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Original articles

Sudden fatal or non-operable bleeding from ruptured intracranial aneurysm

Evaluation by post-mortem angiography with vulcanising contrast medium

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Summary: A series of medicolegal autopsies on 76 patients with fatal outcome following haemorrhage from ruptured intracranial aneurysm comprised 63 surgical patients and 13 non-surgical patients (M:F 6:7; mean age 44.0 ± 18.1 years), all of the latter with sudden fatal course or dramatically poor clinical condition on admission. The medicolegal autopsy was performed because of the sudden and unexpected nature of the death, or to exclude surgical malpractice. Postmortem angiography with vulcanising contrast medium disclosed intraventricular haemorrhage (IVH) in 12 (92%) of the non-surgical fatalities, whereas IVH was thus characterized in only 17 (27%) of the 63 fatalities who had undergone neurosurgery ($P < 0.0001$). The most common type of haemorrhage among surgical cases was, instead, subarachnoid haemorrhage (SAH) ($P < 0.05$). In 35 of the 76 cases (46%), casts of cerebral arteries demonstrated vasospasm-induced segmental narrowings, but such narrowings were no more frequent among the non-surgical cases than in surgical cases, nor did these narrowings correlate with IVH. In non-surgical patients, the haemorrhage most commonly originated from a ruptured aneurysm of the middle cerebral artery ($P < 0.05$), an event more frequently associated with the presence of IVH ($P < 0.05$) than without it. The results indicate that the main cause for sudden and unexpected death or rapidly developed poor non-operable clinical condition of patients with ruptured intracranial aneurysm is an IVH from a middle cerebral artery aneurysm, complicated in many cases by cerebral artery vasospasm.

Key words: Aneurysm cerebral arteries – Intraventricular hemorrhage – Cerebral artery vasospasm – Angiography

Zusammenfassung. Eine Serie von 76 rechtsmedizinischen Obduktionen bei Todesfällen mit tödlichem Ausgang einer Blutung aus rupturierten intrakranialen Aneurysmen umfaßte 63 chirurgische Patienten und 13 nicht-chirurgische Patienten (m:w = 6:7; mittleres Alter 44,0 ± 18,1 Jahre). Sämtliche der letzteren Fälle hatten einen plötzlichen tödlichen Verlauf oder eine infauste Prognose bei der klinischen Einlieferung. Die rechtsmedizinische Obduktion wurde wegen der plötzlichen und unerwarteten Todesart durchgeführt oder zum Ausschluß chirurgischer Fahrlässigkeit. Die postmortale Angiographie mit einem vulkanisierenden Kontrastmedium deckte eine intraventrikuläre Hämorrhagie (IVH) in 12 (92%) der nicht-chirurgischen Todesfälle auf, wohingegen eine IVH in nur 17 (27%) der 63 Todesfälle festgestellt wurde, welche einer neurochirurgischen Behandlung unterzogen worden waren ($p < 0{,}0001$). Der häufigste Typ der Hämorrhagie unter den chirurgischen Patienten war stattdessen eine subarachnoidale Blutung (SAH) ($p < 0{,}05$). In 35 der 76 Todesfälle (46%) zeigten Ausgüsse der Zerebralarterien segmentale Einengungen, welche durch Vasospasmen induziert waren, aber solche Einengungen waren unter den nicht-chirurgischen Fällen nicht häufiger als unter den chirurgischen, auch korrelierten diese Einengungen nicht mit einer IVH. Bei den nicht-chirurgischen Fällen war die Quelle der Hämorrhagie am häufigsten ein rupturiertes Aneurysma der Arteria cerebri media ($p < 0{,}05$); dieser Vorgang war häufiger mit der Anwesenheit einer IVH assoziiert ($p < 0{,}05$) als nicht-assoziiert. Die Ergebnisse zeigen, daß die Hauptursache für den plötzlichen und unerwarteten Tod oder die sich schnell entwickelnde Nicht-Operabilität von Patienten mit rupturierten intrakraniellen Aneurysmen eine IVH aus der Arteria cerebri media ist, welche in vielen Fällen durch cerebrale arterielle Vasospasmen kompliziert werden.

