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Delayed Cerebral Ischaemia: The Pathological Substrate

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Summary

Ischaemic complications both at the level of the cortex and the hypothalamus are well recognised after an aneurysmal subarachnoid haemorrhage. We have studied histological changes in the cortex (53 patients) and hypothalamus (48 patients) in patients who died after an aneurysmal subarachnoid haemorrhage.

Cortical ischaemic lesions were demonstrated in 41 of the 53 patients studied. These changes were more common in patients who had impaired control of systemic blood pressure ($p = 0.0004$) and in patients who died gradually ($p = 0.0003$). Hypothalamic lesions were found in 24 of 48 patients studied; 23 of these patients had widespread associated changes in the cerebral cortex. Patients with moderate/severe cortical changes tended to have hypothalamic lesions and it was uncommon for patients with no cortical lesions to have changes in the hypothalamus ($p = 0.0007$).

We believe that these histological changes are due to a diffuse microangiopathy which develops slowly after a subarachnoid haemorrhage and affects the cortex and hypothalamus. Because the cortical lesions are widespread we postulate that they may be implicated in the aetiology of the well described psychosocial or cognitive problems in patients who survive a subarachnoid haemorrhage.

Keywords: Autoregulation; blood pressure control; cerebral cortex; delayed cerebral ischaemia; hypothalamus; subarachnoid haemorrhage.

Introduction

Acquired ischaemic deficits account for approximately 30% of the early complications of a subarachnoid haemorrhage (SAH)[12] and are felt to be responsible for 15% of patients having a poor outcome[13, 24, 25]. Cerebral vasospasm has been implicated in the aetiology of such deficits[6, 21]. However, the cause of cerebral vasospasm is unknown and its relationship with the occurrence of ischaemic neurological syndromes has not been clearly established. Previous attention has focused on the arteries and a variety of factors that may be involved in the production and maintenance of arterial narrowing[6, 9, 22, 30, 33, 34]. Angiographic vasospasm, a narrowing of a major cerebral artery, is frequently seen between four to twenty-one days after a subarachnoid haemorrhage. It is uncommon within the first four days of a SAH[15] and the peak incidence occurs around day seven[26, 33]. On the other hand the peak incidence of neurological changes attributable to cerebral ischaemia have been demonstrated to occur between days 4 and 5[6, 24]. While the risk of cerebral infarction is increased in patients with compromised cerebral perfusion, little attention has been paid to the aetiology of the deranged perfusion or the effect of SAH on the cerebral cortex and the hypothalamus although ischaemic complications in both have been described after an aneurysmal SAH[1, 3, 4].

In this study we asked three questions. Are there recognisable histological changes occurring in the cortex and hypothalamus after an SAH? If so, is there a relationship between the major risk factors of SAH and the histological changes? Finally, can the histological changes explain some of the clinical syndromes of SAH and the lack of a clear relationship between radiological vasospasm and ischaemic neurological deficits?

Patients and Methods

Consecutive post-mortems were performed in fifty-three patients who had died following an aneurysmal SAH. There was also a control group of eighteen patients, twelve of whom had died following a myocardial infarction (hypotension), one due to hypertensive encephalopathy (a case of malignant phaeochromocytoma) and five cases of malignant glioma with raised intracranial pressure.

Clinical Details

Each patient's record was examined and information on the patient's age, sex, grade on admission (Table 1)[23], blood pressure recordings throughout the length of stay, CT scan, angiogram, op-

Table 1. *Neurological Grade of Patients on Admission*

Grade	Conscious levels[a]	Neurological deficits
1	alert	none
2	alert	minor (cranial nerve palsy)
3	alert	major
4	drowsy	none or minor
5	drowsy	major deficit
6	coma	

[a] Conscious level assessment based on Glasgow Coma Scale[31].
Alert summed coma score of 15, *drowsy* summed coma score of 9–14, *coma* summed coma score of < 8.

erative data, time and form of death was obtained. Blood pressure recordings, using automatic intermittent cuff pressures, were routinely done every four hours or more frequently if required. No antihypertensive drugs were prescribed. The variability of the blood pressure recording was taken into account. If a patient's diastolic pressure varied more than 30 mm/Hg over the course of forty-eight hours or more that patient was classified as having a variable blood pressure[20].

