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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

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ABSTRACT

Objectives: Over the last decade, computed tomography scanners have gained resolution and have become the standard of care in the investigation of neurologically intact patients suffering from acute headache. The added value of the combined assessment of red blood cells count, visual and spectrophotometric xanthochromia, to detect ruptured aneurysmal subarachnoid hemorrhage (ASAH) following a negative head computed tomography (NHCT) was studied.

Methods: The population consisted of all patients who had cerebrospinal fluid tested for spectrophotometric xanthochromia between 2003 and 2009 identified through the clinical-laboratory database and who met all the inclusion criteria: >14 years old, had an initial Glasgow Coma Score of 15, a non-traumatic acute headache with a suspected subarachnoid hemorrhage recorded in the initial ED differential diagnosis and an initial negative head CT scan.

Results: A total of 706 patients were included. LP identified 5 ASAH (prevalence: 0.7%). In these patients, LP parameters were as follows: high red blood cell count (from 1310 to 63,000 × 10^6/L), positive visual xanthochromia in 4 out of 5 ASAH, and positive spectrophotometric xanthochromia in 5 out of 5 ASAH. All ASAH patients were neurologically intact after intervention. No deaths or missed ASAH were reported. Angiographies were performed on 127 patients (19.5%) of which 47 (34.1%) had positive xanthochromia (visual or spectrophotometric).

Conclusions: Considering the low prevalence of ASAH following an NHCT, intense resources were utilized to identify all 5 ASAH. Lumbar puncture analyses combining red blood cell count, visual and spectrophotometric xanthochromia identified all ASAH, allowing intervention and a positive clinical outcome. Our data support 1) that LP identifies the presence of a ruptured ASAH after an NHCT and 2)` that a guide to define a subpopulation of patients who would benefit from a lumbar puncture after an NHCT would be desirable.

Introduction

Subarachnoid hemorrhage accounts for only 4.4% of stroke mortality but occurs at a young age, producing a relatively large burden of premature mortality, comparable to ischemic stroke [1]. It is associated with high mortality and high morbidity. Case fatality ranges from 8.3% to 66.7% [2]. Neurologically intact patients in good clinical condition with symptomatic cerebral aneurysms are commonly misdiagnosed and are more likely to deteriorate clinically than correctly diagnosed patients: thus this subpopulation of patients have a worse overall outcome [3]. Mayer et al. described that among patients initially presenting as a Hunt and Hess clinical grade 1 or 2, an overall good or excellent outcome was achieved in 91% of those with a correct initial diagnosis. Good or excellent outcomes dropped to 53% of patients initially misdiagnosed [3]. In the 1990s, only about 3% of patients with acute headache and normal head third-generation computed tomography (CT) had a subarachnoid hemorrhage [4]. Since missing the diagnosis

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can have life threatening consequences, the small risk of missing a SAH has to be weighed against the fact that a curative treatment exists.

Aneurysmal subarachnoid hemorrhage (ASAH) is a dreadful condition to rule out in the emergency department (ED). It is usually suspected from the clinical presentation, including thunderclap headache, a sudden and severe headache, which is a cardinal symptom of subarachnoid hemorrhage [5]. Head CT scan is a well-established first line test to detect subarachnoid hemorrhage in the ED. A recent Canadian study demonstrated that third generation head CT scans detected all subarachnoid hemorrhage, when performed within 6 h of the onset of symptoms [6]. However, as the time between the onset of the symptoms and the CT scan increases, the sensitivity for subarachnoid hemorrhage detection decreased to 85% for patients scanned after 6 h [6]. Therefore, patients suffering from acute headache with a negative CT are usually further investigated [5,7]. The conservative practice is to use lumbar puncture to verify red blood cell count and the presence of xanthochromia in order to identify patients who would benefit the most from an angiography investigation [5]. This practice has been challenged [8,9] and remains the subject of much debate.