Schlüsselwörter: Hirnbasisarterien-Aneurysma – Ventrikelblutung – Arterielle Vasospasmen – Angiographie

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Introduction

Subarachnoid haemorrhage (SAH) is a common finding at medicolegal autopsy. The most frequent reason for the haemorrhage is a rupture of an intracranial aneurysm, which produces a mortality of over 50% [1]. Many of these patients die suddenly and unexpectedly or progress rapidly into a poor non-operable clinical condition [1, 2], because of which neurosurgery is avoided. Clinically, poor initial prognosis has been ascribed to massive SAH [3] or intraventricular haemorrhage (IVH) [2, 4]. Development of cerebral artery vasospasm also contributes significantly to the mortality of aneurysm patients [5]. Only a few autopsy studies [6] have focused on factors that are associated with sudden and unexpected death in aneurysm patients or lead to a poor non-operable clinical condition. These patients are often subjected to medicolegal autopsy because of the sudden and unexpected nature of their deaths, to exclude trauma, or even because of claims against the surgeon by the relatives for not offering the patient neurosurgery.

In this paper postmortem angiography with vulcanising contrast medium was utilized to characterize non-surgical patients with sudden fatal or non-operable haemorrhage from intracranial aneurysms at autopsy. The results are compared with findings in a series of neurosurgical patients with fatal outcome.

Materials and methods

Autopsy series. The series comprised 76 cases with fatal outcome following rupture of an intracranial aneurysm. Of the patients, 63 underwent neurosurgery at the Department of Neurosurgery, University Central Hospital of Helsinki: 34 were females and 29 males, mean age was 47,3 ± 10,9 years (Table 1).

In 13 patients (17%), who died suddenly or had a poor clinical condition on admission (Table 1), surgery was not performed. Of these non-surgical patients, 7 were female and 6 male, the mean age was 44,1 ± 18,1 years (Table 1). One of the patients with a short history of headache and vomiting was found dead at home; 3 died in the emergency ward. For the other 9 cases, neurosurgery was not offered because of their grave clinical condition.

The medicolegal autopsies were performed at the Department of Forensic Medicine, University of Helsinki. The autopsy was performed on average 5–6 days (range 2–12 days) after death.

Post-mortem angiography from the aortic arch. Angiography was performed from the arch of the aorta before the postmortem. The perfusion was performed using a simple portable device, connected to the compressed air line using quick couplings [7]. No saline preperfusion was used. Briefly, the ascending aorta was cannulated in situ with a PVC mouthpiece, and contrast medium was infused at a pressure of 150 mm Hg for 30 min using disposable PVC tubing. Room temperature vulcanising silicone rubber (Silikon Kautschuk RTV-Vergussmasse K, Wacker-Chemie GmbH., Munich) was used as a contrast medium. The mixture was made radio-opaque with 20% lead oxide. Vulcanising was initiated by adding 2% of vulcanizer (Haerter T) to the solution prior to injection. The mixture vulcanises into a rubbery cast within 2 hours.

Radiographs were taken from an anteroposterior and lateral view using a distance of 100 cm, 55 kV and 300 mAs. The separated brain was radiographed twice at an angle of 5° to obtain stereo X-rays.

Spasm score. Clinical and postmortem angiograms were assessed and scored double-blind, each independently by an experienced neuroradiologist (A. S). The degree of spasm was scored in both series as absent (−), slight (+), moderate (++) or severe (+++).

Statistical calculations. Statistical calculations were performed using Student's t-test or the likelihood-ratio-test.

Results

Surgical patients

In the 63 surgical patients, a total of 86 aneurysms of the intracranial arteries were found (1.4 aneurysms/patient). Multiple aneurysms were detected in 14 of the patients (22%).

Of the 63 ruptured aneurysms, 18 were situated in the medial cerebral artery, 21 in the anterior communicating artery, 12 in the internal carotid artery, 6 in the basilar artery, 3 in the anterior cerebral artery (A. pericallosa), and 3 in the vertebral artery.

Operative vascular complications were revealed in 28 (44%) of the surgical patients due to rupture during dissection or clip application, to obstruction of an uninvolved cerebral artery by aneurysm clip, detachment of the clip, or due to clipping of an uninvolved aneurysm instead of the ruptured one [8].

Non-surgical patients

A total of 18 aneurysms were found in the 13 non-surgical patients (1.4 aneurysms/patient), and 3 patients (23%) had multiple aneurysms (Patients 3, 10, 11). Of the 13 ruptured aneurysms, 8 were situated in the middle cerebral artery, 3 in the anterior communicating artery, one in the basilar artery, and one in the internal carotid artery (Table 1).

Differences between non-surgical und surgical patients

There were no differences in age, sex distribution or number of aneurysms/patient (Table 2).

As expected, the survival time of non-surgical patients was significantly shorter than that of surgical patients (5.3 ± 6.2 days vs 11.1 ± 8.8 days, $P < 0.05$).

