Subarachnoid Hemorrhage Without Detectable Aneurysm
A Review of the Causes

Gabriel J.E. Rinkel, MD; Jan van Gijn, MD, FRCPE; Eelco F.M. Wijdicks, MD

Background: In 15% to 20% of patients with a spontaneous subarachnoid hemorrhage, no aneurysm is found on the first angiogram. This review emphasizes that this group of patients is in fact heterogeneous and describes the clinical features, pattern of hemorrhage on early computed tomographic (CT) scan, prognosis, and proposed management in the several and distinct subsets of these patients.

Summary of Review: Patients in whom no aneurysm is revealed on the initial angiogram can be subdivided mainly according to the pattern of hemorrhage on an early CT scan. In two thirds of these patients the CT scan shows a perimesencephalic pattern of hemorrhage (ie, blood confined to the cisterns around the midbrain); these patients invariably have a good prognosis, which obviates the need for a second angiogram. Patients with diffuse or anteriorly located blood on CT scan are at risk of rebleeding. In most of these patients the source of hemorrhage is an occult aneurysm, but intracranial artery dissections, dural arteriovenous malformations, mycotic aneurysms, trauma, bleeding disorders, substance abuse, or a cervical origin of the hemorrhage should also be considered. Patients with no blood revealed on an early CT scan but with xanthochromic cerebrospinal fluid are extremely rare. These patients deserve a second reading of the scan for blood in the preptontine cistern, which can be the only site of hemorrhage in perimesencephalic hemorrhage.

Conclusions: The prognosis and management of patients in whom no aneurysm is found on the initial angiogram depends on the pattern of hemorrhage on the initial CT scan. Patients should no longer be designated with the umbrella term "angiogram-negative subarachnoid hemorrhage." (Stroke. 1993;24:1403-1409.)

KEY WORDS • aneurysm • angiography • dissection • subarachnoid hemorrhage

In 15% to 20% of patients with spontaneous subarachnoid hemorrhage, no aneurysm is found on four-vessel angiography. A plethora of reports has addressed the outcome in these patients. Early CT scanning, however, was often not performed in these patients; this drawback precludes the recognition of subgroups according to source and prognosis. Moreover, demonstration of blood pigments in the cerebrospinal fluid in patients without CT confirmation of the hemorrhage was required in only a few studies, and the remaining studies may have included patients with innocuous thunderclap headaches followed by a traumatic lumbar puncture. Despite the imperfections in methodology, these studies indicated that the prognosis of patients with "angiogram-negative subarachnoid hemorrhage" is better than that of patients with a detected aneurysm. However, outcome is not always favorable; rebleeding, cerebral ischemia, and acute hydrocephalus have been reported in up to 20% of these patients. Furthermore, 10% to 30% of patients who survive do not recover to their previous state.

The small yield of aneurysms detected by repeat angiography must be weighed against the risks of cerebral angiography. In a recent study complications occurred during repeated angiography of the vertebrobasilar arteries in three of 16 patients in whom the initial angiogram was normal. At present, however, there are no safe techniques that are as reliable as angiography in the detection of aneurysms. High-resolution computed tomography correctly identifies large aneurysms but fails to detect one third of aneurysms smaller than 6 mm. Magnetic resonance (MR) angiography is a promising technique, but its value in detecting "occult" aneurysms has not yet been proved.

According to the pattern of hemorrhage on CT scan, it is now possible to identify subsets within the larger group of patients in whom the initial angiogram reveals no aneurysm. This partition has grave implications for prognosis and management of these patients and allows selection for repeated angiography of only those patients who are at risk of rebleeding. This review describes the clinical features, patterns of hemorrhage on CT scan, prognosis, and proposed management of the different causes of subarachnoid hemorrhage without detectable aneurysm.
argue against a ruptured aneurysm as the source of the hemorrhage. Rupture of a dilated vein or a venous malformation in the preptontine or interpeduncular cistern seems a reasonable hypothesis.

The invariably good outcome and the absence of rebleeding in the long term obviate the need for repeated angiograms.

