately after preoperative embolization of bucrylate-lipiodol mixture showing reduction of AVM nidus (courtesy of Dr Jean Raymond, Notre Dame Hospital, Montreal). **f.** Corresponding CT scan showing embolized material before surgery. **g.** Intraoperative view of AVM nidus which was completely resected. **h.** and **i.** Postoperative angiogram showing complete removal of AVM.
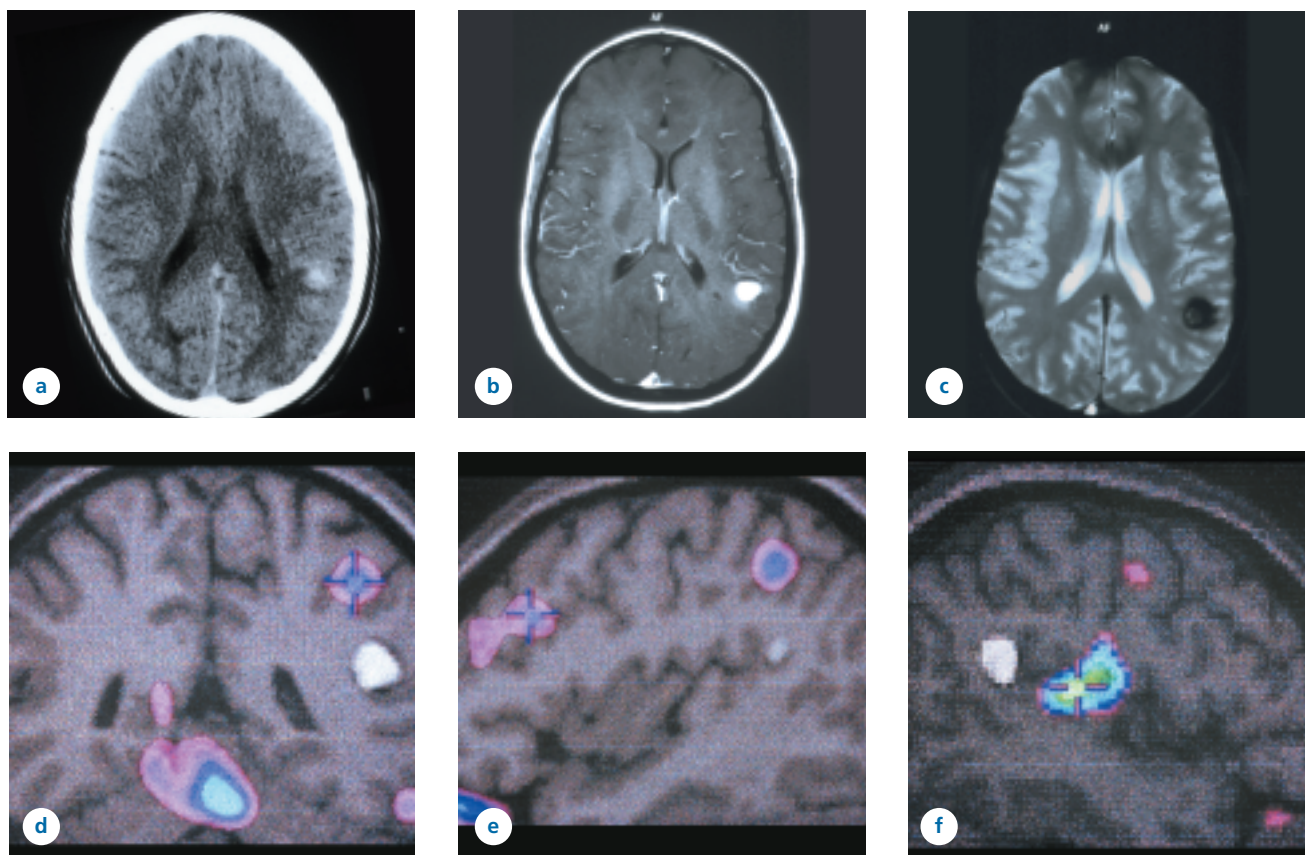
Discussion

Functional neuroimaging and neuronavigation

Preoperative assessment of vascular malformations located within or near highly functional areas of the brain can be achieved using various mapping techniques including functional MRI, magnetoencephalography, PET, single photon emission tomography, and transcutaneous magnetic stimulation *(Table III)*.[13,14]

Functional areas of the brain, such as primary motor cortex or primary somatosensory cortex, can be precisely located and their topographical relationships may be integrated on MRI or CT scan and translated into 3D reconstruction images using frameless stereotaxy with high spatial accuracy.[15,16]

