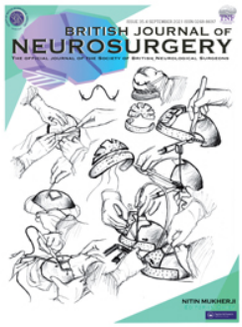

British Journal of Neurosurgery

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/ibjn20

# The value of repeated lumbar puncture to test for xanthochromia, in patients with clinical suspicion of subarachnoid haemorrhage, with CT-negative and initial traumatic tap

Musa China, Samir A. Matloob, Joan P. Grieve & Ahmed K. Toma

**To cite this article:** Musa China, Samir A. Matloob, Joan P. Grieve & Ahmed K. Toma (2021) The value of repeated lumbar puncture to test for xanthochromia, in patients with clinical suspicion of subarachnoid haemorrhage, with CT-negative and initial traumatic tap, British Journal of Neurosurgery, 35:4, 476-479, DOI: 10.1080/02688697.2021.1875398

**To link to this article:** https://doi.org/10.1080/02688697.2021.1875398

© 2021 The Author(s). Published by Informa UK Limited, trading as Taylor & Francis Group.

Published online: 02 Feb 2021.

Submit your article to this journal

Article views: 761

View related articles

View Crossmark data

Full Terms & Conditions of access and use can be found at
https://www.tandfonline.com/action/journalInformation?journalCode=ibjn20

BRITISH JOURNAL OF NEUROSURGERY
2021, VOL. 35, NO. 4, 476–479
https://doi.org/10.1080/02688697.2021.1875398

Taylor & Francis
Taylor & Francis Group

ORIGINAL ARTICLE

OPEN ACCESS Check for updates

# The value of repeated lumbar puncture to test for xanthochromia, in patients with clinical suspicion of subarachnoid haemorrhage, with CT-negative and initial traumatic tap

Musa China[a], Samir A. Matloob[b], Joan P. Grieve[b] and Ahmed K. Toma[b]

[a]Department of Medicine, University College London (UCL) Medical School, London, UK; [b]Victor Horsley Department of Neurosurgery, The National Hospital for Neurology and Neurosurgery, London, UK

**ABSTRACT**

**Objectives:** For the diagnosis of subarachnoid haemorrhage (SAH), the presence of cerebrospinal fluid (CSF) xanthochromia is still considered the gold standard for patients with a thunderclap headache, in the absence of blood on brain CT scan. However, a traumatic lumbar puncture (LP) typically results in high concentrations of oxyhaemoglobin in CSF, impairing the detection of xanthochromia and preventing the reliable exclusion of SAH. In this context, the value of a repeat lumbar puncture has not yet been described.

**Materials and methods:** A retrospective case series of suspected SAH patients, with a negative CT scan and initial traumatic LP, managed with a repeat LP to assess for CSF xanthochromia. Clinical notes, laboratory and imaging results were reviewed.

**Results:** Between August 2011 and January 2020, 31 patients with suspected SAH were referred to our neurosurgical unit following negative CT and traumatic LP. A repeat LP was performed in 7 of the 31 patients, 2.4 days (±0.79 SD) after the first traumatic LP. CSF spectrophotometry analysis from repeated LP in all 7 patients was negative for xanthochromia. No adverse clinical events were recorded on average 18 months following discharge.

**Conclusion:** A repeat LP performed following a traumatic tap can still yield xanthochromia-negative CSF, thereby, excluding SAH, avoiding unnecessary invasive angiography and overall promoting the safer management of these patients.

