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Angiogram negative subarachnoid haemorrhage: Outcomes and the role of repeat angiography

A.A. Khan[a,*], J.D. Shand Smith[a,b], M.A. Kirkman[a], F.J. Robertson[c], K. Wong[c], C. Dott[d], J.P. Grieve[a,b], L.D. Watkins[a,b], N.D. Kitchen[a,b]

[a] Victor Horsley Department of Neurosurgery, The National Hospital for Neurology and Neurosurgery, Queen Square, London, UK
[b] Department of Brain Repair and Rehabilitation, Institute of Neurology, University College London, London, UK
[c] Lysholm Department of Neuroradiology, The National Hospital for Neurology and Neurosurgery, Queen Square, London, UK
[d] University College London Medical School, London, UK

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ABSTRACT

Background: Angiogram negative sub-arachnoid haemorrhage (SAH) is generally considered to have a more benign course than SAH of known cause. There is also variability from centre to centre as to what proportion of angiogram negative SAH patients undergo repeat Digital Subtraction Angiography (DSA). We performed a retrospective study looking at the last four years' of SAH patients at our institution in order to ascertain the clinical course, the nature and results of repeat imaging.
Methods: Retrospective analysis of clinical records and imaging of all patients presenting to our institution with non-traumatic SAH between April 2008 and February 2012 was performed. Results were analysed for presenting grades, blood distribution, complications, outcomes, repeat imaging modalities and findings.
Results: 459 patients with proven non-traumatic SAH of which 50 (11%) had no vascular cause identified on their initial angiogram were identified. The blood distribution was perimesencephalic in 17, non-perimesencephalic in 23, and 10 patients were computed tomography (CT) Negative with a positive lumbar puncture. Eight (16%) patients were complicated by hydrocephalus and 2 (4%) were complicated by vasospasm. Eight patients (16%) underwent repeat cranial DSA with a high suspicion in a multi-disciplinary team setting. None of the repeat angiograms showed an underlying aetiology for the SAH. 76% of patients had a Glasgow Outcome Score of 5 at 6 months. There were no rebleeds.
Conclusions: While generally more benign, angiogram negative subarachnoid haemorrhage can have a complicated clinical course. In our experience repeat DSA should be reserved for cases in which there is significant suspicion of occult vascular lesion. However, evidence-based guidelines are needed to aid the development of management protocols for angiogram-negative SAH and ensuring optimal patient outcomes.

1. Introduction

"Angiogram negative" or "idiopathic" subarachnoid haemorrhage (SAH) accounts for around 15% of SAH [1–4] and is usually divided into peri-mesencephalic (PMC) and non peri-mesencephalic (NPMC) SAH based on pattern of blood on computed tomography (CT) [3,5]. In addition, a subgroup of patients (around 2%) [6] have no evidence of SAH on CT imaging (so-called "CT negative"), but have supporting clinical history and the presence of xanthochromia on lumbar puncture. While angiogram negative subarachnoid haemorrhages tend to have more benign clinical course than their angiogram positive counterparts, clinical outcomes are variable and currently difficult to predict at the time of ictus [3,6,7].

Patients with a history suggestive of SAH but an early negative angiogram often undergo repeat delayed cerebral catheter angiography. Cerebral angiography carries a neurological complication rate in the order of 2.6% (0.1% permanent) and a 0.06% chance of death [8]. Magnetic resonance angiography (MRA) has increasingly replaced catheter angiography in the evaluation of angiogram-negative SAH, as advances in angiographic algorithms and spatial resolution have improved diagnostic accuracy [9,10].

Multiple studies [11–24] have been carried out over the past three decades to assess the utility of repeat catheter angiography. In our centre we perform repeat cerebral angiography only in selected cases where there is a strong suspicion of aneurysmal SAH, after

* Corresponding author at: Victor Horsley Department of Neurosurgery, National Hospital for Neurology and Neurosurgery, Queen Square, London WC1N 3BG, UK. Tel.: +44 7813934502; fax: +44 (0) 203 448 3340.
E-mail address: akbar.khan@uclh.nhs.uk (A.A. Khan).

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discussion in a multidisciplinary team meeting. In this study we present a single centre experience of patients who presented with SAH and had negative initial cerebral angiography.

2. Materials and methods

We performed a retrospective analysis of clinical records and imaging of all patients presenting to our institution with non-traumatic SAH between April 2008 and February 2012. Presenting CT studies were analysed for the presence and distribution of subarachnoid blood (PMC, NPMC and CT-negative).

