DECISION MAKING IN PATIENTS WITH SUBARACHNOID HEMORRHAGE*

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SUMMARY

Diagnostic and therapeutic management options in cases of subarachnoid hemorrhage secondary to aneurysm rupture are discussed. Particular emphasis is given to the diagnosis, medical treatment and timing of surgery. The problems raised by the presence of an intracerebral hematoma, acute hydrocephalus and multiple aneurysms are reviewed. The author also discusses the management of incidental aneurysms, partially treated lesions, familial and genetic aneurysms, lesions which ruptured during pregnancy or associated with arteriovenous malformations, and the question of a negative angiogram in cases of subarachnoid hemorrhage.

RESUMO

Decisão clínica na hemorragia subaracnoideia

O artigo revê as várias opções diagnósticas e terapêuticas em casos de hemorragia subaracnoideia secundária a rotura aneurismática. Dá particular ênfase ao diagnóstico, tratamento médico, e à data da cirurgia em relação à rotura. Trata ainda dos problemas específicos levantados pela presença de hematoma intracerebral, hidrocefalia aguda e aneurismas múltiplos. Analisa criticamente o problema dos aneurismas assintomáticos, parcialmente tratados, familiares ou de base genética, ocorrendo durante a gravidez e associados a malformações arteriovenosas. Finalmente discute as implicações práticas da angiografia negativa em casos de hemorragia subaracnoideia.

In this review I will analyse only management options in subarachnoid hemorrhage (SAH) secondary to aneurysm rupture. Intracranial bleeding related to arteriovenous malformations, cavernous angiomas, tumors or other intracranial processes pose different kinds of questions which are beyond the scope of this paper.

It is important to emphasize that aneurysmal rupture represents about 6.7% of all strokes, and its average incidence is about 10/100.000/year [1]. The seriousness of this condition is well underlined by the fact that 10% will die rapidly, and the global mortality at 3 months is close to 50%. Of the survivors, 25% will have a major disability. A significant number of patients will die or will be severely impaired by the direct effect of the initial rupture, and these cannot be helped. However, early diagnosis, and particularly the recognition of the significance of *warning leaks*, as well as an aggressive detection of complications such as vasospasm, acute hydrocephalus, electrolyte imbalances, etc, will certainly help to improve the bleak outlook of this condition.

I have selected a number of aspects of the clinical problem of HSA secondary to aneurysm rupture to illustrate some of the important options in the pratical management of these patients. Technical aspects of surgery or the role of the new endovascular procedures were purposefully omitted.

The Diagnosis of SAH

The diagnosis of SAH is a clinical one, always requiring confirmation through imaging of the neural structures or examination of the cerebrospinal fluid (CSF) (Fig. 1).

The first test to be obtained in a patient with a suspected SAH is a Computed Tomography of the cranium (CT) which is particularly reliable in the first 72 hours. Indeed, CT is positive in 95% of the cases on the day of SAH, 90% after one day, 80% after 5 days, and 50% after one week [2].

The advantages of an early CT scan are:

— It is a reliable diagnostic technique; — It may demonstrate the aneurysm, thus the advantage of obtaining the study after contrast injection; — It may show the presence of associated lesions such as hydrocephalus or intracerebral hematomas; — It helps in localizing the lesion; — It demonstrates the extent of the subarachnoid clot, having a predicting value regarding the subsequent development of vasospasm.

Lumbar puncture (LP) is indispensable when CT is not available, and when CT is normal or was obtained

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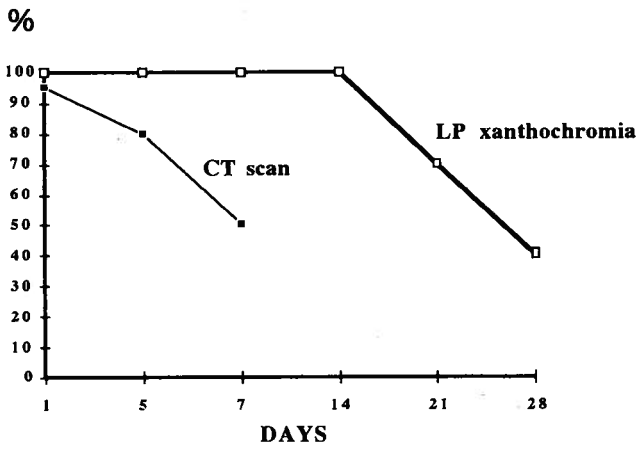

Fig. 1 — Percentage of positivity of CSF findings and CT scan during the four weeks following subarachnoid hemorrhage.

too late after the bleeding episode. It is always preferrable to obtain an LP after CT scan, because of the possible danger of this procedure. In a series of 100 patients suspected to have suffered an aneurysmal SAH, 15 had a nonaneurysmal intracerebral hematoma, 8 of which were in the cerebellum, and one third of the patients with aneurysms had intracerebral hematomas [3].