**ARTICLE HISTORY**
Received 22 August 2020
Revised 10 November 2020
Accepted 8 January 2021

**KEYWORDS**
Aneurysm; cerebrospinal fluid; CT scan; lumbar puncture; subarachnoid haemorrhage; xanthochromia

## Introduction

Subarachnoid haemorrhage (SAH) is a neurosurgical emergency associated with significant mortality and morbidity.[1–3] A computed tomography (CT) scan of the brain is the initial diagnostic imaging modality of choice, with studies reporting a near 100% sensitivity if performed within 6 h of the first onset of symptoms.[4] Patients who present with a clinical history suggestive of a SAH but have a normal CT scan will have a lumbar puncture (LP) performed for cerebrospinal fluid (CSF) spectrophotometry analysis.[5]This is a well-established and practiced diagnostic algorithm.[6]

CT scan sensitivity, however, is time-dependent, falling significantly for patients presenting more than 24–48 h from the first onset of symptoms.[7]The current national guidelines (UKNEQAS) concerning the diagnosis of SAH recommends the use of CSF spectrophotometry to detect the presence of bilirubin, a blood breakdown product, termed xanthochromia.[8] CSF xanthochromia is considered to be the gold-standard investigation to confirm or exclude a SAH following a negative CT, with a near 100% sensitivity for detecting small amounts of blood in the CSF potentially missed by the initial negative CT scan.[4,9] In cases of suspected SAH, misdiagnosis is intrinsically linked with mortality and morbidity which underpins the importance of the LP as a fail-safe investigation. An untreated ruptured cerebral aneurysm can rebleed, eliciting a poor prognosis: an estimated 80% mortality rate or risk of significant permanent disability.[3] Correct initial diagnosis is unequivocally of paramount importance.

However, whilst CSF spectrophotometry is a fail-safe measure employed for those with a negative CT, a scenario commonly encountered in clinical practice is a cohort of CT-negative patients who receive a traumatic tap, where direct needle puncture introduces red blood cells into the subarachnoid space, resulting in equivocal CSF xanthochromia analysis. This is typically reported by the laboratory as 'Oxyhaemoglobin is in sufficient concentration to impair detection of bilirubin' as oxyhaemoglobin, another blood breakdown product, readily forms *in vitro* in high concentrations from a traumatic tap.[1]

A traumatic tap introduces uncertainty into the diagnostic algorithm, conventionally resulting in secondary transfers to local neurosurgical units for unnecessary angiography imaging. These are resource-intensive, invasive and expensive procedures.[4,10] DSA, whilst considered the gold standard for identifying cerebral aneurysms, is not an innocuous procedure, carrying a 1% risk of an acute ischaemic stroke, up to 0.4% chance of access-site haematoma formation[11] and additionally, a near 2% risk of aneurysm re-rupture during the procedure itself.[12] Furthermore,

CONTACT Musa China Musa.china.15@ucl.ac.uk Division of Medicine, University College London (UCL), London, UK

© 2021 The Author(s). Published by Informa UK Limited, trading as Taylor & Francis Group.
This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives License (http://creativecommons.org/licenses/by-nc-nd/4.0/), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited, and is not altered, transformed, or built upon in any way.

the fundamental question of whether a bleed has occurred or not remains unanswered.

In the context of a normal plain CT scan and an unconvincing clinical history, vascular imaging is more likely to detect an unruptured aneurysm than for a bleed to have occurred.[1,4] Approximately 2–3% of the general population harbour an unruptured cerebral aneurysm[4] and the incidence of an actual SAH in the population is estimated to be approximately eight per 100,000 person-years.[13] Endovascular coiling carries a 5% risk of intra-procedural aneurysm rupture[14] and an estimated 2% 30-day mortality or morbidity risk.[15] Late re-bleeding from the aneurysm responsible for the first SAH is still a potential complication following successful coiling or clipping, estimated to be around 2–3% in the first decade following treatment of the ruptured aneurysm.[16] Overall, this highlights the need for an alternative diagnostic strategy which can exclude SAH, limit unnecessary secondary imaging and reduce potential further risks patients are exposed to. For the further investigation of a traumatic tap following a negative CT scan for SAH, the value of performing a repeat LP has not yet been explored.

We describe our practice at the National Hospital for Neurology and Neurosurgery (NHNN) of performing a repeat LP, for CT-negative patients with an initial traumatic tap.