Patients were divided into non-operative and operative groups. Operations were usually done when the patients were Grade 1 or 2 WFNS[32] (range 1–17 days, average 10 days). The time of death from SAH was noted.

Those patients who died within forty-eight hours of a proven subarachnoid haemorrhage including rebleeds were classified as sudden deaths and those whose clinical deterioration was prolonged for more than forty-eight hours and who had suffered no further haemorrhage within that time (either clinical or post-mortem evidence) were classed as gradual deaths.

Angiograms were carried out when the patients were deemed fit for operation and the timing ranged from 1–18 days. The angiograms were reviewed by the Neuroradiologist who reported on the presence or absence of an aneurysm(s), their site(s) and the presence of vasospasm. Where vasospasm was present the Neuroradiologist commented on whether this was focal (confined to the parent vessel of the aneurysm) or diffuse.

The data from the patients' records were tabulated before the results of the histological examinations were obtained.

Postmortem Findings

The brains were fixed in formalin and six weeks later were sliced in the coronal plane. Representative blocks were taken from both frontal lobes at the level of the optic chiasm, the parietal lobes from the sensory-motor cortex, temporal lobes at the level of the mamillary bodies and the occipital lobes at the level of the parieto-occipital sulcus of both the SAH and control group of patients.

Hypothalamic blocks were examined in forty-eight SAH cases and the control group of patients at three levels; the level of the optic chiasm, the level of the tuber cinereum and the level of the mamillary bodies.

The sections were stained with haematoxylin and eosin (H&E), haematoxylin/Van Gieson and Luxol fast blue/cresyl violet.

Histologically the cortical lesions were graded as mild, moderate and severe. Grade 1 changes included mild focal shrinkage of nerve

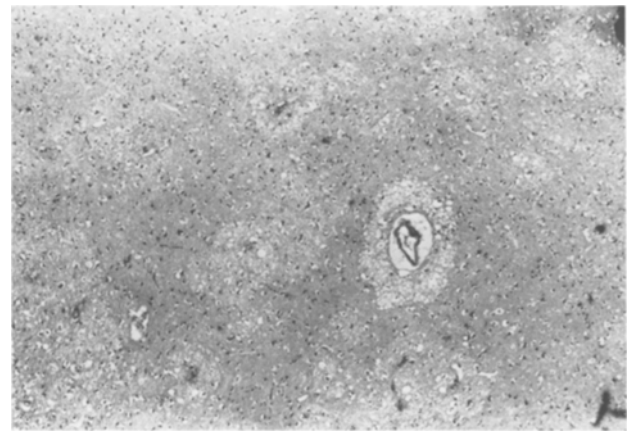

Fig. 1. Cortical ischaemic lesion showing diffuse perivascular spongy changes

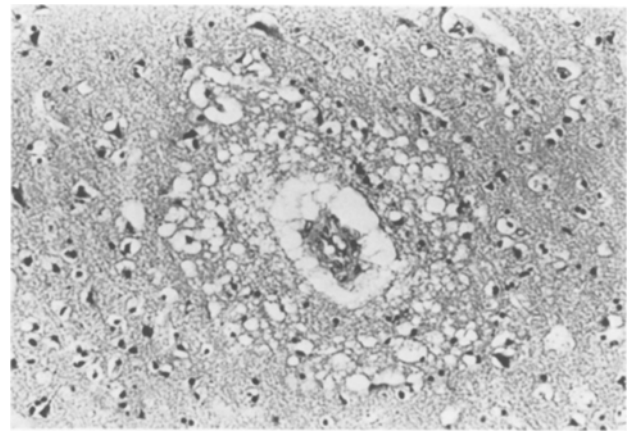

Fig. 2. Higher power view of the perivascular spongy changes and prominent endothelial cells