The only absolutely reliable sign of hemorrhage is the demonstration of xanthochromia in the CSF [4]. If necessary it should be documented by spectrophotometry. Xanthochromia is due to the presence of oxihemaglobin and develops as early as 2 hours following the event, and may be detected in 100% of the cases if the puncture is performed after 12 hours. Xanthochromia is present in 100% of the cases within 2 weeks of the bleeding, 70% at 3 weeks and 40% at 4 weeks.

Cerebral angiography should be obtained at the earliest convenience. In patients with a history suggestive of SAH, seen within 2 weeks of the event, who have normal LP and CT scan the diagnosis of SAH can be safely excluded. If the patient is seen after this period, angiography of MRI angiography may be indicated.

Medical Treatment

There are a number of possible medical problems that arise not only in the preoperative period, but also following the successful clipping of an intracranial aneurysm. I will focus only the problem of delayed cerebral ischemia, which is causally linked to vasospasm because this is still one of the most severe and frequent complications of the disease, about which there is abundant literature, that can be briefly summarized in the following way:

1. Vasospasm is caused by the blood degradation products in the subarachnoid space, among which the most important is oxyhemaglobin [5].

2. *Angiographic* vasospasm is rarely seen before the 4th day, and will peak around the 7th day. 40-70% of the patients will have it, but only 20-30% will be symptomatic [6]. Of these, 50% will make a good recovery.

3. The risk of delayed cerebral ischemia can be predicted by the amount of blood present in the subarachnoid space or in the ventricular system [7].

4. Transcranial Doppler techniques are quite useful in the evaluation of this phenomenon [8].

The following recommendations seem appropriate:

I — The calcium-blocking agent Nimodipine decreases the incidence of delayed ischemia, an effect which does not depend on a vasodilator action [9-11].

II — Volume expansion combined with controlled hypertension and the increase of the cardiac output is now the method of choice for patients with treated aneurysms who have developed signs of ischemia [12]. This treatment requires sophisticated intensive care facilities.

III — Antifibrinolytic therapy offers no advantage [13,14].

IV — The benefits of extensive subarachnoid cleaning of clots during early surgery have not yet been unequivocally demonstrated.

V — A number of treatments still in an experimental stage seem to offer some promise, but require appropriate facilities and well trained teams. These include:

— transluminal angioplasty; — use of thrombolytic agents by cisternal perfusion, such as urokinase and tissue plasminogen activator. Preliminary results with the latter show improvement in patients in grades 3 to 5 [15].

Timing of Aneurysm Surgery

Despite the publication of numerous clinical reports based on either cooperative studies, or series from single institutions, this is still a debated topic [13,16-28]. Before a reasonable stand can be taken concerning the optimal timing for aneurysm surgery, one should consider some data that may influence the decision-making process.

— First of all the percentage of patients who arrive at the neurosurgical centers within the first 48 hours following a SAH is still rather limited, even in countries with more advanced medical care. In the USA the number is 36% [29], and in Amsterdam 30% [30]. In Portugal, 50% of the patients are admitted within 24 hours, 29% between the 1 and 4 th day, and 21% after the 4 th day [31]. In this study the most significant cause of delay was an error in the diagnosis. It was clear that the patients with a more severe neurological status are admitted earlier.

— A rather significant percentage of patients are immediately impaired by the initial rupture, so the results in these cases cannot be affected by any decision concerning the timing of surgery. In fact, the analysis of the causes of morbidity/mortality at 6 months in patients with aneurysmal SAH admitted to North-American centers participating in the International Cooperative Study on timing of aneurysm surgery reveals the following data [22]:

Direct effect of the hemorrhage	13.2%
Vasospasm	12.8%
Rebleed	6.7%
Hydrocephalus	1.7%
Intracerebral hemorrhage	1.4%
Surgical complications	5.2%
Medical therapy complications	0.5%
Others	3.6%

— Concerning the problem of rebleeding, it should be emphasized that this is a diagnosis that requires adequate confirmation which depends, in most instances, on the demonstration of a repeat hemorrhage in the CT scan.

It is clear that rebleeding occurs more frequently in patients in poorer grades (25%) than patients in better grades (9.2%).

Early surgery does not prevent the very early rebleeding (2-6%) that occurs while waiting for surgery[21].

— In my opinion, early surgery is not technically as simple as delayed surgery, except perhaps for the very experienced vascular surgeon. In addition, early surgery requires the precise coordination of a complete medical team, which is not always possible.

