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A prospective study on angiographically negative non aneurysmal spontaneous subarachnoid hemorrhage

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Abstract

Aim: To analyze patients suffering from angiographic-negative and NPM-SAH.

Material and methods: The present prospective study was conducted in the department of neurosurgery of Sri Aurobindo Institute of Medical Sciences, Indore from January 2019 to December 2020. The study comprised of 60 spontaneous subarachnoid hemorrhage patients diagnosed with initial non-contrast CT followed by CTA/MRA Brain. Initial NCCT brain suggestive of subarachnoid hemorrhage and initial negative CTA/MRA patients can be divided into perimesencephalic and nonperimesencephalic pattern. Patients of non-aneurysmal spontaneous subarachnoid hemorrhage were assessed by initial Hunt & Hess scale, GCS, modified fisher grade, WFNS grade (admission status) and modified Rankin scale for clinical outcome.

Results: In this study, WFNS grading 3 and 4 was reported among 14.3%, 23.81% and 2.56%, 0% of the subjects having non-perimesencephalic and perimesencephalic hemorrhage respectively with statistically significant difference as $p<0.05$. Slight and moderate disability was only found among subjects with nonperimesencephalic hemorrhage while no moderate/slight disability was reported among subjects having perimesencephalic hemorrhage. In this study 95.2 % among nonperimesencephalic type SAH having favourable outcome in comparison to 100 % in perimesencephalic type SAH patients at 6 months.

Conclusion: nPMN-SAH patients are associated with higher complication rate and higher incidence of aneurysm. Therefore, we strongly recommend a repeat angiogram in patients with nPMN-SAH pattern on initial imaging.

Keywords: nPMN-SAH, WFNS grade, rankin scale, GCS

Introduction

The term subarachnoid haemorrhage (SAH) refers to the extravasation of blood into the subarachnoid space. Spontaneous subarachnoid hemorrhage (SAH) is an acute and potentially fatal neurosurgical emergency. The incidence of SAH is variable and ranges from 6.5 to 23.9 per 100,000 populations (including all age groups) [1]. As far as the etiology of spontaneous SAH is concerned, around 75% of them are due to ruptured intracranial aneurysms, 5% are caused by arteriovenous malformations (AVMs) and, in remaining cases, no vascular abnormality is evident on angiographic studies[7]. One of the first and most important step in the management of spontaneous SAH is determining the cause of bleed. Initial angiographically negative spontaneous SAH group of patients thus pose a difficult management proposition. This is so because these patients run the risk of re-bleed and its consequences if a structural lesion had been missed on the initial angiogram. That is why many authors have advocated a repeat angiogram after a defined time period to detect these missed cases [2, 3].

Though most authors support the hypothesis that the culprit of the bleeding is of venous origin, the precise mechanism of the bleeding source remains unknown [4]. The initial approach to a non-traumatic SAH requires a non-invasive angiographic study with computed tomography (CT) for therapeutic decision making and risk stratification. The Perimesencephalic SAH subgroup is considered to be associated with excellent outcome and low risk of rebleeding. Unfortunately, data on outcome in patients suffering from angiogram-negative and non-perimesencephalic (NPM) SAH are published often only in small case series and data is scarce for series with more than 50 patients [5]. We therefore analyzed patients suffering from angiographic-negative and NPM-SAH who had been admitted to our institution. Our objective was to analyze factors influencing the clinical outcome in patients suffering from non-aneurysmal and non perimesencephalic (NPM) SAH.

Material and Method

The present prospective study was conducted in the department of neurosurgery of Sri Aurobindo Institute of Medical Sciences, Indore from January 2019 to December 2020. The study comprised of 60 spontaneous subarachnoid hemorrhage patients diagnosed with initial non-contrast CT followed by CTA/MRA Brain and Digital substraction angiography brain. Initial NCCT brain suggestive of subarachnoid hemorrhage and initial negative CTA patients can be divided into perimesencephalic and Nonperimesencephalic pattern. Ethical clearance to carry out the study was obtained from the ethical committee of the institute. The study protocol was explained to the patient/guardian and a written informed consent was obtained from each subject to be enrolled in the study.

Inclusion criteria

All cases were admitted with CTA/MRA Negative spontaneous subarachnoid hemorrhage patients.

Exclusion criteria

Individuals not willing to participate, Traumatic SAH, Lost to follow up and patients diagnosed with structural aneurysmal and vascular malformation case through CT/MR Angiography. & repeat Angiography positive patients.

The data was collected by a preformed structured interviewer-administered questionnaire that was pretested with modifications made prior to its use in the study. The patients were interviewed that requests for the demographic, medical history and previous history of taking any medications, clinico-radiological status and clinical outcome. We assess the patients on detail history and clinical examinations. After this detail routine blood investigation with viral marker along with radiological investigation in form of NCCT brain, CT/MR angiography. Secondary CTA positive patients excluded from study. Patients of non-aneurysmal spontaneous subarachnoid hemorrhage were assessed by initial Hunt & Hess scale, GCS, modified fisher grade, WFNS grade (admission status) and modified Rankin scale for clinical outcome.