**Trauma**

In some patients with shearing injury, pronounced accumulation of blood can be found in the posterior part of the ambient cistern at the level of the tentorial margin. Blood confined to the ambient cistern has also been reported in a patient undergoing anticoagulant treatment, with a relatively mild trauma (fall in the shower). The blood in the ambient cistern may be part of more extensive intracranial hemorrhage, but it can be the main site of hemorrhage (Fig 2). The site of the hemorrhage excludes a ruptured saccular aneurysm as the source of the hemorrhage. The cause of the hemorrhage in these patients is probably the grazing of a vein against the tentorial edge.

**Diffuse or Anteriorly Located Hemorrhage in the Basal Cisterns**

The clinical features and particularly the outcome of patients with diffuse or anteriorly located blood in the basal cisterns are in stark contrast to those of patients with perimesencephalic hemorrhage. In a recent report of 36 such patients, 8 were drowsy or stuporous on admission, and 2 had a focal deficit. During the initial hospital period, 3 patients had a rebleed, which was fatal in 2; 5 patients had symptomatic acute hydrocephalus; and another patient deteriorated from cerebral ischemia. On long-term follow-up, an additional patient died from rebleeding. Altogether, 3 of the 36 patients died and 6 were left disabled as a result of hemorrhage. In two other studies in which patients with angiogram-negative subarachnoid hemorrhage were subdivided according to the pattern of hemorrhage on CT, all patients with complications and poor outcome had a nonperimesencephalic pattern of hemorrhage, whereas all patients with a perimesencephalic hemorrhage had a good outcome. In most patients with poor outcome in these studies, the
center of the bleeding was located in the anterior interhemispheric fissure.

Several causes of bleeding should be considered in patients with a normal angiogram who show a diffuse or anteriorly located hemorrhage in the basal cisterns; in this list, nonvisualized (occult) aneurysms are a large majority.

**Insufficient Examination of the Posterior Circulation**

Despite the widespread use of four-vessel angiography and the technical improvement, angiography of the posterior circulation remains a difficult procedure, and the angiogram should be reviewed for proper visualization of the branches of both vertebral arteries if no aneurysm is found.

A ruptured aneurysm of the posterior circulation can often be suspected from the distribution of the blood on an early CT scan. Up to 85% of these patients show marked intraventricular bleeding that is found predominantly in the fourth (and to a lesser extent in the third and lateral) ventricle. In one fourth of patients with posterior circulation aneurysms, intraventricular hemorrhage is the only finding. Subarachnoid blood, if evident on the CT scan, is usually centered around the midbrain; in addition, it symmetrically extends to the anteriorly located basal cisterns. In patients with such a pattern of hemorrhage, repeated angiography should certainly be performed, with specific attention to the branches of the vertebral arteries.

**Occult Aneurysm**

Although it has been argued that repeating the angiogram is useless, combined data of seven studies on patients with angiogram-negative subarachnoid hemorrhage reveal that 135 repeated angiograms demonstrated no less than 22 aneurysms. If one takes into account that patients with perimesencephalic hemorrhage were not excluded from these series, the yield of follow-up angiograms in patients with diffuse or anteriorly located hemorrhage on CT scan must be even higher.

A hidden aneurysm should be suspected in particular patients with extensive extravasation of blood in the anterior interhemispheric fissure or the sylvian fissure. In a recent report of patients with an initially normal angiogram, a repeated study revealed an aneurysm in 7 of 10 patients with blood predominantly in the anterior interhemispheric fissure and in 1 of 3 patients with blood predominantly in the sylvian fissure. In such patients even a second normal angiogram does not definitively exclude an aneurysm (Fig 3). A third angiogram seems indicated in such patients, although this strategy has never been consistently evaluated.

**Vertebral Artery Dissection**

The proportion of all patients with subarachnoid hemorrhage in whom this is caused by vertebral artery dissection is unknown, but in a recent autopsy series a dissection was found in 5 of 110 patients who died from subarachnoid hemorrhage. Most patients are middle-aged, and approximately one third are being treated for hypertension.

