Incidence of delayed cerebral ischaemia following subarachnoid haemorrhage of unknown cause

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SUMMARY A retrospective study was made of 50 consecutive patients with spontaneous subarachnoid haemorrhage for which no cause was found, looking for evidence of delayed cerebral ischaemia particularly during the first 2 weeks after the bleed. Twenty-three patients had blood visible on the CT scan but only 4-6% developed delayed ischaemia, all of whom made a good recovery. The low incidence of this complication in this group of patients suggests that subarachnoid blood is not a sufficient cause for delayed ischaemia.

Following subarachnoid haemorrhage from a ruptured aneurysm delayed cerebral ischaemia is a common and dangerous complication. It is recognised by a decrease in conscious level and/or the appearance of focal neurological signs, with no evidence of recurrent haemorrhage. Almost all cases occur within two weeks of the initial bleed.^{1,2} In studies where care has been taken to distinguish delayed ischaemia from early rebleeding or other complications the incidence varies from 25-42%, depending upon the timing of surgery, extent of removal of subarachnoid blood, and the use of anti-fibrinolytic drugs (table 1).

Despite its common occurrence the aetiology of delayed cerebral ischaemia is unknown. There is an association with cerebral arterial vasospasm,⁶⁻¹⁰ but the relationship is not clear.^{11,12} Blood and blood products within the subarachnoid space have been implicated in causing vasospasm and ischaemia, and this has led some surgeons to attempt radical removal of all subarachnoid blood at operation.^{4,13}

In order to examine this suggestion, that blood within the subarachnoid space causes delayed cerebral ischaemia, a group of patients with proven spontaneous subarachnoid haemorrhage was studied in whom no aneurysm or arterio-venous malformation was shown on angiography.

Method

The case notes of all patients with subarachnoid haemor-

Table 1 Incidence of delayed ischaemia following a ruptured aneurysm

	Total incidence of delayed ischaemia	Delayed ischaemia causing permanent deficit, infarct or death
Maurice-Williams, 1982 ¹	33%	13%
Bolander <i>et al.</i> , 1984 ³		
early operation	42%	31%
late operation	25%	—
Taneda, 1982 ⁴		
limited blood removal	40%	28%
radical blood removal	30%	11%
Vermeulen <i>et al.</i> , 1984 ⁵		
antifibrinolytics	—	28%
no antifibrinolytics	—	12%

rhage of unknown cause who were investigated at the Institute of Neurological Sciences, Glasgow during 1981-82 were reviewed. Patients were admitted to the study if they fulfilled the following criteria: (1) A history of spontaneous subarachnoid haemorrhage; (2) A CT scan performed; (3) Subarachnoid haemorrhage confirmed by lumbar puncture and/or blood on CT scan; (4) Bilateral carotid and vertebral angiogram failed to show a cause for the haemorrhage.

Patients with a head injury or primary intracerebral haematoma were excluded, but cases of intraventricular haemorrhage were included. One patient was excluded because a CT scan was not performed. The case records were examined for the whole time spent in hospital, paying particular attention to evidence of neurological deterioration in the two weeks following the haemorrhage. Neurological deterioration was defined as a decrease in conscious level, the appearance of focal signs, or both. The clinical grade was assessed on admission to the neurosurgical unit according to Hunt and Hess,¹⁴ but unmodified by systemic disease.

Seventeen patients were discharged home before two weeks by which time all were alert and orientated with no

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Table 2 Age and sex distribution of 50 patients with subarachnoid haemorrhage of unknown cause

Age (yr)	Male	Female
20-29	3	1
30-39	3	3
40-49	5	3
50-59	7	15
60-69	3	7
Total	21	29

Table 3 Clinical details

Number	Hunt & Hess grade (unmodified)					Initial Coma	Hypertension
	I	II	III	IV	V		
50	4	33	11	2	0	7	10

neurological signs. Sixteen of these were assessed later at an out-patient clinic. Direct contact was made with the seventeenth patient and his general practitioner by telephone.

Results

Between the years 1981-82 there were 50 patients who fulfilled the criteria. Their ages ranged from 20-64 years with a mean of 49.2 ± 13.2 SD. Females were more common than males, particularly in the older age group (table 2). Table 3 shows the clinical grade on admission to the Neurosurgical Unit, the occurrence of coma at the time of the bleed, and the presence of hypertension (defined as taking anti-hypertensive drugs and/or blood pressure over 160/90 mm Hg on admission). Of the seven patients who were in coma only two remained in coma for more than 24 hours; these are the only two patients who were Grade IV on admission.

