

Complications After Multidisciplinary Treatment of Cerebral Arteriovenous Malformations

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Summary

Patients and techniques. A series of 67 patients treated for cerebral AVMs with a multidisciplinary approach is reported, with special attention for the complications due to treatment. The malformations were classified after the Spetzler Grading Scale, with 67% low-grade and 33% highgrade AVMs. Three modes of treatment were used: surgical resection, endovascular embolization, and radiosurgery (linear accelerator technique). The actual treatment was: resection alone (25% of cases), embolization plus resection (24%), embolization alone (21%), and radiosurgery (30%), either alone or after embolization or surgery. The following eradication rates were obtained: overall 80%, after resection (with or without embolization) 91%, after embolization alone 13%, after radiosurgery 87%.

Clinical outcome. The outcome was evaluated in terms of deterioration due to treatment. A deterioration after treatment occurred in 19 patients (28%), and was a minor deterioration (19%), a neurological deficit (4%), or death (4%). As far as the mode of treatment is concerned, surgical resection was responsible for deterioration (minor) in 17% of all cases operated upon. Radiosurgery was followed by a minor deterioration in 10% of irradiated cases. Embolization gave a complication in 25% of all embolized cases (minor or neurological deficit, or death). The mechanism of the complications was: resection or manipulation of an eloquent area during surgery, radionecrosis after radiosurgery, ischaemia and haemorrhage (50% each) following embolization. In most cases of haemorrhage due to embolization, occlusion of the main venous drainage could be demonstrated.

Discussion. The haemodynamic disturbances to AVMs and to their treatment are reviewed in the literature. The main haemodynamic mechanisms admitted at the beginning of a complication after treatment of cerebral AVMs are the normal perfusion pressure breakthrough syndrome, the disturbances of the venous drainage (venous overload or 'occlusive hyperaemia'), and the retrograde thrombosis of the feeding arteries.

Conclusions. According the authors' experience, the emphasis of treatment for cerebral AVMs has now shifted from surgical resection to endovascular embolization. One of the explanations is that endovascular techniques are now employed in the most diffi-

cult cases (high grade AVMs). As severe complications of endovascular embolization may also occur for low-grade malformations, the question arises whether surgery or radiosurgery should not be used first for this low-grade group even if embolization is feasible.

Keywords: Cerebral AVMs; endovascular embolization; radiosurgery.

Introduction

The treatment of cerebral arteriovenous malformations (AVMs) which had long been restricted to neurosurgery has lately become more and more multidisciplinary. Modern methods of treatment arose during the past years: first endovascular embolization, and then radiosurgery. These three modes of treatment (surgical resection, endovascular embolization, radiosurgery) may be used either alone or in various combinations [11]. With this multidisciplinary approach, are the complications of treatment still unpredictable and catastrophic? During the period in which surgery was the sole available method of treatment for cerebral AVMs, special interest focussed on complications based on haemodynamic modifications due to the presence of AVM. The question arises nowadays whether, with the new methods of treatment, these haemodynamic complications still exist.

In this paper, we report a series of cerebral AVMs treated by a multidisciplinary approach, with special attention to the complications which occurred after the treatment. Then we review the neurosurgical literature dealing with the haemodynamic disturbances relating to the presence of cerebral AVMs or occurring after the treatment.

Patient and Techniques

Distribution of Patients

Between 1989 and 1993, 67 patients were treated in our Department of Neurosurgery for an intracranial AVM (average 13 per year). These AVMs were classified according to the Spetzler's Grading Scale into five grades (Grade I: 4%, Grade II: 29%, Grade III: 34%, Grade IV: 30% and grade V: 4%). Considering together the low-grade AVMs (I, II and III) and the high-grade AVMs (IV and V), the figures are respectively 67% and 33%. The distribution according to gender was: female 33% and male 67%. According to age, the distribution was: up to 30 years 30%, from 31 to 50 years 54%, and over 50 years 16% (maximum 65 years).

Methods of Treatment

Three modes of treatment were used: surgical resection (in 52% of cases), endovascular embolization (in 60% of cases) and radiosurgery with the linear accelerator technique (30% of cases). These three methods were used either alone or in various combinations, giving four possibilities: resection alone (25% of cases), embolization + resection (24%), embolization alone (21%) and radiosurgery (30%), alone or after surgery or after embolization.

Results

Angiographic Eradication

60 patients underwent post-treatment angiography, and the following figures of complete eradication (calculated on those patients angiographically checked) were obtained:

- 1.) overall: 80%,
- 2.) after surgical resection (with or without embolization): 91%,
- 3.) after embolization alone: 13%,
- 4.) Two years after radiosurgery: 87%.

Clinical Outcome

Outcome evaluation. Clinical results are evaluated in terms of deterioration following treatment, in five groups: 1) No deterioration, 2) minor deterioration, 3) long-lasting neurological deficit, 4) major deterioration, and 5) death. Minor deterioration means a moderate neurological deficit, such as hemianopia, hemiparesis, moderate speech disturbances. Major deterioration means severe neurological deficit or severe intellectual impairment, or vegetative survival, the patients being bed-ridden or dependent for self care. The sub-group "long-lasting neurological deficit" includes patients who present with hemiplegia or aphasia (and so cannot be classified in the "minor deterioration group") but these patients are independent in the daily life and sometimes are able to work (and so they cannot be classified in the "major deterioration group").

In 20 patients, a deterioration occurred after treatment (30%). One of these patients was admitted in a deep coma due to spontaneous rupture of the AVM, and was submitted to a "last chance" or "rescue" operation. She died, and this death cannot be ascribed

to surgery. So the treatment alone was responsible for the deterioration in 19 patients (28% of all patients).