A vertebral artery dissection should be suspected in patients with a recent history of uncommon neck movements (with painting the ceiling, for instance) or of minor trauma such as chiropractic neck manipulation, although dissection can also occur without precipitating trauma. Another clue to the diagnosis may be the presence of lower cranial nerve palsies, Horner's syndrome, or more extensive lateral medullary syndromes.

In dissection with subarachnoid hemorrhage, CT scans show blood throughout the basal cisterns and often intraventricular blood as well, particularly in the fourth and third ventricles. Angiographically the diagnosis rests on the demonstration of narrowing of the artery with signs of intimal flap, a pseudoaneurysm, or a double lumen; however, these features may be absent on an initial angiogram. In a series of 14 patients with a vertebral artery dissection, the first angiogram was normal in 2 and showed only nonspecific arterial narrowing in 2 others; in these 4 patients only the second angiogram revealed the characteristic abnormalities. A second angiogram is not always diagnostic because dissecting aneurysms may resolve spontaneously. CT or MR imaging may detect a thrombus within the false lumen of the dissection, a finding that also confirms the diagnosis.

Rebleeds occur in 30 percent of patients, sometimes within hours of the initial hemorrhage but in other cases after several weeks; these are fatal in half the patients. Approximately half the reported patients have had a good outcome.

**Carotid Artery Dissection**

Very few patients with subarachnoid hemorrhage from carotid artery dissection have been described. The presenting features are the same as in aneurysmal rupture: a severe headache of sudden onset that may be accompanied by focal deficits, a depressed level of consciousness, or both. The patterns of hemorrhage on the CT scans of patients with carotid artery dissection are indistinguishable from those of patients with ruptured saccular aneurysms. CT-documented rebleeds have been reported; these may occur within a few hours of the initial hemorrhage.

The diagnosis should be considered in patients in whom the angiogram shows localized nonspecific nar-
rowing of the carotid artery. Repeated angiograms may disclose the true cause of the hemorrhage in these patients.49

Dural Arteriovenous Malformation

Dural arteriovenous malformations (AVMs) of the tentorium can give rise to a basal hemorrhage that is indistinguishable on CT scan from aneurysmal hemorrhage.51 The anomaly is rare and can be found from adolescence up to old age.

A history of a head injury with a skull fracture should raise the suspicion of a dural shunt, since healing of a skull fracture may be accompanied by the development of a dural AVM.52 In patients in whom CT scanning suggests a tentorial origin of the hemorrhage and in whom the angiogram seems normal, the angiogram should be reviewed again, with the possibility of an AVM in mind. If once again no lesion is found, repeat angiography is indicated, including visualization of the external carotid artery because branches of this artery can be the main or the sole feeders.53 Rebleeding may occur in patients with dural AVMs; in a series of 28 patients, 5 presented with subarachnoid hemorrhage, and 3 of these 5 had one or more rebleeds.54

Spinal Arteriovenous Malformation

Subarachnoid hemorrhage is the mode of presentation in approximately 10% of patients with a spinal AVM; in more than half these patients, the first hemorrhage occurs before the age of 20.55,56 If the malformation is located high in the cervical region, the symptoms at onset may be indistinguishable from those with an intracranial source of subarachnoid hemorrhage,56 and CT may show blood throughout the basal cisterns and ventricles.57 Specific attention should be given to a history of severe pain in the lower part of the neck or pain radiating to the shoulders or arms.57 If even these clues are absent, the true origin of the hemorrhage emerges only when spinal cord dysfunction develops after a delay that may be as short as a few hours or as long as a few years.56,58 Vertebral or spinal angiography can demonstrate the lesion, but this procedure is not always diagnostic,56,58 it is impractical without localizing signs or symptoms, and it carries a greater than 5% risk that persisting neurological deficit will ensue.59 At present, MR imaging in the sagittal plane seems to be the first line of investigation. Rebleeds occur in half the patients who survive the initial bleed,60 and eventually less than 10% of patients who have bled once remain asymptomatic thereafter.61

