

Subarachnoid Hemorrhage -- Role of LP
=====

p Xanthochromia

- "Recently it was contended that it is bloodstained cerebrospinal fluid (CSF) that is important in the diagnosis of subarachnoid haemorrhage (SAH) and not xanthochromia, and also that a normal CT scan and the absence of xanthochromia in the CSF do not exclude a ruptured intracranial aneurysm. The CSF findings were therefore reviewed of 111 patients with a proven SAH. All patients had xanthochromia of the CSF. Lumbar punctures were performed between 12 hours and one week after the ictus. Xanthochromia was still present in all (41) patients after 1 week, in all (32) patients after 2 weeks, in 20 of 22 patients after three weeks and in 10 of 14 patients after four weeks. In six years we identified only 12 patients with sudden headache, normal CT, bloodstained CSF, and no xanthochromia. Angiography was carried out in three and was negative. All 12 patients survived without disability and were not re-admitted with a SAH (mean follow up 4 years). It is concluded that it is still xanthochromia that is important in the diagnosis of SAH and not bloodstained CSF. Furthermore a normal CT scan and the absence of xanthochromia do exclude a ruptured aneurysm, provided xanthochromia is investigated by spectrophotometry and lumbar puncture is carried out between 12 hours and 2 weeks after the ictus."
[Vermeulen M, Hasan D, Blijenberg BG, Hijdra A, van Gijn J. Xanthochromia after subarachnoid haemorrhage needs no revisitation. J Neurol Neurosurg Psychiatry 1989;52(7):826-8]

p Blood in CSF

- Takes 2-4 hours for blood to get into the lumbar area after a SAH.
- "One must be aware of the that however that the presence of xanthochromia may be seen even with a traumatic tap in some cases."
- The mean fall in RBC count from the first to last tube in one study was 74% (Lang, D.T. et. al. Am. J. Clin. Pathol 1990;93:403-405 Rapid Differentiation of Subarachnoid Hemorrhage from Traumatic Lumbar Puncture Using the D-Dimer Assay).
- >Hmm. I thought it was 2-4 hours. Rosen says 4 hours. Where did you >get "at least 12 hours?"
[Vermeulen, J. The diagnosis of subarachnoid haemorrhage. J Neurol, Neurosurg, Psychiatry, 1990;53:365-372. This is an excellent review article. Xanthochromia is only detectable by eye in 1/3 to 1/2 of the cases when it can be picked on spectography.

From: "Simon Brown" <sgabrown@sydney2.world.net>
To: emed-l@itssrv1.ucsf.edu
Date sent: Wed, 11 Oct 1995 16:27:56 +1000
Subject: Re: emed-l traumatic taps

Some words on subarachnoid haemorrhage (SAH) and LPs, and particularly spect analysis. There seem to be a few misconceptions floating around.

Spectrophotometry in this circumstance is NOT used to detect "free hemoglobin", but rather oxyhemoglobin (present in 2-6 hrs following SAH), methaemoglobin (hours, can't recall the exact range) and bilirubin (days). That is, it is used to detect the breakdown components of haemoglobin which produce the visible yellow colour in spun CSF supernatant at higher concentrations. Thus it detects the

bleed that was present BEFORE you do the traumatic tap, and eliminates the need for the infamously inaccurate sequential bottle cell count technique and is much more sensitive than visual inspection for xanthochromia (which misses 30-50% of SAH.) The classic paper on CSF spectroscopy is Barrows et al. (1)

False positives (ie xanthochromia on spect, but no SAH) appear to be common at a rate of around 25-30% when the tap is traumatic (less common when the CSF is clear). False positives may occur with subdurals, ICH and jaundice and various congenital metabolic abnormalities that I have no chance of recalling. Most importantly false positives occur when the CSF is not rapidly examined or spun down and separated for later analysis (2). The reason for this is lysis of cells from traumatic tap and Hb breakdown- blood/CSF left standing develops xanthochromia after 6 hours. A massive traumatic tap does not cause a false positive (measured by spect) unless the sample is left standing.

Cork stoppers also cause spurious xanthochromia (good exam trivia that one!)

So, the value of CSF spectrophotometry in the diagnosis of SAH is:

1. To differentiate a traumatic tap from true SAH, for which it reportedly has 100% sensitivity for SAH when performed from 12 hours to several weeks from the onset of headache (2). Unfortunately specificity may not be as good, but the studies reporting the false negative rate of 25-30% may have been related to leaving bottles standing around.
2. To diagnose SAH at late presentation when the red cells have disappeared.

