Surgery for angiographically occult cerebral aneurysms

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In 15% of patients with spontaneous subarachnoid hemorrhage (SAH), the source of bleeding cannot be determined despite repeated cerebral angiography. However, some patients diagnosed as having "SAH of unknown cause" actually harbor undetected aneurysms. The authors report six patients with SAH who, despite multiple negative cerebral angiograms, underwent exploratory surgery due to a high clinical and radiographic suspicion for the presence of an aneurysm. Brain computerized tomography (CT) scans revealed blood located mainly in the basal frontal interhemispheric fissure in four patients, in the sylvian fissure in one patient, and in the interpeduncular cistern in one patient. The patients were evaluated as Hunt and Hess Grades I to III, and had undergone at least two high-quality cerebral angiograms that did not reveal an aneurysm. Vasospasm was visualized in two patients. Three patients rebled while in the hospital. Exploratory surgery was performed at an average of 12 days post-SAH. Five aneurysms were discovered at surgery and were successfully clipped. All four patients with interhemispheric blood were found to have an anterior communicating artery (ACoA) aneurysm. The patient with blood in the sylvian fissure was found to have a middle cerebral artery aneurysm. These aneurysms were partially thrombosed. No aneurysm was detected in the patient with interpeduncular SAH, despite extensive basilar artery exploration. Five patients had an excellent outcome and one patient developed diabetes insipidus. These results show that exploratory aneurysm surgery is warranted, despite repeated negative cerebral angiograms, if the patient manifests the classical signs of SAH with CT scans localizing blood to a specific cerebral blood vessel (particularly the ACoA) and if a second SAH is documented at the same site.

KEY WORDS: cerebral aneurysm • cerebral angiography • subarachnoid hemorrhage • angiographically occult aneurysm

In a significant number of patients suffering from spontaneous subarachnoid hemorrhage (SAH), the source of bleeding cannot be determined despite extensive neuroradiological investigation. In several published series, a surprisingly large number of patients presenting with the classical signs and symptoms of SAH are found to have negative cerebral angiograms, even when the SAH is confirmed on computerized tomography (CT) scans. It has been estimated that between 13% and 22% of all patients with spontaneous SAH are diagnosed as having "SAH of unknown cause"; however, a small number of these patients actually harbor undetected cerebral aneurysms, and are at risk for additional episodes of bleeding, often with a high risk of morbidity and mortality.

No study has analyzed the practical importance of CT in the surgical management of SAH patients with negative angiograms. Due to a high index of suspicion for the presence of a ruptured intracranial aneurysm, we performed exploratory aneurysm surgery on six patients who presented with clinical SAH (confirmed by CT) and from whom multiple negative cerebral angiograms were obtained.

Clinical Material and Methods

Patient Population

Six patients underwent exploratory aneurysm surgery during the past 5 years. The clinical information is summarized in Table 1. All six patients were women whose age ranged from 36 to 64 years. Each patient presented with the classical signs and symptoms of spontaneous SAH, which was confirmed by CT. Upon admission to the hospital, two patients were in neurological Grade I, three were in Grade II, and one was in Grade III according to the classification of Hunt and Hess.

Radiological Studies

The radiographic findings are summarized in Table 2. Each patient underwent noncontrast-enhanced CT of the brain. In four patients, subarachnoid blood was mainly located in the basal frontal interhemispheric fissure. One patient had a hemorrhage localized to the left sylvian fissure, and another had a focal collection of blood in the interpeduncular cistern. Four-vessel cerebral angiography with multiple views was carried
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TABLE 1
Clinical data for six patients with exploratory aneurysm surgery*

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs)</th>
<th>Sex</th>
<th>SAH</th>
<th>No. of Rebleeds</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>56</td>
<td>F</td>
<td>yes</td>
<td>2</td>
<td>III</td>
</tr>
<tr>
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<td>51</td>
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<td>1</td>
<td>II</td>
</tr>
<tr>
<td>3</td>
<td>36</td>
<td>F</td>
<td>yes</td>
<td>2</td>
<td>II</td>
</tr>
<tr>
<td>4</td>
<td>56</td>
<td>F</td>
<td>yes</td>
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<tr>
<td>6</td>
<td>59</td>
<td>F</td>
<td>yes</td>
<td>0</td>
<td>II</td>
</tr>
</tbody>
</table>

* Patients were graded neurologically according to the Hunt and Hess grading system. SAH = subarachnoid hemorrhage.