Intraventricular haemorrhage (IVH) was revealed in 12 out of 13 (92%) of the non-surgical patients with fatal or non-operable bleeding (Fig. 1), whereas IVH was detected only in 17 (27%) of the 63 patients who underwent surgery ($P < 0.0001$). Intracerebral haemorrhage alone did not predict sudden death or rapid clinical deterioration but was a statistically significant factor ($P < 0.0001$) when combined with IVH. Subarachnoid haemorrhage (SAH) without extension into the brain tissue or ventricles was observed more commonly among surgical patients (2/13 in non-surgical patients vs 35/63 of surgical patients, $P < 0.05$).

Vasospasm-induced segmental narrowings were observed in the vulcanised silicone rubber cast of the cerebral arteries (Fig. 2) in 8 (62%) non-surgical cases and in 27 (43%) surgical cases (n.s.). There was no association

Table 1. Characteristics of sudden fatal or non-operable haemorrhage from a ruptured intracranial aneurysm in 13 non-surgical patients in Helsinki. (SAH = subarachnoid haemorrhage; IVH = intraventricular; IC = intracerebral

No.	Age	Sex	Location of ruptured aneurysm[a]	Post-SAH survival (days)	Type of haemorrhage	Vasospasm[b]
1	27	F	MCA 1	3	IVH IC	++
2	22	M	MCA 1	1	IVH IC	++
3	31	M	MCA 1, AComA 2	17	IVH IC	−
4	33	M	MCA 1	16	IVH IC	+++
5	62	M	AComA 1	11	IVH IC	−
6	32	F	MCA 1	<1	IVH	+++
7	62	F	BasA	12	No circulation	?
8	51	M	AComA 1	2	IVH	−
9	42	F	AComA 1	2	IVH IC	−
10	45	M	MCA 1 BasA	1	IVH IC	+
11	40	F	ICA 2 PComA 1	1	IVH IC	++
12	37	F	MCA 1	1	IVH IC	+++
13	88	F	MCA 1	1	IVH	++

[a] MCA = middle cerebral artery; AComA = anterior communicating artery; BasA = basilar artery; PComA = posterior communicating artery
[b] − no spasm, + to +++ score of spasm-induced segmental narrowing of the cerebral artery

between the occurrence of vasospasm-induced narrowings and IVH.

Compared with surgical patients, non-surgical patients were more frequently ($P < 0.05$) characterized by ruptured aneurysm of the middle cerebral artery.

Table 2. Main features differentiating surgical and non-surgical patients in a series of 76 patients with ruptured intracranial aneurysm in Helsinki in 1982–1990

	Surgery ($n = 63$)	No surgery ($n = 13$)	Significance
Age	47.3 ± 10.9	44.0 ± 18.1	n.s.
Sex M/F	29/34	6/ 7	n.s.
Survival (days)	11.1 ± 8.8	5.3 ± 6.2	$P < 0.05$
Ruptured aneurysm[a]			
MCA	18	8	$P < 0.05$
AComA	21	3	n.s.
ICA	12	1	n.s.
BasA	6	1	n.s.
Other	6	0	n.s.
Type of haemorrhage[b]			
SAH	48	2	$P < 0.05$
IC	23	1	n.s.
IVH	17	12	$P < 0.0001$
IVH and IC	12	11	$P < 0.0001$
Vasospasm score			
No spasm	27	3	n.s.
Slight (+)	4	1	n.s.
Moderate (++)	13	4	n.s.
Severe (+++)	10	3	n.s.
No circulation	9	1	n.s.

[a] MCA = middle cerebral artery; AComA = anterior communicating artery; ICA = internal carotid artery; BasA = basilar artery
[b] SAH = subarachnoid haemorrhage; IC = intracerebral haemorrhage; IVH = intraventricular haemorrhage

Characteristics of patients with and without intraventricular haemorrhage

There were no differences in age, sex distribution, number of aneurysms or presence of vasospasm-induced narrowings between the 29 non-surgical or surgical patients with IVH and 47 patients without IVH (Table 3). The survival time of patients with IVH was significantly ($P < 0.05$) shorter (8.0 ± 7.4 days v.s. 11.6 ± 9.3 days). Most commonly, rupture of aneurysm of the middle cerebral artery alone ($P < 0.05$) led to IVH.

