Incidence of cerebral vasospasm after endovascular treatment of acutely ruptured aneurysms: report on 69 cases

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Cerebral vasospasm is the most common cause of morbidity and mortality in patients admitted to the hospital after suffering aneurysmal subarachnoid hemorrhage (SAH). The early surgical removal of subarachnoid clots and irrigation of the basal cisterns have been reported to reduce the incidence of vasospasm. In contrast to surgery, the endovascular treatment of aneurysms does not allow removal of subarachnoid clots. In this study the authors measured the incidence of symptomatic vasospasm after early endovascular treatment of acutely ruptured aneurysms with Guglielmi detachable coils (GDCs).

Sixty-nine patients classified as Hunt and Hess Grades I to III underwent occlusion of intracranial aneurysms via GDCs within 72 hours of rupture. The amount of blood on the initial computerized tomography (CT) scan was classified by means of Fisher’s scale. Symptomatic vasospasm was defined as the onset of neurological deterioration verified with angiographic or transcranial Doppler studies. Hypertensive, hypervolemic, hemodilution therapy, with or without intracranial angioplasty, was used to treat vasospasm after GDC placement.

Symptomatic vasospasm occurred in 16 (23%) of 69 patients. The clinical grade at admission and the amount of blood on the initial CT were both associated with the incidence of subsequent vasospasm. At 6-month clinical follow-up examination, 12 of these 16 patients experienced a good recovery, two were moderately disabled, and two patients had died of vasospasm.

In conclusion, the 23% incidence of symptomatic vasospasm in this series compares favorably with that found in conventional surgical series of patients with acute aneurysmal SAH. These results indicate that endovascular therapy does not have an unfavorable impact on cerebral vasospasm.

Key Words • cerebral aneurysm • subarachnoid hemorrhage • cerebral vasospasm • endovascular therapy • embolization
and Hess Grades I to III and undergoing GDC endovascular treatment within 72 hours of ictus were included in this study. Five patients who had undergone craniotomy before GDC treatment for attempted surgical clipping (three cases) or for hematoma evacuation (two cases) were excluded from this analysis. These five patients were excluded to eliminate any possible influences of surgical clot removal or brain retraction on the development of symptomatic vasospasm. Patients who had undergone pre-GDC ventriculostomy or lumbar drainage (two cases) were included in this study.

Patient Classification

Sixty-nine patients with acute SAH who were admitted either to UCLA Medical Center (22 patients) or the Methodist Hospital (47 patients) between April 1990 and May 1996 were eligible for this study. Of the 69 patients, 51 were women and 18 were men, and they ranged in age from 26 to 82 years, with an average age of 52 years. Documentation of SAH either by computerized tomography (CT) scanning or lumbar puncture was obtained in all patients. In our institutions, the management protocol for aneurysmal SAH calls for immediate obliteration of the aneurysm to prevent subsequent rerupture. Therefore, patients who would traditionally be considered candidates for delayed surgery underwent immediate endovascular treatment instead. Contraindications for acute surgical clipping included difficult aneurysm locations such as the high basilar tip, giant aneurysm size, or coexisting medical conditions including pregnancy, a history of myocardial infarction, or pulmonary edema.

The 69 patients were classified by admission Hunt and Hess grade. The amount of blood seen on CT scanning was classified by means of Fisher’s scale. Twenty-four patients were treated within 24 hours, 27 between 24 and 48 hours, and 18 between 48 and 72 hours after the initial hemorrhage. Table 1 displays the breakdown of aneurysm locations. Table 2 displays the breakdown of symptomatic vasospasm with GDCs

Treatment of Aneurysms and Patient Management

Aneurysms were embolized by means of GDCs as described by Guglielmi, et al. After successful embolization, patients were admitted to the neurological intensive care units and managed with the same protocol as that used for surgically treated patients. Central venous or Swan–Ganz catheters were used for cardiopulmonary monitoring, and transcranial Doppler (TCD) evaluations were performed in patients at risk for vasospasm. Symptomatic vasospasm, verified by TCD or angiography, was defined as delayed neurological deterioration that could not be attributed to rebleeding, hydrocephalus, intracerebral hematoma, electrolyte abnormalities, or toxic and metabolic factors. Even if TCD or angiographic findings indicated the presence of anatomical vasospasm, this was not considered to be symptomatic vasospasm in the absence of neurological deterioration. The incidence of symptomatic vasospasm was compared with the Hunt and Hess grade (Table 2) and with the amount of the subarachnoid clot (Table 3). The chi-square test for linear trends and Fisher’s exact test were used for statistical analysis.

After the GDC procedure and once the diagnosis of symptomatic vasospasm was established, hypertensive, hypervolemic, hemodilution (3H) therapy was initiated. Calcium channel blockers (nimodipine 60 mg/4 hours) were also administered. At UCLA, patients who developed symptomatic vasospasm despite maximum medical management underwent intracranial mechanical and/or chemical angioplasty. At the Methodist Hospital, angioplasty procedures were not performed.

