Correlation between angiographic vasospasm, hematoma, and ischemic brain damage following SAH


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The correlation between angiographic vasospasm, hematoma, and ischemic brain damage was studied in 29 patients who died as a result of subarachnoid hemorrhage following rupture of a saccular aneurysm. None of these patients was treated surgically. A comprehensive neuropathological examination was undertaken in each case. A significant relationship between the presence and degree of vasospasm and ischemic brain damage was found. Furthermore, even though intracerebral hematoma probably increased the risk of infarction associated with vasospasm, hematoma per se did not increase the incidence of ischemic brain damage.

KEY WORDS • angiographic vasospasm • hematoma • subarachnoid hemorrhage • ischemia

Even though cerebral vasospasm following subarachnoid hemorrhage (SAH) has been recognized angiographically since the early 1950's, its etiology and importance have been the source of considerable controversy. While some clinicians remain unconcerned about its importance, there are many reports that morbidity and mortality rise sharply when vasospasm accompanies SAH following rupture of a saccular aneurysm. It has been suggested that if vasospasm of the cerebral vessels produces a neurological deficit, it probably does so by a reduction of cerebral blood flow, but not all investigators have found such a correlation. It is also known that cerebral infarction is a not uncommon finding in such patients. In spite of these studies, there is continuing doubt about the exact correlation between angiographic evidence of cerebral vasospasm, intracranial hemorrhage, and ischemic brain damage.

More recently, patients with SAH have been studied by both angiography and computerized tomography (CT). For example, Davis, et al., found a correlation between the extent of subarachnoid clot, the clinical grade of the patient, and the severity of spasm preoperatively; and Bryan, et al., and Saito, et al., found a correlation between CT evidence of lucency (presumed cerebral infarction) and severe vasospasm. The association between vasospasm, intracranial hematoma, and cerebral infarction has been reported previously in a group of fatally head-injured patients. Surprisingly few studies, however, have demonstrated clearly similar correlations in patients dying after SAH, and so it was decided to document associations between vasospasm, intracranial hemorrhage, and cerebral infarction following spontaneous rupture of a saccular aneurysm in a group of patients who had not undergone surgery.

Clinical Material and Methods

Patient Population

The series comprised 21 female and eight male patients, ranging in age from 10 to 67 years, who were referred to the Institute of Neurological Sciences from other hospitals in the west of Scotland, and who subsequently died as a result of SAH following rupture of a saccular aneurysm.

The case records were reviewed and, on the basis of the recorded level of consciousness (Glasgow Coma Scale; GCS), a history of headache requiring analgesia, signs of neck stiffness, and severe neurological deficit, the patients were assigned to one of five clinical grades. The grades used were comparable to the levels in the Hunt and Hess system, but were assessed according to more rigorously defined criteria (Table 1):
TABLE 1
Age, sex, clinical grade, survival, and location of saccular aneurysms in 29 patients with SAH*

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Sex, Age (yrs)</th>
<th>Clinical Grade†</th>
<th>Previous SAH</th>
<th>Delay (days)</th>
<th>Site of Rupture</th>
<th>Second Unruptured Aneurysm</th>
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<td>10</td>
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<td>5</td>
<td>It MCA</td>
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</tbody>
</table>

* Abbreviations: MCA = middle cerebral artery; ACA = anterior cerebral artery; ACoA = anterior communicating artery; PCA = posterior communicating artery; SAH = subarachnoid hemorrhage; Angio = angiogram.
† Clinical grading according to Hunt and Hess, as modified.

Grade 1: GCS score of 15 without headache or neck stiffness;
Grade 2: GCS score of 15 with severe headache or neck stiffness;
Grade 3: GCS score of 13 or 14 without severe neurological deficit;
Grade 4: GCS score of 13 or 14 with severe neurological deficit or GCS score of 9 to 12; and
Grade 5: GCS score of 8 or less.

Carotid angiography was performed in each case at a time ranging from less than 24 hours to 33 days after the ictus. The patients survived from less than 24 hours to as long as 10 days after angiography; none was treated surgically. A full neuropathological examination was performed on all patients. The case notes were screened for evidence of hypoxia (PaO₂ of less than 50 mm Hg), hypotension (systolic blood pressure of less than 80 mm Hg for more than 15 minutes), and epilepsy, and a note was made of any drug treatment that the patient had received for these conditions.