— It is unquestionable, however, that early surgery prevents further rebleeding, allows a more agressive treatment of vasospasm and its complications, particularly using hypervolemic-hemodilution hypertensive therapy. Clearing the subarachnoid space of the blood products, when technically feasible, may also be beneficial according to some.

Based on the available literature on the topic and my own experience, the following recommendations are advanced:

— In patients in good grades (I or II) (Table 1) early surgery is clearly favored.

— Patients in grade III should probably be operated early. I am particularly concerned about early surgery for anterior communicating complex aneurysms.

— In patients in grades IV or V and evidence of mass lesion, early surgery is favored.

— In patients with poor grades, or medically unstable, late surgery (after day 11) is favored by many.

— The most critical time for surgery is the 7-10th day, and this period should be avoided.

TABLE 1 — **Clinical grading scale in subarachnoid hemorrhage**

Hunt-Hess Scale
I — Asymptomatic or mild headache.
II — Moderate to severe headache, nucal rigidity, can have oculomotor palsy.
III — Confusion, drowsiness, or mild focal signs.
IV — Stupor or hemiparesis.
V — Coma, moribund, and/or extensor posturing

— Although surgeons with substantial experience in posterior fossa aneurysms state that the same principles apply to these lesions, I believe that the *occasional* posterior fossa aneurysm surgeon will have more technical difficulties operating these lesions early (Fig. 2). It should be stated however, that the timing of aneurysm surgery should always be a matter of individual strategy based on the patient status, the nature and characteristics of the lesion, and personal experience.

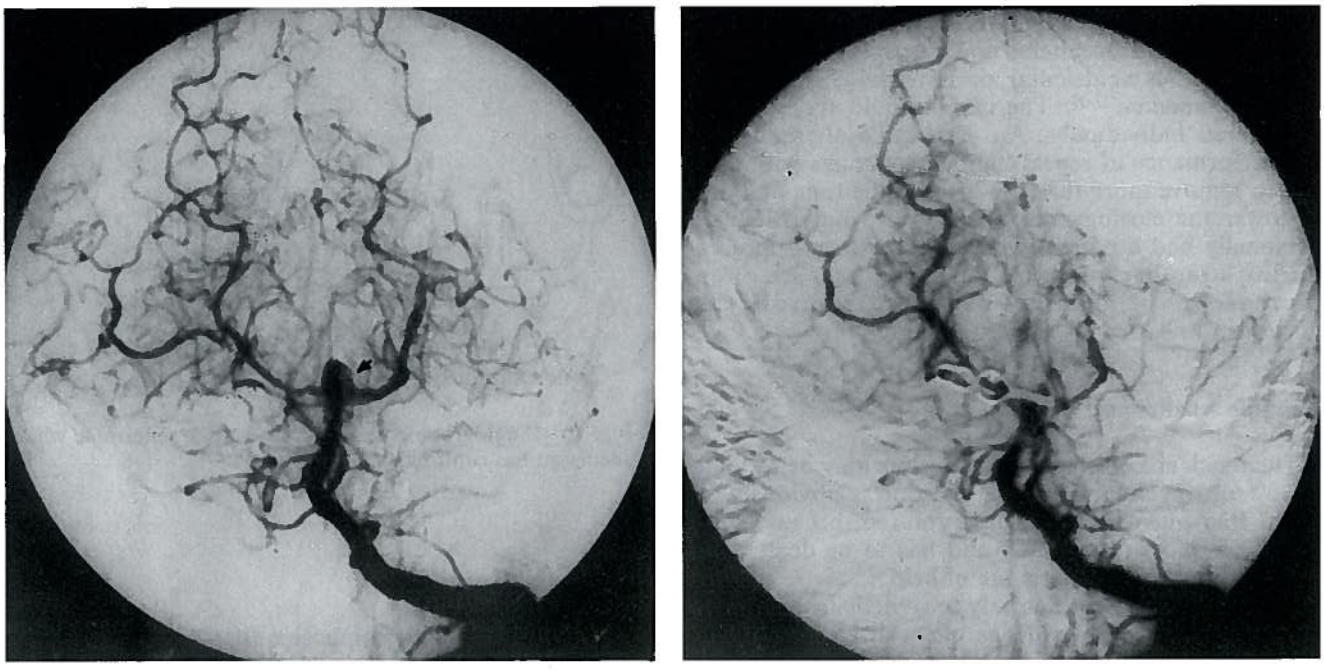

Fig. 2 A — Aneurysm of the tip of the basilar artery (arrow). *B* The aneurysm was excluded with a fenestrated clip. The posterior cerebral artery passes through the ring of the clip.

