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Seizures at the onset of subarachnoid haemorrhage

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Abstract In a prospective study of 253 patients with subarachnoid haemorrhage, 16 (6.3%) had seizures at the onset of bleeding. None had a previous history of seizures. One was an alcoholic. None had metabolic imbalance. Hemiparesis, Hunt's grade > 3, the amount of subarachnoid blood and the presence of an aneurysm were significantly more frequent in patients with seizures at the onset of subarachnoid haemorrhage. Although rebleeding and mortality or severe disability at discharge were more frequent in these patients, seizures were not a significant predictor of prognosis. One of the survivors with early seizures developed recurrent epileptic seizures 1 year later.

Key words Subarachnoid haemorrhage · Seizures · Aneurysm

Introduction

Between 4% and 10% [21] of all patients with subarachnoid haemorrhage (SAH) have seizures at the onset of bleeding. In aneurysmal SAH the percentage is higher (10–26%) [8]. Predisposing factors for seizures occurring at the onset of SAH have not been yet identified. The influence of early seizures on the prognosis of SAH and on late seizures is either not known or controversial. The aims of this study were to describe the prevalence of seizures at the onset of SAH and the associated clinical-radiological features, in an attempt to identify the predisposing factors; to evaluate the influence of seizures on the prognosis of SAH and on the occurrence of late seizures.

Patients and methods

This investigation used the data recorded in our SAH data bank [5] for all cases of SAH admitted to the Departments of Neurology and Neurosurgery from January 1985 to December 1990. Forty-three patients who did not have CT performed on admission were not included. From the remaining 253, we selected those who had seizures within the first 12 h of SAH (onset seizures). We only included seizures observed by the medical staff, ambulance workers or other reliable witnesses. Seizures were defined and classified as generalized or focal according to the recommendation of the International League Against Epilepsy [4]. Previous hypertension (defined according to WHO criteria), high blood pressure on admission (systolic blood pressure > 175 mm Hg or diastolic blood pressure > 120 mm Hg), neurological examination and clinical severity quantified by the Hunt and Hess scale [11] at admission were compared in patients with and without onset seizures. Files of patients with onset seizures were searched for other predisposing factors for seizures, such as alcohol abuse, past history of seizures or metabolic imbalance. Outpatient clinic files of the survivors who were followed up at our institution were also reviewed to look for recurrent seizures.

Two independent observers quantified intracranial blood densities on CT (according to Fisher's grade [7]) and intraventricular blood [10], and identified the presence and localization of intracerebral haematomas, acute ischaemic infarcts and acute hydrocephalus [9] on admission CT.

Four-vessel angiography was performed on all patients eligible for surgery. For the purpose of statistical analysis identified aneurysms were classified as anterior or posterior circulation aneurysms. Among all patients who had surgery only 3 (2 with early seizures) had surgery performed within 1 week of the onset.

To evaluate the effect of onset seizures on prognosis we compared complications during hospitalization, disability at discharge (using the modified Rankin scale [20, 23]) and death of patients with and without onset seizures. Complications were defined as follows: (1) seizures – new seizure occurring after the first 12 h of SAH; (2) rebleeding – sudden headache, deterioration of consciousness or new focal signs, with an increase in the amount of

Table 1 Predisposing factors for seizures at the onset of subarachnoid haemorrhage *(SAH)*

	SAH with onset seizures $n = 16$		SAH without seizures $n = 237$		*P*-value	Odds ratio	95% confidence interval
	n	%	*n*	%			
Hypertension	11	69%	106	48%	NS*	2.7	0.9–8.1
Hemiparesis	5	31%	19	8%	< 0.02	5.2	1.6–16.6
Hunt's grade 4 + 5	4	25%	14	6%	< 0.02	5.3	1.5–18.6
Fisher's grade 3 + 4	13	81%	112	47%	< 0.02	4.8	1.3–17.4
Intraventricular blood grades 2 + 3	2	13%	31	19%	NS	0.95	0.2–4.4
Haematoma	5	31%	37	16%	NS	2.46	0.8–7.5
Ischaemic infarct	–	–	10	5%	NS	–	–
Hydrocephalus	3	19%	49	21%	NS	0.9	0.2–3.2
Aneurysm/no. with angiography	10/11	91%	111/206	54%	< 0.03	8.6	1.1–68.1
Anterior/posterior	7/3	63%/27%	76/ 35	37%/17%	NS	1.1	0.3–4.4