Visual xanthochromia is the yellow discoloration of CSF detected by visual inspection of the supernatant of a centrifuged cerebrospinal fluid [10]. Optimal assessment of visual xanthochromia requires a standardized procedure including trained personnel, appropriate lightening [11], assessment of CSF color against a white background and compared with a similar tube filled with water. Spectrophotometric xanthochromia is the measurement of hemoglobin breakdown products, especially bilirubin which is only formed *in vivo*, allowing to distinguish between a traumatic lumbar puncture tap and a subarachnoid hemorrhage [10,12]. Spectrophotometric xanthochromia is a heterogeneous term referring to all methods that use a spectrophotometer to measure hemoglobin breakdown products such as bilirubin. Among the different spectrophotometric methods, the United Kingdom National External Quality Assessment Service (UKNEQAS) 2008 approach [13] and the iterative method [13] are commonly used. The UKNEQAS 2008 approach consists of drawing a tangent to the scan and calculating the net bilirubin absorbance at 476 nm and the net oxyhemoglobin absorbance at 415 nm. Results are interpreted according to the UKNEQAS 2008 algorithm [13]. The Duiser iterative approach uses a software that isolates the contribution of bilirubin out of the other hemoglobin pigments using iterative calculation [13]. A positive iterative spectrophotometric xanthochromia corresponds to a bilirubin level above 0.20 μmol/L [13]. There is an ongoing debate in the literature on the best xanthochromic approach [14–19]. To date, no prospective, blinded, multi-center study of the diagnostic accuracy of spectrophotometric xanthochromia has been published. While spectrophotometry is widely implemented in Europe, spectrophotometric xanthochromia is available in only 3% of North-American centers [20]. The objective of the present study was to evaluate the clinical outcome of patients with a suspicion of ruptured aneurysmal subarachnoid hemorrhage despite a negative head CT scan and in whom lumbar puncture was performed to assess red blood cell count, visual and spectrophotometric xanthochromia. Lumbar puncture results being a trigger for angiography, an overview of the number and type of angiographies performed in the cohort is also presented.

Methods

Setting and population

The study population consisted of all patients who had their cerebrospinal fluid tested for spectrophotometric xanthochromia between 2003 and 2009 ($n = 1377$) and who met all the inclusion criteria ($n = 706$). Charts were identified through the clinical-laboratory database and were included for review if patients were: >14 years old, had an initial Glasgow Coma Score of 15, a non-traumatic acute headache with a suspected subarachnoid hemorrhage recorded in the initial ED differential diagnosis and an initial negative head CT scan read by a radiologist. The investigation after the initial NHCT was left to the attending physician. Charts were reviewed with a standardized data collection sheet by 2 trained observers. Socio-demographic, clinical features, radiology reports, surgical/radiology interventions and laboratory data were recorded. Inter-observer agreements were assessed and reported. All patients had a lumbar puncture performed by an emergency physician or resident after head imaging. The retrospective design of the study identified consecutive patients. CT scanners were from Siemens (Sensation 4 from 2003 to 2008, Sensation 16 from 2008 to the end of the study).

Outcome of patients discharged from the ED and "Safety-net": as most missed aneurysm rebleed shortly after their initial medical assessment [21], our study had a safety-net for possible missed subarachnoid hemorrhage: the *Hôpital de l'Enfant-Jésus* is the only neurosurgical referral center covering more than half of the province of Quebec (roughly 2 million residents), a false-negative patient discharged from the emergency department would eventually be picked up on a follow-up visit or readmission to the emergency department/hospital or in event of any sudden death through coroner investigation. The presence of medical encounter that occurred after the initial visit to the emergency department was recorded and patients were considered "alive" and free of ASAH. The *Comité d'éthique du CHU de Québec* approved this study (project #2012-1387).