A CT scan was done in 32 patients within three days of their bleed, on 16 within seven days, and on the remaining two patients after the first week. Blood was visible on the scan in 23 patients, the most common site being within the basal cisterns (table 4). Eleven patients had blood at more than one of the main sites.

Bilateral carotid and vertebral angiography was carried out in all patients, but in four cases, for technical reasons, one of the posterior inferior cerebellar arteries could not be visualised. In another four patients angiography was repeated because arterial vasospasm made exclusion of an aneurysm difficult.

Table 4 Distribution of blood on CT scan

Number	Interfrontal	Basal cisterns	Right or left Sylvian fissure	Ventricles
23	6	15	5	8

Table 5 Delayed deterioration in five patients

Patient	Nature of deterioration	Blood on CT scan
1	Died—cardiac failure	Ventricles
2	Died—rebleed	Interfrontal, basal cisterns
3	Transient confusion	Ventricles
4	Transient left arm weakness	No
5	Dysphasia and rt hemiparesis	Basal cisterns, interfrontal, and left Sylvian fissure

Deterioration

Five patients deteriorated within two weeks of the initial bleed. Two of the five died, two recovered completely, but the fifth developed a fixed deficit (table 5).

Patient 1. A 50-year-old hypertensive lady with kyphoscoliosis was admitted four days after sudden onset of headache, neck stiffness and confusion. She remained confused and on admission had a mild left hemiparesis. CT scan showed intraventricular blood but four vessel angiogram was normal. Her neurological condition remained unchanged until three days after admission when she deteriorated over a few hours. Examination showed a severe chest infection, cardiac failure and hypotension. She died several hours later despite treatment, and a post-mortem examination confirmed intraventricular haemorrhage, cardiac failure and acute bronchitis. There were also cerebral and cerebellar boundary zone infarcts consistent with a period of profound hypotension. The site of bleeding was a small area of haemorrhagic necrosis in the posterior part of the interventricular septum. There was no evidence of tumour. This lady's deterioration was most likely due to a chest infection and cardiac failure leading to secondary hypotension and boundary zone infarcts.

Patient 2. A 57-year-old female was admitted on the day of the haemorrhage. She was slightly confused but recovered completely within 24 hours; she had no focal signs. CT scan showed blood in the interhemispheric fissure and ambient cistern but the angiogram was normal. She was discharged back to the referring hospital where she remained well for three days, then suddenly deteriorated. Lumbar puncture showed uniformly blood stained fluid and a diagnosis of rebleed was made (eight days from the first bleed). She was not referred back and died two days later. No post-mortem examination was per-

formed. Presumably the patient had an aneurysm that failed to show on the angiogram.

Patient 3. A 64-year-old woman with ulcerative colitis and hypertension was alert and orientated with no focal signs on admission; CT scan showed intraventricular blood. Immediately following recovery from four vessel angiography performed under general anaesthetic (three days from the bleed) she was confused but had no focal signs. Her confusion resolved within 48 hours and she remained well until discharge. Her deterioration was probably due to the combined effect of cerebral angiography and a general anaesthetic, but delayed cerebral ischaemia cannot be ruled out as a possible cause.

Patient 4. A 20-year-old man was fully alert and orientated on admission, with no focal signs, but complaining of headache and neck stiffness. CT scan and four vessel angiogram were normal, with no subarachnoid blood or vasospasm. Thirty-six hours following angiography (4 days from the bleed) he developed a mild left arm weakness but remained alert. The weakness resolved within several days and he was discharged home. At out-patient follow up he remained completely well. Although his deficit was mild and he remained alert, the deterioration was probably due to delayed ischaemia. No other cause was apparent for the left monoparesis.

Patient 5. This patient showed the clinical picture usually associated with significant delayed cerebral ischaemia. She was a 48-year-old previously well woman, in whom there was a sudden onset of frontal headache, neck stiffness and vomiting but no loss of consciousness. On admission the day after the bleed she was orientated with no focal signs but complained of headache and neck stiffness. CT scan showed subarachnoid blood in the basal cisterns, interfrontal region and left Sylvian fissure. Four vessel angiography was normal (no vasospasm). Seven days after the haemorrhage her conscious level deteriorated and she became dysphasic with a mild right hemiparesis. A repeat CT scan showed a possible area of low density in the left temporal region. Her blood pressure was normal throughout the ill-

ness. No further action was taken and her condition improved spontaneously over the following two weeks. She was discharged home at four weeks from the bleed, fully mobile and independent, but with a mild residual dysphasia.

Of the five patients who deteriorated, delayed cerebral ischaemia probably was the cause in two (patients 4 and 5), and possibly a third (patient 3)—an incidence of 4–6%. Of the two likely cases of delayed cerebral ischaemia one had blood on the CT scan and one did not. Nineteen patients had blood on the CT scan and did not deteriorate.