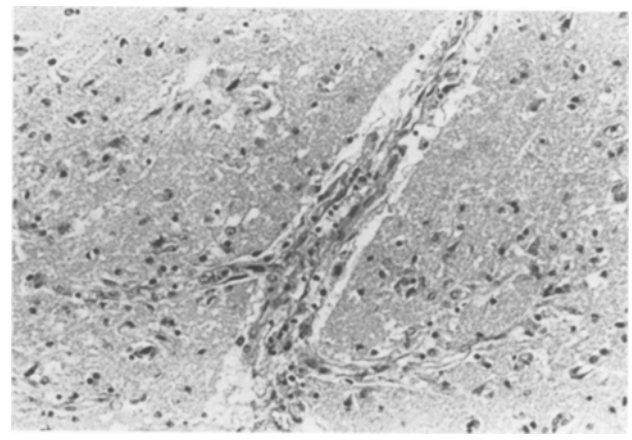

Fig. 3. Hypothalamic lesion. Microinfarction with proliferating vessels, prominent endothelial cells and the presence of scanty macrophages

cells and an increase in the pericellular and perivascular spaces. Grade 2 changes were similar but more widespread and included florid spongy changes in the perivascular region along with swollen endothelial cells. (Figs. 1 and 2). Grade 3 changes denoted marked shrinkage and/or depletion of nerve cells, proliferation of thin walled vessels and focal distribution of macrophages amounting to micro infarction (Fig. 3). Pallor of myelin staining was taken to indicate cerebral oedema.

Patients were grouped into three categories; those with no lesions, those with mild/minimal lesions (Grades 1 and 2) and those with moderate/severe lesions (Grade 3).

Histologically the lesions in the hypothalamus were of three types; Perivascular haemorrhage, micro infarcts and macro infarcts. These lesions were localised in the paraventricular and supra optic nuclei.

Statistical Methods

Test for associations between the various variables in the study were carried out. In each case the null hypothesis was that there was no association. Two different test statistics were used depending on whether or not one or both of the variables were ordinal rather than nominal. If both were nominal the Pearson chi-square statistic was used. On the other hand if one or both were ordinal the Kruskal-Wallis statistic was used. In particular the categories of lesions; none, mild/minimal and moderate/severe were taken as ordinal. For tables with less than five rows and columns exact p-values were calculated using the computer package STATXACT[25]. For the larger tables Monte Carlo methods were used to estimate the exact p-values, again using STATXACT.

Results

There were fifty-three SAH patients (18 males) in the study. The age range was between 22–64 (mean age 47 years). Forty-nine patients were admitted within forty-eight hours of their SAH, the remainder within seven days. Of the 18 control patients, 12 were male and their ages ranged from 30–62 with a mean of 43.4.

Cortical Lesions

Forty-one of the 53 patients had cortical ischaemic lesions and 34 of these patients had focal cerebral oedema. Twenty-five patients had moderate/severe cortical ischaemic lesions, sixteen had minimal/mild lesions and twelve patients had no lesions. None of the control group of patients had cortical lesions.

Relationship Between Blood Pressure and Cortical Lesions

The variability of the blood pressure was assessed in forty-nine patients, four patients' charts being incomplete. Of the forty-nine twenty patients had a variable blood pressure. More patients in the fluctuating blood pressure group had moderate/severe lesions than patients who maintained a steady blood pressure. The relationship between a fluctuating blood pressure and the subsequent development of ischaemic cortical lesions is highly significant ($p = 0.0004$) (Table 2).

Table 2. *Systemic Arterial Blood Pressure Trend*[a] *and the Development of Cortical Ischaemic Lesions*

Lesions	Stable blood pressure	Fluctuating blood pressure
mod/sev	7 (24%)	16 (80%)
mild/min	13 (45%)	2 (10%)
none	9 (31%)	2 (10%)

[a] Charts incomplete in 4 patients.
$p = 0.0004$.

Hypotension was not recorded in any SAH patients while the 12 control patients suffering a myocardial infarction had periods of severe hypotension.

Relationship Between Type of Death and Cortical Lesions

Thirty-four patients died suddenly – the terminal event lasting no longer than 48 hours, eighteen patients gradually and one patient's documentation contained insufficient data for classification. The sudden death group of patients (dying within 48 hours of a haemorrhage) succumbed within a mean of 7 days from their initial SAH. The gradual death group of patients died

Table 3. *Severity of Lesions and Nature of Death*

Lesions	Sudden death	Grading death
mod/sev	10 (29%)	14 (78%)
mild/min	13 (38%)	4 (22%)
none	11 (33%)	0

$p = 0.0003$.