Degree of deterioration. – 13 patients presented with a minor deterioration (68% of all deterioration cases, and 19% of all treated cases), either hemianopia (7 patients) or moderate aphasia (4p) or hemiparesis (2p). In each case the neurological impairment corresponded to the location of the AVM in the corresponding eloquent area

– 3 patients presented with a neurological deficit, also relating to the AVM location (16% of all deterioration cases and 4% of all treated cases),

– 3 patients died after treatment (16% of deterioration cases and 4% of the total series).

Method of treatment and deterioration. – Surgical resection was responsible for 6 cases of deterioration (17% of all operated cases). All were in the "minor deterioration" group. In each case, the deterioration corresponded to the anatomical location of the AVM.

– Radiosurgery was responsible for 2 cases of minor deterioration, due to deferred radionecrosis (10% of all irradiated cases).

– Endovascular embolization was responsible for 10 cases of deterioration (25% of all embolized cases). This deterioration was of the minor type in 5 cases (13% of embolized cases), of the neurological deficit type in 2 cases (5%), and resulted in death in 3 cases (8% of embolized cases).

– One patient is more difficult to classify and could be a complication of the "embolization + resection" type of management (6% of all cases managed with this method). Surgery was planned and carried out 3 weeks after an incomplete embolization for this patient. Under anaesthesia and during the opening of the skull the AVM ruptured. Resection of the AVM could be performed and this patient survived with a neurological deficit.

Mechanism of deterioration. Various mechanisms were responsible for the deterioration in these 19 patients:

– Resection or manipulation of an eloquent area of the brain during surgery (6 patients), responsible for a minor deterioration in each case.

– Radionecrosis after radiation therapy (2 patients). In these cases, the condition was at first severe (neurological deficit) and progressively improved after some months. Eventually the patients suffered a minor deterioration.

– Cerebral ischaemia (5 patients). This ischaemia occurred during the embolization procedure itself,

either through occlusion of an AVM feeder (3 cases, ending with a minor deterioration) or by occlusion of the main trunk of the MCA (2 cases, ending with a neurological deficit). These cases with ischaemia included 2 grade II, 2 grade III, and 1 grade IV AVM.

– Haemorrhage (6 patients). These cases included 1 grade I, 1 grade III, and 4 grade IV AVMs. One patient (grade IV) bled at the beginning of surgery 3 weeks after incomplete embolization of the AVM. Whether this embolization is the cause of the AVM rupture remains hypothetical. In 5 patients haemorrhage could be linked up with endovascular embolization. In 3 of these 5 patients, the rupture of the AVM occurred during the embolization procedure itself, giving a deep coma with decerebrate rigidity. All 3 patients died, despite evacuation of the clot and resection of the AVM in two of them (so called “rescue-operation” despite the desperate clinical status). In the other 2 patients with haemorrhage, the rupture of the AVM occurred during the first week following the embolization procedure (2 days and 5 days). Both these patients were operated upon, their malformation was resected, and they survived with a minor deterioration. On the post embolization angiogram, occlusion of the main venous drainage could be demonstrated in 4 out of these 5 cases of post-embolization haemorrhage.

Illustrative Cases

Case 1: Male, 38 years old, admitted after seizure of the “grand mal” type. The AVM was located in the left temporal lobe (middle part), with several feeders coming from the left MCA, and a steal phenomenon through both the anterior and left posterior communicating arteries. The largest diameter of the nidus was 5 cm. The venous drainage was of the deep type, towards the great vein of Galen, with a large venous ectasia. This AVM was classified as a Grade IV according to the Spetzler's scale. Intravascular embolization was undertaken (September 27, 1990). During the procedure, the AVM ruptured with an intra-temporal haemorrhage. Clinically the patient was in a deep coma with bilateral mydriasis. Despite this desperate clinical status, he was immediately operated upon, the AVM was resected, but the brain remained turgescent and herniated and the patient died rapidly. When reviewing the angiographic images, it was evident that the venous drainage, and particularly the venous ectasia, was partially occluded (Fig. 1).

Case 2: Male, 45 years old. The AVM was located in the right temporal lobe (posterior part), the greatest diameter of the nidus was 3 cm, two feeders came from the right MCA, the venous drainage was superficial (towards both the sagittal and the right transverse sinuses). The AVM was classified as a Spetzler grade I. Intravascular embolization was performed (January 5, 1993), through the right MCA, with a large but incomplete eradication of the malformation: persistance of a small part of the nidus, (filling slowly), late opacification of the venous drainage, disappearing of the drain-

age towards the transverse sinus. Only minimal drainage towards the sagittal sinus was visible (Fig. 2). At the end of the embolization procedure, the patient complained of headache and fell into deep coma. The CT scan showed a huge intra-temporal haematoma. The patient was rapidly operated upon, the AVM resected, the clot evacuated. At surgery the nidus proved to be almost completely occluded, with only one vein, still arterialized. The patient remained comatous and died two days later.

Case 3: Female, 41 years old, admitted after two seizures (Braives-Jackson type). The AVM was located in the left parietal lobe, supplied through 2 long and tortuous feeders (coming from the left MCA and the left PCA). The diameter of the nidus was 6 cm. The drainage was superficial, towards the sagittal sinus. The malformation was classified as a Spetzler grade IV. Intravascular embolization was undertaken (September 15, 1992). The major part of the nidus was occluded, together with the feeder coming from the MCA and the venous drainage. The nidus was still partially supplied through the PCA, but no venous drainage was visible coming out of this residual nidus. Two days later, just prior to discharge, the patient became suddenly comatose, with a right hemiplegia, showing deep haemorrhage on the CT scan. She was taken to the intensive care unit, and progressively recovered. An angiogram performed 3 weeks after the haemorrhage failed to show the AVM, which at the time was thought to be completely eradicated. Despite this constatation, the patient was operated upon and the malformation was resected. The nidus was found occluded, the venous drainage was thrombosed. However, several thin deep feeders were found still patent. The post-operative course was satisfactory, the right hemiplegia recovered, the patient remained with a moderate right hemianopia (minor deterioration), and a post-operative angiogram confirmed the complete eradication of the malformation.