Angiography
The angiography techniques used have been described previously. Briefly, the patients were anesthetized with thiopentone sodium, intubated, and moderately hyperventilated to give a PaCO₂ in the range of 30 to 35 mm Hg. Anesthesia was maintained with 30% O₂/70% N₂O, supplemented with fentanyl (Sublimaze), pentazocine (Fortral), or thiopentone. Contrast medium was injected by hand into the common carotid artery, and serial films were taken on a Barr and Stroud manual cassette changer.*

Arterial spasm was considered present when there was smooth circumferential tapered narrowing of cerebral arteries, with the sites of branching being relatively less affected. The severity of the spasm was determined by relating the caliber of the artery in spasm to that of the nearest area of apparently normal vessel, although in some cases when a long section was involved an estimate had to be made. When the reduction in caliber was less than one-third, the spasm was classified as Grade 1; when the reduction was between one-third

* Manual cassette changer (no longer being produced) was manufactured by Barr and Stroud, Caxton Street, Glasgow, Scotland.
Vasospasm and cerebral ischemia

### TABLE 2
Incidence and distribution of arterial spasm identified in hemispheres with and without ischemic brain damage*

<table>
<thead>
<tr>
<th>Associated Ischemic Brain Damage</th>
<th>Total Hemispheres</th>
<th>Spasm</th>
<th>Location of Spasm</th>
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<tr>
<td></td>
<td></td>
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<tr>
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<td>22</td>
<td>4</td>
<td>1</td>
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</tbody>
</table>

* Basal = distal internal carotid artery and/or proximal anterior and middle cerebral arteries; ACoA = anterior communicating or peripheral anterior cerebral artery; MCA = peripheral middle cerebral artery.

and two-thirds, Grade 2; and when it was greater than two-thirds, Grade 3. The distribution of spasm was recorded in each case.

Displacement across the midline of the internal cerebral vein or branches of the anterior cerebral artery, or both, was also recorded. When the displacement was between 1 and 5 mm, it was classified as Grade 1; when it was between 6 to 10 mm, Grade 2; and when it was greater than 10 mm, Grade 3. The autopsy findings were subsequently reviewed to establish whether or not an intracerebral hematoma had been identified, thus ensuring that the intracerebral space-occupying lesion was due, at least in part, to a hematoma, and not wholly to infarction with brain swelling.

### Neuropathology

The brains were fixed by immersion for at least 3 weeks in a 10% formal saline solution before dissection. Large representative bilateral blocks were taken from the cerebral and cerebellar hemispheres and from the brain stem. They were embedded in celloidin, and sections cut at 30 μm were stained by the method of Nissl using cresyl violet, and by Woelke’s modification of Heidenhain’s method (for examination of changes in myelin). The sections then were examined using a Watson stereomicroscope at a magnification between x 10 and x 40. Infarction was easy to identify in the longer surviving patients, whereas in patients surviving only 1 to 2 days the specific features of the ischemic cell process5,6 were identified by conventional light microscopy. Histological abnormalities were charted on line diagrams of the brain, the analysis of which formed the basis of this study.

A comprehensive autopsy was undertaken in every case. It included an examination of the full length of the common and internal carotid arteries and inspection of the upper and lower ends of the vertebral arteries. In many cases, the arch of the aorta and the neck arteries were removed in a single block and were dissected after fixation. Both the intracranial and extracranial cerebral arteries were examined at several levels.

### Statistical Evaluation

Statistical significance was determined by the chi-square test.

### Results

Three patients had a recorded episode of hypoxia, six experienced a period of hypotension, and five had one or more seizures after the initial SAH. Six patients were receiving antihypertensive drug therapy and one patient was 28 weeks pregnant at the time of presentation. None of the patients received antifibrinolytic therapy. Twenty-seven patients underwent bilateral carotid angiography and the other two had unilateral carotid angiography, which provided a total of 56 angiograms for analysis in this study. The results are based on a correlation between the angiographic appearances and the presence or absence of ischemic damage in the cortex of 56 hemispheres. Arterial spasm was documented in 26 (46%) of the 56 hemispheres; the distribution (Table 2) and the severity of spasm (Table 3)

### TABLE 3
Severity of arterial spasm and degree of midline displacement identified in hemispheres with and without ischemic brain damage

<table>
<thead>
<tr>
<th>Associated Ischemic Brain Damage</th>
<th>Total Hemispheres</th>
<th>Spasm Grade*</th>
<th>Midline Shift Grade*</th>
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<td></td>
<td></td>
<td>3 2 1 Total</td>
<td>3 2 1 Total</td>
</tr>
<tr>
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<td>1 1 1 1</td>
<td>1 1 1 3</td>
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<tr>
<td>absent</td>
<td>22</td>
<td>1 1 2 4</td>
<td>1 3 3 4</td>
</tr>
</tbody>
</table>

* For definition of grading see Materials and Methods, under Angiography.
were recorded. Arterial spasm was not seen on the carotid angiograms in 30 hemispheres. Intracerebral hematomas were present in 22 (39%), and hematomas combined with spasm in 13 hemispheres (23%).