Discussion

The present results suggest that intraventricular haemorrhage (IVH) is the most important cause of sudden death as well as rapidly progressing poor clinical condition of the patients with ruptured intracranial aneurysm. The most common location of subarachnoid haemorrhage (SAH) is the base of the brain [1]. When the fundus of the aneurysm is embedded in the brain, the haemorrhage may not leak into the subarachnoid space, but be contained in the brain tissue or reach the ventricles. Rupture into the ventricles occurs in about 28–40% of cases with SAH [4, 6]. The mortality rate of patients with IVH is 33–64% (2, 4). In line with our results, in a clinical series of 84 non-survivors after SAH, 54% had IVH, whereas this was observed among survivors only in 29% [3]. In survivors following IVH, the haematoma disappears from the ventricles in 3–8 weeks (9). An IVH may develop so rapidly that it produces a diffuse mass effect that cannot be compensated for by efflux of the cerebrospinal fluid and reabsorption. The bleeding may itself interfere with the CSF flow and rapidly increase the intracranial pressure [1]. Clinically this may mimic an acute intracerebral "hypertensive" haemorrhage. Increased intracranial pressure causes herniation of the

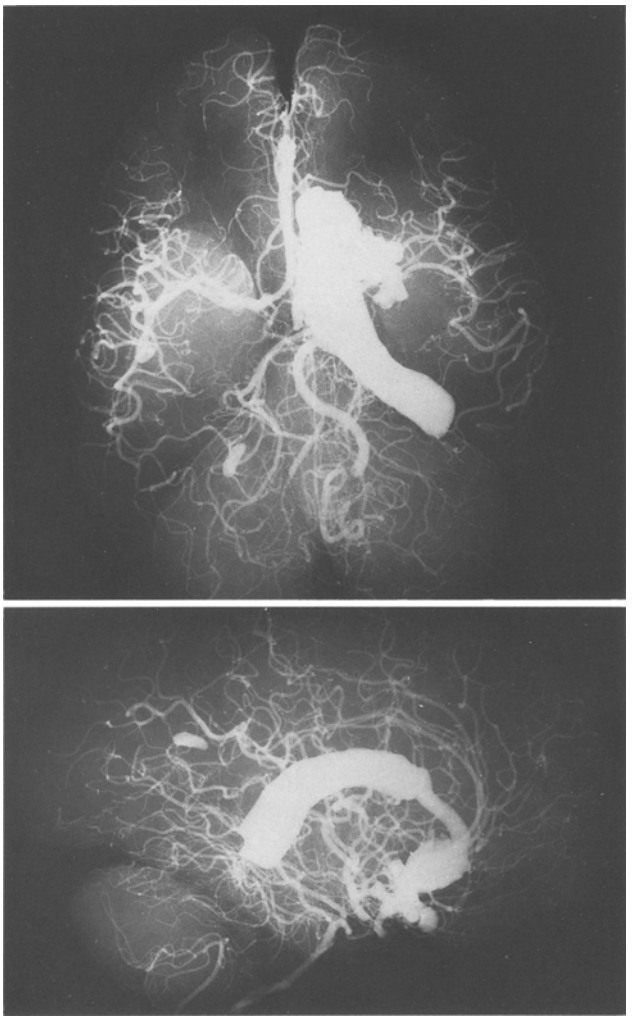

Fig. 1. Intraventricular haemorrhage from rupture of aneurysm of the right middle cerebral artery. Haemorrhage extending into posterior horn of right lateral ventricle *(top)*. Lateral X-ray from separated brain *(bottom)*

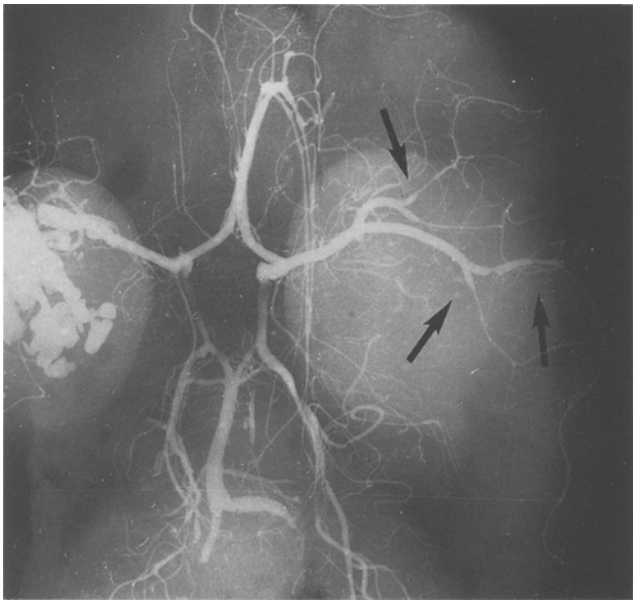

Fig. 2. Vasospasm-induced severe segmental narrowings *(arrows)* of affected and especially of the uninvolved middle cerebral arteries. Subarachnoid haemorrhage from ruptured aneurysm of right middle cerebral artery. Haemorrhage ruptured into right temporal lobe and extended also into ventricles