Table 4. *Ischaemic Lesions in Patients Dying Within and After One Week*

Lesions	Within a week		After a week	
	Sudden	Gradual	Sudden	Gradual
mod/sev	4	2	6	12
mild/min	8	–	5	4
none	6	–	5	0

$p = 0.0019$.

Table 5. *Relationship Between Location of Aneurysm, Site of Infarction or Swelling and Presence and Severity of Ischaemic Cortical Lesions*

Site of infarction	Location of aneurysm	Severity of lesions
LT AC	ACoA	severe LT > RT
LT AC	ACoA	severe
RT AC	ACoA	minimal LT > RT
RT O	RT PCoA	severe
LT MC	LT ICA	severe RT > LT
RT MC	RT MCA	severe
RT MC	RT ICA	severe
LT MC	LT ICA	moderate
Site of swelling	**Location of aneurysm**	**Severity of lesions**
RT hemisphere	RT MCA	none
LT hemisphere	LT MCA	mild
diffuse	multi	none
RT hemisphere	RT MCA	minimal
diffuse	ACoA	severe
RT hemisphere	RT PCoA	severe

LT left, *RT* right, *ACoA* anterior communicating artery aneurysm, *MCA* middle cerebral artery aneurysm, *ICA* internal carotid artery aneurysm, *PCoA* posterior communicating artery aneurysm, *multi* multiple aneurysms, *AC* anterior cerebral artery territory, *MC* middle cerebral artery territory, *O* occipital artery territory.

within a mean of 14 days from their presenting SAH (only two of these patients died within one week of their initial SAH).

Significantly Table 3 shows that all patients in the gradual group had a lesion; these were severe in 78%. By contrast 32% of the patients in the sudden group had no histological lesions demonstrated ($p = 0.0003$). As shown in Table 4 there were more patients with moderate/severe lesions who died gradually after seven days. This was also a significant association ($p = 0.0019$).

None of the other variables assessed were statistically associated with the presence of cortical ischaemic lesions.

Table 5 shows the relationship between the location of the aneurysm, the site of infarction or swelling and the presence and severity of the cortical lesions. There is no correlation between the site of infarction or swelling and the severity of the cortical lesions. Eight patients had cerebral infarction and these patients tended to have severe cortical ischaemic lesions while this was the case in only two of the six patients with cerebral swelling.

In Table 6 the histological lesions are tabulated against age, sex, grade on admission and site(s) of aneu-

Table 6. *Relationship Between Severity of Lesions and Age, Sex, Grade on Admission and Location of Aneurysm*

Clinical feature		None	Histological lesions	
			Minimal/mild	Moderate/severe
Age	< 49	5 (20%)	8 (32%)	12 (48%)
	> 50	7 (25%)	8 (28%)	13 (46%)
Sex	male	4 (22.2%)	5 (28%)	9 (50%)
	female	8 (22.9%)	11 (32%)	16 (46%)
Grade	1	4 (40%)	4 (40%)	2 (20%)
	2	1 (9.1%)	2 (18%)	8 (73%)
	3	2 (25%)	3 (37.5%)	3 (38%)
	4	1 (33.3%)	0	2 (67%)
	5	1 (14.3%)	3 (43%)	3 (43%)
	6	3 (21.4%)	4 (29%)	7 (50%)
Aneurysm[a]	ACoA	2 (20%)	3 (30%)	5 (50%)
	MCA	6 (30%)	4 (20%)	10 (30%
	ICA/PCoA	0	6 (43%)	8 (57%)
	V-B	2 (50%)	2 (50%)	0
	Multi	2 (50%)	1 (25%)	1 (25%)
	Others	0	0	1 (100%)

[a] *ACoA* anterior communicating artery aneurysm, *MCA* middle cerebral artery aneurysm, *ICA* internal carotid artery aneurysm, *PCoA* posterior communicating artery aneurysm, *V-B* vertebro basilar artery aneurysm, *multi* multiple aneurysms.

$p = > 0.1430$ in all cases.