TABLE 2
Radiological data for six patients with exploratory aneurysm surgery

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Location of SAH on CT Scan*</th>
<th>Angiogram†</th>
<th>Vasospasm</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>interhemispheric</td>
<td>negative (2)</td>
<td>yes</td>
</tr>
<tr>
<td>2</td>
<td>interhemispheric</td>
<td>negative (3)</td>
<td>no</td>
</tr>
<tr>
<td>3</td>
<td>interhemispheric</td>
<td>negative (2)</td>
<td>no</td>
</tr>
<tr>
<td>4</td>
<td>sylvian</td>
<td>negative (2)</td>
<td>no</td>
</tr>
<tr>
<td>5</td>
<td>interpeduncular</td>
<td>negative (2)</td>
<td>no</td>
</tr>
<tr>
<td>6</td>
<td>interhemispheric</td>
<td>negative (2)</td>
<td>yes</td>
</tr>
</tbody>
</table>

* SAH = subarachnoid hemorrhage; CT = computed tomography.
† Numbers in parentheses indicate the number of times angiography was performed.

Both the interval between the onset of SAH and the initial angiographic study ranged from 0 to 5 days (mean 2 days). A second cerebral angiogram was performed in five patients between 7 and 10 days after SAH (mean 8 days). One patient underwent a third angiographic investigation on Day 28 post-SAH. Two of the six patients had angiographic evidence of vasospasm on the initial study. No aneurysm could be demonstrated in any of the 13 total angiograms performed in this patient population.

Incidence of Rebleeding

Three patients (50%) experienced another hemorrhage while in the hospital, after the initial angiographic study. Two patients rebled twice, and one patient had a single rebleed. Computerized tomography documented that each episode of rebleeding occurred at the identical site of the original SAH. The recurrent hemorrhages were noted at an average of 6 days following the initial SAH. One patient (Case 3) had undergone prior clipping of an anterior communicating artery (ACoA) aneurysm 7 days prior to suffering two further episodes of hemorrhage localized to the interhemispheric fissure. Two additional high-quality angiograms failed to reveal an aneurysm.

Surgical Technique

All six patients underwent exploratory surgery an average of 12 days following the initial SAH. At surgery, the suspected intracranial vessel was explored first. Four patients with blood in the interhemispheric fissure underwent a right pterional craniotomy. After the internal carotid artery (ICA) was identified on that side and the sylvian fissure was split, a right gyrus rectus cortectomy was performed and the ACoA complex was exposed. After aneurysmal clipping, the ICA and its branches, the middle cerebral artery (MCA), and the basilar apex were exposed and inspected.

The patient with blood in the left sylvian fissure (Case 4) underwent surgical exploration via a left pterional craniotomy, and a right subtemporal approach was used in the patient with blood in the interpeduncular cistern (Case 5). In the latter patient, we inspected the basilar apex, the P1 segment of the posterior cerebral arteries, and the superior cerebellar artery segments.

Results

Operative Findings

Table 3 shows a summary of our results. Five aneurysms in six SAH patients were discovered at surgery and were clipped uneventfully. Each of these aneurysms was noted to be partially thrombosed. Four aneurysms were in the ACoA complex and one was at the left MCA bifurcation. All four patients whose CT scans localized blood to the interhemispheric fissure were found at exploration to have an ACoA aneurysm as the source of their SAH. In the patient with blood in the interpeduncular fossa (Case 5), no aneurysm was found despite extensive exploration of the basilar artery.

The three patients who experienced episodes of rebleeding while in the hospital were found to have aneurysms at exploratory surgery. One patient (Case 3) had undergone clipping of an ACoA aneurysm 1 week prior to two subsequent hemorrhages in the basal frontal interhemispheric fissure. Two follow-up angiograms failed to reveal another aneurysm. At surgery, a second partially thrombosed aneurysm was found next to the originally clipped lesion, which had probably developed at the site of an incompletely occluded aneurysmal neck.

Outcome

Five of the six patients in the present study (83%) had an excellent outcome and returned to their preop-

TABLE 3
Operative findings in six patients with exploratory aneurysm surgery*

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Operative Findings*</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>ACoA aneurysm</td>
<td>excellent</td>
</tr>
<tr>
<td>2</td>
<td>ACoA aneurysm</td>
<td>excellent</td>
</tr>
<tr>
<td>3</td>
<td>ACoA aneurysm</td>
<td>diabetes insipidus</td>
</tr>
<tr>
<td>4</td>
<td>MCA aneurysm</td>
<td>excellent</td>
</tr>
<tr>
<td>5</td>
<td>no aneurysm</td>
<td>excellent</td>
</tr>
<tr>
<td>6</td>
<td>ACoA aneurysm</td>
<td>excellent</td>
</tr>
</tbody>
</table>

* ACoA = anterior communicating artery; MCA = middle cerebral artery.
Illustrative Case Report

This 56-year-old woman (Case 1) suffered the sudden onset of a severe headache. She was admitted to another hospital where the diagnosis of SAH was made based on clinical as well as CT findings (Fig. 1). A four-vessel cerebral angiogram revealed neither an aneurysm nor vasospasm. While in the other hospital, she suffered a second SAH. Upon transfer to our hospital, a second series of four-vessel cerebral angiograms was obtained with multiple views; however, they failed to reveal the source of hemorrhage (Fig. 2). Two days following the second angiogram, the patient experienced a third SAH. At exploratory surgery, a bilobed, partially thrombosed ACoA aneurysm was found and successfully clipped. The patient made a complete recovery.