Aneurysm Rupture Associated With a Large Intracerebral Hematoma

The presence of a large intracerebral hematoma secondary to a ruptured aneurysm is observed in about 4-17% of the cases[32]. Most patients will be grade III or higher, and quite often this is a life-threatening situation, implying emergency surgery. The following guidelines can be offered:

— Patients in grade III or IV of Hunt and Hess should be operated promptly.

— Surgical intervention in grade V patients is quite debatable. It can be stated, however, that patients with decerebrate posturing, anisocoria or dilated pupils and a marked midline shift will practically never survive. Other factors of bad prognostic significance are advanced age and coma as the presenting picture.

— It is usually preferrable to evacuate the hematoma and try to deal with the aneurysm (mortality rate 25-50%), than to evacuate the hematoma only (mortality rate 69-100%)[33].

When cerebral angiography cannot be obtained expeditiously it may be justified to evacuate the hematoma and explore the related vessels — e.g. the middle cerebral complex and the internal carotid for a temporal lobe clot — to look for the culprit[34]. The morbidity and mortality in these situations is always quite high.

Aneurysm and Acute Hydrocephalus

In large series of patients with ruptured aneurysms the incidence of hydrocephalus is approximately 20%, which is symptomatic in about one third of them[35,36]. The presence of hydrocephalus is an ominous sign, since there is a higher incidence of rebleeding in these patients. However, ventricular drainage should be instituted with great parsimony since many of these patients will improve spontaneously and an increase in incidence of hydrocephalus and vasospasm in patients with continous ventricular or cisternal drainage has been documented[37-39]. The cases should therefore be considered individually. An acceptable alternative is the performance of repeat lumbar punctures with care not to remove more than 15-20 ml at the time and not to lower the closing pressure below 15 mm H2O[37]. I personally had a patient whose aneurysm re-ruptured during a lumbar puncture, probably because of an increase in the gradient of pressure across the aneurysm wall.

Multiple Aneurysms

The incidence of multiple aneurysms may be as high as 30% of the cases. The first question is obviously to try to find out which one has ruptured, because that one is the most threatening and has to be dealt with first. The following criteria are of help[40]:

— Clinical signs, particularly focal deficits.

— CT (and MRI) evidence of localized collections of blood.

— Angiographic signs (Fig. 3):

— focal spasm

— focal mass effect

— aneurysm nipples

— the larger one

— the one with a more irregular shape

— change in shape in successive angiograms (less helpful)

Using this criteria an accurate diagnosis may be reached in about 97.5% of the cases.

Once the ruptured aneurysm is identified it should be operated, and all the accessible ones should be dealt with in the same intervention if technically feasible[41]. Here again, individual expertise is of utmost importance.

The non-treated remaining lesions should be dealt with as incidental aneurysms, following the principles outlined below.

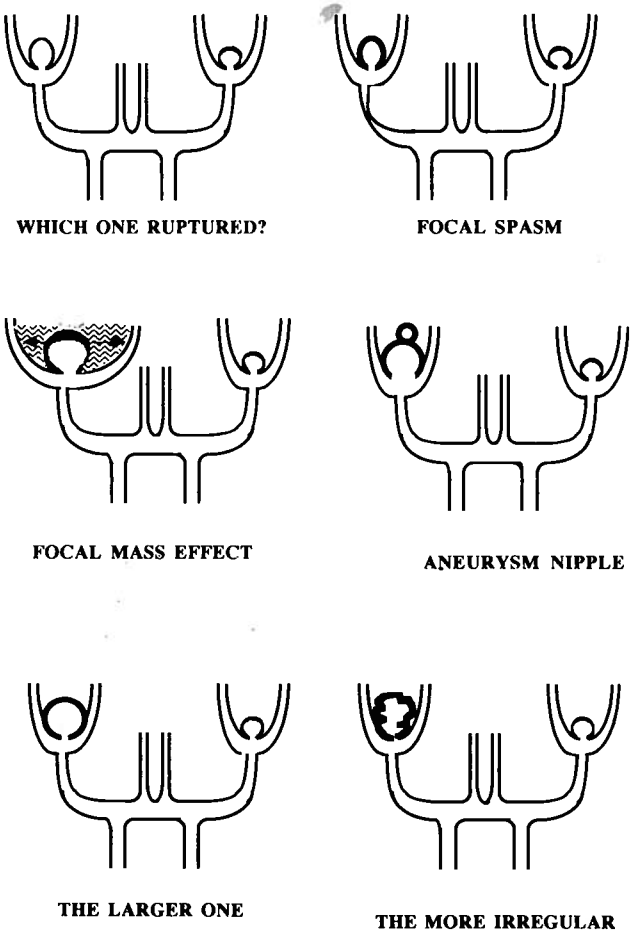

Fig. 3 — Angiographic findings that help to determine which aneurysm has ruptured.

