Delayed neurological deterioration following resection of arteriovenous malformations of the brain


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Object. The aim of this study was to analyze delayed neurological deficits following surgical resection of arteriovenous malformations (AVMs).

Methods. The authors report on a consecutive series of 200 patients with angiographically proven AVMs of the brain that were surgically resected between January 1989 and June 1998. The 30-day mortality rate for patients in this series was 1%, with one death caused by AVM resection and one death attributed to basilar artery aneurysm repair following successful AVM resection. The Spetzler–Martin grading system correlated well with the difficulty of surgery. No permanent incidence of morbidity resulted from resection of Grade I or II AVMs; the percentage of patients with a significant neurological deficit due to resection was 7.8% for those with Grade III lesions and 33.3% for those with Grade IV or V AVMs. However, this grading system did not accurately predict the development of delayed neurological deficits.

Ten patients (5%) developed delayed neurological deficits after recovering from anesthesia and surgery. The delayed deficit was due to hemorrhage in four of the 10 patients and all four had undergone resection of AVMs measuring at least 4 cm in diameter. An increase in blood pressure during the first 8 postoperative days precipitated hemorrhage in these patients. Edema arising as a consequence of propagated venous thrombosis (two patients) was associated with extensive venous drainage networks rather than large AVM niduses. Both hemorrhagic and edematous complications can be included under the umbrella term of "arterial-capillary-venous hypertensive syndrome" to describe the common underlying pathogenesis accurately. An additional four patients developed a delayed deficit as a result of vasospasm. Vasospasm occurred when resection had involved extensive dissection of proximal anterior and middle cerebral arteries; in such cases the incidence of vasospasm was 27%.

Conclusions. On the basis of their analysis of these complications, the authors recommend strict blood pressure control for patients with lesions measuring 4 cm or more in diameter (particularly those with a deep arterial supply). Thromboprophylaxis with aspirin and heparin is prescribed for patients with extensive venous drainage networks, and prophylactic nimodipine therapy and angiographic surveillance for vasospasm are suggested for patients in whom extensive dissection of proximal anterior or middle cerebral arteries has been necessary.

KEY WORDS • brain lesion • arteriovenous malformation • surgery • complication

MORBIDITY and mortality rates for patients who have undergone surgical resection of arteriovenous malformations (AVMs) of the brain since 1980 vary markedly among series. Morbidity rates ranging from 7.8 to 30% and mortality rates ranging from 0 to 12.5% have been reported in the literature. Factors that explain these disparate results include differences in case selection, changes in operative technique, and the evolution of postoperative care over time. These factors make comparison among series difficult, a difficulty compounded by the lack of agreement on definitions and terminology for complications of AVM surgery and postoperative care.

Spetzler and Martin introduced a grading system that has been independently and prospectively validated and confirmed to have predictive capabilities. One of the major advantages of this grading system is its ability to improve interseries comparisons. This has become particularly important when comparing different treatment modalities (such as focused radiation treatment and surgery). Despite the advances that the Spetzler–Martin system brings to an analysis of surgical risk, a further investigation of results is needed to anticipate, prevent, and treat specific delayed postoperative complications.

Neurological complications may arise from both the surgical procedure and postoperative care. Prevention and management of these complications is clearly different. Deficits that present immediately on recovery from anesthesia are, for the most part, due to intraoperative events that can be minimized by correct patient selection as well as meticulous surgical technique and judgment. In contrast, delayed neurological deterioration results from complications that appear during the postoperative period. Several complications are recognized that have different...
risk factors and causes, and these may be prevented by tailoring postoperative management to the patient’s risk factors. The aim of this series was to analyze delayed neurological complications that occur after patients have recovered from AVM surgery, to determine the risk factors for different delayed complications, and to make recommendations for tailored postoperative management based on the perceived risks of delayed neurological deficits.

Clinical Material and Methods

Patient Population

Between January 1989 and June 1998, 200 patients aged 11 to 73 years underwent surgical resection of angiographically proven AVMs of the brain. Of these patients, 54.5% had presented with an intracranial hemorrhage and 27% with seizures; the remaining 18.5% presented with headaches or a focal neurological deficit unrelated to hemorrhage or received the diagnosis of AVM by chance. All patients were prospectively graded according to the Spetzler–Martin system; 59% were assigned Grade I or II, 32% Grade III, and 9% Grade IV or V. The locations of the AVMs included the cerebrum in 88% of patients, the cerebellum in 9%, and the brainstem in 3%.