Case 4: Female, 42 years old, admitted after two seizures (“grand mal” type). The AVM was located in the right parietal area, the greatest diameter of the nidus was 5 cm, the venous drainage was superficial, through the sagittal sinus (Spetzler grade III). Intra-vascular embolization was carried out (October 13, 1993), a 50% reduction of the volume of the nidus was obtained, with a late filling of the venous drainage. A second embolization procedure was planned one week later and the patient was discharged. She was readmitted as an emergency 5 days later, stuporous, without neurological deficit, the CT scan showing an intra-cerebral and intraventricular haemorrhage. After four days in the intensive care unit, she was operated upon. At surgery, the nidus was found almost completely occluded, one superficial arterial feeder remained patent, the venous drainage was completely thrombosed. At the end of the resection, the deeper part of the nidus, next to the ventricle, was thrombosed, but several small and thin arterial feeders were still patent. The patient recovered after surgery, presenting with a moderate left hemianopia (minor deterioration), the eradication of the AVM proved to be complete on the post-operative angiogram.

Discussion

In the neurosurgical literature, various haemodynamic disturbances have been described, relating to a cerebral AVM. These disturbances, caused by the existence of the malformation itself, may also be responsible for complications after treatment of the AVM.

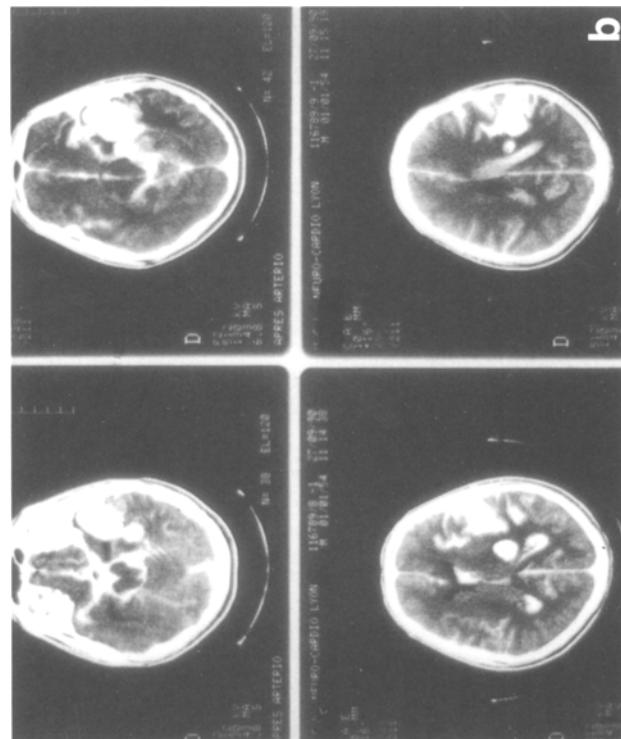
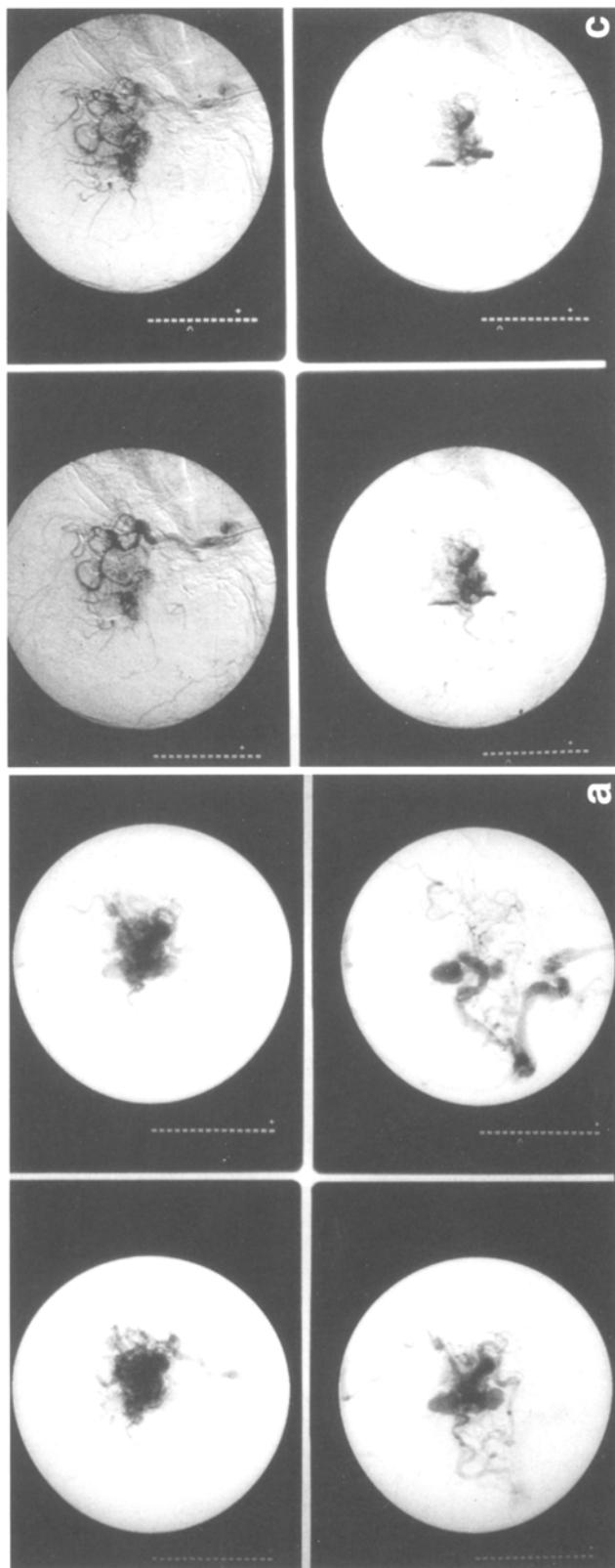