There was focal ischemic damage in the cortex of 34 (60%) of the 56 hemispheres (excluding necrosis due to cardiorespiratory arrest, status epilepticus, and agonal hypotension, and necrosis within the distribution of the posterior cerebral artery as a result of tentorial herniation). In 28 (82%) of these 34 hemispheres there was infarction within the distribution of either the anterior or the middle cerebral arterial territory, or both; and in six there was infarction in the boundary zones between the distributions of the major cerebral arteries, particularly in those between the territories of the anterior and middle cerebral arteries.

Using the criteria defined by Adams and Graham, there was evidence of raised intracranial pressure in 24 of the 29 patients; in 16 of these 24, there was ischemic damage in the cortex. The majority of the patients, therefore, died from the effects of raised intracranial pressure with tentorial herniation and resultant damage to the brain stem; the rest died from intercurrent infection.

There was a variable amount of atheroma in the intracranial and extracranial arteries, but 26 patients had neither angiographic nor postmortem evidence of appreciable stenosis or occlusion. Of the remaining three patients, one had fibromuscular hyperplasia of the carotid artery, one had thrombosis of the common carotid artery following angiography, and in one the internal carotid artery had been ligated therapeutically some 2 years previously. The findings in these latter three patients were included in the analysis, as there was no correlation between the findings at death and the preexisting vessel disease. A congenital variation of the circle of Willis and/or its major branches was identified in seven patients.

Evidence of left ventricular hypertrophy in the absence of valvular heart disease (greater than 350 gm) was identified post mortem in 17 patients. One patient had active pulmonary tuberculosis, and another had bilateral hydronephrosis and hydronephrosis because of obstruction at the bladder neck.

### TABLE 4

<table>
<thead>
<tr>
<th>Associated Ischemic Brain Damage</th>
<th>Hematoma Location</th>
<th>Frental</th>
<th>Temporal</th>
<th>Elsewhere</th>
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<tr>
<td>absent</td>
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<td>1</td>
<td>3</td>
<td>0</td>
</tr>
</tbody>
</table>

\* Abbreviations: ACA = anterior cerebral artery; MCA = middle cerebral artery.

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**Correlations**

**Arterial Spasm**

Of the 26 hemispheres with spasm, with or without a coexisting intracerebral hematoma, there were 22 in which ischemic damage was present in the cortex (Table 3). In 20 hemispheres the ischemic damage was in the distribution of the affected artery; in one there was spasm of the middle cerebral artery and ischemic damage within the distribution of the ipsilateral anterior cerebral artery; and in one there was infarction in the arterial boundary zone.

Of the 34 hemispheres with ischemic damage, there was arterial spasm in 22 (65%), as compared with four (18%) hemispheres with spasm among the 22 nonischemic hemispheres ($p < 0.005$). Furthermore, we found evidence of vasospasm in 21 (75%) of the 28 hemispheres in which there was infarction within arterial territories, whereas there was evidence of vasospasm in only four (18%) of the 22 hemispheres without infarction ($p < 0.001$).

Severe spasm (Grade 2 or 3) correlated significantly with the presence of ischemia ($p < 0.01$), particularly when arterial territory infarction was considered. There were 15 hemispheres with arterial territory infarction in which the vasospasm was either Grade 2 or 3, as compared with only two hemispheres without ischemic hemispheres in which a similar degree of vasospasm was found ($p < 0.005$).

Considering only those hemispheres with spasm but without an intracerebral hematoma, 10 (63%) of the 16 hemispheres with ischemic damage had spasm, whereas only three of 18 hemispheres (17%) without ischemia had spasm ($p < 0.025$). This was even more striking when only infarction in arterial territories was considered; 10 (77%) of 13 hemispheres with arterial territory infarction had spasm, as compared to 17% (three of 18) of hemispheres with spasm but no infarction ($p < 0.005$). There was no correlation between boundary zone infarction and the presence of spasm.