Laboratory assessment of cerebrospinal fluid xanthochromia

Visual and spectrophotometric xanthochromia were performed on fresh, centrifuged, light protected cerebrospinal fluid kept at room temperature and analyzed immediately after arrival to the laboratory on a 24/7 basis. Visual analysis was performed by observing the supernatant of a cerebrospinal fluid sample centrifuged at room temperature for 10 min and 900 g: CSF was described as xanthochromic if the color was yellow. Visual assessment was made by the technologist on duty. The technologists were not systematically instructed to compare the CSF with a similar tube filled with water and against a white background. Spectrophotometric analysis of cerebrospinal fluid was performed right after visual assessment, using a quartz cuvette compared against a blank made of ultra-pure water, and scanned from 350 nm to 700 nm using a Cary100 spectrophotometer (Varian). Absorbencies at different wavelengths were acquired and transferred to the software Microsoft Excel. Resulting scans were analyzed using 2 methods: 1) the United Kingdom National External Quality Assessment Service (UKNEQAS) 2008 approach [13] and 2) the Duiser iterative approach [22]. The UKNEQAS 2008 approach was performed automatically by drawing a tangent to the scan and calculating the net bilirubin absorbance at 476 nm and the net oxyhemoglobin absorbance at 415 nm. Results were interpreted by author AG according to the UKNEQAS 2008 algorithm [13]. Of note, these results were not transmitted to the attending physician since the UK NEQAS approach was under evaluation. The Duiser approach was performed using the DuiserSoft®. The results were transmitted to the physician as μmol/L of bilirubin obtained from the iterative calculation [22]. A positive spectrophotometric xanthochromia corresponded to a bilirubin level above 0.20 μmol/L.

ASAH definition

Aneurysmal subarachnoid hemorrhage was defined as: 1) presence of any aneurysm and 2) either positive visual xanthochromia or $>5 \times 10^6$ [6] red blood cell/L in the last lumbar puncture tube [23]. To avoid misclassifying as ASAH an incidental aneurysm with a traumatic LP, positive cases according to the definition were further reviewed by two physicians using a standardized data collection sheet (AG, ME). In case of disagreement, medical charts were sent to a neurosurgeon for a third opinion. Good clinical outcome was defined as identification of any ruptured ASAH (if present) leading to intervention and preserved neurological functions on follow-up.

Estimated sensitivity and specificity of xanthochromia

Visual xanthochromia being part of the definition of ASAH and in the absence of angiograms performed on all participants, classical diagnostic accuracy assessment of xanthochromia was not performed. Estimated performance of xanthochromia was made using the clinical outcome "identification of ruptured ASAH (if present) leading to intervention and preserved neurological functions on follow-up" as an alternative to the lack of reference standard.

Angiography

The decision to perform an angiography as well as the type of angiography was to the discretion of the ED physician or neurosurgical consultant. Various types of angiography were performed including invasive (catheter angiogram) and non-invasive (e.g., CT-angiogram) techniques. Typically, the patients undergo a first non-invasive test as part of the secondary evaluation step of probable ASAH and then an invasive procedure to confirm/treat the aneurysm based on neurosurgeon decision.

Statistical analyses

Univariate analyses were used to describe the population and the ASAH group. Inter-observer agreements were calculated using simple and weighted kappa statistic. Estimated sensitivity, specificity, positive predictive value and negative predictive value of all xanthochromia detection techniques are presented with 95% confidence interval. Statistical analyses were performed using SAS software (Cary, NC, USA) version 9.2.

Results

Flow diagram 1 indicates that between 2003 and 2009, 1377 xanthochromia analyses were performed (Fig. 1). Among these, 706 patients had a medical chart at the *Hôpital de l'Enfant-Jésus* and met all our inclusion criteria. Five (5) patients had a confirmed ruptured aneurysmal subarachnoid hemorrhage (ASAH prevalence: 0.7%). Flow diagram 2 indicates classification results for ASAH for each xanthochromia technique (visual, iterative spectrophotometric, UK NEQAS 2008 spectrophotometric) (Fig. 2). Mean (±SD) age of the cohort was 41 ± 14 years while mean age of the 5 subarachnoid hemorrhages was 49 ± 6 years (NS). Female gender represented 52% of the cohort and 60% of the subarachnoid hemorrhage patients. Clinical characteristics are detailed in Tables 1 and 2. Kappa statistics for inter-observer agreement was ≥0.6 for clinical data and main outcome. Our review showed 211 patients (30.5%) had a medical evaluation in the 12 months after their acute headache index visit, none reported missed subarachnoid hemorrhage. No deaths were reported through provincial coroner's offices.

Added value of lumbar puncture using a combined approach (red blood cell count, visual and spectrophotometric xanthochromia)

Lumbar puncture identified 5 ASAH. Table 2 describes the five aneurysmal subarachnoid hemorrhages with negative head CT. Good clinical outcome was defined as identification of ruptured ASAH leading to intervention and preserved neurological functions on follow-up.