Fig. 1. Case 1. (a) Left carotid angiogram before embolization (lateral view). Note the deep venous drainage into the great vein of Galen and the straight sinus, with a venous ectasia. There is an additional drainage, superficial, directly into the lateral sinus. Note the intracranial steal around the malformation. (b) CT scan after onset of the haemorrhage, during the embolization procedure (intracerebral, intraventricular and subarachnoid haemorrhage). (c) Post-haemorrhage angiogram (left carotid, lateral view). Note 1) the incomplete occlusion of the nidus, 2) the partial occlusion of the venous ectasia, with embolic material inside, 3) the suppression of the deep venous drainage, with persistence of the superficial drainage

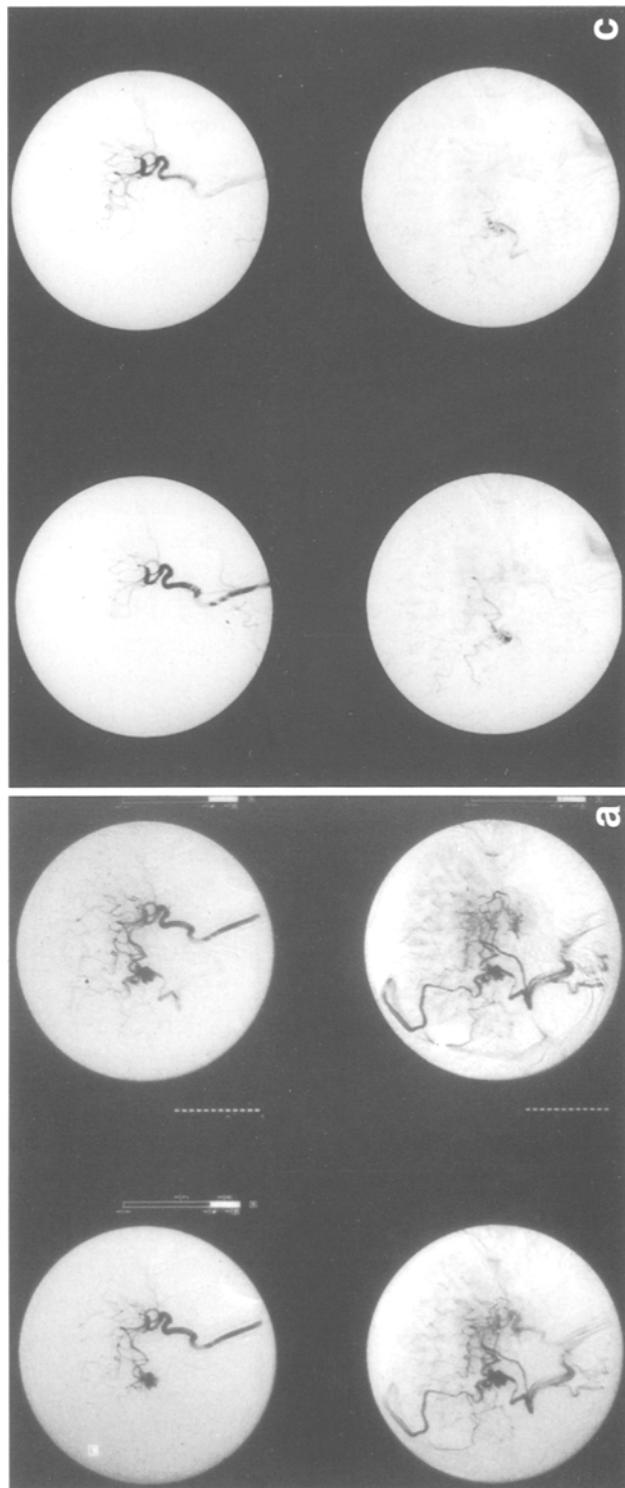


Fig. 2. Case 2. (a) Right carotid angiogram (lateral view). Note the venous drainage, towards the sagittal sinus and towards the lateral sinus. (b) CT scan after onset of the haemorrhage, demonstrating a huge right intra temporal haematoma.

(c) Right carotid angiogram (lateral view) after embolization. Note the incomplete occlusion of the nidus, and the suppression of the venous drainage towards the sagittal sinus. The drainage towards the lateral sinus is very slow and does not reach the sinus itself

Circulatory Modifications Due to the AVM

In the presence of an AVM, changes in the vessels relating to the malformation have been documented. The *pressure in the feeding arteries* is reduced, and becomes much lower than the systemic pressure, as demonstrated by means of intra-operative Doppler sonography investigations [4, 12, 15, 26]. In the feeding arteries, Nornes [26] found a mean arterial pressure of 56 mm Hg. The decrease of this low arterial pressure was proportional to the number and to the length of these arteries. On the contrary, the *pressure in the draining veins* is increased, and the figures are far higher than in the normal veins: Nornes [26] found a mean venous pressure of 15 mm Hg. As a consequence of both a low arterial pressure and a high venous pressure, the *perfusion pressure* of the surrounding brain is reduced. There may be some exceptions, and Pertuiset [29] described some cases in which the venous pressure was found low: in these cases, the venous drainage was unique and went into the sagittal sinus via an enlarged vein of Galen.

