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Non-Aneurysmal Subarachnoid Haemorrhage (NASAH): The Role of Spinal Imaging in the management Pathway Single Centre Experience

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ABSTRACT

Background: NASAH constitute 10-20 % of all spontaneous subarachnoid haemorrhages (SAH) as no structural causes for the haemorrhage were detected despite extensive neuroimaging investigations. The optimal diagnostic pathway is still open to question.

Objective: To evaluate the diagnostic yield and the utilization rate of Magnetic Resonance Imaging (MRI) for spinal column routinely used in identifying a structural lesion in patient with NASAH.

Methods: In this retrospective study, adult patients admitted to the Walton Centre/Liverpool/UK between the 1/2009 and 05/2018 with spontaneous NASAH were surveyed. A multidisciplinary team examined the utilization rate, mean time, and the diagnostic yield of the following imaging tests: Computed Scan, Computed Tomography Angiography, Digital Subtraction Angiogram, cervical and whole spine MRI. The assessment was during hospital admission and for long term follow-up (6-24 months).

Results: During that period, 450 patients with spontaneous NASAH were treated in the hospital. In 76 patients (17%), an entire spinal axis by standard T1- and T2-weighted MR-imaging was done. While cervical T1- and T2-weighted MR-imaging was conducted in 156 patients (24.5 %). In all the 232 patients (51.5%), MR-imaging for the spinal axis did not identify any underlying spinal anomaly that contributing to the SAH formation.

Conclusion: In spontaneous NASAH patients, traditional use of spinal axis MR-image has a very low diagnostic yield. Therefore, MRI for possible causes of NASAH is not routinely recommended unless there are focal neurological deficits to suggest a cranial or spinal pathology.

Keywords: Subarachnoid haemorrhage. Non-aneurysmal subarachnoid haemorrhage Cerebrovascular diseases. Magnetic resonance imaging. Spinal cord vascular anomaly. Spinal cord imaging

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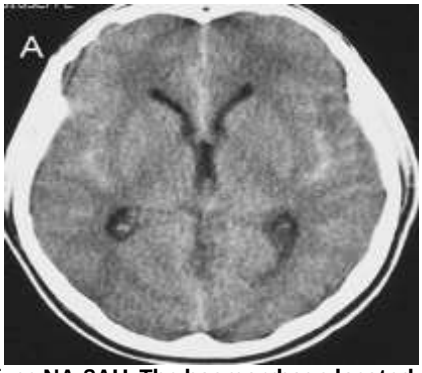
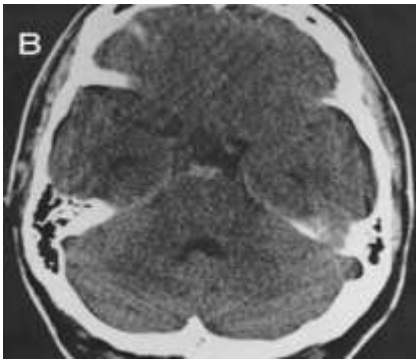
INTRODUCTION

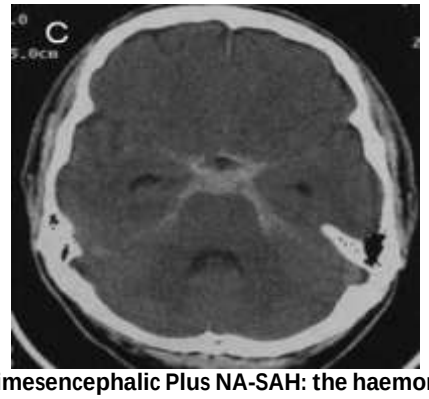
In about 15-20% of spontaneous SAH patients, no secondary causes of the bleeding such as cerebral aneurysm or arteriovenous malformation (AVM) could be identified despite the performance of different imaging modalities. These patients would be diagnosed as non-aneurysmal spontaneous subarachnoid haemorrhage patients (NASAH) [1-4]. The more recent classification of NASAH was introduced by Aladi et al [5] and divided the NASAH into five subgroups according to their initial CT scan findings as flow: perimesencephalic, perimesencephalic-plus, diffuse, superficial, and CT -negative with Lumber Puncture (LP) positive NASAH. All these patients, Computerised Tomography Angiography (CTA), Digital Subtraction Angiography (DSA) and \ or brain and spinal Magnetic Resonance Imaging (MRI) were done to confirm the diagnosis of NASAH. This is summarized in figure (1)