Time between headache onset and lumbar puncture was estimated greater than 12 h in 466 patients (67.5%), with a median of 13 h. Clinical outcome of confirmed angiographic ASAH in NHCT patients was used as a reference standard to assess estimated sensitivities and specificities. Xanthochromia performed as follows [95% CI]: *visual*: sensitivity 80% [28.4–99.5]; specificity 98.7% [97.5–99.4]; area under the curve (AUC) 89.4 [69.8–100]; *spectrophotometric iterative method*: sensitivity 100% [47.8–100]; specificity 91.9% [89.6–93.9]; AUC 95.9 [94.9– 96.9]; *spectrophotometric United Kingdom National External Quality Assessment Service 2008*: sensitivity 100% [47.8–100]; specificity 98.1% [96.7–99.0]; AUC 99.1 [98.5–99.5]. No deaths were reported.

False positive for aneurysmal subarachnoid hemorrhage

Iterative spectrophotometric xanthochromia had 56 (7.9%) false positive results and included 38 (5.3%) analytical false positive results as well as 18 (2.5%) biological false positive results (7 meningitis, 10 non-aneurysmal subarachnoid hemorrhage, and 1 hyperbilirubinemia disease). The UKNEQAS 2008 spectrophotometric xanthochromia gave a total of 13 (1.8%) false positive results. Among these 13 patients, 9 patients had "non-aneurysmal subarachnoid hemorrhage" as final

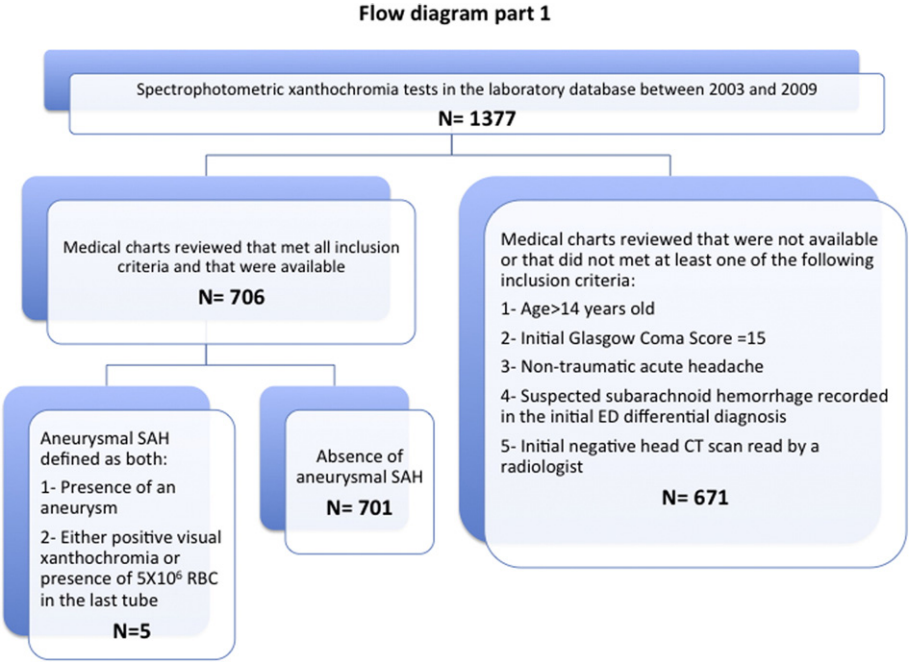

Fig. 1. Flow diagram part 1: recruitment of patients, inclusion/exclusion criteria.