Localization of speech function is best performed using activated PET scanning, since functional MRI is more sensitive to activation of motor areas. Interestingly, functional cortical reorganization has been observed in patients with AVMs: in some patients, the primary motor cortex may undergo a certain shift towards the premotor cortex and language areas may even migrate from the dominant hemisphere to the contralateral side.[17-19]

Results of surgical treatment of AVMs

Excellent results and high obliteration rates can be achieved after microsurgical resection of small AVMs

Preoperative embolization
Electrophysiological monitoring (somatosensory evoked potential, direct cortical stimulation)
Surgery on awake patient
Intraoperative angiography
Image-guided surgery
Ultrasound localization
Endoscopy

Table III. Surgical adjuncts for cerebral vascular malformations.
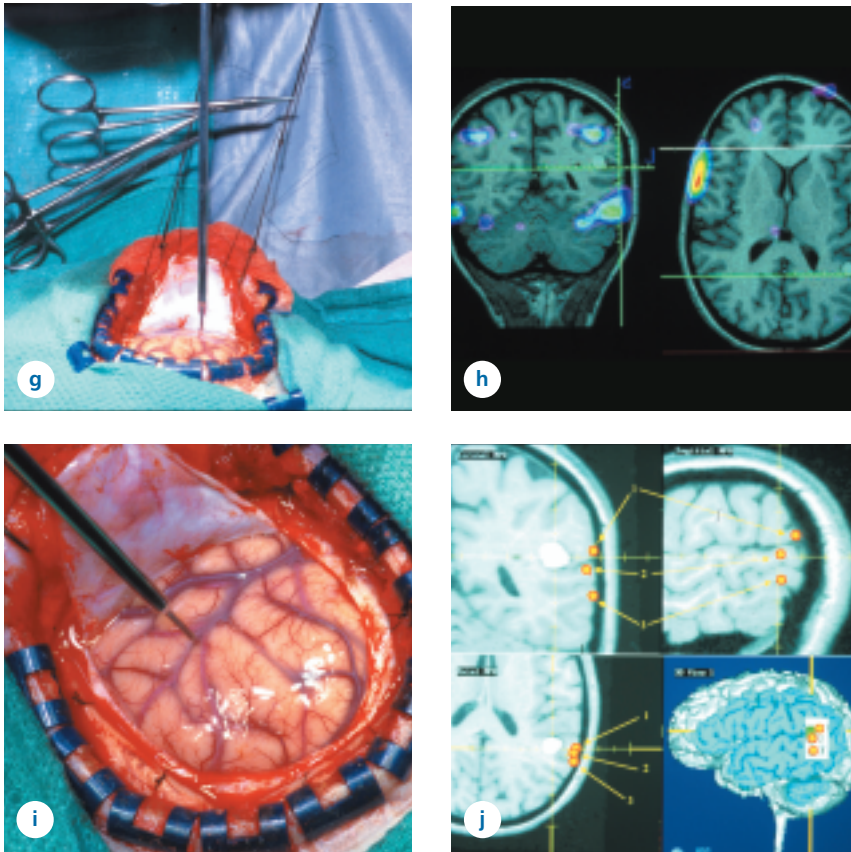
Figure 5. a. Computed tomography scan 48 hours after a generalized convulsion showing a small left parietal hemorrhagic lesion (case 3). **b.** and **c.** Magnetic resonance imaging (MRI) scan in T2-weighted and T1 with gadolinium showing cavernous angioma with recent perifocal hemorrhage. **d.** Positron emission tomography (PET) scan showing focal increase in cerebral blood flow (CBF) following word repetition minus silence in left parietal lobule. **e.** and **f.** Activated PET scan integrated on MRI showing increased CBF in superior-parietal lobule, visual cortex, and motor speech area following calculation minus reading. **g.** Viewing wand of neuronavigational system ISG allowing for image-guided localization (frameless stereotaxy). **h.** 3D reconstruction of MRI scan for neuronavigational localization and selection of three different possible accesses: target 2 was finally selected for a trans-sulcal approach. **i.** Intraoperative close-up picture showing cortical surface and before transsulcal approach. **j.** Intraoperative reconstruction of integrated PET scan and MRI images showing progression of the target localization (crossing of scaled lines indicating the actual localization of the probe tip).