Evaluation of Patients

Clinical follow-up evaluations were performed a minimum of 6 months after GDC treatment. Outcome was defined according to the Glasgow Outcome Scale. Data on outcome were obtained from the report of the referring physician, the report of the treating physician, or telephone conversation with the patient or patient’s relative.

Results

Incidence of Symptomatic Vasospasm

Symptomatic vasospasm occurred in 16 (23%) of 69

<table>
<thead>
<tr>
<th>Fisher's Scale</th>
<th>No. of Cases (%)</th>
<th>No. W/ Vasospasm (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>6 (6)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Group 2</td>
<td>10 (15)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Group 3</td>
<td>47 (68)</td>
<td>13 (28)</td>
</tr>
<tr>
<td>Group 4</td>
<td>6 (9)</td>
<td>2 (33)</td>
</tr>
<tr>
<td>not available</td>
<td>2</td>
<td>1 (50)</td>
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patients. Its incidence was identical at the two institutions, with five of 22 patients developing symptomatic vasospasm at one institution and 11 of 47 patients at the other. The correlation between Hunt and Hess grades on admission and the development of symptomatic vasospasm was as follows: two (10%) of 20 patients with Grade I; four (22%) of 18 patients with Grade II; and 10 (32%) of 31 patients with Grade III developed symptomatic vasospasm. The clinical grade on admission was associated with the incidence of symptomatic vasospasm (Table 2; chi-square test for linear trend, p = 0.0658).

The amount of the cisternal clot on the initial CT was also associated with the development of symptomatic vasospasm. None of the 14 patients with Fisher Grade I or 2 developed vasospasm, whereas 13 (28%) of the 47 patients with Grade 3 and two (33%) of the six patients with Grade 4 developed symptomatic vasospasm. In two patients the grade could not be determined, and one of these developed vasospasm. Statistical analysis showed that the difference between Grade 2 (thin clot) and Grade 3 (thick clot) was significant (Fisher's exact test, p = 0.0285). However, the difference among Grades 1, 3, and 4 was not significant because of the small number of patients in the sample (Table 3).

Complications Due to Aneurysm Treatment

There were no deaths related to the procedure. There were five complications (7%): one patient had worsened brainstem compression caused by a giant basilar bifurcation aneurysm that required subsequent surgical decompression and clipping; in one patient the aneurysm ruptured during the endovascular procedure (however, with the immediate delivery of additional GDCs, the aneurysm was completely obliterated and the patient recovered completely); and three patients suffered thromboembolic events (two of them recovered completely after receiving thrombolytic therapy and one had a permanent deficit). Seven patients (10%) underwent surgical clipping in the chronic phase of SAH in the months following subtotal or incomplete occlusion of their aneurysms with GDCs.

Management and Outcome in Patients Who Developed Symptomatic Vasospasm

Of the 16 patients who developed symptomatic vasospasm, 12 were treated with 3H therapy only and four with 3H therapy and intracranial balloon or chemical angioplasty; there were no complications (Table 4). Of the 12 patients with good outcomes, two were originally classified as Hunt and Hess Grade I, three as Grade II, and seven as Grade III. The two patients with moderate disability caused by vasospasm were originally Grade III. The two patients who eventually died of vasospasm were originally Grade II or III (Table 5).

Overall Outcome

The overall 6-month clinical outcomes in the 69 patients are presented in Table 5. The causes of morbidity and mortality are given in Table 6. No aneurysm rebled in this series.

Discussion

Cerebral vasospasm is the major cause of morbidity and mortality in patients admitted to the hospital after aneurysmal SAH. Although its etiology is not fully established, the incidence, distribution, and severity of vasospasm are correlated to the location and volume of blood clot deposited in the basal cisterns by the ruptured aneurysm. It has been suggested in clinical studies that early surgical evacuation of the cisternal blood clot may reduce the incidence of vasospasm. This has been proven in experiments conducted in primates. Despite this, the largest clinical series reports that vasospasm remains the most significant cause of death and disability even in patients undergoing early surgery. Furthermore, there is no clear evidence that early surgery significantly reduces the severity of vasospasm. Despite progressive improvements in spasm treatment such as 3H therapy and the use of calcium channel blockers, additional risk factors may play an important role in the development of vasospasm after early surgery. The failure of early surgery to reduce the incidence of vasospasm may be due to the difficulty in removing subarachnoid clots. Alternatively, it is conceivable that surgery may affect vasospasm because of extensive retraction of the brain or overmanipulation of main arteries. Stornelli and French, Sundt and Whisnant, and Alcock and Drake also have cautioned that early surgery with or without preoperative spasm is more likely to precipitate postoperative vasospasm. Öhman, et al., also reported that early surgery was associated with a significantly higher number of hypodense areas consistent with cerebral infarction than that found in operations performed after Day 3 post-SAH.
Incidence of vasospasm with GDCs

We did not include patients with Grades IV or V in this series because it is difficult to diagnose accurately neurological deterioration caused by vasospasm in such patients. In our series of GDC-treated cases, 10% of patients with Grade I, 22% of patients with Grade II, and 32% of patients with Grade III developed symptomatic vasospasm. This compares favorably with conventional surgical series.