Ablation Method

Surgery alone was performed in 80% of the cases and in combination with preoperative selective particulate embolization in 20% of the cases. In general, the patients selected for embolization had AVMs that were Spetzler–Martin Grades III or greater, with vascular anatomy that was considered favorable for degree of obliteration without neurological risk. Embolization preceded surgery by 6 to 7 days and the embolic agent was a mixture of Avitene, polyvinyl alcohol, absolute alcohol, and contrast agent.

During surgery the patient’s systolic blood pressure was maintained at 80 to 100 mm Hg. Surgical dissection focused mainly on the AVM margin, using a wide sulcal opening where appropriate. Only occasionally was a zone resection used.

Postoperative blood pressure was strictly controlled by maintaining a maximum systolic pressure of 110 mm Hg for a maximum of 7 days in patients with an AVM nidus that measured more than 3 cm in diameter.

Neurological Complications

Regardless of their eventual outcome, all patients suffering from deterioration in neurological function other than seizures between recovery from anesthesia and hospital discharge were considered to have a delayed neurological deficit. Final outcome was assessed 3 months after hospital discharge, and the patients’ conditions were classified as normal, abnormal but independent, dependent, or dead.

Statistical Analysis

Patients were stratified according to Spetzler–Martin grading of their AVMs: less than Grade III, Grade III, and greater than Grade III. Statistical comparisons were made using this stratification because previous studies have found this stratification to be significant in predicting outcome.7 Statistical comparison was made using Fisher’s exact test. The significance level was set at a probability value less than 0.05.

Results

Overall Results

Two hundred patients with angiographically demonstrated AVMs of the brain underwent surgical resection. The overall 30-day operative mortality rate due to AVM resection in this group was 0.5%. An additional patient died as a complication of surgery for a basilar artery aneurysm performed within 30 days of AVM surgery. The incidence of new neurological deficits present 3 months postoperatively is presented in Table 1. No patient who had an AVM with a Spetzler–Martin grade of less than III sustained a new permanent neurological deficit, although 15.6% of patients with Grade III AVMs developed a new deficit, including the patient who died as a result of basilar artery aneurysm repair following successful AVM removal. The difference between these two groups was significant (p < 0.0001). New neurological deficits occurred in 44.4% of patients who had Spetzler–Martin Grade IV or V AVMs. This was significantly different from outcomes in patients with Grade III AVMs (p < 0.02). New deficits caused no significant downgrading of the quality of life in 50% of the patients with Grade III AVMs, but new deficits did produce a reduction in the quality of life in 75% of patients who had Grade IV or V AVMs. Early postoperative angiography was performed in all patients and repeated surgery for a residual AVM was necessary in two. Following these procedures, angiographically demonstrated cure was confirmed in all 200 patients.

Delayed Neurological Deficits

A delayed onset of neurological deterioration developed in 10 patients during the first 9 days following surgery (Table 2). Six of these patients recovered to normal condition by 3 months; one patient recovered to the preoperative level of deficit; one patient exhibited a new permanent neurological deficit that did not interfere with quality of life; one patient was significantly impaired but independent in activities of daily living; and one patient worsened to a vegetative state.