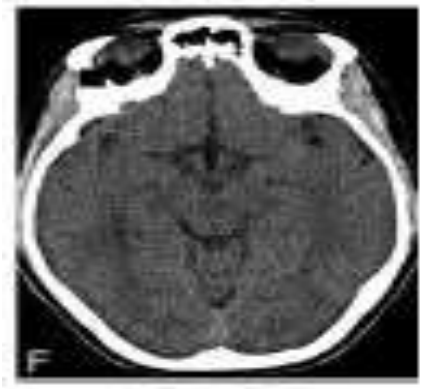
A- Diffuse NA-SAH: The haemorrhage located mainly on the basal cistern and extend to the interhemispheric cistern, Sylvain cistern, suprasellar cistern, and the cerebellopontine angle cistern.



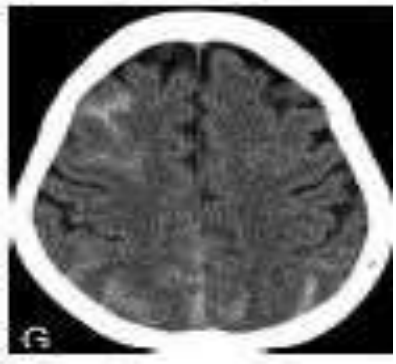
B- Perimesencephalic Plus NA-SAH: Where the haemorrhage concentrated immediately anterior to the midbrain without extension of blood to the ambient cistern or to the basal part of the Sylvain fissure.



C- Perimesencephalic Plus NA-SAH: the haemorrhage focused directly anterior to the midbrain, with blood expansion to the ambient cistern and to the caudal part of the Sylvain fissure, but without the complete filling of the anterior interhemispheric fissure.



D illustrates negative cranial CT scans in patients presented with a thunderclap headache. Xanthocromic changes was found in the Lumberpuncture of the SAH patient.



E shows peripheral location of haemorrhage at the brain sulci and no blood was found in the bsalcristen.

Figure 1: Illustrates from A-E figures the classification of NA-SAH patients

Bleeding origin and the real causes of the haemorrhage in NASAH patient are still under speculation despite of the advancement in the neuroimaging procedures during the last decade. Theories includes micro aneurysms or micro angiomas that endure thrombosis at the time of haemorrhage, or the bleeding source could be a venous or capillary rupture around the midbrain [6,7]. Also, the basal vein of Rosenthal was draining into another venous system rather than the vein of Galen venous system and could be the cause of the bleeding [8]. However, there was no clear explanation for the actual role of these venous abnormalities in SAH formation [9,10].

A spinal vascular anomaly has been reported as a cause of NASAH, but its incidence is unknown and rare [11-13]. However, failure to visualise this bleeding source will spark a serious spinal cord complication such as acute spinal haemorrhage or myelopathy with more deterioration in the clinical condition and delay the management protocols [14]. During the last decade, many published studies systematically looked for the spinal origin of haemorrhage in patient with NASAH [11,12,15,16]. However, the major limitations of the aforementioned studies were related to the retrospective nature of the data collection and small number of sample-population. Also, the exact incidence rate of the spinal causes of the haemorrhage were not discussed in reliable manner.

In this study, our aim is to examine the role of conventional MR- imaging of the entire spinal axis in search for a spinal origin in non-aneurysmal SAH. The study will review the neuroimaging modalities used for the diagnosis of NASAH patients during the initial hospital admission and follow-up period. The result of the study could be used to enhance the care pathway for NASAH patients.

METHODOLOGY AND MATERIALS

Study Design

The study was an observational retrospective review for the patient's information that were collected from a tertiary neuroscience centre to evaluate the investigation pathway of NASAH patients. The site of the study was The Walton Centre Foundation Trust, Fazakerley/Liverpool/ United Kingdom. It is a specialised neuroscience centre serving a population of the 3.5 million in the northwest of England. A

multidisciplinary team composed from neurovascular, neurosurgeon, neuroradiologists, and statistical analyst from The Walton Centre carried-out the data collection and analysis process for the information.