* Not statistically significant ($P > 0.05$)

Table 2 Clinical course and prognosis of SAH

	SAH with onset seizures $n = 16$		SAH without seizures $n = 237$		*P*-value	Odds ratio	95% confidence interval
	n	%	*n*	%			
Rebleeding	7	44	20	10	< 0.001	8.4	2.8–25.1
Haematoma	2	12.5	12	5.9	NS*	2.7	0.5–13.2
Acute hydrocephalus	–	–	26	12.9	NS	–	–
Rankin grade > 3 or death at discharge	7	43	38	17	< 0.05	4.1	1.4–11.6

* Not statistically significant ($P > 0.05$)

blood on repeated CT or at autopsy; (3) acute hydrocephalus – deterioration of consciousness with only hydrocephalus on repeated CT.

For statistical analysis we used the chi-square test with correction for continuity or Fisher's exact test when appropriate, odds ratio (OR), differences between proportions (DP) and their respective 95% confidence intervals (95% CI).

Results

Of the 253 SAH patients, during the study period 16 had seizures within 12 h of the onset (6.3%). None of the 43 patients excluded had seizures. In 11 patients seizures occurred within 1 h of the onset and in 5 between 1 and 12 h. In 6 patients seizures were observed by the emergency room medical staff, in the remaining 10 by relatives or other reliable witnesses. In 15 patients fits were apparently generalized. Between 12 and 24 h after onset, 4 of these patients experienced recurrent seizures (2 generalized and 2 focal). Owing to either poor medical condition or severe disability with no indication for surgery, angiograms were not performed in 32 SAH patients (14%) without onset seizures and in 5 patients (31%) with onset seizures (95% CI: –5% to +41%). No further seizures were observed during hospitalization in patients with onset seizures. Anticonvulsive medication, usually phenytoin 300 mg/day, was prescribed in all patients with onset seizures.

Predisposing factors for seizures at the onset of SAH

There were no demographic differences between SAH with and without onset seizures [males: 7 (44%) vs 137 (58%) (DP = 14%; 95% CI –39.2% to +11.1%); mean age: 43 vs 51 years (95% CI –14% to +5%)].

None of the patients with onset seizures had a history of previous seizures, a hypertensive peak (systolic blood pressure ≥ 175 mm Hg and/or diastolic blood pressure ≥ 120 mm Hg), or metabolic imbalance on admission. One patient was an alcoholic. Previous hypertension, intraventricular blood, presence of haematoma, ischaemic infarct or hydrocephalus on CT, and location of aneurysms were similar in SAH patients with and without onset seizures. Subjects with onset seizures were more frequently hemiparetic, in stupor or coma with a Hunt's grade ≥ 4, had higher amounts of subarachnoid blood on CT and in 10 of the 11 on whom angiography was performed an aneurysm was detected; all these differences are statistically signifi-

cant (Table 1). Although the risk of seizures associated with each one of these factors was high (ranging between 4.8 and 8.6), some of their 95% Cls were wide. Because of the low prevalence of haematomas, our study may lack the requisite power to exclude confidently a role of haematoma as a predisposing factor for seizures.

Influence of onset seizures on SAH prognosis and late seizures

During hospitalization rebleeds were significantly more frequent in patients with onset seizures (Table 2). Six of these patients rebled, 5 of them fatally. Rebleeding occurred on the 1st (1 case), 2nd (1), 4th (1) and 7th (3) day, always before surgery. The OR for onset seizures as a predictor of rehaemorrhage was 3.4 (95% Cl: 1.3–8.5).