In the feeding arteries, the *flow velocity* is increased [12, 16]. By means of transcranial Doppler sonography (TDS), Lindegaard [16] measured the blood flow velocity in the basal arteries. In the arteries feeding the AVM, he found a high flow velocity (mean 124 cm/sec instead of 65 cm/sec in normal arteries), and a low pulsatility index (median 0.48 compared to 0.87 in normal arteries). The flow velocity was also found increased in the carotid arteries in the neck [2, 28].

The *vasomotor reactivity* was found altered, in vivo and in vitro. Hassler [12] using in vivo microvascular sonography measurements, found a poor vasomotor reactivity to CO₂ changes in the AVM feeders. Murasko [24] took isolated fragments of feeding arteries of AVM and tested them in vitro with various vaso-active substances; he compared the in vitro results with the spontaneous vessel activity (spasm, ectasia, postoperative course). He found that some of the AVMs had non-reactive feeders in in vitro testing, and that these vessels had also no spontaneous activity. He could not find any histological basis for the lack of reactivity, and made the hypothesis that these vessels segments might act as passive conduits in vivo.

The Steal Phenomenon

An intracranial steal may be induced in the surrounding brain by an AVM, as demonstrated by blood flow studies and by CO₂ reactivity measurements.

The *regional cerebral blood flow* was often found decreased in cases of AVM, especially in sites near to the malformation [4, 6, 15, 27, 41]. Batjer [6] found a decrease of the blood flow ipsilaterally and contralaterally to the AVM. He found a more severe steal in older patients and in patients with progressive deficit. Lo [17] using a biomathematical analysis of haemodynamic alterations in AVMs demonstrated that the vascular steal is inversely proportional to the haemodynamic resistance of the AVM: an AVM with lower resistance will shunt more blood away from the surrounding vessels. The relationship between the size of the AVM and the severity of the steal remains controversial: Batjer [6] found no relationship. On the contrary, for Leblanc [15] the steal is more severe for large AVMs. Contrary to these studies in which a reduced CBF was found, Young [42, 43] found a normal CBF, around the AVM. However, Al Rhodan [1] recently stated that these CBF studies, performed with different techniques, make direct comparison inaccurate; moreover in the cases of Xenon measurements, areas of hypoperfusion may not be revealed due to impairment in the delivery of the indicator in the region of interest.

The CO₂ reactivity is modified in the brain surrounding the AVM. Normally, the administration of Acetazolamide produces changes in the tissue CO₂ which provoke vessel dilation, and increase the rCBF by 35%. In cases of AVM, this CO₂ reactivity has been frequently found reduced. This fact is in favour of a decreased perfusion pressure and thereby proves the presence of a steal [4, 15, 31]. But these findings have been criticized. The CO₂ reactivity was sometimes found normal [42, 43], which indicates a dissociation between pressure autoregulation (lost) and CO₂ reactivity (maintained). Last of all, Batjer [5] reported a patient with an AVM who developed a fatal hyperaemic complication and in whom the CO₂ reactivity was increased (more than normally) before any treatment. This constatation indicated that the vessels surrounding the AVM were still capable of further dilation after Acetazolamide delivery. Then Batjer studied [8] a series of patients with rCBF and Acetazolamide administration. An increase of vasodilation was noted in the following conditions: 1) patients with perforator recruitment, 2) patients with angiographic steal phenomenon, 3) patients who developed ischaemic complications, 4) patients with poor neurological outcome.

Steal demonstration using other methods. Apart

from the angiographic demonstration of steal, which is well known, Leblanc [15] using intra-operative fluorescein angiography described an early filling of feeders, nidus and veins, and a late filling of the arteries in the surrounding cortex. He also found, in PET studies, a fall in glucose metabolism proportional to the size of the AVM.

Mechanism of the Clinical Manifestations

The changes described above may be responsible for the onset of spontaneous clinical manifestations. Various mechanisms have been advocated.

(1) *The size of AVM and the pressure in the feeding arteries.* Spetzler [32] studied the relationship between the size of an AVM and its propensity to haemorrhage. He measured the pressure in the arteries feeding the AVMs, and found that smaller AVMs had higher feeding artery pressures than larger ones. He concluded that, if perfusion pressure increases as AVM size decreases, then smaller AVMs with higher feeding pressure would be more likely to haemorrhage than large AVMs under low pressure. And in patients whose AVM had ruptured, he actually found a significantly higher pressure in the feeding arteries. This disparity in feeding artery pressure could also explain the fluctuating neurological deficit with large AVMs (the steal symptoms). The low feeding artery pressure would be likely to provide a low perfusion pressure to the surrounding cortex, thereby producing relative ischaemia.

(2) *The strength of the shunt walls.* This parameter was studied by Lo [17] with his biomathematical model: He demonstrated that haemorrhage occurs when the transmural stress exceeds the strength of the shunt walls. The transmural stress is proportional to the vessel radius and inversely proportional to the wall thickness. Therefore, large thin-walled shunts would be more likely to rupture.

(3) *The steal phenomenon.* Manchola [18] also tried to relate AVM haemodynamics with clinical findings, and calculated the flow volume to the AVM, by means of transcranial Doppler and angiographic data. He found that patients with haemorrhage had significantly lower flow volume than patients having other symptoms and signs. Conversely, patients presenting with neurological deficit had higher flow volumes than other patients (which favour the hypothesis of a steal).

(4) *The role of the venous drainage.* Taneda [39] studied the response of the CBF to hypotension in the

presence of an AVM. Before the resection of the AVM, he found regions in the brain where CBF increased in response to hypotension. After total resection of the AVM, this increase in the CBF was no longer obtained. This phenomenon could be explained by the increased pressure on the venous side of the AVM circulation: As a consequence of the shunt, there is an increased back-pressure and so a reduction in the perfusion pressure in the territory of the veins draining the AVM. Therefore, decrease in systemic arterial blood pressure, transmitted to this venous system, could reduce the elevated venous blood pressure and increase the CBF in the corresponding tissue around the AVM.