The study population

Patients admitted to the hospital with NASAH from the 1st of January 2008 to the 31st of December 2018 were included in this review. NASAH is a class of the haemorrhagic stroke caused by a bleeding into the subarachnoid space around the brain. No secondary vascular aetiologies for the bleeding could be identified despite the performance of the different imaging modalities (angiogram negative for aneurysms and intracranial vascular malformation). The selected patients were admitted to the hospital with a clinical history of non-traumatic spontaneous SAH that was documented by bleeding findings in a non-contrast cranial CT scan. Another group of patients included were presented with a negative non-contrast cranial CT scan for SAH, but lumbar puncture was positive for Xanthochromia/bilirubin. In both previous SAH groups, no added information related to the bleeding sources were recorded after doing different angiographic procedures such as CTA, DSA, and \or MRA. No age limitation was obtained.All

Radiological assessment

All the selected patients have a non-contrast cranial CT scan were flowed by CTA with intravenous contrast, conducted on 64-slice scanner. According to the results, the patients were classified into five sub-groups: -

1) Perimesencephalic NASAH: blood was precisely located anterior to the midbrain without extension of blood to the ambient cistern or sylvian fissure.

2) Perimesencephalic plus NASAH: the blood located directly anterior to the midbrain with expansion to the ambient cistern and sylvian fissure.

3) Diffuse NASAH: the haemorrhage located on the basal cistern and extended to the interhemispheric, sylvian, suprasellar, and cerebellopontine cistern.

4) Superficial NASAH: the blood located at the periphery of the brain without any filling to the basal cistern

5) CT-negative/LP positive NASAH: the patients presented to the Emergency Department (ED) with a thunderclap headache but with negative brain CT scan and typical xanthocromic changes in the cerebrospinal fluid (CSF). Xanthochromia is the hallmark of SAH diagnosis, and it defines as yellow CSF discolouration due to the presence of blood. The preferred technique for detecting Xanthochromia is spectrophotometry as it can differentiate CSF pigments per their different absorption of light. SAH diagnosis depends on the detection of a net bilirubin absorbance of more than 0.0007 absorbance unit (AU) at a wavelength of 458 nanometres.

All the above groups underwent DSA and procurement of the images was achieved by 2D and 3D-DSA using single-plane angiographic unit (Philips Medical System, Netherland). Iodinated Contrast material was injected through the femoral vein to visualise the vertebral, internal and external artery. Another DSA was done for the patients during follow-up period from 90 days to 7 years. If the there are any contraindication for contrast injection such as chronic renal failure (CRF), the patient offered a brain MRI and MRA instead. In addition, if no intracranial causes for the bleeding where proved by the neuroradiologist, the patients offered a spinal cord MRI and MRA with T1 and T2 weighted arrangement in sagittal position.

Statistical analysis

Data was analysed using SPSS software (version 22.0) for windows. The parametric variables were presented as percentages or numbers, and the statistical test of choice to define if variation occurred between the groups was the Pearson chi-squared test. The non-parametric variable presented as mean (± standard deviation), and the relation between the groups was analysed through independent-measures *t* test. The revenue of spinal MRI was figured through dividing the number of NASAH patients with spinal origin of the haemorrhage by the total number of the NASAH patients who subjected to spinal axis MRI. The proportion was given with reciprocal 95% confidence interval (CI). P value of less than 0.05 and 0.001 during statistical analysis was agreed as significant and highly significant respectively.

RESULTS

Study population

2251 patients with SAH admitted to the neurovascular ward in The Walton Centre during the period from the 1st of January 2008 to the 31 of December 2018. Aneurysmal SAH was the diagnosis in 80% (n=1801) patients, while NASAH was the diagnosis in the remaining 20% (n=450) patients. Chi-Square test showed that there was no significant statistical difference in the rate of hospital admission for both patients' groups with p value; 0.882.

Patients characteristics

The male proportion account for 66% (n=300), while the female patient was 34% (n=150), with male to female ratio of 2:1. The mean age of male population was 42.1 years, while it was 53.4 years in female gender. The higher incidence rate of the haemorrhage was recorded in sixth decade (50-59 years), and it formed 30% (n= 90) of male patients and 25% (n=37) of female patients. The study show that hypertension was the main independent vascular risk factor for developing NASAH, which occurred in 21% (n=96). Moreover, Diabetes Mellitus (DM) and Ischemic heart disease (IHD) were the main risk factor in 12% (n=54) and 43% (n=43) patients respectively, while smoking and alcohol consumption were reported in 113 (37.66%) and 151 (50.33%) patients respectively. The most common presenting symptom was a sudden onset headache that occurred in 94% (n=425), while focal neurological symptoms was presenting in 12% (n=51). Loss of consciousness was the initial symptoms in 11% (n=49), whereas 5% (n=23) presented with other symptoms such as photophobia, seizure, and confusion. Neck pain found in 9% (n=39), and thoracolumbar pain 5% (n=24) patients.