Severe disability at discharge with a Rankin grade ≥ 4 or death was significantly more frequent in patients with onset seizures (Table 2). However, onset seizures were not a significant predictor of disability or death (OR = 1.4; 95% Cl: 0.6–3.4).

Five of the non-disabled survivors were regularly examined (mean follow-up = 34 months) at the outpatient clinic. Anticonvulsvie medication was prescribed in all cases for at least 12 months. At 3 months none reported seizures. At 1 year, one patient experienced recurrent seizures that were difficult to control.

Discussion

In the present series the frequency of seizures within 12 h of the onset of SAH was 6.3%, a figure within the range mentioned in the literature [12, 14, 17–19, 22], except for the series of Bonita and Thomson [3] and Bassi et al. [1], where no seizures were observed at onset, and the series of Biller et al. [2] and Hart et al. [8], who reported 21% and 19%, respectively. However, Biller et al. studied SAH in young patients (15–45 years old) while Hart et al. included only patients with aneurysmal SAH. Some authors [6, 21] mentioned that movements resembling those of the decerebrate state can occur during transient unconsciousness at the onset of SAH, but clonic jerking, clenched teeth and cyanosis are absent. Hart et al. [8] mentioned that probably many of the reported "seizures" are not epileptic but decerebrate fits, due to a sudden increase in intracranial pressure. In our series the fits were observed by the medical staff, family or a reliable witness and we only included patients who had unquestionable seizures.

Predisposing factors for onset seizures have not yet been identified because previous series analysed seizures occurring during hospitalization and/or after aneurysmal surgery that can have different determinants from onset seizures. Features associated with the occurrence of seizures in SAH included haematomas and anterior circulation aneurysms [17], previous hypertension, ischaemic infarct shown on late CT and duration of coma longer than 1 h [16], and even a higher prevalence of vertebrobasilar aneurysms [8]. Because many of the predisposing factors are associated, they should be analysed by multivariate techniques. However, the small number of SAH subjects with seizures does not permit this type of analysis and limits the conclusions of our study. We did not find any instance of metabolic disturbance or previous epilepsy. Alcoholism was a relevant precipitant of onset seizures in one patient. Detection of an aneurysm, independently of its localization, hemiparesis, Hunt's grade > 3, and a larger amount of subarachnoid blood were the major predisposing factors for onset seizures in SAH. A large amount of subarachnoid cisternal blood was found to be significantly more frequent in SAH patients with seizures [16]. An eventual mechanical effect of the blood near the motor cortex area or the insula can account for the association between hemiparesis and the occurrence of seizures at the onset of SAH. The release of large amounts of glutamate might account for the induction of epileptic seizures [13]. Moreover, the presence of blood in the subarachnoid spaces generates lipid peroxides from oxygen free radical reactions catalysed by iron and by haemoglobin degradation products as well as by the oxidative catabolism of arachidonic acid [15]. Although these might be critical factors in the induction of brain oedema and brain injury, they are less likely to contribute to such an early phenomenon as onset seizures.

Patients with onset seizures had more rebleeds during hospitalization. Rebleeding did not happen on the same day as the seizure and so it is difficult to establish a cause and effect relationship. In Öhman's series [16] a significant severe disability at discharge was also found in SAH subjects who sustained seizures, while in the series of Hart et al. [8] no correlation was found either with severe disability at discharge or death. They found a higher mortality, or severe disability at discharge, in patients with onset seizures.

All our patients were treated with anticonvulsant drugs during hospitalization. This seems reasonable because 25% of the patients experienced early recurrences. Long-term prophylactic treatment is more controversial. Early seizures are not an independent predictor of late ones [9]. The small number of patients with long-term follow-up does not allow a confident conclusion on this aspect, but prophylactic anticonvulsant treatment for 1 year failed to prevent the development of recurrent seizures in 1 of 5 patients.

In conclusion, large amounts of subarachnoid blood and damage to the motor cortex are likely to be two of the factors involved in the genesis of onset seizures, but these seizures are not a significant predictor of prognosis.

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