(5) *The regional cerebral atrophy.* Tanaka [38] described on MRI morphological changes related to the haemodynamic dysfunction in areas remote from the AVM. He compared these changes to the "diaschisis phenomenon" (which correspond to reversible changes occurring after acute stroke): In cases of AVM, hypoperfusion can end in secondary atrophy in the basal ganglia. Tanaka proposed to call these irreversible morphological changes the "diaschisis-like phenomenon" caused by metabolic depression due to the decrease in CBF, being different from the steal phenomenon and responsible for clinical manifestations.

Haemodynamic Modifications Occurring After Resection of the AVM

Excision of the AVM produces immediate haemodynamic changes in the surrounding brain [4, 5, 7, 12, 15, 25, 26, 30, 31, 35, 43] and these changes convert a shunt flow into a perfusion flow [15]. The arterial pressure increases and becomes normal. Nornes [26] found an increase from 56 to 76 mm Hg (average). Hassler [12] also found an increase of arterial pressure by 60% to normal values after occlusion of the feeding vessels. The venous pressure decreases and becomes normal (from 15 to 0 mm Hg, average for Nornes). These modifications result in an acute increase in the arteriovenous pressure gradient [43] and so the cerebral perfusion pressure increases and becomes normal. The flow velocity decreases and becomes normal [12]. The cerebral blood flow increases in the ischaemic rim around the AVM [15]. This increase may become exaggerated: the rCBF may rise over the normal values, up to two times the pre-resection values [25, 35] and may reach the remote areas, from 2 to 4 cm from the resection site [4]. In

most cases, the CO₂ reactivity is restored to normal, and sometimes may show an hyperresponsiveness [5, 8].

Haemodynamic Complications Following the Eradication of AVM

Complications may follow the eradication of the AVM. These complications have been described mostly after surgical excision, but also more recently after endovascular occlusion of the AVM. They may occur after complete or partial eradication of the malformation, both intra- and postoperatively and consist of brain oedema and/or haemorrhage in the normal surrounding parenchyma. These complications have been related to haemodynamic mechanism, but this precise mechanism is far from being clearly understood. Several theories have been developed so far.

(1) *The normal perfusion pressure breakthrough (NPPB) theory* was proposed by Spetzler in 1977 [31]. In the presence of a large AVM, the relating vessels offer no resistance to blood flow. The consequence is an intracranial steal and the surrounding hemisphere is ischaemic. On the contrary, the small surrounding vessels (not relating to the AVM) offer a high resistance to blood flow and must remain maximally dilated to correct the chronic steal and the chronic ischaemia. Thus, the conjunction of a chronic ischaemia and of a chronic vessel dilation induces a state of vasomotor paralysis which results in a *loss of autoregulation* in the brain surrounding the AVM. After occlusion of the malformation, the flow is redirected to the surrounding hemisphere, and this ischaemic hemisphere returns to a normal perfusion pressure. But, due to the loss of autoregulation, the paralysed vessels supplying the functional brain are unable to constrict in response to this suddenly elevated perfusion pressure. So there is an impossibility to increase the resistance of the arterial network (which has been chronically dilated) to regulate this new pressure, and hence an impossibility to protect the capillaries. Therefore the conjunction of occlusion of the AVM and of loss of autoregulation results in disruption of the capillary bed: *the capillary breakthrough*, responsible for oedema and haemorrhage in the adjacent brain.

This NPPB theory which is supposed to occur only in large AVMs (that is not very frequently), has had supporters and detractors. The supporters [4, 10, 15, 28] advocate that this breakthrough complication may well be explained by the pre-operative decrease of the

cortical arterial pressure, of the CBF, and of the CO₂ reactivity, and by the postoperative normalization of these parameters. And Young [43] proposes a scheme with four possible haemodynamic responses to AVM occlusion: 1) No change in AV gradient with shunt occlusion. 2) Increased pressure gradient with appropriate autoregulatory vaso-constriction and no CBF increase. 3) Increased pressure gradient with impaired autoregulatory vasomotion and resultant CBF increase. 4) Same as 3) but with perfusion related complications.

However, several criticisms have been directed against the NPPB theory. Hassler [12] for example does not agree with this hypothesis, for he found no modification of pressure and flow velocity (neither before nor after AVM resection) in the remote brain arteries, but only in the feeders of the AVM. For Morgan and Sundt [21] this denomination (NPPB) is not appropriate, and this complication should rather be called normal pressure hyperperfusion breakthrough. Their hypothesis is that surgery, and especially multi-staged surgery, could end into an "acute-on-chronic hypoperfusion", with the following mechanism: in the presence of both chronic hypoperfusion and loss of autoregulation, an intra-operative deep hypotension could increase both the surrounding ischaemia and the capillaries lesions, and could favour the occurrence of micro infarcts. So, when the arterial pressure returns to normal, the occurrence of oedema and haemorrhage could be facilitated.