The value of diagnosing a traumatic tap is that it avoids angiography and it's attendant morbidity... but this may become a moot point if the (much safer) MRI angiography is well validated and becomes more available.

As to timing of the LP, Vermuelen's study (3) is the only good-sized study that demonstrates spectroscopic analysis for xanthochromia to be acceptably sensitive (100%) and all samples were taken 12 hours or more after the onset of symptoms. He quotes one article (4) that I just haven't been able to get my hands on that reports false negatives if samples are taken earlier than this. I have my doubts- on the basis of other work (smaller numbers &/or in-vitro studies) CSF xanthochromia should be present in practically all SAH at 4-6 hours.

So, you can either:

1. LP early if CT is negative and accept that bloody tap equals cerebral angiography and it's risks. Serial bottle cell counts simply do NOT work AT ALL and should not even rate a mention.

2. LP at 4-6 hours if CT is negative and accept that negative xanthochromia in the presence of a bloody tap is PROBABLY a good negative predictor for SAH, but may miss the occasional SAH (we just don't know the sensitivity in this time frame)

3. LP after 12 hours if CT is negative and accept that there is a small risk of re-bleeding during this time. Balance this risk of rebleeding versus the risk of unnecessary angiography if LP is done early when xanthochromia may be unreliable and the tap is bloody. I suspect the risk of rebleed is miniscule in the CT-normal GCS 15 patient, much less than the quoted 4% overall rebleed rate. Also, there's no point rushing in to the LP in the middle of the night if angiography can't be done until the morning.

4. Do fancy tests like CSF D-Dimers and hope they work.

5. Warm up the MRI and damn the torpedoes.

Our neurosurgeons seem to prefer option 2, and they seem keen to do angios in the middle of the night. I'm not sure I agree entirely, but it seems reasonable and we'll get their backup -hopefully- if things go wrong.

The guys at the hospital over the river from us want to do a study of approach number 2, and also look at CSF D-Dimers. Unfortunately the numbers will be hard to get (only one or two CT-negative SAHs a year at their hospital), so we may never know for sure unless lots of people get interested and join in.

REFERENCES:

1. Barrows-LJ; Hunter-FT; Banker-BQ. The Nature and clinical significance of pigments in the cerebrospinal fluid. Brain 1955;78:59-80

2. Resurreccion-EC; Rosenblum-JA. Common cases of spurious xanthochromia in cerebrospinal fluid. Angiology 1972 Feb; 23(2): 105-10.

3. Vermeulen-M; Hasan-D; Blijenberg-BG; Hijdra-A; van-Gijn-J. Xanthochromia after subarachnoid haemorrhage needs no revisitation. J-Neurol-Neurosurg-Psychiatry 1989 Jul; 52(7): 826-8.

4. Walton-JN. Subarachnoid Haemorrhage. Edinburgh; Livingston, 1956.

////////////////////////////////////\n
Simon Brown MBBS
Department of Emergency Medicine
Royal Brisbane Hospital

An interesting article "the Clinical Spectrum of Unruptured Intracranial Aneurysms" Arch Neurol vol50, p265-269 March 1993 reports a subgroup of patients with acute HA and no SAH- postulate that the "thunderclap HA" may occur with acute expansion of aneurysm (sort of like AAA) or with

acute thrombosis of aneurysm.

In a simliar manner studies have yielded conflicting numbers regarding the sensitivity of CT scan in diagnosing SAH. The reason for this is that these studies have included patients who were scanned at different time intervals after the ictus. If performed within 48 to 72 hours of bleeding some have found 100% sensitivity for CT (1). In one very interesting 'time lapse' study in which serial CT scans were performed on patients with SAH the following was found (2):

| DAYS | 0-2 | 3-5 | 6 | 7 | 8 | 9 | 18-22 |
|----------------------------|-----|-----|----|----|----|---|-------|
| # scanned | 68 | 8 | 10 | 12 | 11 | 8 | 10 |
| extravasated blood | 64 | 7 | 7 | 5 | 2 | 1 | 1 |
| only non-specific findings | 4 | 1 | 1 | 2 | 5 | 2 | - |

Within the first 72 hours 100% sensitivity was again demonstrated. The authors, however concede the following: A low threshold for diagnosing SAH on CT was used that included not only the demonstration of extravasated blood in the basal cisterns and fissures but more subtle findings such as increased density of the tentorium (as in the last row above). Furthermore this series did not include patients with 'warning leak' where others have shown only 55% sensitivity of CT scanning (3). The latter study, however, did not specify the times at which the scanning was performed.

After about a week, or so, it is exceptional to find blood on CT scan after SAH and some have argued that, if present, is evidence of rebleeding but this is disputed (2).

