The notion of "warning leaks" in subarachnoid haemorrhage: are such patients in fact admitted with a rebleed?

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Abstract

***Objective*—Often patients with subarachnoid haemorrhage (SAH) recall a recent episode of acute severe headache, usually interpreted as a "warning headache" or first SAH. An alternative explanation is recall bias. The clinical and radiological features of patients with SAH were studied in relation to previous headaches or later rebleeding.**

***Methods*—Patients with either a previous headache episode or a subsequent rebleed were selected from the SAH database in Utrecht within 1 month of the index SAH. The clinical condition was graded on the World Federation of Neurological Surgeons (WFNS) scale. The CT was reviewed and the amounts of subarachnoid blood, hydrocephalus, and intraventricular, intracerebral, and subdural blood were rated. Proportions were compared by unpaired or paired *t* test.**

***Results*—Forty four of 390 patients (11%) had had a severe headache before their index SAH (11 of these had a subsequent rebleed); 31 other patients had a rebleed in hospital but no preceding headache. Patients with and without preceding headache did not differ in level of consciousness (14 of 44 *v* 11 of 31 were comatose), nor in any of the radiological features. After rebleeding (42 patients), 37 of 42 patients were comatose (*v* 11 of 42 before), and CT showed higher proportions of intracerebral haemorrhage (17%), intraventricular haemorrhage, (27%), and hydrocephalus (12%) than baseline scans. Intraventricular haemorrhage was twice as frequent after rebleeding than at baseline.**

***Conclusions*—The clinical and radiological features of patients admitted with SAH after a preceding bout of headache did not differ from those without such an episode, and are clearly dissimilar from those after documented rebleeds. The findings challenge the existence of minor "warning headaches".**

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Rebleeding occurs in one third of patients with aneurysmal subarachnoid haemorrhage (SAH),[1 2] and is a major cause of poor outcome.[3] The risk of rebleeding is highest during the first 3 weeks after the initial episode of SAH.[4–6] If patients survive a rebleed, further rebleeding episodes are in the offing.[1] Therefore many neurologists and neurosurgeons favour clipping of the aneurysm soon after rerupture, also if the patient's clinical condition is less than optimal, and despite the lack of controlled evidence for this regimen.

Up to 60% of patients with SAH recall an episode of sudden, unusually severe headache days to weeks before the index episode. Such headaches have often been interpreted as a "warning leak".[7–9] In a population based study we found, however, that the radiological appearance of subarachnoid haemorrhage associated with first ever episodes of acute, severe headache without loss of consciousness or focal deficits, did not differ from the usual pattern with aneurysmal ruptures, and provided no evidence for the existence of small leaks.[10] This contradicts the time honoured concept that "sentinel headaches" should be interpreted as a first (minor) SAH.[7–9 11] The practical implication of that notion is that patients with SAH who had a previous warning headache are in fact admitted with a rebleed, are at increased risk of further rebleeds and poor outcome, and are candidates for immediate operation. The alternative explanation for a "sentinel headache" might be that it was in fact unrelated to SAH, but that in the context of serious brain disease the earlier episode is overinterpreted (recall bias).[10]

We studied the clinical and CT features in patients with SAH on admission, with or without a history of previous headache, to investigate if such characteristics are helpful in distinguishing a warning headache suggestive for previous SAH from an innocuous headache episode before the initial SAH. A further group for comparison consisted of patients with an episode of rebleeding after admission.

Methods

The study population was selected from the SAH database of the University Hospital Utrecht for the period 1993 through 1996, 390 patients in total. We selected all patients with (1) SAH and an aneurysm established by conventional angiography, CT angiography, or necropsy[12 13]; and (2) either a previous bout of sudden headache 1 month or less before the index SAH, or a rebleed within 1 month after the established index SAH (regardless of previous headache episodes). Data about previous headaches as well as rebleeding were obtained from the patient's medical chart, recorded by

attending neurologists at the time of admission, and prospectively completed for the SAH database by one of us (GJER). A previous headache episode was diagnosed if patients or their relatives on direct questioning reported a sudden and unusually severe headache, lasting for at least 1 hour, with or without loss of consciousness or focal symptoms, and with a symptom free interval or marked improvement of symptoms before the index SAH.[14] Rebleeding was defined as an episode after a proved index SAH, with (1) a sudden decrease in level of consciousness, with or without new focal signs or loss of brainstem reflexes, or only a sudden severe increase of headache[1]; and (2) an increased amount of blood compared with the baseline CT on admission, or—in the absence of an increased amount of blood—exclusion by CT of alternative explanations, especially infarction or hydrocephalus, and also exclusion of cardiac arrythmias by means of continuous electrocardiographic bedside monitoring.[15]