Recent haemodynamic studies exploring the CBF, ended also in criticisms against the NPPB theory. To test the mechanism of NPPB phenomenon, Young [44] measured the CBF before and after resection of the AVM, and again after increasing the mean arterial pressure by 20 mm Hg. Immediately after resection, he found a significant increase in CBF, but no further increase after elevation of the systemic arterial pressure. This experiment demonstrated that the vessels around the AVM were still able to constrict in reaction to an increased perfusion pressure, and that the autoregulation was preserved. So, even if there are probably certain cases in whom complications occur as a result of impaired autoregulation, there is also a general hyperperfusion response that does not involve pressure autoregulatory mechanisms. Young and his colleagues [45] conducted a second study using induced hypertension during embolization procedures. In the patient studied, rCBF did not change after induced hypertension. The authors concluded

that these patients were not in a "pressure-passive" state, but that there could exist in response to chronic hypotension a downward shift of their autoregulatory curve to the left, thereby adaptating the lower limit of autoregulation in affected vascular territories. The role of the CO₂ reactivity was also criticized by Batjer [8] after his study using CBF and administration of Acetazolamide: patients who developed hyperaemic complications actually demonstrated an increased vasodilation (greater than in normal brain tissue), and this fact does not support the NPPB theory. For Batjer these findings could suggest smooth muscle derangements in cerebral vasculature in some AVM patients.

(2) *Disturbances of the AVM drainage* have also been advanced as a source of post treatment complications. Miyasaka [20] pointed out that postoperative haemorrhagic infarction caused by thrombosis in the draining veins should be considered as a distinct complication after removal of an AVM. In his experience several arguments were in favour of the venous origin of such a complication: no evidence of residual AVM, delayed onset of the haemorrhage (inconsistent with the time course of a NPPB or with insufficient haemostasis), good correlation between the location of the haemorrhage and the occlusion of the draining vein, and multifocal haemorrhage affecting both the gray and the white matter. More recently, two theories, very similar to each other, have been proposed regarding the venous mechanism of post-treatment complications.

a) *The theory of "venous overload"* was proposed by Wilson [40]: For this author, interference with venous drainage represents the single factor responsible for almost all clinically significant complications of AVMs following treatment. A spontaneous thrombosis of a major draining vein may cause occlusive hyperaemia and abrupt neurological deterioration. This venous complication could be related with the time. Early deterioration (first day or so) could reflect differing degrees of venous restriction, and late deterioration (after several days) could be attributed to delayed thrombosis of one or more critical draining veins. In Wilson's opinion, the NPPB theory exists, but is neither common nor a universal explanation for complications related to the AVM eradication. In some cases, a combination of both NPPB and hyperaemia due to venous occlusion could be responsible for these complications.

b) *The theory of "occlusive hyperaemia"* was proposed by Al-Rhodan, Sundt, and co-workers [1].

These authors emphasized the role of the veins that drain the AVM as well as the surrounding brain parenchyma. Inadvertent embolization or surgical ligation of these veins is likely to precipitate passive hyperaemia and engorgement with subsequent haemorrhage and brain oedema, and a secondary reduction in arterial perfusion. The conclusion of Al-Rhodan's study is that two separate but interrelated mechanisms may be responsible for the complications of haemorrhage and oedema following the resection of high flow AVMs: 1) Stagnant arterial flow in former AVM feeders and in their parenchymal branches, with subsequent worsening of the existing hypoperfusion and ischaemia, and subsequent haemorrhage and oedema. 2) Obstruction of the venous outflow system of brain adjacent to the AVM, with subsequent passive hyperaemia, engorgement, and further arterial stagnation. In addition, disturbed autoregulation at the microcirculation level may play a role.

(3) *Retrograde thrombosis of the feeding arteries*. Nornes [26] pointed out that the length of the feeders is a very important factor: in his experience, no brain swelling was observed in cases with short feeders. In the contrary, there is a high risk in cases with feeders longer than 8 cm. Hassler [12] agrees on this risk due to the length of the feeders. Miyasaka [9] also described this complication, which was found in 6.6% of all his cases, and in 14% of medium-sized and large AVMs. He suggested that the development of retrograde thrombosis could be due partly to slow flow in the former feeding arteries that was observed immediately after AVM removal and partly to pathological changes in these vessels due to long-standing haemodynamic stresses.

Therapeutic Implications

Therapeutic measures are proposed on the basis of the theories described above.

(1) *The prevention of the NPPB*. The principle of the method for the prevention, as established by Spetzler [31], is to gradually increase perfusion to the ischaemic hemisphere by graded occlusion of the AVM. This aim may be obtained through staged ligation or staged embolization of feeding arteries [23, 26, 31], or through multistaged resection [28, 31]. Postoperative hypotension is recommended [4, 10, 15, 25, 31]. Intra-operative hypotension is more controversial: sometimes recommended [25, 26, 28], but sometimes not [21, 46], for lowering the blood pressure during surgery could increase the pre-existing

ischaemia and the hyperaemic complications. Some authors have proposed partial temporary clamping of the cervical carotid artery rather than lowering the systemic arterial pressure. This arterial clamping may be performed either intra-operatively [9, 28] or post-operatively [35, 36] or both, lasting for several days and then gradually tapered off. Several additional measures have been proposed during the post-operative period [15]: intensive care unit during at least 24 hours, reduced fluid intake, administration of diuretics and osmotherapy, and if ICP raises, barbiturate coma.

(2) *Prevention of occlusive hyperaemia* (or of the venous overload). In this hypothesis [1] in which occlusive hyperaemia is a greater risk than NPPB, the staged surgical resection is not recommended (except if technically necessary). Whether the AVM resection is accomplished in one or multiple stages, with or without embolization, several precautions must be taken to reduce the risk of occlusive hyperaemia: avoiding injury of veins that drain both the AVM and the surrounding brain parenchyma; clipping of the terminal arteries as close to the malformation as possible, and protection of the vessels that supply normal brain beyond the malformation; avoidance of excessive intravascular hypotension that could increase cerebral ischaemia and predispose to sludging, aggregation and clumping of formed elements (platelets and red blood cells) in the draining veins. Wilson [40] also thinks that reducing the fluid intake during the postoperative period and using the various means of reducing oedema might increase the risk of venous thrombosis. He recommends to assure an adequate blood volume, to avoid haemoconcentration, and even to give aspirin and low-dose heparin therapy immediately after surgery.