Classification of NA-SAH patients

The selected NASAH patients was classified into five subcategories according to their initial non-contrast brain CT scan as pure perimesencephalic NASAH, which was the

largest subgroup with 42% (n=190). Next was CT- negative \ LP-positive NASAH subgroup with 28% (n=125). Lumber Puncture (LP) was done within the first 24 hours after a negative CT scan for any bleeding in 82% of the patient, whilst in the remaining 12%, the procedure was done after 24 hours after cranial CT- scan. The third group was the diffuse NASAH with 14% (n=65), flowed by perimesencephalic-plus group with 11% (n=50). The smallest subgroup on the study was the superficial NA-SAH with only 5% (n=20) patients.

Hunt and Hess grading scale (H&H) was used by the clinician to evaluate the clinical presentation of all selected NASAH patients [17], while the neuroradiologists used Fisher scale to grade NASAH patients according to the blood distribution on the initial CT scan [18]. Good presenting clinical status was recorded in 91 % (n=410) of the patient's sample, with grade I-II in H&H grading scale and 1-2 grade in Fisher scale. On the other hand, unfavourable clinical status was recorded in 9% (n=40) admitted to the hospital with diffuse NASAH. This is summarised in in below table (1)

Table 1: Illustrates the classification of NASAH patients according to the distribution of haemorrhage on the presenting CT scan

NASAH groups*	No & % **	H &H grade ***	Fisher grade
Pure Perimesencephalic	190 (42 %)	I	2
Perimesencephalic plus	50 (11 %)	I-II	2
CT****-negative /LP positive	125 (28%)	I	1
Diffuse	65 (14 %)	III-VI	3-4
Superficial	20 (5%)	I	2

NA-SAH*= Non-aneurysmal subarachnoid haemorrhage, No&% **= Numbers and percentages, H&H***= Hess and Hunt grade, and CT-negative/LP positive**** = Computerised Tomography/Lumber Puncture.

Radiological Evaluation

All patients presented to the ED with signs and symptoms of SAH have been offered cranial CT- scan to diagnose SAH. The initial CT-scan performed within the first 24 hours of the haemorrhage in 91% (n=410) and after 24 hours in the remaining 9% (n=40). The patients who diagnosed by lumber puncture were presented afterward than 24 hours after bleeding ($p< 0.05$). All the 2251 patients with SAH underwent Computerised Tomography Angiography (CTA) except in 3% (n=15) patients who have contraindication for contrast injection such as CRF or pregnancy. Brain MRI & MRA were offered by the hospital as an alternative neuroimaging procedure for these patients and an aneurysm was diagnosed in 10 patients (ASAH), whilst no vascular aetiologies were founded in the other five patients (NASAH). Digital Subtraction Angiography (DSA) was done in 92% (N=411) patient with NASAH and no secondary vascular aetiologies were visualised in all patient (100%). Second DSA was offered during hospital admission for 81% (n=365) and no further causes for the haemorrhage were detected. The median time for repeat, same admission follow-up DSA was 10 (IQR=7) days after admission. No added information was obtained regarding the source of the bleeding and the diagnostic index was 0% for neuroimaging. Delayed flow-up DSA between 3 to 24 months was offered to 34% (n=152) patients and pericallosal aneurysm was discovered in one patient, which was surgically removed without further complication. The diagnostic index of delayed DSA is only 0.6 % ($p < 0.005$).

Routine brain MRI was done in 67% (n=310) and brain MRA in 54% (n=245) of NASAH patients, whereas brain MRV was offered to 17% (n= 76) only. All the aforementioned MR-imaging show normal finding and no secondary vascular aetiology for bleeding in patients with NASAH was discovered. The diagnostic yield of these radiological investigation in NASAH was 0%. Moreover, conventional whole spinal axis MR-imaging was done in 17% (n=76) patients, while cervical T1- and T2-weighted MR-imaging was conducted in 25% (N=156) patients. All the 232 patients have normal MR-imaging for the spinal axis except in one patient presented with negative CT/positive LP where the MR-imaging showed a cervical ependymoma with small bleeding. The tumour was surgically removed without any complication. The diagnostic yield of MR-imaging for the spinal axis account for only 1% with CI of 1.1-3.4 and p value was less than 0.005.

DISCUSSION

This retrospective cohort study reviewed the role of MR-imaging for the brain, cervical, and entire spinal axis in 450 patients presented to the ED with NASAH diagnosis. The result of this single-centre study reveals the extremely low diagnostic index of brain MRI (3%), cervical MRI (0.6 %), and whole cord MRI (0%) in the management of NASAH. The aforementioned neuroimaging is routinely ordered at the hospital for NASAH patients during the diagnostic journey.