Amount of Blood Clot

In 1980, Fisher, et al.,38 developed a system for classifying the amount of subarachnoid clot present on CT scans and showed a strong correlation between the size and location of clot and the incidence, severity, and site of subsequent vasospasm. Adams, et al.,1 confirmed that thick collections of blood displayed on CT scans were highly predictive of cerebral ischemia. Duration of exposure to blood adjacent to cerebral arteries may also affect the development of vasospasm. Handa, et al.,37 demonstrated that the critical period of blood exposure appeared to be approximately 72 hours in primate models and that the direct removal of thrombus prior to that threshold prevented the development of vasospasm. The concepts of cisternal drainage and intracisternal administration of recombinant tissue plasminogen activator (TPA) are based on the significance of these observations. Our results showed that the incidence of symptomatic vasospasm following endovascular treatment was associated with the amount of cisternal clot found on the initial CT scan. By eliminating any possible contributions to vasospasm from surgical mechanical manipulation, this may be a more accurate reflection of the effect of clot volume on the development of vasospasm.

Incidence of Permanent Neurological Deficit Caused by Vasospasm

Öhman, et al.,36 reported on 228 patients with Hunt and Hess Grades I to III who were divided into groups receiving nimodipine or placebo. Delayed cerebral ischemia caused permanent neurological deficits in 14.3% of the patients in the nimodipine group and 27.7% of those in the placebo group. Awad, et al.,39 reported that death or major neurological deficit resulting from vasospasm occurred in 6.7% of all patients.

In our study, the overall morbidity rate due to vasospasm was 2.8% and the mortality rate was also 2.8% (clinical evaluation at 6 months post-SAH). A combined morbidity and mortality rate of 5 to 6% from delayed cerebral ischemia is acceptable by today’s standards.

Protection From Rebleeding During Critical Period of Vasospasm

The GDC embolization procedure was successful in preventing rebleeding throughout the period of subsequent vasospasm treatment (including aggressive 3H therapy and chemical and/or mechanical angioplasty). This experience may lead to a new strategy for treatment of patients with an acutely ruptured aneurysm.52 Both early surgery (with retraction of a tight brain) and delayed treatment (leaving a ruptured aneurysm unprotected for more than 2 weeks) carry risks, and the debate concerning timing of aneurysm clipping persists.
tion of the aneurysm with GDCs in the acute stage allows therapies preventing and treating vasospasm to be safely administered over the following days. If embolization of the aneurysm is incomplete and surgical clipping is eventually required (seven [10%] of 69 cases in this series) the surgery can be performed as an elective procedure in a nonedematous brain. Although there are anecdotal reports of GDCs making clipping technically difficult,12,13,18 larger series have shown that when post-GDC clipping was performed (in a minority of cases), the subsequent surgery was more often made safe by the improvement in the patient’s condition in the interval than made hazardous by the presence of GDCs within the aneurysm.19

Potential Role for Intrathecal Thrombolysis

One limitation of the endovascular technique remains the inability to evacuate a subarachnoid clot. Although the incidence of symptomatic vasospasm in this series is acceptable, this does not trivialize the importance of the subarachnoid clot. To the contrary, the correlation demonstrated between the volume of the blood clot and the incidence of vasospasm accentuates the role of the clot and the theoretical benefit of removing it.

Intrathecal infusion of thrombolytic agents has been proposed as one means of evacuating the clot and decreasing the incidence of vasospasm. Findlay, et al.,4 demonstrated that the incidence of vasospasm could be markedly reduced in primates by lysing the subarachnoid clot within 48 hours by means of intrathecal fibrinolytic therapy. Some clinical studies have also shown the effectiveness of thrombolysis of subarachnoid clots using TPA or urokinase.7,34,45,50,52 According to these reports, intrathecal administration of TPA or urokinase may reduce in primates by lysing the subarachnoid clot. To the contrary, the correlation demonstrated between the volume of the blood clot and the incidence of vasospasm accentuates the role of the clot and the theoretical benefit of removing it.

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Conclusions

The overall incidence of symptomatic vasospasm in this series was 23%. Seventy-five percent of patients who developed symptomatic vasospasm achieved good clinical status by the 6-month clinical follow-up review. The rate of vasospasm correlated with the patient’s clinical grade on admission and with the amount of cisternal blood clot found on initial CT scans. Early obliteration of the aneurysm with GDCs allowed aggressive treatment including 3H therapy and intracranial angioplasty for vasospasm. There were no cases of rebleeding after GDC treatment in this series. These results indicate that endovascular treatment does not have an unfavorable impact on cerebral vasospasm. In spite of the fact that this study focused only on patients with Hunt and Hess Grades I to III, the results compare favorably with surgical and natural history outcomes in patients with similar neurological grades. Although the 6-month outcome data are reassuring, we strongly encourage further research to reduce (and possibly prevent) the still significant incidence of post-SAH symptomatic vasospasm.

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