Table 7. *Distribution of Blood on CT Scan Done Within 3 Days of Haemorrhage and Severity of Ischaemic Lesions*[a]

Lesions	No blood	Blood basal cisterns/ subarachnoid haemorrhage	Intraventricular/ intracerebral blood
mod/sev	2 (40%)	9 (53%)	13 (52%
min/mild	2 (40%)	4 (24%)	8 (32%)
none	1 (20%)	4 (24%)	4 (16%)

[a] Number of patients = 47 (2 patients not scanned). (4 patients scanned after 3 days).
p = 0.8972.

Table 8. *Relationship Between Angiographic Spasm and Cortical Ischaemic Lesions in 28 Patients*

Lesions	None	Spasm localised	Spasm diffuse
mod/sev	5 (56%)	1 (20%)	9 (64%)
min/mild	2 (22%)	3 (60%)	4 (29%)
none	2 (22%)	1 (20%)	1 (7%)

p = 0.2612.

Table 9. *Influence of Operation on the Development of Ischaemic Cortical Lesions*

Lesions	No operation	Operated patients
mod/sev	18 (45%)	7 (54%)
mild/min	12 (30%)	4 (31%)
none	10 (25%)	2 (15%)

p = 0.5358.

rysm(s). There was no significant relationship ($p > 0.1430$ in all cases).

The presence or absence of blood on the CT scan made no difference to the incidence of the histological lesions (Table 7). There was a higher percentage of moderate/severe lesions and fewer patients with normal histology with diffuse spasm in the twenty-eight patients who had cerebral angiography. The numbers are small and this does not reach statistical significance (Table 8). Thirteen patients had an operation and the incidence of histological lesions in these patients showed little difference to the non-operated group (Table 9). Eight of the 13 patients died within 36 hours of their operation. Four had severe cortical lesions, 2 moderate and 2 had no lesions. Of the 8 patients, 6 had been ventilated prior to death. Four of these patients had severe cortical lesions, 1 moderate and 1 had no lesions. There was no significant relationship between timing of operation, type of operation (all aneurysms were clipped), post operative deterioration, time of death and cortical lesions.

Table 10. *Frequency of Cortical Ischaemic Lesions in Patients With and Without Hypothalamic Lesions*

	Cortical lesions		
	none	mild/min	mod/severe
Hypothalamic lesions	1	8	15
No hypothalamic lesions	12	6	6

p = 0.0007.

Table 11. *Site of Aneurysms in Patients With and Without Hypothalamic Ischaemic Lesions*

	Lesions	No lesions	p value
ACoA	8	2	p = 0.0141
MCA	7	11	
ICA	8	3	
V-B	0	4	
Multi	1	3	
Others	0	1	

Hypothalamic Lesions

The histological changes in the hypothalamus were analyzed in forty-eight patients. The ages of these patients ranged from 22–64 (mean 47). Twenty-four patients had no evidence of ischaemic changes in the hypothalamus. There were no hypothalamic lesions in the control group.

Factors Associated with the Development of Hypothalamic Lesions

As shown in Table 10 patients with moderate/severe cortical lesions tended to have hypothalamic lesions and it was uncommon for patients with no cortical lesions to have hypothalamic changes (p = 0.0007).

Table 11 shows the site of aneurysms in patients with and without ischaemic change in the hypothalamus. Patients with an aneurysm in the anterior cerebral and internal carotid artery territories tended to more frequently develop ischaemic change in the hypothalamus (p= 0.0141).

Table 12. *Relationship Between the Frequency of Hypothalamic Lesions and Blood Pressure, CT Appearances, Vasospasm, Operation and Mode of Dying*

Total	BP Death				CT			Vasospasm			Operation	
	St	F	S	G	none	SAH	Par/Ven	None	L	D	Yes	No
H + 24	10	12	11	13	4	5	14	3	1	7	17	7
H − 24	18	6	19	5	1	1	5	3	3	7	18	6
p value	0.0689	0.1246					1.000			0.7319		1.000

H hypothalamic (+ = present and − = absent, *G* gradual, *S* sudden, *St* stable, *F* fluctuating, *L* local, *D* diffuse, *Par* parenchymal *Ven* intraventricular.

Table 13. *Neurological Grade on Admission in Patients With and Without Ischaemic Hypothalamic Lesions*

Grade	Number of patients	
	Lesions	No lesions
1	3	7
2	7	3
3	2	6
4	1	1
5	4	2
6	7	5

p = 0.3259.