Of the 98 selected patients, 23 other patients were excluded from the study for the following predefined reasons: no history obtainable from the patient or relatives to prove or disprove a previous episode of headache (10); use of anticoagulant drugs (one), in which bleeding is more extensive[16]; first CT performed more than 1 week after the onset (six); history of recent head injury (one); a history of a ruptured aneurysm (three); subsequent rupture of a second aneurysm (one); or deterioration after lumbar puncture in the referring hospital (one). The seventy five remaining patients were divided in three subgroups: patients with a preceding bout of headache before the index SAH (33), patients with rebleeding after admission (31), and patients with both characteristics (11) (fig 1). The clinical condition on admission was assessed by means of the World Federation of Neurological Surgeons (WFNS) grading scale[17] (this scale combines the Glasgow coma scale (GCS) and the presence or absence of focal signs: grade I implies GCS score 15 without focal deficits, grade II and III GCS score 14–13 with absence (II) or presence (III) of motor deficit, grade IV GCS 12–7, and grade V GCS 6–3, either with or without motor deficit).

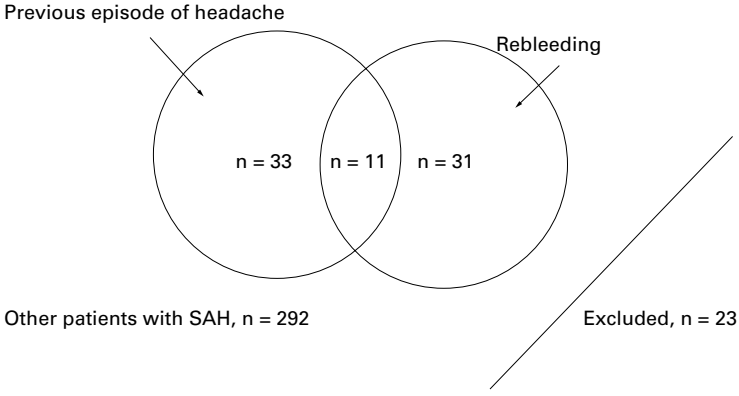

Figure 1 Patients with SAH included in this study, and the numbers of all other patients with SAH seen during the study period (1993–6).

We dichotomised between good (WFNS I-III) versus poor (WFNS IV-V) condition on admission.

Brain CT was performed on the day of the ictus in 68 (91%) of the 75 patients. Patients with rebleeding in hospital had undergone immediate CT, in the great majority within 1 hour after deterioration. For the purpose of this study one of us (FHHL) graded the CT on admission and after the first rebleed, without access to the clinical features. The amount of subarachnoid blood was quantified as follows: 10 fissures and cisterns were separately graded as: 0 (no blood), 1 (sedimentation), 2 (not completely filled), or 3 (completely filled).[18] Totals were classified as large amounts (20–30), moderate amounts (10–20), and small amounts or no blood at all (0–10). Hydrocephalus was defined as a bicaudate index or third ventricle size exceeding the 95th percentile for age.[19 20] Intraventricular haemorrhage (IVH) was dichotomised into absent (no ventricular blood or only sedimentation) or present (clots, ventricles partly or completely filled with blood). Intracerebral haematoma (ICH), hypodensity (oedema or infarction), and subdural haematoma (SDH) were also classified as present or absent.

We made four different comparisons: firstly, the clinical and radiological features on admission of 44 patients with antecedent headache episodes versus 31 without (11 in the first and all in the second group would eventually rebleed, but we considered that as irrelevant for the initial SAH); secondly, the CT features before and after rebleeding in 42 patients; thirdly, the intervals between the preceding headache episode and the index SAH versus the intervals between index SAH and rebleeding; and fourthly the CT features in the patients with previous headache episodes versus those with rebleeding— before and after exclusion of the overlapping group. We compared proportions between groups by means of their mean differences, based on either the unpaired or paired t test, as appropriate, with their corresponding 95% confidence intervals. We used the Mann -Whitney U test to compare cisternal blood scores between the different groups.

Results

In the 75 included patients (fig 1), the mean age was 51 (SD 13) years; range 21–79 years) and the proportion of women two thirds (n=49), without any difference between the three subgroups. Of the 44 patients who had preceding headache before SAH, 28 (64%) had consulted a physician, and in 18 SAH was not considered. Ten patients were referred for the initial episode, but had a second attack with headache or loss of consciousness before reaching the hospital. Sixteen patients did not contact their general practitioner for their headache.