## Material and methods

A retrospective review of all of the available CSF spectrophotometry reports, recorded from August 2011 to January 2020, in the neuroimmunology department database at our institution was performed. CSF spectrophotometry analysis was investigated and reported by neuroimmunologists, in accordance with UKNEQAS guidelines.[8]

This is a retrospective case-series with no identifiable patient information. Patient consent was not applicable and no experimental trial on human subjects was conducted requiring ethics committee approval.

Patients with inconclusive CSF xanthochromia results were selected for further review. For all patients within LP inconclusive group: CT scans performed at initial presentation, electronically available clinical notes and CSF biochemistry data were reviewed. Patients with a negative CT and clinical or biochemical indications of receiving an initial traumatic LP and who received a second LP for SAH exclusion were identified.

Electronically available clinical notes and CSF biochemistry data for these patients were analysed further to determine key patient clinical characteristics, review angiography outcomes and record any adverse neurovascular events following discharge.

## Results

Between August 2011 and January 2020, our study identified 775 CSF spectrophotometry reports performed for patients with negative non-contrast CT scans for subarachnoid haemorrhage.

Fifty-two percent were women and the ages ranged from 16 to 89 years (mean 47.8 ± 14.97 SD).

Six hundred and ninety-five (89.7%) reports were negative, 29 (3.74%) were positive, 20 (2.58%) were inadequate and 31 LP samples (4%) were equivocal.

Twenty-eight of the 31 patients with equivocal CSF spectrophotometry analysis underwent angiography (CT/MR/DSA) of which 0 aneurysms were identified. Fifteen had CTA, 11 had MRA and 2 DSAs were performed following negative CT but no vascular abnormality was identified. Reasons for not performing angiography for 3 patients: for 2 patients an alternative diagnosis was determined more likely and 1 patient had self-discharged prior to scheduled angiography. All 31 patients were discharged with no significant adverse neurovascular events noted in the patient's clinical notes up to 18 months following discharge.

Seven of the 31 patients within the LP equivocal group were identified as having received a repeat LP for CSF spectrophotometry analysis following a negative CT scan and an initial traumatic LP (Table 1).

All seven patients presented to Accident and Emergency departments describing severe, sudden onset headache with five patients describing it as '*worst ever*' and 10/10 on visual analogue pain scale rating. Six patients had CT scan performed within 12 h of symptom onset and one patient had a CT at 12–18 h. All LPs were performed more than 12 h following first onset of symptoms. Seven CTAs were performed (five at NHNN and two at district general hospitals (DGHs) before transfer to NHNN) with no vascular abnormalities identified. Two patients had additional DSA, with no aneurysms detected.

**Table 1.** Study patients characteristics: Negative xanthochromia with repeat LP.

| Patient | Symptom(s) | Time from symptom onset to CT-scan | Initial LP xanthochromia | Repeat LP xanthochromia result | Repeat LP image-guided/Grade of performing clinician | CTA findings | Time from presentation to discharge |
|---|---|---|---|---|---|---|---|
| 40/M | Sudden onset headache | 12–18 h | LP Equivocal ('*bloody tap*') | Negative | Non-image guided/ Specialist registrar | None[a] | 8 days |
| 48/F | Thunderclap headache | 12–18 h | LP Equivocal ('*likely traumatic tap*') | Negative | Fluoroscopy-guided LP/Consultant Neuroradiologist | None | 5 days |
| 48/M | Thunderclap headache | 6–12 h | LP Equivocal ('*likely traumatic tap*') | Negative | Non-image guided/ Specialist registrar | None | 3 days |
| 51/M | Headache/ Dizziness/Nausea | 6–12 h | LP Equivocal ('*multiple attempts*') | Negative | Non-image guided/ Specialist registrar | None | 4 days |
| 53/M | Thunderclap headache/Nausea | 0–6 h | LP Equivocal ('*5 attempts/ difficult LP*') | Negative | Fluoroscopy-guided LP/Consultant Neuroradiologist | None[a] | 6 days |
| 57/M | Thunderclap headache/Nausea | 6–12 h | LP Equivocal ('*traumatic*') | Negative | Non-image guided/ Specialist registrar | None | 4 days |
| 59/M | Thunderclap headache | 6–12 h | LP Equivocal | Negative | Non-image guided/ Specialist registrar | None | 5 days |

[a]Digital Subtraction Angiography also performed, no aneurysm detected.
M: Male; F: Female.