Cases of Hemorrhage or Edema

Hemorrhage or edema developed in six patients (Cases
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<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs), Sex</th>
<th>Site of AVM</th>
<th>AVM Size (cm)</th>
<th>S–M Grade</th>
<th>Preop Deficit</th>
<th>Time From Surgery to Deterioration</th>
<th>Delayed Deficit</th>
<th>Cause of Deterioration</th>
<th>3-Mo Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>65, M</td>
<td>sylvian fissure</td>
<td>2</td>
<td>III</td>
<td>dysphasia</td>
<td>9 days</td>
<td>worsening dysphasia</td>
<td>vasospasm</td>
<td>same as preop</td>
</tr>
<tr>
<td>2</td>
<td>36, M</td>
<td>medial basal frontal</td>
<td>2</td>
<td>I</td>
<td>normal</td>
<td>7 days</td>
<td>confusion</td>
<td>vasospasm</td>
<td>normal</td>
</tr>
<tr>
<td>3</td>
<td>20, M</td>
<td>parietal convexity</td>
<td>6</td>
<td>IV</td>
<td>normal</td>
<td>6 days</td>
<td>GCS 3, fixed pupils</td>
<td>hemorrhage</td>
<td>vegetative</td>
</tr>
<tr>
<td>4</td>
<td>42, F</td>
<td>frontal parasagittal</td>
<td>4</td>
<td>III</td>
<td>leg weakness</td>
<td>2 days</td>
<td>GCS 4</td>
<td>hemorrhage</td>
<td>hemiparesis &amp; poor memory</td>
</tr>
<tr>
<td>5</td>
<td>62, F</td>
<td>frontal convexity</td>
<td>2.5</td>
<td>I</td>
<td>normal</td>
<td>2 days</td>
<td>headache, progressive hemiparesis, &amp; confusion</td>
<td>propagated venous thrombosis</td>
<td>normal</td>
</tr>
<tr>
<td>6</td>
<td>18, M</td>
<td>frontal parasagittal</td>
<td>4</td>
<td>III</td>
<td>normal</td>
<td>8 hrs</td>
<td>GCS 4, fixed pupils</td>
<td>hemorrhage</td>
<td>hand weakness</td>
</tr>
<tr>
<td>7</td>
<td>48, F</td>
<td>basal frontal</td>
<td>4.5</td>
<td>III</td>
<td>normal</td>
<td>7 days</td>
<td>hemiparesis</td>
<td>vasospasm</td>
<td>normal</td>
</tr>
<tr>
<td>8</td>
<td>28, F</td>
<td>sylvian fissure</td>
<td>2</td>
<td>II</td>
<td>normal</td>
<td>6 days</td>
<td>dysphasia</td>
<td>vasospasm</td>
<td>normal</td>
</tr>
<tr>
<td>9</td>
<td>16, F</td>
<td>temporal</td>
<td>1</td>
<td>II</td>
<td>normal</td>
<td>5 days</td>
<td>headache &amp; dysphasia</td>
<td>edema</td>
<td>normal</td>
</tr>
<tr>
<td>10</td>
<td>52, M</td>
<td>frontal</td>
<td>4</td>
<td>II</td>
<td>dysphasia</td>
<td>8 days</td>
<td>confusion, aphasia, hemiparesis</td>
<td>hemorrhage</td>
<td>normal</td>
</tr>
</tbody>
</table>

* GCS = Glasgow Coma Scale; S–M = Spetzler–Martin.

In each case postoperative angiography demonstrated no filling of the AVM. Four of these patients suffered from hemorrhage into the bed of the AVM resection or into the ventricle. These four patients had AVMs that measured at least 4 cm in diameter; in three of these cases the AVMs were fed by deep perforating vessels (lenticulostriate or choroidal arteries). The onset of clinical deterioration with hemorrhage was dramatic in each case, with three patients suddenly demonstrating deterioration to a Glasgow Coma Scale<sup>26</sup> score less than 5 (Fig. 1). All patients experienced an increase in blood pressure prior to hemorrhage. All but one of these patients was in the intensive therapy unit undergoing careful blood pressure surveillance at the time of hemorrhage. A systemic blood pressure increase (from < 120 mm Hg to 130–160 mm Hg) was documented to have preceded clinical deterioration in those patients in the intensive therapy unit. In the patient on the neurosurgical ward who had refractory hypertension (Case 10), systolic blood pressure rose from 140 to 160 mm Hg 1 hour before clinical deterioration. Surgical evacuation and barbiturate-induced blood pressure control were used for treatment in each case. Outcome was poor in two cases and good in the remaining two cases. Each of these four patients underwent a second postoperative angiography session following the hemorrhage and hematoma evacuation, which confirmed AVM ablation.

Cases of edema (Cases 5 and 9) presented less dramatically. The patient in Case 5, who had a small (2.5 cm) superficial AVM with extensive venous drainage (Fig. 2), exhibited gradual deterioration with headaches, confusion, and hemiparesis commencing 2 days after surgery. Noncontrast-enhanced CT scanning demonstrated hyperdense superficial venous drainage, suggesting propagated venous thrombosis underlying the deterioration. The case was managed with administration of low-dose heparin and aspirin, and the patient then made a gradual and complete recovery. The patient in Case 9 had a small (1-cm nidus) AVM in the temporal lobe with extensive superficial drainage. She began having headaches and dysphasia co-incident with a systolic blood pressure elevation from 100 to 130 mm Hg on postoperative Day 5. A CT scan confirmed edema and hyperdense redundant draining veins. On rapid reduction of systolic blood pressure to 100 mm Hg, the patient’s headaches resolved quickly but her dysphasia took several weeks to resolve.

Although hemorrhage was only seen to occur in AVMs that were 4 cm in diameter or larger, there was no significant difference between the patients’ Spetzler–Martin grades and the incidence of hemorrhage or edema.