Table 1 CT features of index SAH in patients with and without a previous headache

Feature	With previous headache episode(%)	Without previous headache episode (%)	Difference between proportions (%) (95% CI)
Number	44	31	44 *v* 31
Hydrocephalus	6 (14)	3 (10)	4 (−11 to 19)
Intracerebral haematoma	18 (41)	10 (32)	−9 (−31 to 13)
Intraventricular haemorrhage	11 (25)	10 (32)	7 (−14 to 28)
Subdural haematoma	2 (5)	0 (0)	5 (−2 to 11)
Amount of cisternal blood:			
0–10	14 (32)	14 (42)	13 (−9 to 36)
10–20	7 (16)	4 (13)	−3 (−19 to 13)
20–30	23 (52)	13 (42)	−10 (−33 to 13)

Table 2 CT features of all patients after rebleeding compared with the baseline CT . Percentages are given in parentheses

	All patients with rebleeding		
Feature	Initial CT	CT after rebleeding*	Difference between proportions (95% CI)
Number	42	41	
Hydrocephalus	5 (12)	10 (24)	12 (3 to 17)
Intracerebral haematoma	15 (36)	21 (52)	17 (2 to 28)
Intraventricular haemorrhage	14 (33)	25 (60)	27 (9 to 32)
Subdural haematoma	1 (2)	2 (5)	2 (−2 to 2)
Amount of cisternal blood			
0–10	19 (45)	18 (44)	p Mann-Whitney *U test* 0.92
10–20	5 (12)	11 (27)	
20–30	18 (43)	12 (29)	

*CT of one patient after rebleeding was not available for review.

CLINICAL AND CT FEATURES IN PATIENTS ADMITTED WITH SAH, WITH AND WITHOUT PRECEDING HEADACHE

On admission, there was no difference in level of consciousness between the patients with and without preceding headache (14 of the 44 patients with preceding headache were comatose on admission, versus 11 of the 31 without preceding headache).

There were no significant differences in amount of cisternal blood (Mann-Whitney *U* test p=0.92) and in severity of intraventricular or intracerebral haemorrhage or in the proportion of patients with hydrocephalus between patients with and those without a previous headache episode (table 1). Subgroup analysis of 22 patients who had had their previous headache episode less than 3 days before the presenting haemorrhage again failed to show any differences with the group of patients without a warning headache (data not shown).

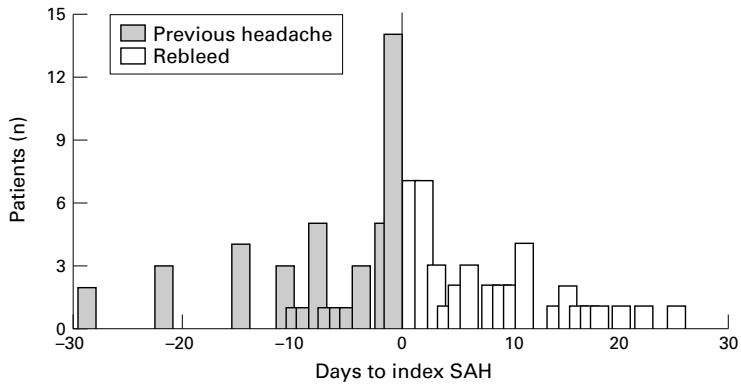

Figure 2 Time interval between previous headache or rebleed and index SAH.

CLINICAL FEATURES AND COMPARISON OF CT FEATURES AFTER REBLEEDING WITH THOSE ON ADMISSION

Shortly after rebleeding, 37 of 42 patients (88%) were comatose, of whom 10 patients became again alert within 24 hours (one had aphasia), versus 11 patients of 42 (26%) who were comatose after the first episode of SAH (eight of them distinctively deteriorated on the Glasgow coma scale).

The pairwise CT features of 42 patients before and after rebleeding are summarised in table 2 (in one patient the CT after rebleeding was not available for review).

For the group as a whole, hydrocephalus, intracerebral haematoma, intraventricular haemorrhage, and subdural haematoma were all more frequent after rerupture of the aneurysm. Except for subdural haemorrhage, all these differences were statistically significant. By contrast, large amounts of cisternal blood were more common on the initial CT. Hydrocephalus after rebleeding was associated with intraventricular haemorrhage in nine out of 10 cases. The CT features after rebleeding were similar for patients with and those without an episode of headache before admission. A subgroup analysis of 15 patients who had their rebleed within 3 days after the index SAH showed no differences from the entire group of patients who rebled.

INTERVALS BETWEEN PREVIOUS HEADACHE EPISODES AND INDEX SAH, AND INTERVALS BETWEEN INDEX SAH AND REBLEEDING

In the group with preceding headache, 37 patients had experienced a single attack of sudden severe headache, five patients had had two attacks, and two patients three attacks. Of the 42 patients with a rebleed, 31 had a single rebleed, nine had two, one had three, and one patient four rebleeds. The time intervals between warning headache and index SAH or between index SAH and rebleed are shown in fig 2 (in the case of several attacks, the shortest interval to the index SAH is given). Both for warning headache and rebleed, a first peak occurred within 1 day, and a second, smaller peak at 7–14 days before or after index SAH. Most warning headaches and rebleeds occurred within 2 weeks from the index SAH.