Qualitative indicators within the clinical notes suggestive of initial traumatic LP were observed in five of the seven patients, including the phrases: '*traumatic tap*', '*multiple attempts*' and '*bloody tap*'. All seven repeat LPs were performed at the NHNN and all CSF spectrophotometry analysis was reported by the hospital laboratory as negative for xanthochromia with no haem pigments detected (oxyhaemoglobin or bilirubin). All repeat LPs were performed by either a senior grade neurosurgical registrar (ST5+) or consultant neuroradiologist. Repeat LP was performed on average 2.4 days (±0.79 SD) following the first initial traumatic LP. All seven patients were discharged on same day as negative repeat LP with an average time, from first hospital presentation to discharge, of 5 days (±1.63 SD). No significant adverse neurovascular events were noted in the patient's clinical notes on median average follow-up of 18 months following discharge (range: 6–50 months).

## Discussion

Traumatic taps are not unexpected, with up to 20% of LPs estimated to be a traumatic tap, and often result in equivocal CSF xanthochromia analysis.[4] Whilst there is no clear guidance on what constitutes a traumatic tap,[4,12] national guidelines advocate that the final interpretation of an LP should be a combination of CSF xanthochromia analysis and the clinical presentation of the patient.[2] In the clinical notes of six of our seven patients who received a repeat LP, it was highlighted in their clinical notes that a traumatic tap was suspected through phrases such as 'bloody tap', 'difficult tap' and 'likely traumatic tap' (Table 1), justifying our clinical reasoning for performing a repeat LP for these specific patients. In our study, CSF spectrophotometry analysis from the repeated LP yielded a negative result, with no detectable CSF haem pigments (bilirubin and oxyhaemoglobin). In these patients, it was therefore deemed highly unlikely a bleed had occurred. All seven patients underwent CTA, prior to the repeat LP, which yielded no vascular abnormalities. Subsequently, all seven patients were discharged on the same day following the repeated LP, without requiring further investigations or experiencing any adverse neurovascular events. Despite this, patients with a normal CT scan and a suspected traumatic LP are frequently referred to regional neurosurgical centres, for further imaging partly reasoned as a 'fail-safe' to identify any potential vascular abnormality, due to the significant mortality and morbidity associated with a missed initial diagnosis.[17] The indiscriminate use of angiography imaging like this could be exposing some patients to unnecessary complications from both angiography imaging and neurosurgical interventions that may follow, as previously outlined in this paper.[1,4,5]

The repeat LP was performed on average 2.4 days (±0.79 SD) following the initial equivocal LP. This can be reasoned arbitrarily to the time taken for patients from local district general hospitals, to be referred and admitted at our tertiary level neurosurgical unit, undergo angiography imaging subsequently reported negative for aSAH and then for a repeat LP to be performed. To our knowledge, there is a paucity of literature examining how quickly blood in the CSF disappears in this population following traumatic tap.[1] However, the following premise still holds value: a repeat LP performed too soon following a traumatic tap, for example, less than 12 h, could very much return another equivocal CSF analysis, as high concentrations of oxyhaemoglobin as a result of in vitro lysis of red blood cells from the initial traumatic tap, mask the detection of bilirubin.[1] Whilst inversely, a delay in performing a repeat LP does not inform treatment decisions, may increase risk of morbidity and mortality from a potential missed diagnosis and for innocuous admissions, as exhibited by our study population, further delays discharge.[1,10] Whilst we demonstrate there is still value in performing a repeat LP 2–3 days following a suspected initial traumatic tap, ultimately, the decision to perform and when should be decided on a case-by-case basis resting on the clinical judgement of the attending clinician.