Second follow-up CTA and DSA was ordered to nearly three-quarter of the patients during same admission, and no secondary vascular aetiology for bleeding was discovered and the diagnostic index for both procedures were nearly 0%. In addition, late follow-up DSA was done in about half of NASAH patients, and none of the follow-up neuroimaging was positive for any pathology to explain bleeding source apart from only one patient with diffuse NASAH. In this patient, peri-callosal aneurysm was missed during initial angiographic assessment and discovered during late follow-up DSA and surgically removed without complication. The reason behind that could be due to thrombosis inside the aneurysm, vasospasm, or incompetent radiological assessment [19,20]. The diagnostic index of late follow-up neuroimaging in our study was about 0.6% and matched similar study that disclosed a diagnostic yield of repeat angiographic investigation between 0% -30% [21-23].

Our study highlighted the minor role of brain MR-imaging in the management pathway of NASAH patient, and the diagnostic index was nearly 3 %. The logic behind that referred to the aneurysmal rupture as the main pathology for bleeding in SAH, and DSA is the gold standard diagnostic image not MR-imaging. In fact, brain MR-imaging should not routinely prescribe to SAH patients unless having contraindication for CTA and DSA such as pregnancy or CRF. This outcome is matching the conclusion of many other researches that reported a diagnostic index between 0%-3% [24-27]

The diagnostic role of cervical MR-imaging in management pathway of NASAH patients was extremely low, and reported in this research with only 0.6%. Our patient with spinal source of the SAH was a 45 years old female presented to ED with recurrent headache for the last 2 days and negative past-medical history. Brain CT scan show no sign of haemorrhage flowed by LP, which show a clear xanthocromic changes. CTA & DSA were arranged and the patient considered as NASAH patient after normal result. However, cervical MRI show benign tumour and removed surgically without complication. This result is aligned with the outcomes of three more studies, which highlighted that the spinal origin of SAH is commonly happened in CT- negative\ LP positive NASAH patient's group [12,16,28]. However, the small size and benign origin of the tumour did not lead to any sort of intracranial haemorrhage or further complication such as myelopathy. Though, the diagnostic index compering with the clinical relevance was very low and the study will not recommend for routine spinal axis MRI in all NASAH patient.

The outcomes of our large sample size study echo those from smaller previous papers, which documented a diagnostic role of spinal MRI in NASAH management between 0% to 4% [29-33]. While the conclusion of two big studies was in line with our result and support the low diagnostics index of spinal axis MR-imaging in management pathway of NASAH. The first one was a literature meta-analysis, which reviewed the data of 538 NASAH patients. The study showed a diagnostic index for cervical MRI as 1.3% (95% CI, 0.5% - 2.5%) [34]. The second one was a multicentre retrospective cohort study for the record of 752 patients with NASAH from 7 research centre in the United Kingdom and United State of America. The study concluded that the diagnostic role is very low and less than 1% regardless of the type of haemorrhage [35].

Our single-centre research has serval strength points. First, to our information, this is the largest available study from single-centre experience defining the diagnostic yield of spinal MR-imaging in management pathway of NASAH patients. This large set of patients' data could be counted as a true representative for NASAH patients who admitted to a hospital. Secondly, the study outcomes highlighted the importance of early diagnosis of NA-SAH patients as the care-pathway has great differences and in no doubt divers from that of aneurysmal SAH. Thirdly, long term follow-up neuroimaging (range from 90 days to 7 years) helped the study to evaluate with more certainty the aetiology of NA-SAH.

Limitations

The study has several constrain such as those related to the retrospective design with a probability of selection bias, which is a limiting factor in any retrospective analysis. Next, missing data was a major confounding factor, and the study was limited by the availability and quality of the recorded patients' information. Lastly, not all patients offered a contrast-enhancement MR-angiography for the spinal axis as a small AV fistula could be visualise, and the minimal element was only sagittal T1 and T2 image.

CONCLUSION

The study demonstrates that NASAH patients is a defined bleeding category and formed one in five of all SAH patients. There is a great variation in the management pathway of those patient worldwide, which increase the demand for the development of a gold standard and universally accepted guideline for the management. The role of spinal MR-imaging in chasing spinal origin of the bleeding is low, and the routine prescription for NA-SAH patients is not mandatory unless the patients have a focal neurological singe. Cost- effectiveness of spinal MR-imaging in relation to the clinically relevant could be a study for future work.

CONFLICT OF INTEREST

None

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