Incidental Aneurysms

It is important to emphasize that I am referring to unruptured asymptomatic lesions (Fig. 4). Unruptured symptomatic aneurysms which may manifest themselves as intracranial mass lesions or cause neurological

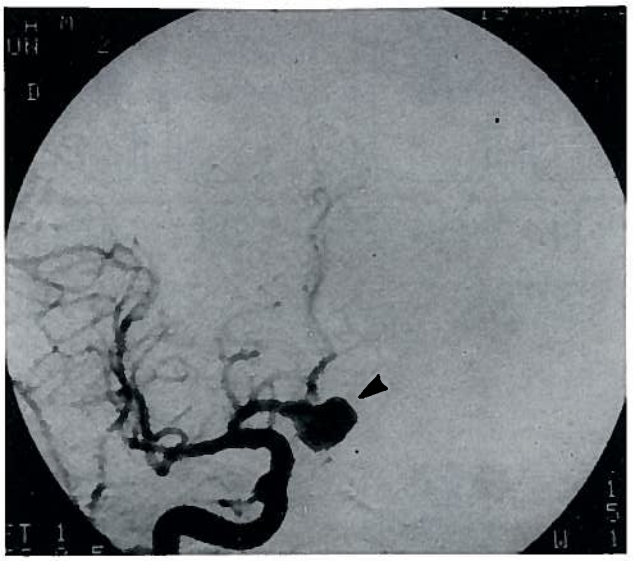

Fig. 4 — Large incidental anterior communicating aneurysm (arrow) found initially in a CT scan. On surgery the sac was heavily calcified and the lesion was wrapped.

symptoms by compression of adjacent structures raise different therapeutic challenges.

If one considers that in autopsy series the incidence of intracranial aneurysms is about 5%, it is quite apparent that the majority of these lesions never ruptures. On the other hand, it is generally accepted that the average size of a ruptured aneurysm is about 7--7,5 mm, although there have been documented ruptures in smaller lesions. In such cases it is possible that partial collapse or thrombosis of the sac may have occurred. The risk of rupture of these incidental aneurysms has been estimated to be about 1-2%/year.

With these data in mind, the following guidelines appear reasonable[42,43]:

— aneurysms measuring less than 5 mm should be followed. Repeat angiography every 2 to 5 years is suggested.

— aneurysms larger than 10 mm should be operated.

— aneurysms with sizes between 5 (7 to some authors) and 10 mm should be considered for surgery, taking into consideration the surgical risk, the age of the patient, the characteristics of the lesion, and the surgeon's experience.

Partially Treated Aneurysm

Occasionally, satisfactory clipping of the aneurysmal sac is not possible and a segment, usually close to the neck, is left. It may also happen that a postoperative angiogram reveals that a complete exclusion of the aneurysmal sac did not take place. The risk of rupture of these aneurysmal *rests* is around 0.38-0.79%/year[44] and therefore these should be managed as *incidental* aneurysms. The morbidity/mortality of the surgical approach to these lesions does not warrant the re--exploration[45], although aneurysmal sacs may regrow from residual necks[46].

I want to emphasize that careful wrapping of the aneurysmal sac with muslin gauze or other adhesive materials that may be considered safe and effective, if the whole lesion is surrounded by the protective material[13,47,48] (Fig. 5).