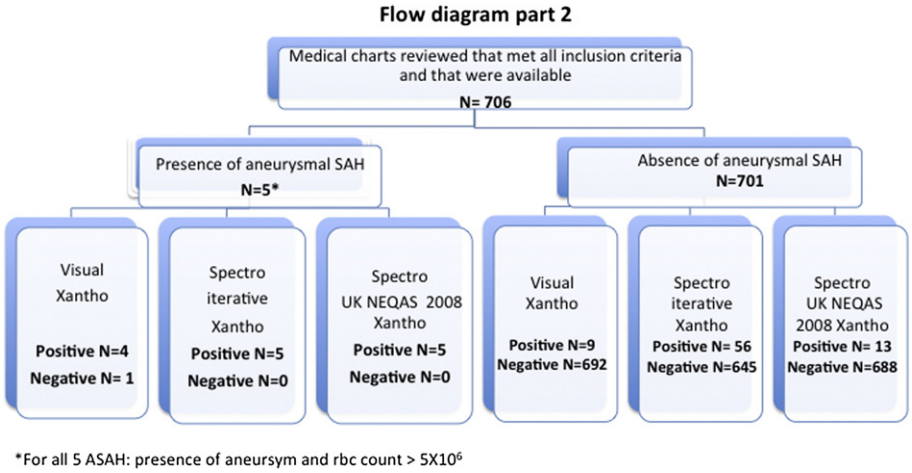

Fig. 2. Flow diagram part 2: visual and spectrophotometric xanthochromia results in patients with and without aneurysmal SAH.

diagnosis. All 13 patients had false positive iterative spectrophotometric xanthochromia while 7 had false positive visual xanthochromia. No false negative results were recorded for spectrophotometric xanthochromia, while visual xanthochromia gave one false negative.

Angiographies in relationship with lumbar puncture results

A total of 127 patients had angiography (17.9%), of which 11 had a second angiogram. A total of 11 angiograms were catheter angiograms (Table 3). A total of 91 angiographies (12.9%) were performed in patients with negative xanthochromia (both visual and spectrophotometric), while 0.6% of them ($n = 4$) were catheter angiographies. Angiographies performed on patients with false positive iterative spectrophotometric xanthochromia for ASAH included a total of 31 angiographies (4.4%), of which 6 were catheter angiograms (final diagnosis: non-aneurysmal subarachnoid hemorrhage ($n = 3$), headache ($n = 2$) and hyperbilirubinemia ($n = 1$)). Three of these angiographies were performed in patients who also had false positive visual xanthochromia along with false positive UKNEQAS 2008 spectrophotometric xanthochromia and high red blood cell count. The UKNEQAS 2008 spectrophotometric xanthochromia results were not provided to physicians, thus no data for angiography rate for patients managed with this spectrophotometric approach are available.

Discussion

The prevalence of ruptured aneurysmal subarachnoid hemorrhage in our cohort of neurologically intact patients having a negative head CT scan was only 0.7%, a prevalence which is much lower than the 3% previously reported [4] but close to a recent reported prevalence of 1.5% [24]. The most probable explanation is that the increased accessibility to CT scanners as well as their gain in diagnostic performance between 1995 and 2003 allowed the diagnosis of more subarachnoid hemorrhage at the imaging step. Therefore, CT should continue to be a first-line investigation, performed as soon as possible, as illustrated in a previous multicenter study [6,25].

Table 1
Characteristics of the population.

Characteristics	
Number of CSF samples sent for analysis	1377
Number of patients meeting inclusion criteria	706
Number of ruptured aneurysmal subarachnoid hemorrhage identified in NHCT	5
Prevalence of ruptured aneurysmal subarachnoid hemorrhage	0.7
Mean age of included patients	41 (±14)
Mean age of subarachnoid hemorrhage positive patients	49 (±6)
Female gender, all patients included in the study (%)	52%
Female gender, subarachnoid hemorrhage positive patients (%)	60%
Mortality, number of patients	0
Morbidity, number of patients	0

NHCT: negative head computed tomography.