Estimates approximate up to 150 patients per 250,000 population annually in the UK, present with symptoms suspicious of SAH but have a negative brain CT scan, and of whom only about 2–3% will have had SAH.[1] The significance of this is that patients who are investigated with angiography imaging, are more likely to be exposed to the risk of an incidental aneurysm finding versus being diagnosed with aneurysmal SAH.[1,4] In our study, of the 24 patients within the equivocal LP group who did not receive a second LP, 21 were investigated with further angiography imaging in the form of CTA or MRA. No cerebral aneurysms were identified with vascular imaging within this LP group and a retrospective review of their clinical notes noted no further adverse cerebrovascular events in the 12 months following discharge. There is a need to delineate the genuine few who require angiography and an alternative approach is required for patients with no evidence of haemorrhage on CT imaging and who experience a traumatic LP. In this context, to the best of our knowledge, the value of performing a repeat LP has not yet been explored. We envisage our practice will mitigate unnecessary transfers to local neurosurgical units and could alleviate the over-reliance on angiography to investigate a traumatic LP.[4]

In our study, of 775 LPs performed following a negative CT scan, 89.7% yielded a negative CSF xanthochromia analysis. 91% (728/796) of CSF spectrophotometry reports retrospectively reviewed at another UK tertiary level neurosurgical unit,[7] were also negative for xanthochromia in the investigation for SAH. In view of this, we may be underestimating the sensitivity of CT imaging for SAH, with recent studies reporting a near 100% sensitivity of CT if performed within 48 h of ictus onset.[6,18,19] In our seven study patients, CT imaging was performed within 18 h of the first onset of symptoms which is well within the time-frame expected to benefit from high CT scan sensitivity for SAH. In the context of our observation that almost 90% of LPs performed following a normal CT scan were negative, in combination with a strong clinical suspicion or indication that a traumatic tap has occurred in these specific patients, affords us greater confidence that our approach is safe. By demonstrating a repeat LP can return a negative LP result, leaves no doubt there is value in performing a repeat LP for this specific clinical scenario.

Our case-series is limited by a small sample size and retrospective study design. Overall, given the relatively small patient population, CT-negative and initial traumatic tap with equivocal CSF spectrophotometry analysis, we advocate that a case-series approach is a reasonable option for exploring possible refinements to CSF analysis and SAH exclusion in clinical practice. Despite the retrospective nature of our case series, the availability of clinical and laboratory data, CT scan results and further secondary investigation outcomes provide robust and unambiguous results from which meaningful conclusions can be made.

A lumbar puncture itself is not without limitations. An LP is a technically difficult procedure, which can be uncomfortable for patients with up to 30% experiencing a post-LP dural headache.[4] The number of LP attempts directly correlate with the extent of dural damage, so fewer attempts could be associated with a reduced incidence of complications which include post-LP

headache, bleeding and local infection.[20] In the clinical notes of five of our seven patients, it was documented that the initial LP was 'difficult' or had been attempted 'multiple times'. By proposing a second LP, we may actually amplify the risk of patients experiencing these complications, however, the potential risks from performing a repeat LP have to be balanced against the potential risk of missing a SAH and the significant mortality and morbidity associated with a missed initial diagnosis.[3] Ultimately, the clinical judgement of the attending clinician and, equally, the patient's tolerance will determine the number of LP attempts undertaken. Whilst we outline the potential limitations of an LP, we believe these are still outweighed by the adverse effects of angiography and the additional risk of complications associated with neurosurgical interventions, all of which this practice could potentially limit in this small select group of patients.

## Conclusion

For the investigation of SAH, in patients with a traumatic LP and a negative CT scan, performing a repeat LP can still yield CSF analysis negative for xanthochromia, definitively ruling out SAH. We described our practice which allowed for the discharge of these specific patients without requiring further investigations or experiencing adverse clinical events in the 18 months following discharge.

## Informed consent

Informed consent was obtained from all individual participants included in the study.

## Authors contributions

All authors were involved in all aspects of the manuscript.