**Cases of Vasospasm**

Neurological deterioration developed in four patients with angiographic confirmation of vasospasm between Days 6 and 9 following surgery. Two of these cases previously have been reported.<sup>13</sup> All patients were treated with intravenously administered nimodipine and three patients also underwent papaverine angioplasty. No patient underwent hypertensive therapy for fear of precipitating hemorrhage or edema.

Each case in which vasospasm developed required extensive exposure of the A<sub>1</sub>, M<sub>1</sub>, or M<sub>2</sub> arterial segments. In the entire series, only 15 patients required this extensive exposure of distal internal carotid and proximal anterior and middle cerebral arteries. In no case was it thought that there was significant subarachnoid bleeding. All patients had fully recovered 3 months after surgery. Statistical comparison using Fisher’s exact test found that for the prediction of vasospasm there was a significant difference between those patients who underwent basal dissection and those who did not (p < 0.001). There was no significant difference between the patients’ Spetzler–Martin grades and the incidence of vasospasm.

**Discussion**

The overall surgical results of this series are similar to the results of other studies reported recently.<sup>1,8,19,21,25</sup> Patients with Spetzler–Martin Grade I or II AVMs had no
new permanent neurological deficits. Patients with Grade III AVMs had a 15.6% risk of death or new permanent neurological deficit (50% of these deficits had no major impact on their quality of life), and those with Grade IV or V had a 44.4% risk of death or new permanent neurological deficit (25% of these deficits had no major impact on the patient’s quality of life).

In this series the Spetzler–Martin grading system correlated well with operative difficulty (Table 3). However, it proved to be less of a predictor for the development of delayed neurological deficits. Nine of the 10 patients in whom a delayed deficit developed had an AVM with a grade less than IV. Thus, further discriminators are necessary when evaluating potential predictors for delayed postoperative complications. Broadly subclassifying these delayed deficits into arterial-capillary-venous hypertensive (ACVH) syndromes (hemorrhage and edema) and vasospasm assists in analyzing the potential therapeutic interventions that may reduce the incidence of such postoperative complications.

**Fig. 1.** Case 3. Magnetic resonance image (A), angiograms (B and D), and CT scans (C and E) demonstrating a large parietal AVM (A and B) that was excised without complication (C). Postoperative angiography (D) confirmed no early venous filling. However, on postoperative Day 6 the patient experienced a rise in blood pressure and sustained a devastating intraventricular hemorrhage (E).

**Arterial-Capillary-Venous Hypertensive Syndrome**

Patients with either normal perfusion pressure breakthrough, proximal feeding vessel rupture, or propagated venous occlusive syndromes have as their underlying common pathophysiological perturbation localized intravascular pressure rise.2,23 This may result in either vessel rupture or interference with capillary function. Difficulty can arise when ascribing one of the various labels (for example, “normal perfusion pressure breakthrough” or “venous occlusive hyperemia”) as the exclusive mechanism for clinical deterioration. In addition, it may be that more than one process is involved. In Case 9 thrombosis was observed within the draining varix (a result that was expected), but this was not necessarily the sole reason for development of edema because it is uncertain whether normal venous outflow was compromised. Similarly, some researchers may argue that postoperative hemorrhage occurring in the distribution of diaphanous feeding arteries in a patient with elevated blood pressure may be
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caused by a ruptured residual AVM because of the pathological nature of these vessels. This confusion is not surprising, given the lack of a sharp transition from a normal vessel to an AVM vessel. This may explain, in part, the diametrically opposed views that have been argued regarding the existence of normal perfusion pressure breakthrough. In the four patients who sustained hemorrhage as a manifestation of ACVH syndrome, the diameter of the AVM nidus was at least 4 cm, and three of these patients also had a deep feeding vessel. These characteristics are also associated with intraoperative problems.

In the two cases in which venous insufficiency is believed to have played a role, the pattern of venous drainage may have predisposed to the genesis of these complications. In both patients these were extensive and redundant venous networks, despite the small size of the AVM nidus. Although one might speculate that a more distal stenosis of intracranial venous circulation may have contributed to the development of such a venous outflow hypertrophy and to the subsequent thrombosis of this system, none was identified in either of these two cases. With the compromise in venous outflow, a subsequent capillary hypertension above the level of blood-brain barrier competency will cause edema and the reduction in blood flow may produce infarction. This has been termed "venous occlusive hyperemia."