Data collection

- After written informed consent, variables *viz*. sex, mode of presentation, clinical symptomatology, and clinical as well as radiological findings and various risk factors.
- Clinical, radiological investigations, surgical details, outcome data were recorded.
- The clinical follow-up observation was carried out by outpatient and inpatients review.
- The patients were regularly followed up at 6 week, 3 months & 6 months.
- All the data was recorded in a pre-designed and pre-tested proforma.
- Patients were examined at admission, 6 week, 3 months & 6 months. Clinical outcome is studied with help of Modified Rankin Scale at regular interval 6 week, 3 months & 6 months. AT time of admission patients assess with help of GCS Score, Hunt & Hess scale, WFNS grading and bleeding pattern on fisher grading on NCCT brain.

Statistical analysis

Data so collected was tabulated in an excel sheet, under the guidance of statistician. The means and standard deviations of the measurements per group were used for statistical analysis (SPSS 22.00 for windows; SPSS inc, Chicago, USA). Difference between two groups was determined using student t-test as well as chi square test and Fisher Exact Test. The level of significance was set at $p < 0.05$.

Results

Out of 60 subjects, 21 (35%) were having non-perimesencephalic hemorrhage and 39 (65%) were having perimesencephalic hemorrhage diagnosed on initial bleeding pattern on NCCT Brain. In our study, 61.9% and 69.23% of the subjects were male having non-perimesencephalic and perimesencephalic hemorrhage respectively. In both groups male were more than females. Mean age among subjects having nonperimesencephalic and perimesencephalic hemorrhage was 45.67±11.39 and 43.03±15.44 years respectively. In overall study spontaneous non-aneurysmal subarachnoid hemorrhage more common among 40-60 year age group patients.

Table 1: Distribution of angiographically negative patients turned out to be positive on second CTA

Second CTA	Nonperimesencephalic Hemorrhage		Perimesencephalic Hemorrhage	
	N	%	N	%
Positive	2	8.69	0	0
Negative	21	91.31	39	100
Total	23	100	39	100

Initially there were 62 patients diagnosed with NCCT Brain suggestive of SAH with Initial negative CTA which then goes for second CTA. In second CTA 02 patients comes to positive with 9.68%. Initially there were 23 subjects having nonperimesencephalic hemorrhage, out of which 02 turned out to be positive on second CTA (8.69%). None of subjects with perimesencephalic hemorrhage turned out to be positive on second (table 1).

Table 2: Hunt & Hess grading, WFNS, GCS grading at admission among the study subjects

Hunt & Hess Grade	Nonperimesencephalic Hemorrhage		Perimesencephalic Hemorrhage		Chi Square	P value
	N	%	N	%		
1	2	9.52	10	25.64	1.97	0.28
2	16	76.19	28	71.8		
3	2	9.52	1	2.56		
4	1	4.76	0	0		
					t test	p value
Mean±SD	2±0.63		1.87±0.52		0.71	0.40
WFNS Grade					Chi Square	p value
1	8	38.09	26	66.67	6.81	0.04*
2	5	23.81	12	30.77		
3	3	14.3	1	2.56		
4	5	23.81	0	0		
					t test	p value
Mean±SD	1.67±0.91		1.44±0.72		1.16	0.29
GCS Grade					Chi Square	p value
≤12	5	23.81	0	0	8.11	0.02*
13-14	8	38.09	13	33.33		
15	8	38.09	26	66.67		
Total	21	100	39	100		

Hunt & Hess grading 3 and 4 was reported among 9.52%, 4.76% and 2.56%, 0% of the subjects having non-perimesencephalic and perimesencephalic hemorrhage respectively with statistically insignificant difference as p>0.05. WFNS grading 3 and 4 was reported among 14.3%, 23.81% and 2.56%, 0% of the subjects having non-perimesencephalic and perimesencephalic hemorrhage respectively with statistically significant difference as p<0.05. GCS grade ≤12 was reported among 23.81% of the subjects having non-perimesencephalic hemorrhage. GCS grade 15 was found among 38.09% and 66.67% of the subjects having non-perimesencephalic and Perimesencephalic hemorrhage respectively (table 2).

Table 3: Modified Rankin Scale at follow up (different intervals) among the study subjects

MR Scale	Nonperimesencephalic Hemorrhage		Perimesencephalic Hemorrhage		Chi Square	P value
	N	%	N	%		
At 6 Weeks						
0	13	61.9	36	92.3	10.48	0.01*
1	4	19.05	3	7.7		
2	1	4.8	0	0		
3	3	14.3	0	0		
At 3 Months						
0	15	71.4	37	94.9	6.81	0.03*
1	3	14.3	2	5.1		
2	1	4.8	0	0		
3	2	9.52	0	0		
At 6 Months						
0	15	71.4	37	94.9	6.49	0.01*
1	4	19.05	2	5.1		
2	1	4.8	0	0		
3	1	4.8	0	0		

*: statistically significant

Slight and moderate disability was only found among subjects with nonperimesencephalic hemorrhage while no moderate/slight disability was reported among subjects having perimesencephalic hemorrhage. When subjects were compared w.r.t. MR scale at different intervals among according to nonperimesencephalic and perimesencephalic hemorrhage, it was found to be statistically significant as p<0.05 (table 3). In this study 95.2 % among nonperimesencephalic type SAH having favourable outcome in comparison to 100 % in perimesencephalic type SAH patients at 6 months.