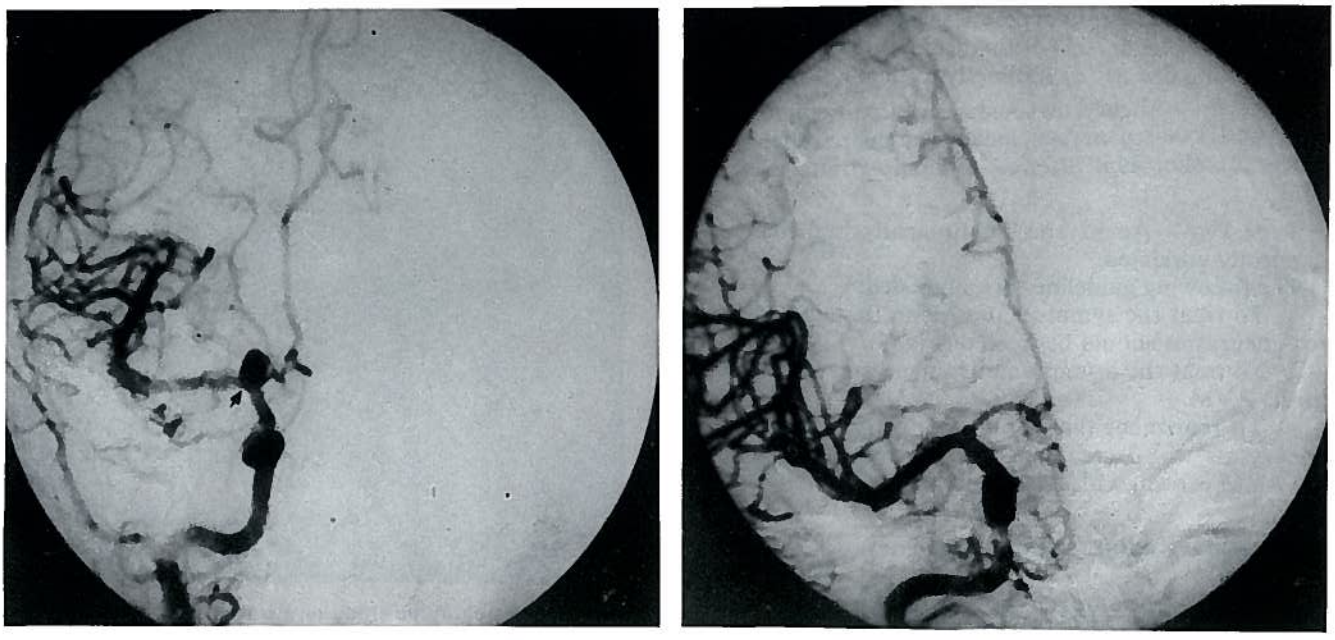

Fig. 5 A — Aneurysm of the bifurcation of the internal carotid artery (arrow). *B* Angiography three weeks after wrapping showing total occlusion of the sac.

Familial Aneurysms and Predisposing Disorders

A question that is raised often concerns the need to study the relatives of patients with intracranial aneurysms because there have been reports of families in which an autosomal dominant inheritance pattern can be recognized[49]. Aneurysms in identical twins have also been described[50]. Angiography is only indicated when more than one member has suffered an SAH.

Another question relates to the evaluation of the vascular tree in patients with pathologies in which it is known that intracranial aneurysms occur with a higher incidence. Some are hereditary, either autosomal dominant like Marfan's syndrome or polycystic kidney disease, or recessive like the pseudoxanthoma elasticum or the Ehler-Danlos syndrome (type III collagen deficency); others, such as aortic coarctation or fibromuscular dysplasia have no genetic base.

Levey et al[51] carried out a decision analysis on whether angiographic investigation was justified in patients with polycystic kidney disease, and the answer was negative, since the study was only beneficial if the presence of the lesion was higher than 30%, the surgical complication rate was below 1%, and the patient was younger than 25. The improvement of non-invasive techniques such as magnetic ressonance angiography may however change the present perspective.

Intracranial Aneurysms in Patients with Arteriovenous Malformation (AVM)

Approximately 10% of the patients with AVM will have an associated intracranial aneurysm[52,53]. In a recent series of the Neurological Institute of New York the cause of the SAH was the aneurysm in 46% of the cases, the AVM in 33% and in the remaining 21% it was not possible to identify the causal lesion. Sa and Stein considered[53] four types of aneurysms (Fig. 6):

Type I — Aneurysms of the proximal major arteries contributing directly or indirectly to the malformation.

Type II — Aneurysms located on superficial feeders.

Type III — Aneurysms located on deep feeders (e.g. posterior choroidal arteries, lenticulo-striate arteries, etc).

Type IV — Aneurysms anatomically and hemodinamically unrelated.

The following guidelines are suggested:

— To treat the symptomatic lesion first. All ruptured aneurysms should be treated (Fig. 7).

— To treat the asymptomatic aneurysms if adjacent to the AVM.

— To remember that a number of the flow-related aneurysms will decrease in size, or even disappear if the AVM is dealt with effectivelly.

Aneurysmal Rupture During Pregnancy

Intracranial hemorrhage in pregnancy occurs in 0.01-0.05% of cases, with a mortality of 40-50%. Eclampsia is probably the most common cause but aneurysms and AVM may also be responsible. In a recent review aneurysms were the culprit in 77% of the cases and AVM in 23%[54]. From an analysis of the pertaining literature[54,55] the following pratical points can be emphasized:

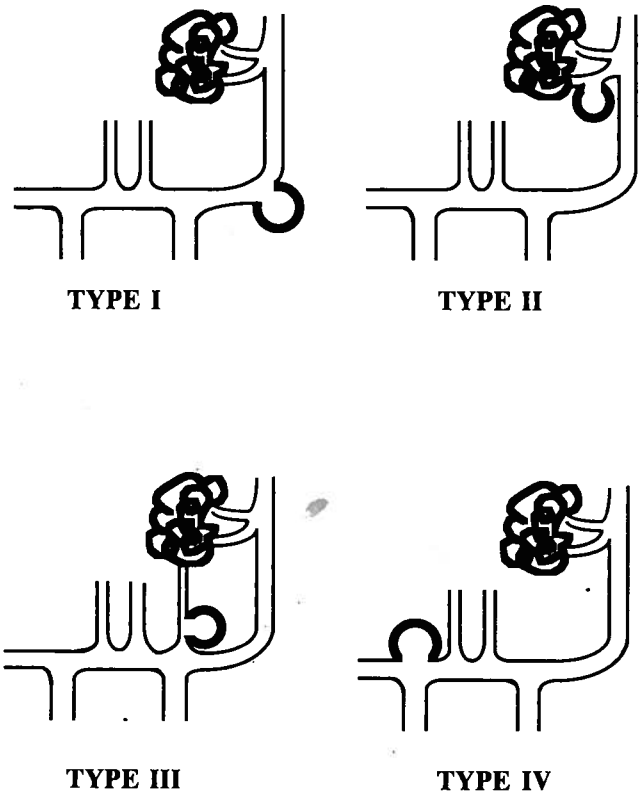

Fig. 6 — Association of aneurysms and arteriovenous malformations (see text).

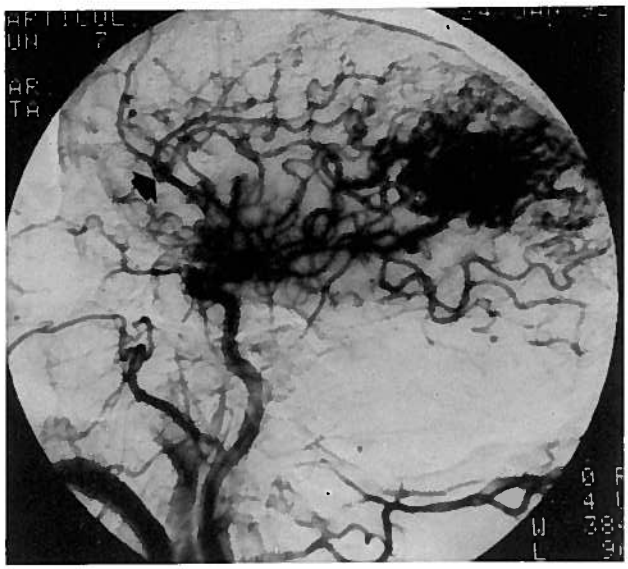

Fig. 7 — Angiographic study of a patient with a large parietal arteriovenous malformation. The cause of the patient's subarachnoid hemorrhage was, however, a small pericallosal aneurysm (arrow).

— The risk of hemorrhage increases with the advance in gestational age.

— Rupture rarely occurs during delivery.

— Once the SAH has been documented angiography should be performed. Care should be taken to shield the uterus and to avoid maternal dehydration.

— The surgical management should be carried along similar lines to any intracranial aneurysm.

— Anticonvulsant prophylasis is indicated.

— Due to the risk of maternal dehydration, mannitol and diuretics should be used with care.

— There is no contra-indication to the use of steroids, but the fetal risks of Nimodipine are still unknown.

— For the non-treated patients the risks of cesarean section and vaginal delivery are similar.

Subarachnoid Hemorrhage and Negative Angiography

The first question is, of course, to correctly define ***negative angiography*** (Fig. 8). A complete study requires the visualization of all major intracranial vessels including both posterior inferior cerebellar arteries. The study has to be of good quality, and vasospasm should not be present.

Negative angiography in the presence of a well documented subarachnoid hemorrhage occurs in 4--27% of the published series [56]. These are patients who are generally in good shape. There is a low incidence of focal deficits, rebleeding or delayed ischemia. A particularly benign pattern is the so-called *perimesencephalic hemorrhage* [57-59]. It is important, however, to exclude a basilar bifurcation aneurysm in these patients. In such cases, nimodipine or hemodilution/hypertensive therapy is not justified. Rebleeding, cerebral ischemia and residual disability occur only in patients with an aneurysmal pattern of hemorrhage on the initial CT [59].

In some cases of negative angiography it may be justified to study the whole spine, particularly if back pain or signs and symptoms pointing to cord pathology are present. MRI or complete myelography may then be used as screening techniques.