Discussion

We have identified a small group of patients presenting with clinical as well as radiographic SAH who, in spite of several negative cerebral angiograms, harbor intracranial aneurysms that otherwise would have gone undetected. This group of patients whose aneurysms were discovered at exploratory surgery would have previously been diagnosed as having "SAH of unknown etiology"[1.2.6.8.12.17.18.19] and, unquestionably, some of these patients would have rebled and died[20]. The brain CT findings in these patients strongly suggested the presence of an aneurysm. By excluding such patients from this categorization, one merely strengthens the claim that true "SAH of unknown etiology" has a favorable prognosis.

CT Findings in Occult Cerebral Aneurysms

In all four cases in which CT showed focal blood in the interhemispheric fissure, an ACoA aneurysm was found at surgery, despite at least two negative angiograms. In other words, SAH in this location was found to be highly predictive of the discovery of an ACoA aneurysm at exploratory surgery. Endo and Suzuki[11] and Di Lorenzo and Guidetti[9] each reported two patients who presented with SAH and, despite negative angiography in each patient, underwent exploratory surgery with successful clipping of an ACoA aneurysm.

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Only a few studies have described the blood distribution on CT scans in patients with SAH of unknown etiology. It is established that the distribution of blood within the cisterns may indicate the site of an aneurysm; however, no prior study has recommended exploratory surgery on the basis of the CT findings in conjunction with a strong clinical suspicion for an aneurysmal SAH. Iwanaga, et al., showed that focal blood in the interhemispheric fissure was highly predictive of an ACoA aneurysm on repeat angiography, even if the initial angiogram was normal. Our finding of a ruptured ACoA aneurysm in all four patients with interhemispheric blood on the CT scan substantiates their speculation that exploratory craniotomy may disclose an "active" ACoA aneurysm in patients with this CT finding.

In agreement with other authors, we found that SAH localized to the interpeduncular region on CT correlates with a nonaneurysmal origin of the hemorrhage. Van Gijn, et al., suggested that SAH in the perimesencephalic cistern might originate from veins or capillaries around the midbrain. Others have proposed leakage from the lenticulostriate or thalamoperforating vessels as the source of focal blood around the basal cisterns. Giombini, et al., noted psychological symptoms in their patients which they attributed to ischemia of the limbic lobe structures. Some authorities have attributed the bleeding to a microaneurysm or microanangioloma that undergoes thrombosis or "self-repair" at the time of hemorrhage. Extensive exploration of the basilar artery failed to reveal any abnormality in our patient with an interpeduncular SAH, lending strength to the above reports. Therefore, exploratory surgery should not be attempted in patients with SAH localized to the interpeduncular cistern if the cerebral angiograms do not reveal an aneurysm.

Angiography in Occult Cerebral Aneurysms

The question of whether a four-vessel cerebral angiogram should be repeated following an initially normal study has been debated extensively in the literature. Forster, et al., argued that repetition of angiography is seldom justified unless further episodes of hemorrhage occur. Brismar and Sundhärö stated that a normal pan-angiographic evaluation, with oblique views demonstrating all arterial bifurcations, almost excludes the possibility of an aneurysm. We have observed here that this is not always true. However, others have established false-negative angiogram rates of 11.7% to 16% in patients whose initial angiographic studies were negative, but in whom aneurysms were discovered on repeat angiography. Some have recommended repeating the study whenever a condition such as vasospasm, hematoma, or brain edema may have masked the cause of bleeding.

Several explanations have been offered for the non-visualization of an existing cerebral aneurysm on serial arteriography. The possible mechanisms include vasospasm, narrowing of the aneurysmal neck, alterations in blood flow, observer error, technical factors, and intra-aneurysmal thrombosis as promoted by systemic hypertension, cerebral vasospasm, a narrow neck, and antilibrinolytic therapy. In addition, temporary thrombosis of the aneurysmal sac with subsequent recanalization has been described. At surgery, we found each of the five aneurysms to be partially thrombosed, in agreement with this theory.