Discussion

Previous reports have shown that the prognosis of patients with subarachnoid haemorrhage for which no cause is found, both in the short and long term, is better than in those with subarachnoid haemorrhage due to an aneurysm; in particular the rebleed rate is low (table 6).

The principal aim of previous studies was to ascertain the prognosis; the incidence of delayed deterioration was discussed only briefly, if at all. Some early studies would in any event have been unsuitable for identifying cases of delayed ischaemia. The CT scan was not available to exclude primary intracerebral haematoma, and vertebral angiography was not routine; a number of the cases must have deteriorated due to rebleeding from posterior circulation aneurysms.

The three most recent reports^{20–22} all comment on the incidence of delayed deterioration but their series cannot be compared to the present study. Hayward²⁰ reported three cases of transient deterioration, but included in his study head injured patients and two patients with intracerebral haematomas; only four patients had blood on the CT scan compared with 23 in this study. Sundbärg *et al.*²¹ reported 128 patients with subarachnoid haemorrhage of unknown cause and stated that 11 had delayed cerebral ischaemia; seven of these died or were permanently disabled. Their series started in 1968 and it is therefore not possible to correlate

Table 6 Prognosis following subarachnoid haemorrhage of unknown cause

Author	Number of patients	Length of follow-up (yr)	Total mortality	Rebleed rate
Walsh, 1956 ¹⁵	93	2–15	16%	12%
Dunsmore, 1956 ¹⁶	81	1–10	27%	21%
af Björkstén, 1957 ¹⁷	61	1–8	5%	8%
Höök, 1958 ¹⁸	138	1–10	11.5%	7%
Levy, 1960 ¹⁹	76	1–8	10.5%	1.5%
Hayward, 1977 ²⁰	51	1–3	0	0
Sundbärg, 1982 ²¹	128	3–13	4%	3%
Béguelin, 1983 ²²	42	1–5	12%	2%

these results with the CT scan findings, or to exclude primary intracerebral haematomas. The study of Béguelin and Seiler²² is also inadequate. Of 42 patients five died from "ischaemic complications". All five were receiving anti-fibrinolytic drugs, which are known to increase the incidence of cerebral ischaemia,^{5,23} and three of the five did not have a CT scan. The post mortem findings were not reported, and the causes of death are therefore uncertain.

The present study described 50 patients with proven subarachnoid haemorrhage not related to head injury or intracerebral haematoma. Fifteen patients had blood visible within the basal cisterns, which in aneurysmal subarachnoid haemorrhage is consistently associated with a high incidence of vasospasm and delayed cerebral ischaemia.^{8-10,24-26} Two patients had a mild transient neurological deterioration, and in one case (patient 3) this was most likely due to the general anaesthetic and angiography as it occurred only three days following the bleed. Only one patient developed a fixed deficit, and even her eventual outcome was satisfactory.

The incidence of delayed ischaemia in our group of patients (4-6%) is lower than that with subarachnoid haemorrhage caused by an aneurysm (25-42%). This suggests that the mere presence of blood in the subarachnoid space is not sufficient cause for delayed ischaemia. There may therefore be other factors, specific to patients who have an aneurysm, that predispose to the development of ischaemia.

Smith *et al*²⁷ showed that severe vasospasm and an associated angiopathy are related to haemorrhage within the wall of the affected intracranial artery; they found that blood around the arteries had little effect. As most aneurysms are situated on major intracranial vessels, rupture of an aneurysm may lead to intramural haemorrhage. In cases of subarachnoid haemorrhage with normal angiograms the bleed may be from small vessels or tiny angiomas,²⁸ and intramural haemorrhage within a large vessel would not occur. This mechanism could explain the case of Friedman *et al*, where there was arterial vasospasm (accompanied by neurological deterioration) in association with an aneurysm that had not ruptured but probably enlarged.²⁹

There may also be genetic differences between patients who have an aneurysm and those who do not.³⁰⁻³² If so, then there may be inherent abnormalities in the arteries of patients with aneurysms that also predispose to the development of spasm.

Whatever the mechanism the outlook for these patients is good, provided they survive the initial effect of the haemorrhage. The incidence of rebleeding and of delayed ischaemia is low and most patients can therefore be mobilised early (in this

study 17 patients returned home within two weeks, and a further 20 within three weeks). Even the two or three patients who developed delayed ischaemia all made a good recovery, and no patient showed the fulminant picture of massive infarction and death seen so commonly after subarachnoid haemorrhage from an aneurysm.

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