Additional benefit of lumbar puncture

Our results demonstrate that the combination of red blood cell count, visual and spectrophotometric xanthochromia after a negative head CT scan, was useful to identify additional 5 subjects with ASAH that benefited from treatment. Red blood cells and visual xanthochromia being elements of the definition of ASAH, the present study does not permit to compare between visual versus spectrophotometric xanthochromia; neither does it permit a reliable diagnostic accuracy assessment of spectrophotometric xanthochromia. In order to assess reliably the diagnostic accuracy of spectrophotometric xanthochromia, a standardized spectrophotometric method should be used and studied in a prospective, multi-center and blinded fashion against a gold-standard method for ASAH, usually angiography. As angiographies are not performed on all participants, an alternative reference standard is usually used in accuracy studies which can introduce a reference standard bias. Using the clinical outcome of intervention on confirmed ASAH as an alternate reference standard, an estimation of the diagnostic accuracy of xanthochromia is proposed. Visual assessment missed 1 of the 5 aneurysmal subarachnoid hemorrhages. Both spectrophotometric definitions identified all 5 subarachnoid hemorrhages and therefore demonstrated an estimated sensitivity of 100%, but the low number of events impairs the statistical significance of this result (IC 95% [47.8–100], $p = 0.06$). Iterative spectrophotometric xanthochromia detected all five ruptured aneurysmal subarachnoid hemorrhages and was associated with 31 angiographies (4.2% of the cohort). Of note, false positive for iterative spectrophotometric xanthochromia included analytical false positive (38% or 5.3%) as well as biological false positive results (18% or 2.5% of the cohort), such as non-aneurysmal subarachnoid hemorrhage and meningitis. Analytical false positive in the iterative method was caused by the lack of correction for a high baseline signal, pushing the bilirubin signal above the 0.20 μmol/L threshold. The UK NEQAS method corrects for high baseline signal, thus the false positive rate for UKNEQAS 2008 spectrophotometric xanthochromia was four times lower than the false positive rate of iterative spectrophotometric xanthochromia (13 patients versus 56 patients) and it can be hypothesized that this approach would result in fewer angiographies than iterative spectrophotometric xanthochromia. Visual xanthochromia gave 9 false positive results, of which 7 were biological false positive results (6 non-aneurysmal subarachnoid hemorrhage and 1 meningitis), and one false negative result for aneurysmal subarachnoid hemorrhage.

Table 2
Description of the 5 additional aneurysmal subarachnoid hemorrhage identified by lumbar puncture.

Age	Gender	Estimated CT delay	Result CT	Time TCH to LP	First tube RBC $\times 10^6$	Last tube RBC $\times 10^6$	Visual	UK spectrophotometry	Iterative spectrophotometry	Aneurysm localisation	Aneurysm size (mm)	SAH grade	SAH Fischer	Intervention	Outcome
59	F	>96 h	Negative	>96 h	31,300	32,250	+	+	+	SB	15	G1	F1	Craniotomy clipping intubation	Good
43	F	2.5 h	Negative	19 h	116,000	63,000	+	+	+	PCA	13 X 6.5	G1	F2	GDC coiling	Good
45	M	>24 h	Negative	>24 h	20,600	21,550	+	+	+	ACA	NM	G2	F2	GDC coiling	Good
50	M	>6 d	Negative	>6 d	1350	1310	+	+	+	ATA	5 X 6 X 4	G1	F1	Craniotomy clipping	Good
46	F	>3 w	Negative	>3 w	5100	6200	–	+	+	ACA	3 X 4 X 5	NM	NM	GDC coiling	Good

M: male, F: female, TCH: thunderclap headache, CT: computed tomography, h: hours, d: days, w: weeks, LP: lumbar puncture, RBC: red blood cells, Visual: visual xanthochromia, UK spectrophotometry: United Kingdom National External Quality Assessment Service 2008 spectrophotometric xanthochromia, SAH: ruptured aneurysmal subarachnoid hemorrhage, NM: not mentioned, ACA: anterior communicating artery, ATA: anterior temporal artery, PCA: posterior communicating artery, SB: Sylvian bifurcation. Clinical outcome "good" refers to preserved neurological functions on follow-up.

Table 3
Total number of angiographies and catheter angiograms in patients with a negative head computed tomography.

Angiographies	*n*	% of cohort
No angiography performed ($n = 703$ patients)	576	81.9
Total number of angiographies performed	138	19.5
Number of patients who had angiographies ($n = 703$ patients)	127	18.1
Catheter angiograms ($n = 703$ patients)	11	1.6
Angiographies in patients with negative xanthochromia (visual and spectrophotometric, $n = 632$ patients)	91	12.9
Catheter angiograms in patients with negative xanthochromia (visual and spectrophotometric $n = 632$ patients)	4	0.6
Angiographies in false positive iterative spectrophotometric xanthochromia ($n = 56$ FP patients)	31	4.4
Catheter angiograms in false positive iterative spectrophotometric xanthochromia patients	6	0.9
Catheter angiograms in patients who also had false positive visual xanthochromia and high red blood cell count ($n = 56$ FP patients)	3	0.42

Is a lumbar puncture necessary?