(less than 3 cm in diameter). According to Pikus et al,[8] a 98% postoperative removal rate was achieved on postoperative angiography with less than 8.3% permanent morbidity and no mortality in 74 cases. Similar figures were obtained by Schaller and Schramm[20] in 62 cases of small AVMs with 98% angiographic exclusion and only 3.2% permanent neurologic deficit.

Results of stereotactic radiosurgery and AVMs

Radiosurgery consists of stereotactic application of a single high-dose irradiation of the AVM nidus producing a progressive thrombosis of the lesion over a period of several months. The currently used methods include gamma knife, linear accelerator, and heavy particles such as proton beam therapy.[21-24] It is thought that ionizing radiation induces a proliferation of myofibroblasts within the connective tissue stroma of the AVM nidus as well as some endothelial proliferation.[25,26] AVM obliteration has been achieved in 80% of lesions

smaller than 3 cm in diameter with a hemispheric localization: using gamma knife radiosurgery in 220 patients with adequate follow-up as defined by a postoperative angiogram 24 months after treatment, excellent results were obtained by Pollock et al[22] in 73 patients with hemispheric localization and lesions smaller than 4 cm³ (diameter 2 cm or less) with low morbidity and mortality. Recently, Chang et al[21] have developed a mathematical model for decision making in AVMs that takes into account several variables, such as age, size, presence of previous rupture, and life expectancy for both surgery and radiosurgery.

Endovascular treatment of AVMs

Embolization techniques have evolved considerably during recent years in becoming both safer and more efficacious.[27,28] More refined, flow-directed microcatheters can deliver polymerizing acrylic substances such as *N*-butyl-cyanoacrylate into even distal portions

of the nidus. Using the superselective catheterization methods, most AVMs cannot be permanently occluded, since recanalization of the nidus occurs in the periphery of the lesions. Morbidity related to endovascular treatment consists of distal embolization and hemorrhage which remain below 8% in most series.[29] Most often, embolization is used to reduce the size of the nidus either preoperatively, thus facilitating the surgery by decreasing blood flow substantially, or before radio-surgery in large AVMs that would otherwise have a lower obliteration potential.

Cavernous malformations

In spite of some reports of successful treamtent of CMs with stereotactic radiosurgery,[10,30] the management of symptomatic lesions remains surgical: in a recent review of 97 CMs treated surgically at the Massachusetts General Hospital, only 4.1% of patients had permanent neurologic deficits and the vast majority were rendered seizure-free.[9] Risk factors for increased postoperative deficits included location within the brainstem and basal ganglia. Due to the relatively small size of these lesions and their localization within the subcortical areas making their visualization difficult on the cortical surface, neuronavigational techniques are particularly well suited for surgery of CMs.

Conclusions

Functional neuronavigation represents one of the most interesting advances in recent adjunctive technology in neurosurgery: the possibility of integrating functional information about anatomical localization of eloquent areas into a 3D frameless stereotaxy system enhances the accuracy of the surgical procedure in helping localize the lesion and its immediate topographical relationships. Navigational systems are mostly represented by three different types of "pointer systems": (i) the mechanically directed "viewing wand" type, transmitting the spatial information through an arm to the computer; (ii) instrument-based pointers using infrared light–emitting diodes and spatial sensors that transmit the information to the computer and reconstruct it as 3D images; and (iii) microscope-based pointer systems where the automated focus represents the target of the system allowing the superimposed reconstructed images to be seen directly through the microscope.[16,31]

The management of vascular malformations of the brain remains to some extent controversial but the following conclusions can be drawn: small volume malformations (less than 3 cm in diameter) that have bled can be safely removed using microsurgical techniques with excellent results, and the utilization of functional neuronavigation for lesions located in eloquent areas adds even further safety in preserving function. Larger AVMs that have presented with hemorrhage can be treated surgically after preliminary embolization but will have higher morbidity rates.[32] Stereotactic radiosurgery can be offered to patients with relatively small lesions who present with symptoms other than hemorrhage, such as epilepsy, or for lesions located in the basal ganglia or brainstem. For CMs, the present trend is to remove the lesion surgically if hemorrhage has been demonstrated or if epilepsy cannot be controlled.