After all the above let me make the following consession (since I often bludgeon people over the head with consensus statements when they are to my liking as in the case of unstable angina): the AHA says: "The accuracy of CT in documenting SAH diminishes after 24 hours. Thereafter the diagnosis is often dependent on lumbar puncture" (4). Do they thus mean to imply that before 24 hours one may rely upon CT scan alone? Reading further: "When clinical features suggest SAH, lumbar puncture is a critical diagnositic procedure in patients with sudden-onset diffuse headache. In fact lumbar puncture is the only diagnostic procedure that will uncover small SAHs" (5). Why they choose to emphasize the presentation as one of 'diffuse headache' to highlight the need for LP is a mystery to me inasmuch as (small) sentinel bleeds typically present with hemicranial or periorbital pain (3). As an aside, in a very revealing passage, they observe "Patients suspected of having SAH or meningitis whose neurological examinations, including gait are normal and who will not be hospitalized if their CSF were clear should have a lumbar puncture in the physician's office or emergency ward. In this cirsunstance, CT is a low yeild procedure and can probably be ommitted unless the CSF is bloody or xanthochromic." I

won't pull out my refernces (which I think I produced recently) that show that LP is a safe procedure in SAH unless the patient has focal findings or is obtunded.

Having said that, let me observe that I perform LPs on every patient I suspect of having an SAH who has a normal CT but do not do serial CK testing in the ED.

H. Louzon MD

(1) Bassi et. al. Warning Signs in Subarachnoid Hemorrhage: A Cooperative Study.

Acta Neuro Scan 1991;84:227-281

(2) Gijn et. al. The Time Course of Aneurysmal Haemorrhage on Computed Tomograms.

Neuroradiology 1982;23:153-156

(3) Leblanc The Minor Leak Preceding Subarachnoid Hemorrhage. J

Neurosurg 1987;

66:35-39

(4) Caplan LR, Flamm ES, Mohr JP, Toole J, Plum F, Fisher CM, Drake CG, Peerless SJ Lumbar puncture and stroke. A statement for physicians by a Committee of

the Stroke Council, American Heart Association.

Circulation 1987 Feb;75(2):505A-507A

(5) *ibid.*

Even with last generation SCAN false negative being at least 7% (1), and could go to 16% if bleeding occurred > 24 hours (I just discard a comment from Harvey yesterday: was his point against or with that position of diminish sensitivity over time?).

(In the study bellow, it is said that LP identified all patient -- but as these SAH were probably diagnosed by this LP, you can't say much about the number of patient who didn't get a SCAN and no LP and where in fact SAH.)

May be we just circle now?

SENSITIVITY OF NEW-GENERATION COMPUTED TOMOGRAPHY IN SUBARACHNOID HEMORRHAGE

Sames, T.A., et al, Acad Emerg Med 3(1):16, January 1996

BACKGROUND: Since CT scanning with older generation scanners is insensitive in at least 10% of patients with acute nontraumatic subarachnoid hemorrhage (SAH), lumbar puncture (LP) is recommended when SAH is suspected and the CT scan is reported as normal. Theoretically, however, newer generation CT scanners might provide greater diagnostic accuracy.

METHODS: This retrospective study, from the Joint Military Medical Centers in San Antonio, TX, reviewed findings in 181 patients aged 13-86 in whom acute nontraumatic SAH was ultimately diagnosed, and who had undergone CT scanning with newer-generation scanners (third generation

or more recent). The accuracy of the initial radiology interpretation (by either a neuroradiologist, a general radiologist or a radiology resident) was examined.

RESULTS: The sensitivity of the initial CT scan was 91.2% overall, 93.1% in patients with symptoms for less than 24 hours, and 83.8% in those with symptoms for more than 24 hours. The sensitivity was not significantly influenced by the low-contrast resolution characteristics of the 17 scanners that were employed. Lumbar puncture was diagnostic for SAH in all patients with "normal" CT scans.

CONCLUSIONS: Even with newer generation CT scanners (and even without considering other patients in whom the diagnosis may have been missed because of a false-negative CT scan), a substantial subset of patients with acute nontraumatic SAH had a "normal" initial scan interpretation, particularly among those whose symptoms had been present for more than 24 hours. Therefore, LP should be performed in all patients with normal CT scans and symptoms suggestive of SAH.

| Alain Vadeboncoeur MD |

I know we have 'talked' recently on this topic, but, I am curious what people think about the recent retrospective study done at Brown. (Sidman, et al; Subarachnoid Hemorrhage Diagnosis: Lumbar Puncture is Still Needed When the CT Scan is Normal; AEM, Sept. 96, Vol 3, No. 9, pages 827-831.)