Given that aneurysmal subarachnoid hemorrhage can be morbid or lead to death if undiagnosed, and the fact that a curative treatment is available, lumbar puncture is widely used to detect a ruptured aneurysm in patients with a negative head CT. The current ED management resulted in the identification of all 5 subarachnoid hemorrhages missed by CT as well as good outcome for all patients in our cohort (no mortality and no morbidity). However, it also resulted in an overwhelming amount of lumbar punctures performed in patients with undifferentiated acute headaches, exposing them to post lumbar puncture headaches as well as being resource intensive. A prospective study evaluating clinical decision rules designed to better orient the management of acute headache patients, protecting them from unnecessary investigations is currently ongoing [23,25,26].

Lumbar puncture performs particularly well in patients presenting late after the onset of the acute headache episode. Of the 5 patients having aneurysmal subarachnoid hemorrhage and a negative head CT scan, 4 patients were scanned days after the onset of symptoms, consistent with the decline in sensitivity of the CT for subarachnoid hemorrhage detection, and the gain in sensitivity of the lumbar puncture as time from acute thunderclap headache increases. Given the present data, investigation of the benefit of using LP in delayed presentation should be included in prospective studies. One particular patient was scanned 2.5 h after the onset of an episode of headache accompanied with fainting, neck stiffness and vomiting. The patient experienced a similar but less intense episode a few weeks prior, followed by moderate intensity headaches in the subsequent weeks up to the day of the second thunderclap headache episode. The lumbar puncture was performed 19 h after the onset of the headache and was positive for both visual and spectrophotometric xanthochromia. As this is a retrospective study, delay and timeline of tests, as well as onset of headache should be interpreted with caution. No study provides data on the optimal time frame to perform a lumbar puncture in patients with a negative head CT scan in ED. In patients with a negative head CT scan, the minimal amount of time required for bilirubin to become detectable in the cerebrospinal fluid as well as the minimal amount of blood that needs to enter the cerebrospinal fluid to give a positive xanthochromia remain unknown.

Limitations

Absence of a reference standard applied to all patients

Angiograms to establish presence or absence of aneurysm were not performed on all subjects. Various types of angiography were performed (invasive catheter angiogram vs. non-invasive technique such

as CT-angiogram) to the discretion of the ED physician. No consensus exists on a single definitive test to diagnose subarachnoid hemorrhage or on a "gold standard definition", thus no single definition entirely captures all aneurysmal subarachnoid hemorrhages while excluding all non-subarachnoid hemorrhage patients. A very conservative sensitive definition was used in the present study in order to not miss any patient that could possibly have a subarachnoid hemorrhage. All of those patients were reviewed by 2 or 3 physicians, thus we believe that patients that could have been mislabeled as subarachnoid hemorrhage positive based on the definition (e.g., incidental aneurysm with a traumatic lumbar puncture tap) were identified and reclassified correctly.

Low number of events

Only five patients met inclusion criteria and had confirmed ASAH. In the absence of gold standard and blinding, sensitivity and specificity calculations must be interpreted carefully as previously suggested [27]. With all lumbar puncture parameters being available to the physician, it is difficult to accurately isolate the contribution of either visual or spectrophotometric xanthochromia to the observed outcome.

Conclusions

In conclusion, prevalence of aneurysmal subarachnoid hemorrhage was very low following a negative head CT scan. Despite excellent patient outcomes, intense resources were utilized to identify these 5 aneurysmal subarachnoid hemorrhages. Lumbar puncture analyses combining red blood cell count, visual and spectrophotometric xanthochromia identified all ASAH, allowing intervention and a positive clinical outcome. To our knowledge, this study is one of the first to establish the outcome of patients using a combined approach consisting of red blood cell count along with both visual and spectrophotometric xanthochromia to predict subarachnoid hemorrhage from aneurysmal rupture in neurologically intact patients after a negative head CT scan using new generation scanners.

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