The combined management of cerebral vascular malformations is best achieved by a well-integrated multidisciplinary team that includes neurosurgeons, interventional neuroradiologists, neurologists, and radiation oncologists.[33] Refinement of neurosurgical techniques and pre- and intraoperative neurophysiological monitoring have led to a reduction in surgical morbidity and mortality in selected cases. Radiosurgical techniques are also to be considered although they do not immediately remove the source of bleeding due to the progressive intranidal myoendothelial and fibroblastic proliferation. Patients should be given detailed information about the natural history of their lesions and the various therapeutic alternatives. ❑

Consideraciones funcionales y topográficas en el manejo quirúrgico de las malformaciones vasculares cerebrales

Las tres alternativas de tratamiento para las malformaciones arterio venosas intracraneales son la resección, la embolización endovascular y la neurocirugía estereotáxica. En raros casos la malformación puede ser erradicada utilizando sólo una de estas opciones; la mayoría de las veces se requiere de una combinación de alternativas, incluso de las tres juntas. Los avances más recientes se han producido en la neurorradiología intervencionista con la introducción de las imágenes en tres dimensiones de alta definición y la embolización endovascular del interior del nido, hiperselectiva, utilizando microcatéteres y cables microguías, lo que produce ventajas significativas en términos de rapidez, eficacia y seguridad. La desvascularización del nido está ahora más perfeccionada, lo que se expresa en el aumento del intervalo de tiempo entre las sesiones de embolización. Por su parte las imágenes de resonancia magnética funcional de alta resolución juegan un papel valioso en la preparación pre-embolización y el seguimiento post-embolización.

Considerations fonctionnelles et topographiques dans la prise en charge des malformations cerebrales vasculaires

Les malformations vasculaires cérébrales susceptibles de suites opératoires sont principalement représentées par les malformations artérioveineuses (MAV) et les malformations caverneuses. La tomodensitométrie, l'imagerie par résonance magnétique couplée ou non à l'angiographie, l'angiographie conventionnelle font partie des examens neuroradiologiques préopératoires standard qui permettent d'évaluer les relations topographiques exactes entre le foyer malformatif, les pédicules artériels nourriciers et le drainage veineux. L'anatomie des lésions situées près ou à l'intérieur des zones cérébrales éloquentes peut être précisée à l'aide de nombreux examens comme l'IRM fonctionnelle, la tomographie par émission de positon et l'encéphalographie magnétique qui peuvent ensuite être intégrés à un système de navigation neurologique. Celui-ci, couplé à une chirurgie sélective guidée par image, peut diminuer la morbidité chirurgicale. L'embolisation préopératoire, en réduisant le débit sanguin à travers la MAV, peut parfois en faciliter l'ablation. Les malformations caverneuses peuvent aussi bénéficier de techniques très sélectives et peu invasives.

REFERENCES

1. Ojeman RG, Crowell RM, eds. Arteriovenous malformations of the brain. In: *Surgical Management of Cerebrovascular Disease.* Baltimore, Md: Williams & Wilkins; 1983:264-286.
2. Yamada S, Brauer FS, Knierim DS. Direct approach to arteriovenous malformations in functional areas of the cerebral hemisphere. *J Neurosurg.* 1990;72:418-425.
3. Kurl S, Saari T, Vanninen R, Hernesniemi J. Dural arteriovenous fistulas of superior sagittal sinus: case report and review of literature. *Surg Neurol.* 1996:250-255.
4. Yasargil MG. Pathological considerations. In: *Microneurosurgery IIIA*. New York, NY: Thieme Medical Publishers Inc; 1987:49-211.
5. Spetzler RF, Martin NA. A proposed grading system for arteriovenous malformations. *J Neurosurg.* 1986;65:476-483.
6. Norris JS, Valiante TA, Wallace WJ, et al. A simple relationship between radiological arteriovenous malformation hemodynamics and clinical presentation: a prospective, blinded analysis of 31 cases. *J Neurosurg.* 1999;90:673-679.
7. 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;73:387-391.
8. Pikus HJ, Beach ML, Harbauch RE. Microsurgical treatment of arteriovenous malformations: analysis and comparison with stereotactic radiosurgery. *J Neurosurg.* 1998;88:641-646.
9. Amin-Hanjani S, Ogilvy CS, Ojemann RG, Crowell RM. Risks of surgical management for cavernous malformations of the nervous system. *Neurosurgery.* 1998;42:1220-1228.
10. Chang SD, Levy RP, Adler JR, Martin DP, Krakovitz PR, Steinberg GK. Stereotactic radiosurgery of angiographically occult vascular malformations: 14-year experience. *Neurosurgery.* 1998;43:213-218.
11. Moriarity JL, Wetzel M, Clatterbuck RE, et al. The natural history of cavernous malformations: a prospective study of 68 patients. *Neurosurgery.* 1999;44:1166-1173.
12. Amin-Hanjani S, Ogilvy CS, Candia GJ, Lyons S, Chapman PH. Stereotactic radiosurgery for cavernous malformations: Kjellberg's experience with proton beam therapy in 98 cases at the Harvard cyclotron. *Neurosurgery.* 1998;42:1229-1238.
13. Leblanc R, Meyer E, Bub D, Zatorre RJ, Evans AC. Language localization with activation positron emission tomography scanning. *Neurosurgery.* 1992;31:369-373.
14. Schlosser MJ, Luby M, Spencer DD, Awad IA, McCarthy G. Comparative localization of auditory comprehension by using functional magnetic resonance imaging and cortical stimulation. *J Neurosurg.* 1999;91:626-635.
15. Fandino J, Kollias SS, Wieser HG, Valavanis A, Yonekawa Y. Intraoperative validation of functional magnetic resonance imaging and cortical reorganization patterns in patients with brain tumors involving the primary motor cortex. *J Neurosurg.* 1999;91:238-250.
16. Muavecic A, Steiger HJ. Computer assisted resection of cerebral arteriovenous malformations. *Neurosurgery.* 1999;45:1164-1171.