Discussion

It is generally recognized that NASAH has a more preferable outcome than aSAH, recent studies suggest that the management of the nPMN-SAH subgroup should be more rigorous in light of its more severe clinical courses and outcomes [6]. As nPMN-SAH is a diagnosis of exclusion, some controversial issues remain regarding the management of these patients that have negative initial CTA findings. Despite numerous studies utilizing multiple imaging modalities, the bleeding source of NASAH has not been elucidated [7].

In our study, males were comparatively more as compared to females in the present study. Asma Bashir *et al* [8], Sunil K Gupta *et al* [5] and P. Canhao *et al* [10] revealed similar results too.

In this study, Hunt & Hess grading 3 and 4 was reported among 9.52%, 4.76% and 2.56%, 0% of the subjects having non-perimesencephalic and perimesencephalic hemorrhage respectively. Similarly Asma Bashir *et al* [8] in their study reported that HH grades 3 or above were mostly seen in patients with nPMSAH. Sunil K Gupta *et al* [5] also noted that 23.7% patients in poor grade (IV/V) and 76.3% having good grade HHS I-III. No patients in PMN type have poor grade but 26.5% in npmn type, which similar to our study.

In this study, WFNS grading 3 and 4 was reported among 14.3%, 23.81% and 2.56%, 0% of the subjects having non-perimesencephalic and perimesencephalic hemorrhage respectively with statistically significant difference as p<0.05. Similarly Asma Bashir *et al* [8] and As Konczalla *et al*[10] reported similar findings.

In our study, GCS grade ≤12 was reported among 23.81% of the subjects having non-perimesencephalic hemorrhage. GCS grade 15 was found among 38.09% and 66.67% of the subjects having non-perimesencephalic and perimesencephalic hemorrhage respectively. Similarly Asma Bashir *et al* [8] in their study found that at discharge 9% of the subjects with non-perimesencephalic hemorrhage were having 3-5 GOS at discharge. In a study by Alhoobi, *et al* [11], patients with NPM-SAH had initial severe symptoms with low GCS (GCS ≤12) as all patients with WFNS Grade IV had NPM SAH, and 3 of them had GCS <10 as compared to the PM-SAH.

At admission, Moderate and slight disability was found among 3 (14.3%) and 5 (23.8%) subjects having nonperimesencephalic hemorrhage while no moderate/slight disability was reported among subjects having perimesencephalic hemorrhage. After 6 weeks, 3 months and 6 months; moderate disability was reported among 3 (14.3%), 2 (9.52%) and 1 (4.8%) subjects having nonperimesencephalic hemorrhage respectively. When subjects were compared w.r.t. MR scale at different intervals among according to nonperimesencephalic and perimesencephalic hemorrhage, it was found to be statistically significant as p<0.05. Similarly Asma Bashir *et al*[8] in their study found that at discharge 11% of the subjects with non-perimesencephalic hemorrhage were having 3-6 mRS at discharge. Juergen Konczella *et al* [12] also reported similar type of finding.

At the end of 6 month, unfavorable outcome was revealed only in one subject (4.8%) having nonperimesencephalic

hemorrhage in the present study. Liang Xu *et al* [13] reported that patients with PMN-SAH had a better clinical outcome at 3 months after ictus with respect to both mRS ($p < 0.001$) and GOS ($p = 0.003$). In a study by Raghavendra N *et al* [14], better outcome was seen in good number of patients (79.5%) especially in patients with PMSAH group (91%) and even delayed cerebral ischemia was less in PMSAH patients when compared to the patients NPMSAH. These results were in accordance with our study.

Long-term follow-up in our study is limited by heterogeneity in patient age and time to last clinical follow-up. Although time to clinical follow-up within 6 month was not significantly different between groups, patients with each form of nonperimesencephalic or perimesencephalic hemorrhage must be followed for a longer period of time specially in nonperimesencephalic hemorrhage, on average.

Conclusion

Managing SAH patients with negative initial CTA findings can be challenging. Based on the results of our present study and a review of the pertinent literature, the PMN-SAH subgroup usually has a benign clinical course and a repeat CTA very seldom reveals a ruptured intracranial aneurysm. More importantly, nPMN-SAH patients are associated with higher complication rate and higher incidence of aneurysm. Therefore, we strongly recommend a repeat CTA in patients with nPMN-SAH pattern on initial imaging.

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