PMC haemorrhage was classified according to the established definition of Van Gijn et al., "a centre of haemorrhage located immediately anterior to the midbrain or within the pre-pontine cistern, with or without extension to the ambient cisterns; absence of complete filling of the anterior inter-hemispheric fissure; absence of extension of blood into the lateral sylvian fissure, except for minute amounts; and absence of frank intraventricular haemorrhage" [25].

Presenting criteria documented included patient demographics, Fisher grade, WFNS grade and presence and distribution of blood on initial CT imaging. We also recorded length of hospital stay, clinical complications of subarachnoid during admission and Glasgow outcome score (GOS) both at discharge and at last known follow up. All follow up imaging was reanalysed by two neuroradiologists, documenting timing, imaging modality and any new relevant findings. Statistics were performed on the data using SPSS 16.0 (SPSS Inc., Chicago, IL).

2.1. Imaging protocols

2.1.1. Decision regarding further imaging

All patients who had an initial negative cerebral angiogram were discussed at a weekly neurovascular multidisciplinary team meeting, attended by interventional neuroradiologists and vascular neurosurgeons. Here a decision was made with regards to further management and imaging, based on the clinical information and radiological findings. Similar to many neurosurgical centres, no formal protocol is in existence for management of these patients currently.

2.1.2. Angiography

Angiography was performed on an Axiom Artis Zee (Siemens, Erlangen, Germany) biplane angiography system once appropriate consent had been obtained. Utilising a 4 fr common femoral artery sheath, selective injections were made using a 4F catheter into both internal and external carotid arteries and at least one vertebral artery. Standard angiography was obtained in all patients to ensure all pial and dural arteries were adequately visualised. All procedures were performed or supervised by an experienced neuroradiologist and later reviewed in a multidisciplinary meeting.

2.1.3. MRI/MRA

The MRI studies were performed on either a Siemens Magnetom 1.5T (Espree, Avanto) or 3T (Trio, Skyra) MRI scanner. Sequences used were T1 saggital, T2 axial, coronal fluid attenuated inversion recovery (FLAIR), axial T2*, diffusion weighted imaging (with apparent diffusion co-efficient [ADC] map), intracranial time of flight MRA and susceptibility weighted imaging (SWI).

3. Results

459 patients with proven non-traumatic SAH underwent formal angiography during the time period of this study. From this cohort, 50 patients (11%) had no vascular cause identified on their initial angiogram. Thirty were male, with a mean age of 52.5 years [range = 25–84 years].

3.1. Clinical presentation

Patients were divided into three subgroups based on blood distribution on presenting CT scan: perimesencephalic (PMC); non-perimesencephalic (NPMC); and a CT negative group (with positive CSF studies) (CTN) (Table 1). The commonest symptom experienced was of a sudden onset headache (80%), followed by vomiting (30%), neck pain/stiffness (18%), collapse/loss of consciousness (12%), photophobia (10%), confusion (8%), and seizures (2%) (Table 1). Six percent of patients had a slow onset headache.

3.2. Clinical outcomes

Longest hospital stays were seen in the NPMC group (median 10 days) and shortest in the CTN group (median 5 days) (Table 2). The clinical course was more complicated in the NPMC patients with seven requiring external ventricular drain (EVD) insertion for hydrocephalus, two developing clinical vasospasm, and one of these suffering a permanent neurological deficit (all Fisher grade

Table 1
Data on basic demographics, Fisher and WFNS grades in our cohort.

	Perimesencephalic	Non perimesencephalic	CT Negative
Total number	17	23	10
Median age (range)	49 (29–66)	56 (37–64)	52 (25–74)
Male:female	12:5	14:9	4:6
Presenting symptoms			
Sudden onset headache (%)	17 (100)	16 (70)	7 (70)
Slow onset headache (%)	0 (0)	1 (4)	2 (20)
Vomiting (%)	6 (35)	5 (22)	4 (40)
Collapse/loss of consciousness (%)	1 (6)	4 (17)	1 (10)
Neck pain/stiffness (%)	4 (24)	4 (17)	1 (10)
Photophobia (%)	3 (18)	2 (9)	0 (0)
Confusion (%)	1 (6)	2 (9)	1 (10)
Seizure (%)	0 (0)	0 (0)	1 (10)
WFNS grade			
1	14	17	9
2	2	4	–
3	1	–	–
4	–	2	1 (seizure)
Fisher grade			
1	–	–	10
2	–	1	–
3	17	20	–

CT = computed tomography; WFNS = World Federation of Neurosurgical Societies.