**Intracerebral Hematoma**

Of the 22 hemispheres with intracerebral hematoma, there were 18 with ischemic damage in the cortex: 15 with infarction in arterial territories and three with boundary infarction (Table 3). In 18 (53%) of the 34 hemispheres with cortical infarction there was an ipsilateral hematoma, as compared with four (18%) of the 22 nonischemic hemispheres in which a hematoma was present ($p < 0.025$). When the different distribution patterns of ischemic brain damage were considered, significant correlations were seen when the 15 hemispheres in which a hematoma coexisted with arterial territory infarction were compared with the four hemispheres with hematoma but without ischemia ($p < 0.025$). There was no significant relationship between boundary zone infarction and the presence or absence of intracerebral hematoma. Hematomas associated with displacement of midline cerebral vessels by greater than
5 mm correlated significantly with the presence of infarction (p < 0.05).

There was an exact correlation between the site of hematoma formation and location of ischemic damage in the 15 hemispheres with infarction within the distribution of arterial territories (Table 4). The eight hemispheres in which there was a hematoma in the frontal region had infarction within the distribution of the anterior cerebral artery; and in the seven hemispheres in which the hematoma was in the temporal region, there was infarction within the distribution of the middle cerebral artery.

Arterial Spasm and Intracerebral Hematoma

Arterial spasm and intracerebral hematoma were found combined in 12 (35%) of the 34 hemispheres with cortical infarction, as compared with one (5%) of the 22 hemispheres in which there was no ischemic damage (p < 0.025). The results are summarized in Table 5. There also was a significant relationship between infarction within arterial territories and the presence of spasm and a hematoma (p < 0.025). A comparison of the hemispheres in which there were both spasm and a hematoma with the hemispheres that had neither of these showed that the presence of both lesions increased the likelihood of infarction (p < 0.005), and in particular increased the likelihood of arterial territory infarction (p < 0.001).

Neither Spasm Nor Intracerebral Hematoma

Spasm and hematomas were absent in only six of the 34 hemispheres with cortical infarction, as compared with 15 of the 22 nonischemic hemispheres (p < 0.001). There was also a correlation between the absence of spasm and hematoma and the absence of infarction within arterial territories (p < 0.001).

There was no correlation between ischemic brain damage and other conceivably causal or exacerbating factors, such as the time interval between ictus and angiography or between angiography and death, the extracranial or intracranial location of the disease, the development of epilepsy, or an episode of hypoxia. The findings show a significant relationship between spasm, the site of intracerebral hematoma, or both, and the presence and location of ischemic damage within arterial territories of the ipsilateral cortex.

Discussion

Clinical Importance of Vasospasm

Despite the many clinical and experimental studies of angiographic vasospasm, there is as yet no uniform agreement regarding its clinical relevance. Most of the recent reports reflect the opinion that vasospasm increases the risk of ischemic brain damage after aneurysm rupture. Other results refute the importance of vasospasm in adding to morbidity or mortality after SAH, leaving the relationship between vasospasm and brain ischemia in doubt.

Although not all patients with angiographic vasospasm have neurological deficits, deficits generally occur when spasm is widespread and severe. Vasospasm correlates with the patient's clinical grade at the time of angiography and with the presence of contralateral hemiparesis, but not with confusion or depressed levels of consciousness (unpublished observation). When neurological abnormalities accompany vasospasm, changes in consciousness may occur in patients with vasospasm around aneurysms in any location, but focal paresis is most prevalent in patients with middle cerebral artery aneurysm rupture and surrounding vasospasm, and abulia is seen with spasm of the anterior cerebral arteries.

Preoperative vasospasm appears to increase the risk of death or disability after aneurysm surgery. Severe spasm is reported to produce higher mortality and greater morbidity than does mild or moderate spasm, although the relationship between severe spasm and poor clinical grade has not been observed in all series. Nonetheless, the fear of these effects of vasospasm has led many surgeons to modify their management of ruptured intracranial aneurysms, to try to prevent progressive neurological injury or death from...
cerebral ischemia after what would seem to be appropriate and technically faultless treatment of SAH.

**Saccular Aneurysms, SAH, and Infarction**

Robertson, et al. found cerebral infarcts in five of 93 cases of ruptured aneurysm. An incidence of 45% was reported by Wilson, et al. Tomlinson, in a series of 32 cases, reported infarcts in 78% of cases; 40% of these were massive infarcts. Of 17 patients examined by Hirano, et al., seven had cerebral infarcts, of whom five had undergone surgery; only two of 11 who did not have surgery had infarcts. Birse and Tom found cerebral infarction identified mainly by light microscopy in seven of eight patients with anterior cerebral artery aneurysms; none had undergone surgery, but all had had angiography. In addition, among seven patients with middle cerebral or posterior communicating artery aneurysms (six of whom had undergone surgery), five also had cerebral infarcts. Crompton, in a series of 159 patients, reported a 75% incidence of significant cerebral infarction, which he defined as necrosis of one-third or more of the cortical distribution of one of the major arteries, or ganglionic necrosis of 5 mm in diameter or more. In a study of 105 cases, some with and others without angiography or surgery, Schneck described cerebral infarcts in 58%. Tomlinson, in his second series of 75 cases which included the 32 cases reported previously, again found massive infarcts in 40% and smaller lesions in an additional 40%.