Experimentally, it has been demonstrated that there is a loss of astrocytic foot processes surrounding capillaries in the brain subjected to chronic arteriovenous shunting. It may be that the brain surrounding an AVM is more prone to ACVH damage with intracapillary pressure elevation because of these changes.

Development of Vasospasm

Clinically significant vasospasm developed in four patients. Although only 2% of patients developed this com-

<table>
<thead>
<tr>
<th>Spetzler–Martin Grade</th>
<th>No. of Patients</th>
<th>Patients Worse or Dead at 3 Mos</th>
<th>ACVH Syndrome</th>
<th>Vasospasm in Survivors</th>
</tr>
</thead>
<tbody>
<tr>
<td>I or II</td>
<td>118</td>
<td>0 (0%)</td>
<td>3 (2.5%)</td>
<td>2 (1.7%)</td>
</tr>
<tr>
<td>III</td>
<td>64</td>
<td>10 (15.6%)*</td>
<td>2 (3.1%)</td>
<td>2 (3.1%)</td>
</tr>
<tr>
<td>IV or V</td>
<td>18</td>
<td>8 (44.4%)*</td>
<td>1 (5.6%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

* Significant difference with preceding group by Fisher's exact probability test comparing Spetzler–Martin Grade I or II with Grade III (p < 0.001) and comparing Spetzler–Martin Grade III with Grade IV or V (p < 0.02). Other comparisons were nonsignificant.
plication, it only occurred in those who required extensive exposure of the A\textsubscript{1}, M\textsubscript{1}, or M\textsubscript{2} arterial segments. For the group of patients undergoing such extensive basal cisternal dissection, the incidence of symptomatic vasospasm was 27%. Although subarachnoid blood presumably underlies the trigger for vasospasm, no patient was found to have a significant subarachnoid hemorrhage on postoperative CT scanning. It may well be that there is an increased vasoreactivity in such vessels.\textsuperscript{3,13} These vessels may be more sensitive to the agents normally responsible for vasospasm, making this complication possible without a large volume of subarachnoid blood. In managing vasospasm, hypertensive, hypervolemic, hemodilution therapy is contraindicated because of the potential to precipitate the ACVH syndrome.

**Postoperative Management**

Arteriovenous malformations larger than 4 cm in diameter (with deep perforating feeding vessels) appear to be those at the greatest risk for developing hemorrhage with elevation of blood pressure in the first 8 days following surgery.\textsuperscript{14} Patients with these AVMs may benefit from aggressive blood pressure management and intensive monitoring during this period.

Arteriovenous malformations with extensive venous drainage may benefit both from blood pressure control and prophylaxis against thrombosis. Although both low-molecular-weight heparin and aspirin (alone or in combination) have been used in this series, they have a relatively long halflife, and we now use continuous infusion of low-dose heparin in those patients believed to be at risk. Caution must be exercised in using this regimen in patients with larger lesions who are at risk for postoperative hemorrhage with blood pressure lability.

Vasospasm can be anticipated in 27% of patients undergoing extensive dissection of the A\textsubscript{1}, M\textsubscript{1}, or M\textsubscript{2} arterial segments, regardless of the presence or absence of subarachnoid blood on postoperative CT scanning. Because of the potential problems associated with the use of induced hypertension (particularly during the first 8 days with larger lesions), management must be restricted and rests, in part, on nimodipine therapy and selective angioplasty. Intravenously administered nimodipine has the molecular-weight heparin and aspirin (alone or in combination) therapy and selective angioplasty. Intravenously administered nimodipine has the dual theoretical advantage of providing a reduction in delayed ischemic neurological deficit and a reduction in blood pressure. Rather than performing early postoperative angiography in patients who are at risk for vasospasm (only 1% of patients in this series required reoperation for residual AVM), it may be appropriate to delay the procedure until the period in which vasospasm is likely to be present. Angioplasty has been performed using papaverine in our patients, but caution needs to be exercised, with potential increased vasoreactivity of AVM feeding arteries.\textsuperscript{13} As yet, we have no experience with balloon angioplasty because of our concern that proximal arteries may be less robust or harbor focal thin walls at potential aneurysm sites, predisposing to their rupture during such procedures.

**Conclusions**

To reduce the incidence of postoperative complications, consideration should be given to stringent postoperative blood pressure management for 8 days in cases of larger AVMs, the use of prophylaxis against thrombosis in cases with extensive venous drainage systems, and the use of nimodipine therapy and surveillance angiography in cases requiring extensive dissection of larger arteries at the base of the brain.

**References**

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