Hypothalamic lesions were more frequent in patients with a varying blood pressure but this just failed to reach statistical significance (p = 0.0689, Table 12).

While patients who die gradually are more likely to have hypothalamic change this also fails to achieve significance (Table 12).

There is no significant correlation between the changes in the hypothalamus and the distribution of blood on CT scan, angiographic vasospasm or the influence of surgery (Table 12).

There was no correlation between neurological grade on admission and the subsequent development of ischaemic changes in the hypothalamus (Table 13).

Discussion

Cerebral ischaemia is widely regarded as a major cause of increased morbidity and mortality following a subarachnoid haemorrhage[6, 11, 13, 16, 24, 33]. Most previous studies have concentrated on the pathophysiology of cerebral blood vessels with little attention being paid to the effect of cortical changes on outcome. Crompton demonstrated areas of cerebral infarction related to the major arteries[3, 4] and changes suggestive of infarction are often seen on CT scans[5, 14, 24]. There is an association between the occurrence of these changes and neurological deficits[24]. However, patients may deteriorate in the absence of the CT scan changes and on other occasions may have a scan appearance of infarction but yet remain neurologically intact. The relationship of these changes to angiographic vasospasm is even more uncertain though they are assumed to be ischaemic.

This prospective study was designed to determine the occurrence of cortical changes after a subarachnoid haemorrhage, the relationship of these changes to various risk factors and whether syndromes of cerebral ischaemia could be related to histological changes in the cerebral cortex.

Cortical lesions were present in 78% of the SAH patients studied and 61% of these patients had moderate or severe lesions. The lesions were widespread, discrete and in many sections the lesion had a central blood vessel.

Histologically these lesions resemble those commonly seen in hypertensive encephalopathy. However, we did not observe the vessel necrosis which occurs in that condition[10]. Byrom in the 1950's demonstrated similar cerebral lesions in animals[2]. In animal experiments using the Goldblatt method[8] to produce renal ischaemia he was able to show that those animals who developed a high fluctuating blood pressure were more likely to develop ischaemic lesions of the cortex. He suggested that loss of autoregulation of blood pressure was a factor in producing this cerebral pathology. However, in the control group of 18 patients no cortical or hypothalamic lesions were found. While 6 of these patients died as a result of raised intracranial pressure,

the remaining 12 died following myocardial infarction and hypotension.

Eighty per cent of the patients with moderate/severe lesions had a fluctuating blood pressure. This in our view supports Byrom's observations and may reflect a profound disturbance of autoregulation of the cerebral blood vessels which particularly affects the micro-circulation in the cortex. This loss of autoregulation has been previously described[11]. However, we have noticed two additional effects of subarachnoid haemorrhage on blood pressure, the loss of the diurnal rhythm[20] and secondly the occurrence of major fluctuations of the diastolic blood pressure. It would seem that both these effects may result from loss of autoregulation. Thus the auto-regulatory disturbance would appear to be much more extensive than has previously been appreciated. This leads us to postulate that disturbed neural control may be a factor.

The failure of hypotension or raised intracranial pressure in the control group to produce similar ischaemic cortical changes to the SAH patients is to be expected. In the SAH group no hypotension was recorded nor were there any events comparable to those occurring in the patients with myocardial infarction. The significant cardiovascular findings in the SAH patients was the presence of a fluctuating blood pressure. The observation cofirms the complexity of the pathophysiological processes initiated after a SAH[28].

The significant relationship between gradual deterioration and death and the severity of the cortical lesions lends support to the concept of an ischaemic process developing over a period of time. This is supported by two previous observations. Firstly, the time of maximum occurrence of deterioration due to delayed ischaemia[5, 24] and secondly, the evidence of a progressive fall in cerebral blood flow during the first ten days after a subarachnoid haemorrhage[19]. This time related structural change would appear to be dependent on additional factors, both central and systemic.

There was no significant correlation between the severity of the cortical lesion and age, sex, position of the aneurysm or operations. We reviewed in detail the timing of operation, operation, time of death and presence of cortical lesions. There was no indication that the operative procedure played a significant part in the cortical or hypothalamic changes.