In summary, it was thought initially that cerebral infarction in patients with SAH from the rupture of a saccular aneurysm was uncommon or rare. However, a considerably higher incidence has been reported subsequently, probably indicating more widespread awareness of the association between these two entities. The incidence of ischemic brain damage also depends on patient selection and early management of the patients, and especially on whether surgery is performed soon after ictus or is delayed. It also depends on the histological techniques (small paraffin or large celloidin sections) used to identify whether or not, and to what extent, ischemic damage is present. In our study, infarction of the cortex was a common complication, occurring in 60% of hemispheres.

**Pathogenesis of Cerebral Infarction**

Previous studies have paid little attention to the possible effects of angiography and surgery on the incidence and distribution of cerebral infarction; hence, few reports have demonstrated the correlation between vasospasm and cerebral infarction. Our study was restricted to patients who had not had an operation, so unless angiography caused infarction, the 60% infarction rate in our series must be the result of the effects of aneurysm rupture alone.

Various mechanisms for infarction with SAH have been proposed; namely, spasm alone or in combination with intracerebral hematomas, the mass effect of some aneurysms, extension of aneurysm thrombus into the parent vessel, or extracranial vascular occlusion might give rise to cerebral infarction after aneurysm rupture. Tomlinson presented a detailed discussion of some of these mechanisms in reporting the results of autopsy in patients who died after aneurysm rupture. He noted that infarction after SAH was not more frequent in older patients—a finding that argues against, but does not exclude, a role of atheroma. Furthermore, he did not find any emboli arising from aneurysm thrombus, and there was no difference in infarction rates between patients who had thrombus of the aneurysm sac and those who did not. There was also no evidence that thrombi extended distally from the site of aneurysm formation along major arteries. He found no association between infarction and systemic hypotension, pulmonary complications, or the use of medications.

Tomlinson identified SAH near a number of infarcts, and proposed that the tearing of small vessels by hematomas might result in necrosis of subjacent brain. Crompton described necrotic vessels within subarachnoid hematoma, but Tomlinson identified only rare examples of arteries in such hematomas and found no torn vessels in distended sulci. Nonetheless, he felt there was "good reason to suppose that subarachnoid hematomas are of prime importance in the pathogenesis of cerebral infarction in this condition, largely through stretching or distorting the major arteries, thereby inducing spasm in them, and possibly through tearing of their small branches." More recent studies have confirmed by CT finding that large collections of subarachnoid blood significantly increase the likelihood of vasospasm and cerebral infarction.

Perhaps the theory that has aroused the most controversy is that cerebral infarction subsequent to SAH is due to vasospasm of cerebral arteries. Schneck, in his first series, found that 65% of 23 patients with vasospasm had infarcts, but 82% of 28 patients without vasospasm also had lesions. In a second series, Schneck and Kricheff reported vasospasm in 62%, and no vasospasm in 38%, of patients with infarction—but, when they viewed the cases another way, they found that 62% of patients with infarction and 57% of those without infarction had vasospasm. They concluded that there was little direct correlation between the two entities, but speculated that vasospasm may be an initial cause of cerebral ischemia which, when aggravated by surgery or compression by a hematoma, progressed to frank infarction. Crompton, however, did find a possible relationship when he recorded vasospasm in 37% of 109 patients with cerebral infarction and in only 12% of 33 patients without infarction. He found in almost every case that the infarct occupied part or all of the territories of the arteries affected by vasospasm, but he did not consider vasospasm to be the only cause.

Our study clearly demonstrates a significant relationship between the presence and degree of vasospasm and ischemic brain damage. Although we found that intra-
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cranial hematoma probably increased the risk of infarction associated with vasospasm, hematoma alone did not increase the incidence of infarction. We believe that these data support the contention that vasospasm contributes adversely to outcome after aneurysm rupture, and that research into defining methods for preventing and treating cerebral vasospasm should be encouraged.

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References

36. Schneck SA: On the relationship between ruptured intra-

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