## ORCID

Musa China http://orcid.org/0000-0001-9562-3769

## References

1. Beetham R. CSF spectrophotometry for bilirubin-why and how? *Scand J Clin Lab Invest* 2009;69:1–7.
2. Gangloff A, Nadeau L, Perry JJ, *et al.* Ruptured aneurysmal subarachnoid hemorrhage in the emergency department: clinical outcome of patients having a lumbar puncture for red blood cell count, visual and spectrophotometric xanthochromia after a negative computed tomography. *Clin Biochem* 2015;48:634–9.
3. Roos YB, de Haan RJ, Beenen LF, *et al.* Complications and outcome in patients with aneurysmal subarachnoid haemorrhage: a prospective hospital based cohort study in the Netherlands. *J Neurol Neurosurg Psychiatry* 2000;68:337–41.
4. Long B, Koyfman A. Controversies in the diagnosis of subarachnoid hemorrhage. *J Emerg Med* 2016;50:839–47.
5. Dawkins AA, Evans AL, Wattam J, *et al.* Complications of cerebral angiography: a prospective analysis of 2,924 consecutive procedures. *Neuroradiology* 2007;49:753–9.
6. Perry JJ, Alyahya B, Sivilotti MLA, *et al.* Differentiation between traumatic tap and aneurysmal subarachnoid hemorrhage: prospective cohort study. *BMJ* 2015;350:h568–h568.
7. Bakr A, Silva D, Cramb R, *et al.* Outcomes of CSF spectrophotometry in cases of suspected subarachnoid haemorrhage with negative CT: two years retrospective review in a Birmingham hospital. *Br J Neurosurg* 2017;31:223–6.
8. Tormey W, O'Shea P, Brennan P. National guidelines for analysis of cerebrospinal fluid for bilirubin in suspected subarachnoid haemorrhage. *Ann Clin Biochem* 2012;49:102–3.
9. Bonita R, Thomson S. Subarachnoid hemorrhage: epidemiology, diagnosis, management, and outcome. *Stroke* 1985;16:591–4.
10. Ditta M, Galea J, Holland J, Patel HC. Lumbar puncture and the diagnosis of CT negative subarachnoid haemorrhage: time for a new approach? *Br J Neurosurg* 2013;27:599–602.
11. Alakbarzade V, Pereira AC. Cerebral catheter angiography and its complications. *Pract Neurol* 2018;18:393–8.
12. Saitoh H, Hayakawa K, Nishimura K, *et al.* Rerupture of cerebral aneurysms during angiography. *AJNR Am J Neuroradiol* 1995;16:539–42.
13. Etminan N, Chang H, Hackenberg K, *et al.* Worldwide incidence of aneurysmal subarachnoid hemorrhage according to region, time period, blood pressure, and smoking prevalence in the population: a systematic review and meta-analysis. *JAMA Neurol* 2019;76:588–97.
14. Ihn Y, Shin S, Baik S, *et al.* Complications of endovascular treatment for intracranial aneurysms: management and prevention. *Interv Neuroradiol* 2018;24:237–45.
15. Wiebers D. Unruptured intracranial aneurysms: natural history, clinical outcome, and risks of surgical and endovascular treatment. *Lancet* 2003;362:103–10.
16. Wermer MJ, Greebe P, Algra A, Rinkel GJE. Incidence of recurrent subarachnoid hemorrhage after clipping for ruptured intracranial aneurysms. *Stroke* 2005;36:2394–9.
17. McCormack RF, Hutson A. Can computed tomography angiography of the brain replace lumbar puncture in the evaluation of acute-onset headache after a negative noncontrast cranial computed tomography scan? *Acad Emerg Med* 2010;17:444–51.
18. Mark DG, Pines JM. The detection of nontraumatic subarachnoid hemorrhage: still a diagnostic challenge. *Am J Emerg Med* 2006;24:859–63.
19. Sames TA, Storrow AB, Finkelstein JA, *et al.* Sensitivity of new-generation computed tomography in subarachnoid hemorrhage. *Acad Emerg Med* 1996;3:16–20.
20. Ahmed SV, Jayawarna C, Jude E. Post lumbar puncture headache: diagnosis and management. *Postgrad Med J* 2006;82:713–6.