There are fewer Grade 1 patients on admission with severe lesions compared to patients classed as Grade 6, though no clear trend emerges on assessing all the neurological grades on admission. The strong association between cortical lesions and time would suggest that grades on admission will be less reliable in determining the extent of the lesions than an assessment of the clinical progress of the patient. This study shows that grade on admission does not determine the extent of the cortical lesions and we suspect that the severity of the haemorrhage[7, 29] is likely to be a more sensitive indicator as to the subsequent cortical changes.

While there was no significant relationship between the cortical lesions and blood on CT scans, this was probably due to the fact that the information obtained did not indicate the severity of the haemorrhage. In order to do this we should have assessed the extent of the blood clot and the number of sites affected[5, 7]. However, some authors have commented on the difficulty of measuring thickness due to anatomical variations of the cisterns and fissures, their variable planes, the different local concentration of blood, thickness of the CT slices and problems related to partial volume effects. In addition there is progressive isodensity with time[5]. There is therefore considerable doubt as to the relative value of such assessments.

The failure to obtain a significant association between angiographic vasospasm and the cortical lesions was not surprising since the angiogram only gives information about the larger cerebral vessels and only 53% of our patients had angiography. However, this study indicated no clear relationship between the occurrence of histological infarction related to a major cerebral vessel and the severity of cortical lesions.

Histological abnormalities in the hypothalamus following a subarachnoid haemorrhage have been previously described[3]. These changes were of three types and were felt to be due to ischaemia or haemorrhage and there was a strong association with autonomic dysfunction. Recent animal work has supported this clinical observation[1]. The relationship between the cortical and hypothalamic histological changes had not been previously examined and any association between these changes and systemic disturbances has been a matter of speculation.

However, in this study hypothalamic lesions occurred in 24 (50%) of the patients studied and of these only one did not have an associated cortical lesion. Sixty-five per cent of patients with hypothalamic lesions had moderate/severe cortical lesions. Significantly fewer of the patients without hypothalamic changes had cortical lesions. While the presence of hypothalamic lesions was clearly shown there may be a more subtle disturbance of hypothalamic function that

could be demonstrated by other methods, i.e., electron microscopy, audioradiography which could highlight a cause and effect relationship.

Not surprisingly, as previously reported[3], there was a correlation between the site of certain aneurysm and hypothalamic lesions.

Ischaemic hypothalamic lesions occurred more often in patients with a fluctuating blood pressure although this did not reach statistical significance. This further supports the view that there is an impairment of systemic autoregulation. This impairment may be associated with a disturbance of the cerebral microcirculation and hypothalamic control may be involved in both autoregulatory systems[35].

While the cortical lesions have been clearly illustrated and their relationship to some of the risk factors following a subarachnoid haemorrhage demonstrated, the mechanisms producing these ischaemic changes remain ill defined. However, the study does offer some explanation with regard to the clinical deterioration of patients following a subarachnoid haemorrhage without CT scan or angiographic abnormalities. The extensive distribution of the lesions may help explain some of the neurological sequelae that occur after a subarachnoid haemorrhage. In particular the lack of drive, loss of concentration, memory deficits and lethargy that occur in some of these patients[17, 27].

In conclusion this study demonstrates the presence of ischaemic lesions throughout the cortex and the hypothalamus in patients following a subarachnoid haemorrhage. A strong correlation between the cortical lesions and gradual neurological deterioration suggested a time element. In addition there was a significant association between the occurrence of hypothalamic lesions and severe cortical changes indicating the extensive nature of the disturbance. A significant relationship between the cortical lesions, hypothalamic lesions and variable blood pressure was noted. This led us to question the part played by the loss of autoregulation of blood pressure, the cerebral micro-circulation and the role of neural control in the pathophysiology of an aneurysmal subarachnoid haemorrhage.

It is not surprising, given the nature of these histological lesions, that conventional imaging (CT scanning and angiography) cannot be used to predict outcome accurately in patients who have sustained an aneurysmal SAH. Magnetic resonance imaging may be of value in the detection of these widespread, discrete ischaemic lesions and digital image analysis coupled with PET scanning data may facilitate their early detection. The ability to image these widely distributed lesions may enable us to explain some of the early and late cognitive changes that have been associated with subarachnoid haemorrhage[17, 27].

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