Trauma

In most patients with trauma, the subarachnoid hemorrhage is located in the superficial cortical sulci, adjacent to a fracture or intracerebral contusion. Particularly in patients with basilar frontal contusions, the pattern of hemorrhage can resemble rupture of an anterior communicating artery aneurysm. In patients with direct trauma to the neck or with head injury that provokes vigorous neck movement, the trauma can immediately be followed by a massive basal hemorrhage that results from a tear or even a complete rupture of one of the arteries of the verteobasilar circulation.62,63 These lesions are often rapidly fatal.62,63

Mycotic Aneurysms

The most frequent causes of mycotic aneurysms are infective endocarditis and aspergillosis. In patients with infective endocarditis, most aneurysms are located on distal branches of the middle cerebral artery, but approximately 10% of the aneurysms are more proximally located.64 Rupture of a mycotic aneurysm gives rise to an intracerebral hematoma in most patients, but some patients have a pattern of hemorrhage indistinguishable on CT from that of a ruptured saccular aneurysm.65 CT-documented rebleeds have been reported.65 Most patients present with valve endocarditis before subarachnoid hemorrhage occurs, but rupture of a mycotic aneurysm can be the initial manifestation of infective endocarditis.66,67 In older series, 10% of mycotic aneurysms were missed by angiography,68 but even now the initial angiogram may be normal. The aneurysms in these patients can be found on repeated angiograms69; however, if angiography is repeated after too long an interval, it may be truly normal because mycotic aneurysms can resolve after antibiotic therapy.64

Mycotic aneurysm in patients with aspergillosis are usually located on the proximal part of the vertebrobasilar or carotid artery.69 Rupture of such an aneurysm causes a massive subarachnoid hemorrhage in the basal cistern, indistinguishable from that associated with a saccular aneurysm.70 In some cases the initial angiogram is normal and only repetition of the study reveals the aneurysm.70 Rupture of a mycotic aneurysm in patients with aspergillosis is often fatal.69

Cocaine Abuse

In half the patients with subarachnoid hemorrhage related to the use of the alkaloid form of cocaine, no aneurysm is demonstrated by angiography.71 The pattern of hemorrhage revealed on CT scan is indistinguishable from that of a ruptured saccular aneurysm,72 and the diagnosis rests on a confirmatory history or the results of toxicological tests. Rebleeds do occur, even in patients with a normal angiogram.73 Outcome seems poor for these patients: four of five recently reported patients had died after the cocaine-related subarachnoid hemorrhage.73 The source of the hemorrhage in patients without an aneurysm is unknown. Although biopsy-proven vasculitis has been found in patients with cocaine abuse,74 angiograms of patients with subarachnoid hemorrhage related to cocaine abuse do not show changes suggestive of vasculitis.73,75

Sickle Cell Disease

Subarachnoid hemorrhage is a rare complication of sickle cell disease.76 Thirty percent of patients with sickle cell disease and subarachnoid hemorrhage are children.77 CT scans performed in these children show blood in the superficial cortical sulci; angiograms reveal no aneurysm but often show multiple distal branch occlusions and leptomeningeal collateral circulation.77 The subarachnoid hemorrhage is attributed to rupture of these collaterals. The outcome is poor: only three of the 11 recently reviewed children had a good outcome.77 Most adult patients with sickle cell disease–related subarachnoid hemorrhage have an aneurysm. The hemorrhage is located diffusely in the basal cisterns,78 and
the outcome is comparable to that of patients with ruptured saccular aneurysms.77

Coagulation Disorders
Anticoagulation-related subarachnoid hemorrhage seems rare. In a series of 116 patients with anticoagu-
lant treatment and intracranial extracerebral hemor-
rrage, 7 had only subarachnoid hemorrhage. In two of
these 7 patients the hemorrhage was associated with
trauma, and in two other patients an aneurysm was
found by angiography.79 Thus, in only three of these
patients no other cause for the hemorrhage than anti-
cogulation was found.