Table 3. Characteristics of patients with or without intraventricular haemorrhage (IVH) in a series of 76 patients with ruptured intracranial aneurysm in Helsinki in 1982–1990

	IVH ($n = 29$)	Non-IVH ($n = 47$)	Significance
Age	45.1 ± 14.6	48.1 ± 10.9	n.s.
Sex M/F	14/15	21/26	n.s.
Survival (days)	8.0 ± 7.4	11.6 ± 9.3	$P < 0.05$
Ruptured aneurysm			
MCA	14	12	$P < 0.05$
AComA	7	12	n.s.
ICA	2	11	n.s.
BasA	3	4	n.s.
Other	3	8	n.s.
Vasospasm[a]	14	21	n.s.

[a] Slight (+) to severe (+++)

cerebellum and damage of the brainstem with resulting death due to respiratory paralysis. The progression of the condition occurs rapidly and the patient may die within 1 or 2 hours from the onset of the bleeding. In the present series, all except one of the non-surgical patients reached the hospital.

In the present study, angiography at autopsy was applied to improve the quality of the autopsy diagnostics [7]. It reliably differentiates between aneurysm bleeding from intracerebral haemorrhage, ruptured arteriovenous malformation [10], hypertensive haemorrhage or ruptured vertebral artery [11] prior to the dissection. The present results also show that cerebral artery spasm-induced segmental structural narrowings of the arterial wall can easily be detected at necropsy using the angiographic technique with vulcanising contrast medium. Clinically, cerebral artery vasospasm, the most dreaded complication following aneurysm rupture, is also diagnosed by the narrowings observed in the pre- or postoperative angiography or directly on the operating table [12]. The common consequence of vasospasm is a cerebral infarct. Cerebral vasospasm is suggested to be due to long-lasting nonphysiological (sustained) smooth-muscle constriction, or to structural change at the vessel wall, or to a combination of both. It has also been proposed [14] that pathological findings ascribed to spasm are artifacts caused by insufficient fixation techniques, and that subendothelial proliferation and medial myonecrosis attributed to vasospasm are nonspecific findings indistinguishable from changes seen in atherosclerosis. Conventional histopathological verification of vasospasm is thus difficult and time-consuming [13, 14]. Using post-mortem angiography, vasospasm was demonstrated in 35 (46%) of the present series of 76 patients, in line with data on the occurrence of vasospasm in clinical series [5].

Vasospasm is initiated by a complex mechanism involving the action of vasoactive substances released from the haemorrhage. It is thought to involve 3 phases [15]. The first phase is characterised by smooth muscle contraction, which is followed by inflammatory necrosis of the vessel wall with resulting narrowing of the artery. This is followed in the third phase by vasodilatation. Post-mortem angiography may thus disclose the second phase of vasospasm, whereas early smooth muscle contraction as well as late vasodilatation remain undetected. The segmental nature of the narrowings observed was incompatible with the suggestion that the finding is caused by atherosclerosis and closely resembled typical findings seen in clinical angiograms on spastic cerebral arteries. Moreover, dissection of the arteries at spasm disclosed no atherosclerotic changes.

In this study, the development of the vasospasm was not associated with the occurrence of IVH. The prerequisite for vasospasm is the occurrence of blood bathing the artery, whereas in cases with IVH most of the blood bursts into the ventricles.

Rupture of the middle cerebral artery was the most important cause of IVH, whereas an aneurysm of the anterior communicating artery was found ruptured in only 7 (24%) of the cases. This contrasts with other reports in which 48–53% of IVH were due to rupture of the aneurysm of the anterior communicating artery [6], and rupture of an aneurysm of the middle cerebral artery most commonly (39%) resulted in intracerebral haematoma [6].

The present results indicate that the most important feature characterising non-surgical patients with sudden or unexpected death or rapid poor progression following rupture of intracranial aneurysm is the bursting of the haemorrhage into the cerebral ventricles. This rupture most commonly occurred in an aneurysm of the middle cerebral artery and was often associated with cerebral artery vasospasm.

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