PATIENTS WITH PREVIOUS HEADACHE EPISODES AND PATIENTS WITH REBLEEDING IN HOSPITAL: COMPARISON OF CT FEATURES

Table 3 shows CT features of 44 patients with SAH and a previous headache episode (including 11 with a later rebleed), and of 31 patients after rebleeding in hospital, without a headache episode before admission. In patients with a rebleed, intraventricular haemorrhage was twice as frequent as in patients with a previous headache episode. By contrast, cisternal blood scores showed a trend towards smaller amounts with rebleeding than with an index episode of SAH after a preceding bout of headache. The risk differences were in the same range if the comparison was limited to the baseline scans of the 33 patients with a bout of

Table 3 CT features on admission in patients with a previous headache episode, compared with follow up CT of patients with a rebleed in hospital, without headaches before the presenting SAH

Feature	Index SAH with previous headache (%)	At rebleed, no previous headache (%)	Difference between proportions (%) 95% CI
Number	44	31	
Hydrocephalus	6 (14)	5 (16)	3 (−14 to 19)
Intracerebral haematoma	18 (41)	17 (55)	14 (−9 to 37)
Intraventricular haemorrhage	11 (25)	17(55)	30 (8 to 52)
Subdural haematoma	2 (5)	1 (3)	−1 (−10 to 7)
Amounts of cisternal blood			
0–10	14 (32)	13 (42)	10 (12 to 32)
10–20	7 (16)	11 (36)	20 (0.4 to 40)
20–30	23 (52)	7 (23)	−30 (−51 to 9)

headache before the presenting SAH but no further rebleeding in hospital.

Discussion

The notion of "warning leaks" or "sentinel headaches" has originated from the finding, in many studies, that up to 50% of patients with subarachnoid haemorrhage recall on admission an episode of unusual, sudden, severe headache some days to weeks before. If such premonitory headaches would truly represent a first SAH, the ictus on admission is a rebleed.

This implication is made unlikely, at least in general, by our findings in this study. Firstly, the proportion of patients in coma and the severity of subarachnoid, intraventricular, or intracerebral haemorrhage is similar in patients with or without a previous bout of headache. Secondly, clinical condition severely worsened after rebleeding in most patients and CT after an in hospital rebleed showed features that, on average, were much more severe than those of patients with premonitory headaches and also on comparison with the baseline scans of the same patients. The main differences on CT were that patients with rebleeding in hospital had a higher rate of intracerebral and especially intraventricular haemorrhage, and also of hydrocephalus than on their corresponding baseline CT, but lesser amounts of cisternal blood. The CT features after rebleeding were in keeping with those from a previously published series of 39 patients, in which rerupture was accompanied by intraventricular haemorrhage in 41%, by an intracerebral haematoma in 18%, and by both in 10%, and 31% had purely SAH.[1] Despite the difference in the average patterns of haemorrhage between rebleeding and the index SAH, the overlap is so extensive that the CT features cannot be used to diagnose rebleeding from a single scan.

There might be objections to the fact that our finding of preceding bouts of headache not being associated with a difference in clinical or radiological features should be attributed to selection bias, in that the patients without premonitory headaches were those who would later have a rebleed. However, a previous study showed that clinical and radiological characteristics were similar for those who later went on to rebleeding and those who did not.[1] Another potential criticism is that our criteria for premonitory headaches were too loose. Yet we had only 11% of patients with this type of headache in our series, which is markedly lower than the 20%-60% of patients with SAH with a "warning leak" in other studies.[21–26] The higher proportions in the other studies may have been caused not only by recall bias,[10] but also by a higher proportion of initially missed diagnoses of true SAH (referral bias).[27 28]

A history of a previous headache episode also failed to show an association with special clinical or radiological characteristics when the analysis was confined to those in whom the premonitory bout was recent (less than 3 days), or if there was a history of repeated attacks.

We can only speculate about the causes and pathophysiological mechanisms of preceding non-haemorrhagic headache before aneurysmal rupture. We suspect that recall bias is an important factor. Other potential explanations are a sudden growth of an aneurysm, such as occurs in patients with sudden onset of headache and oculomotor palsy, but without haemorrhage,[29 30] or intramural dissection within the aneurysmal wall.[31 32]

In conclusion, the clinical and radiological features of patients with attacks of severe headache before presenting with overt SAH are so similar to the average baseline characteristics and sufficiently dissimilar from documented rebleeds to doubt the usual implication that the presenting haemorrhage in patients with premonitory headaches is in fact a rebleed. Together with our earlier finding that episodes of acute headache in the general population represent average and not minor subarachnoid haemorrages[10] this leads us to challenge the existence of minor "warning leaks" as a common phenomenon in patients with aneurysms. Of course, we do not wish to imply that the diagnosis of SAH cannot be missed.

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