Severe coagulopathy other than by anticoagulant is
also a rare cause of hemorrhage confined to the sub-
arachnoid space. In a recent series of 13 patients with
intracranial hemorrhage after liver transplantation, only
three had a subarachnoid hemorrhage on CT.80 In all
patients but one in this series, the intracranial hemor-
rrage was associated with systemic bleeding.80

Pituitary Apoplexy
Pituitary apoplexy has been proposed as one of the
causes of subarachnoid hemorrhage of unknown
cause.81 The initial features consist of a sudden and
severe headache, followed by nausea, vomiting, neck
stiffness, and sometimes a depressed level of conscious-
ness.82 The hallmark of pituitary apoplexy is that most
patients suffer a decrease in visual acuity or double
vision. In one series of 15 patients, only 2 had normal
visual acuity; 9 had an oculomotor nerve palsy, 6 an
ducbens nerve palsy, and 3 a trochlear nerve palsy.83
CT and MR scanning indicate the pituitary fossa as the
source of the hemorrhage; in most instances the ade-
noma itself is also visible.84,85

Miscellaneous Causes
Other (exceedingly rare) lesions that can give rise to
subarachnoid hemorrhage in the basal cisterns and a
normal angiogram are a cervical tumor, such as a
meningioma,85 and rupture of a small circumferential
artery in the pontine cistern.86

Patients With Normal CT Scan
and Normal Angiogram
Patients with clinical features of spontaneous sub-
arachnoid hemorrhage and xanthochromia in the cere-
brospinal fluid (demonstrated by spectrophotometry) in
whom no blood is found on a CT scan performed within
3 days of onset of hemorrhage deserve a second reading
of the scan. Particular attention should be paid to the
prepontine cistern because in some patients with a
“perimesencephalic” hemorrhage this cistern is actually
the only one in which subarachnoid blood is seen.28 We
found only three normal CT scans in a personal series of
116 patients with subarachnoid hemorrhage and a
normal angiogram.87 The CT scans of these patients
were made on the first or second day after the hemorrhage.
All three had a good outcome after a median period
follow-up of 55 months.

Conclusions
The pattern of hemorrhage on an early CT scan is an
invaluable guide to the management of patients with
subarachnoid hemorrhage in whom no aneurysm is
found on the initial angiogram (Table). The potential
risks of angiography debar injudicious repeat studies.

Patients with perimesencephalic hemorrhage (blood
confined to the cisterns around the midbrain, perhaps
with some extension to the suprasellar cisterns but not
to the anterior interhemispheric fissure, lateral sylvian
fissure, or the ventricles) run an uncomplicated course
and invariably have an excellent outcome, also in the long term. A ruptured vein is the most probable cause, although this has not yet been confirmed. Follow-up angiography is not indicated in these patients.

Patients with a pattern of hemorrhage in the basal cisterns that is more extensive than that of the perimesencephalic type are at risk of a fatal rebleed from an occult aneurysm; we therefore urge follow-up angiograms in this group unless review of the initial angiogram reveals signs of vertebral artery dissection or a mural AVM. An occult aneurysm should be suspected particularly in patients with thick, localized clots in the anterior interhemispheric or sylvian fissure, and even a second normal angiogram does not definitively exclude an aneurysm in these patients.

Other, but rare causes of extensive hemorrhage in the basal cisterns without a detectable aneurysm are trauma, mycotic aneurysm, bleeding disorders, cocaine abuse, or a spinal AVM. The diagnosis of trauma and mycotic aneurysm is usually straightforward from the history. Cocaine abuse should specifically be queried and can be confirmed by results of toxicological tests. Bleeding disorders can be inferred from systemic bleeding, history, and appropriate laboratory tests. Pain radiating to the shoulders or to the arms suggests a cervical origin of the hemorrhage.

Patients with true subarachnoid hemorrhage (xanthochromic cerebrospinal fluid) in whom no blood is found on an early CT are extremely rare. If there are no features suggestive of a spinal AVM, repeat angiography is warranted; this is especially true in patients with focal deficits or loss of consciousness because these features are incompatible with an idiopathic perimesencephalic hemorrhage.

The term "angiogram-negative subarachnoid hemorrhage" is meaningless in both individual patients and follow-up studies if no specification of the pattern of hemorrhage on CT is given. Physicians, researchers, and editors should abandon this blanket term.

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G J Rinkel, J van Gijn and E F Wijdicks

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