Conclusion

Aneurysmal rupture is often a catastrophic event which kills and disables a large number of young, productive people. Its management imposes a number of

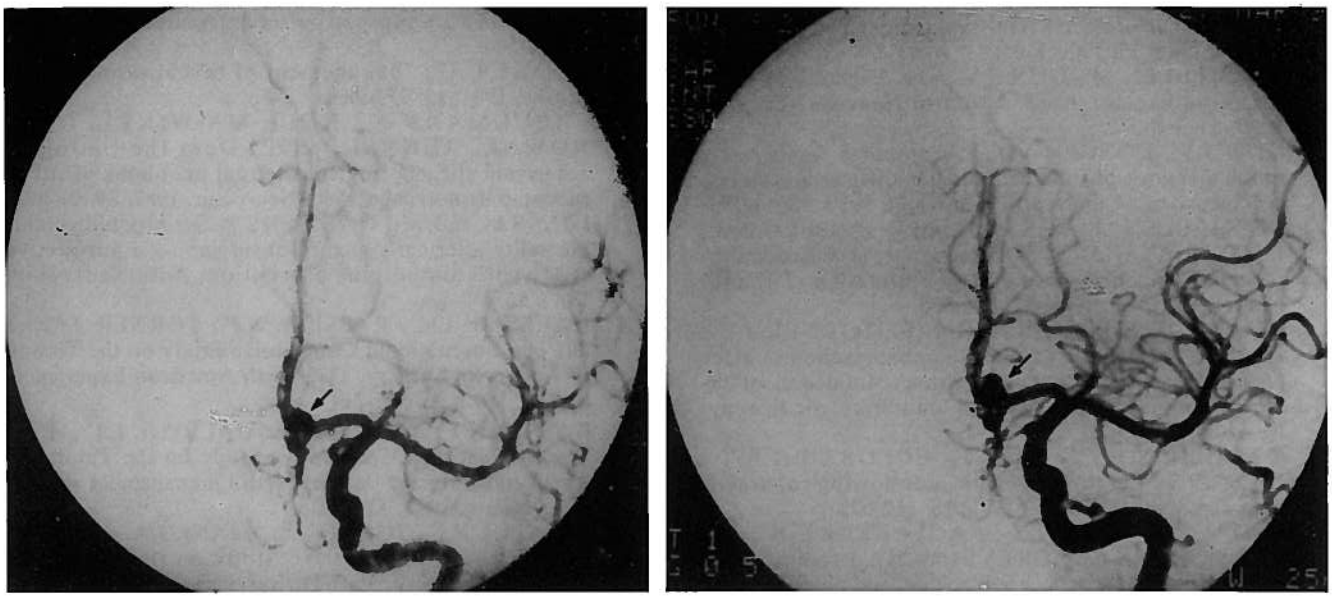

Fig. 8 A — Angiography of a patient with a subarachnoid hemorrhage considered normal. Note that the anterior communicating complex is suspicious (arrow). *B* Angiography one year later shows clearly the aneurysm (arrow).

This group of patients is probably quite heterogenous. It may be that in some cases there was a small intracranial aneurysm that exploded and self destructed. In cases where vasospasm, or an intracerebral hematoma are present, or when there is a second bleeding episode the angiographic study should be repeated.

It is also apparent that a number of these patients have a false SAH. These are individuals who develop a crushing headache and as part of their evaluation suffer a traumatic spinal tap, and quite often one can observe multiple puncture holes on their lower back.

options, some of which were considered in this lecture. We should strive to improve the diagnosis and care of these patients and the following guidelines, slightly modified from Weir [60], will certainly contribute decisively.

— Prevention of pre-hospital death; — improving cardiopulmonary ressuscitation.

— Early correct diagnosis, particularly of *warning leaks*; — better education of health care personnel; — better education of the public regarding the significance of sudden-onset severe headache; — widespread use of CT for the investigation of these headaches.

— Early corrective surgery in appropriate medical facilities in selected cases.

— Prevention of delayed ischemic deficit; — avoidance of dehydratation, antifibrinolytics and adverse cardiac, hematological and respiratory events; — clot removal?; —cisternal perfusion with fibrinolytic drugs?; — increase perfusion (hypertension, hypervolemia, increased cardiac output) at the onset of ischemic signs.

— Prevention of delayed deterioration; — CSF shunting; — treatment of depression; — appropriate rehabilitation.

— Screening for aneurysms in groups at risk; — familial cases (two or more immediate relatives with known aneurysms); — polycystic kidneys, coarctation of the aorta, fibromuscular dysplasia, etc; — partially treated, or not definitively treated cases.

It is clear that some of decisions that have to be made are not always based on undisputable scientific evidence. We are reminded that *when you don't have all the facts, you sometimes have to draw on your own experience*[61].

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