17. Leblanc R, Meyer E, Zatorre RJ, Klein D, Evans AC. Functional imaging of cerebral arteriovenous malformations with a comment on cortical reorganization. *Neurosurg Focus.* 1996;1:1-6.

18. Leblanc R, Meyer E. Functional PET scanning in the assessment of cerebral arteriovenous malformations. *J Neurosurg.* 1990;73:615-619.

19. Morgan MK, Sekhon LHS, Finfer S, Grinnell V. Delayed neurological deterioration following resection of arteriovenous malformations of the brain. *J Neurosurg.* 1999;90:695-701.

20. Schaller C, Schramm J. Microsurgical results for small arteriovenous malformations accessible for radiosurgical or embolization treatment. *Neurosurgery.* 1997;40:664-674.

21. Chang HS, Nihei H. Theoretical comparison of surgery and radiosurgery in cerebral arteriovenous malformations. *J Neurosurg.* 1999;90:709-719.

22. Pollock BE, Flinckinger JC, Lunsford LD, Maitz A, Kondziolka D. Factors associated with successful arteriovenous malformation radiosurgery. *Neurosurgery.* 1998;42:1239-1247.

23. Porter PJ, Shin AY, Detsky AS, Lefaive L, Wallace MC. Surgery versus stereotactic radiosurgery for small operable cerebral arteriovenous malformations: a clinical and cost comparison. *Neurosurgery.* 1997;41:757-766.

24. Young C, Summerfield R, Schwartz M, O'Brien P, Ramani R. Radiosurgery for arteriovenous malformations: the University of Toronto experience. *Can J Neurol Sci.* 1997;24:99-105.

25. Szeifert GT, Kemeny AA, Timperley WR, Forster DMC. The potential role of myofibroblasts in the obliteration of arteriovenous malformations after radiosurgery. *Neurosurgery.* 1997;40:61-66.

26. Gewirtz RJ, Steinberg GK, Crowley R, Levy RP. Pathological changes in surgically resected angiographically occult vascular malformations after radiation. *Neurosurgery.* 1998;42:738-741.

27. Fournier D, TerBrugge KG, Willinsky R, Lasjaunias P, Montanera W. Endovascular treatment of intracerebral arteriovenous malformations: experience in 49 cases. *J Neurosurg.* 1991;75:228-233.

28. Paulsen RD, Steinberg GK, Norbash AM, Marcellus ML, Lopez JR, Marks MP. Embolization of rolandic cortex arteriovenous malformations. *Neurosurgery.* 1999;44:479-486.

29. Purdy PD, Batjer HH, Samson D. Management of hemorrhagic complications from preoperative embolization of arteriovenous malformations. *J Neurosurg.* 1991,74:205-211.

30. Pozzati E, Giangaspero F, Marliani F, Acciarri N. Occult cerebrovascular malformations after irradiation. *Neurosurgery.* 1996;39:677-683.

31. Nimsky C, Ganslandt O, Kober H, et al. Integration of functional magnetic resonance imaging supported by magnetoencephalography in functional neuronavigation. *Neurosurgery.* 1999;44:1249-1256.

32. Sadasivan B, Hwang YK. Large cerebral arteriovenous malformations: experience with 27 cases. *Surg Neurol.* 1996;45:245-249.

33. Munshi I, MacDonald RL, Weir BKA. Intraoperative angiography of brain arteriovenous malformations. *Neurosurgery.* 1999;45:491-499.