Rebleeding

While several studies have concluded that "SAH of unknown cause" has a benign prognosis, a number of patients eventually succumbed to a subsequent hemorrhage. Various series have reported rebleeding rates of 4.7% to 8.6%; some of these patients were later found to have aneurysms that were not detected during the initial diagnostic evaluation. Similar to all patients with unclipped aneurysms, their risk of rebleeding is significant. Due to the significant danger of rebleeding, as with all unoperated aneurysms, identification of those patients with angiographically occult aneurysms is crucial. This is clearly supported by the fact that three (50%) of the six patients in our study rebled while in the hospital and eventually were found at surgery to have aneurysms.

Management Strategies

Several authors have discussed their management protocols for patients presenting with clinically and CT-verified SAH, in whom the angiographic study is negative. In general, if the initial arteriogram shows evidence of vasospasm, then the study is repeated between 1 and 8 weeks later. If the second angiogram is negative, then the patients are discharged home and told to resume their usual activities of daily living. These patients are then followed clinically. However, if there is no vasospasm on the initial study, the patients are checked for evidence of a bleeding diathesis, systemic hypertension, drug ingestion, or symptoms suggestive of a spinal arteriovenous malformation, such as pain, myelopathy, or radiculopathy. The workup would then include a complete myelogram or, preferably, an MR image of the spine, followed by a spinal angiogram if either of the initial tests is suspicious for a vascular malformation.

On the basis of our finding of a positive surgical exploration in five of the six patients with negative angiographic evaluations, we propose an alternative management protocol for this small subgroup of patients in whom the index of suspicion for an aneurysmal SAH is high. If the CT scan localizes the hemorrhage to a specific cerebral blood vessel, particularly the ACoA, in a patient with clinically evident SAH, then four-vessel cerebral angiography should be repeated 1 week later. Furthermore, even if the repeat angiographic studies are unrewarding, we consider that exploratory surgery is justified in patients whose SAH is predominately basal interhemispheric in location. In agreement with previous studies, we believe that angiographically negative interpeduncular and perimesencephalic hemorrhages should not be explored. Even though exploration of the one patient with SAH localized to the sylvian fissure was positive for an MCA bifurcation aneurysm, we believe that further studies will be necessary to substantiate exploration of patients with this
CT finding. One may question our reason for repeating the angiogram in any patient with a localized basal frontal interhemispheric hemorrhage if we eventually operate on all such patients regardless of a negative study. We stress, as was found by Iwanaga, et al., that there is a significant probability of discovering an ACoA aneurysm on the repeat study in patients with this CT finding. If an aneurysm is detected on the repeat study, then the vascular anatomy can be defined preoperatively and the operative strategy can be optimized. If exploratory surgery is undertaken, one should approach the suspicious vessel first, and should be prepared to inspect the entire ipsilateral ICA and MCA distribution, as well as the ACoA complex and basilar apex regions.

While we believe that exploratory aneurysm surgery is justified when there is a high index of suspicion for an ACoA aneurysm on the basis of the clinical presentation, localized blood on a CT scan, or recurrent SAH in the same location, others have used different criteria to select surgical candidates. Di Lorenzo and Guidetti justified their decision to operate on the basis of their patients’ young age, absent history of hypertension or blood dyscrasias, CT evidence of blood in the basal and midline cisterns, and the presence of marked arterial spasm. However, the mean age of our patient population (54 years) was significantly older than that of Di Lorenzo and Guidetti’s patients. None of our patients had evidence of a blood dyscrasia. Similarly, the presence or absence of hypertension would not have altered our decision regarding surgical intervention, insofar as our explorations were based on the clinical and CT evidence. Angiographic vasospasm was not found to be predictive for the presence of an angiographically occult aneurysm in this series of patients.

It is not our intention to promote mistakes through excess, leading to useless operations. There are several shortcomings with our study. We do not know the number of patients on our service with true SAH of unknown etiology, nor do we know the number of patients whose aneurysms were discovered on repeat angiography, following an initially negative study. However, based on our limited experience with six patients, we believe that we have identified a small population of patients with angiographically occult aneurysms in whom exploratory surgery appears justified on the basis of clearly defined criteria. At present, aneurysms of the ACoA complex appear to be the only lesions that fall into this category. All of the currently available data suggest that angiographically negative interpeduncular and perimesencephalic SAH is not aneurysmal in origin and should not be explored in the face of a negative angiogram.

Conclusions

We conclude that exploratory aneurysm surgery is warranted in spite of repeated negative angiograms if the patient manifests the classical signs and symptoms of SAH with brain CT scans localizing blood to a specific cerebral blood vessel, particularly the ACoA, and if a second SAH is documented at the same site. We believe that the location of SAH blood on CT scans is more predictive than vasospasm for the location of a ruptured occult cerebral aneurysm. We consider that exploratory aneurysm surgery should not be attempted in perimesencephalic SAH if the cerebral angiogram is negative.

References

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