(3) *The role of selective embolization*. Intravascular embolization has been advocated either as sole treatment of AVMs, or more often as a pre-operative method in the combined management of AVMs [11]. Several questions arise as far as the efficacy and the innocuousness of embolization is concerned. Is there a benefit after embolization on the haemodynamic disturbances due to the malformation? The angiographic suppression of the intracranial steal due to the AVM is a common finding even after partial eradication. Sugita [33] reported a case demonstrating the correction of the steal phenomenon and the restoration to normal of a visual field defect after embolization. Takeuchi [37] investigating the effects of embol-

ization on cerebral haemodynamics in AVMs by means of the SPECT technique, confirmed that there is an acute flow redistribution immediately after embolization of AVMs. This improvement of the cerebral perfusion was found particularly marked in patients with no history of haemorrhage, or when the embolization had caused no new infarction in the surrounding normal brain, or when the nidus itself was occluded (and particularly with liquid emboli such as IBCA). After partial embolization, the improved cerebral circulation did not last. The second question is: are there specific haemodynamic complications due to the embolization procedure itself? Immediate and delayed complications of the embolization have been reported, very similar to that described above in our experience. Spetzler [32] reported several AVM ruptures occurring several days to weeks after trans-femoral embolization that converted a large AVM into a smaller one. He explained this complication by the AVM feeding artery pressure: following embolization of a large AVM, the resistance to flow increases and the feeding artery pressure in the remaining lesion is elevated. Spetzler's conclusion is that the usefulness of partial embolization as the sole treatment for AVMs should be seriously questioned, and the goal of treatment for AVMs should be complete obliteration. Jafar [14] observed a transient ischaemic event in one patient (5%) and a haemorrhagic complication in 3 (15%) requiring emergency surgery with subsequent recovery: The haemorrhage occurred during the embolization procedure in one case, and within 24 to 72 hours in two other cases. The third question is: Does the embolization reduce the rate of complications occurring after the resection of AVMs? The fact that embolization may favour the development of the smaller deep feeding vessels, which could increase the difficulty of surgery, seems well accepted [14, 22]. In our series, we observed no haemodynamic complications after surgery, with or without embolization. Various opinions are expressed in the recent literature. Morgan [22], discussing the complications of surgery for AVMs, concluded that in his experience no NPPB or intra-operative haemorrhage occurred since the introduction of selective embolization. Yound [45] had the same experience with a limited group of patients who went to surgery after embolization. Jafar [14] compared a series of patients treated by pre-operative embolization and surgery, and a series of patients treated by surgery alone. In patients operated on after embolization, he observed a 15%

rate of postoperative haemorrhage (and overall a 3% death rate). Nevertheless he concluded that transfemoral embolization with NBCA is a safe and beneficial adjunct therapy to the surgical resection of AVMs. Embolization makes larger-sized, higher-grade AVMs surgically equivalent to smaller-sized, lower-grade lesions, by reducing operative time and blood loss. Takeuchi [37] observed in his series one case with hyperperfusion on SPECT two weeks after embolization, together with a NPPB phenomenon occurring at the end of the operation which was performed three weeks after embolization. He concluded that the hyperaemic state due to embolization probably continues for two or three weeks after embolization. Awad [3] in a series of AVM patients treated by staged embolization followed by surgical excision concluded that this mode of treatment did not completely eliminate postoperative intracranial hypertension, which was observed in 28% of the cases, and more frequently in AVMs greater than 6 cm in maximum diameter with no mortality.

Conclusion

The review of the literature demonstrates that the complications occurring after treatment of cerebral AVMs may be either not based on haemodynamics, or based on haemodynamics [21]. Not based on haemodynamics are the resection of eloquent brain, the post-resection oedema and haemorrhage, the rupture of occult retained AVM, and the new onset of seizures. Based on haemodynamics are the NPPB phenomenon, the venous and arterial occlusion of vessels of normal parenchyma, the retrograde thrombosis of feeding arteries, and the venous overload or occlusive hyperaemia phenomenon.

In our experience:

- Complications of resection (with or without pre-operative embolization) remained minor and only due to the resection or to the manipulation of the corresponding brain area. No haemodynamic complication occurred in this group.

- Complications of radiosurgery (alone, or after embolization, or after incomplete resection) remained so far infrequent and of the minor type, relating to the anatomical site of the AVM.

- Complications of endovascular embolization were the most frequent and the most severe ones, responsible for all the deaths due to treatment. They were all of haemodynamic origin, either with ischaemic

in 50% of cases (no mortalities) or with haemorrhage in 50% of cases (with all the fatal cases). In most of cases with haemorrhage the mechanism was occlusion of the venous drainage. These complications of embolization occurred mainly in high-grade AVMs, but also, to a lesser extent, in low-grade cases. So, in our experience, the emphasis of the treatment of AVMs, which once was devoted to surgical resection, has now shifted to endovascular embolization. As far as high-grade AVMs are concerned, this shift of treatment (surgery or embolization) is quite understandable and acceptable, for these malformations remain the most difficult and the most dangerous to treat, even with embolization. We will continue to submit these cases to pre-operative or pre-irradiation embolization. In any case, the patient and the family should be warned that the embolization technique remains a procedure of risk, contrary to the idea taking root in the mind of the population at large. But several complications after embolization occurred also in cases with low-grade AVMs, which are the best cases for surgery (or in some cases for radiosurgery, depending on the greatest diameter). After this experience, we tend to select these low-grade cases more and more frequently for direct resection (or radiosurgery) and to refrain from proposing embolization even if technically feasible. Even if the risk of embolization in this sub-group is infrequent, the severity of the complication outstrips the risk of surgery or radiosurgery.

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