Utilizing retrospective chart review and an 'arbitrary' group defining criteria of less than or greater than 12 hours from time of symptom onset to CT scan. Their data find a sensitivity of 100% (95% CI = 95%-100%) for the third generation scanners in the diagnosis of SAH for patients presenting within 12 hours of symptom onset. The January 96 issue of AEM includes a study from San Antonio in which 24 hours from symptom onset was the cut-off, the data found a sensitivity of 93% in these 'early' presenters.

>An MRA was recommended and that was to have been performed during her >observation.

>

>The rbc's seen in the csf were from the 4th tube. I did not check the >first tube.

>

>I usually perform my lp's with the pt sitting up. I did not check >opening pressure

If it is important for you to know the pressure while performing an LP in the sitting position, extension tubing may be added from the needle to the approximate level of the foramen magnum. The manometer attached at that level should give an accurate reading, at least enough to know if the CSF pressure is grossly elevated.

Personally I attempt all LPs at least once in the lateral position and sit them up if unsuccessful.

Visualializing the fundi is fine as a gross test of elevated ICP but, if I recall correctly, there is a delay of several hours from its onset to the occurence of papilledema. The converse, excluding raised ICP, can be

done reliably, I am told, if spontaneous venous pulsations (SVP) are visible in the fundus vessels. Their absence, however, may occur normally in a few percent of the population with normal ICP. So if you see SVP you have reliably excluded the presence of clinically significant ICP elevations.

Our laboratory has a standard protocol for performing CSF analysis and routinely counts cells in the first and last tubes whether you order it or not. I realize that this sounds heretical to some of our strangely silent Aussie friends who have cautioned us against using this method in the past but, in truth, unless you are willing to subject all of your traumatic taps to angiography or have 24 hour availability of MRA, you have little choice. I am skeptical of the suggestion that one perform repeat lumbar puncture after an interval corresponding to 12 hours (when xanthochromia can be reliably detected per Vermullen's study (1)) as I see no reason why the initial traumatic tap, which presumably introduced blood into the CSF as well as your tube, would not result in CSF xanthochromia after that interval. Console yourself with the realization that some academic emergency physicians are satisfied to exclude SAH solely by the absence of blood demonstrable on CT when performed within 12 hours of the ictus (2).

Furthermore, let me point out that when testing for xanthochromia most laboratories have an assistant hold the CSF supernatant up against a sheet of white paper, a notoriously insensitive (and non-specific) technique. I don't know how many hospital laboratories have the capability (much less the enthusiasm) for performing spectrophotometry at 3 o'clock in the morning.

Other than testing for the presence of xanthochromia several other techniques have been advocated to distinguish traumatic tap from SAH. The use of a D-dimer assay have been proposed (3) but its reliability has not been confirmed (4). To my knowledge, a study done in infants which purports to show a discrepancy in RBC MCV between blood and CSF samples in CNS bleeds (5) has not been confirmed in adults. In any case, when is the last time your laboratory reported the MCV in your CSF cell counts?

Bottom line in this case is that your neurologist gave you good advice (do an MRA if you're not sure). That's why I'm perplexed that you thought that he was not very helpful.

H. Louzon MD

(1)

Vermullen et. al. Xanthochromia After Subarachnoid Hemorrhage Needs No Revisitation. J Neuro Neuros Psych 1989; 52(7):826-.

(2)

Singal A Tap in Time. AEM 1996;3(9):823

(3)

Lang DT, Berberian LB, Lee S, Ault M
Rapid differentiation of subarachnoid hemorrhage from traumatic lumbar
puncture using the D-dimer assay.
Am J Clin Pathol 1990 Mar;93(3):403-5

The D-dimer assay of 40 cerebral spinal fluid (CSF) samples accurately differentiated subarachnoid hemorrhage (SAH) from traumatic lumbar puncture. The D-dimer assay was positive in all six patients with subarachnoid hemorrhage. Negative D-dimer values were obtained in control groups of 14 patients with hemorrhagic CSF secondary to traumatic lumbar puncture (LP) and in 20 patients with normal CSF. The D-dimer assay proved to be a better test than xanthochromia or the decline in erythrocyte count in sequentially collected tubes in differentiating subarachnoid hemorrhage from traumatic LP.

(4)

Page KB Howell SJ Smith CM Dabbs DJ Malia RG Porter NR Thickett KJ
Wilkinson GM
Bilirubin, ferritin, D-dimers and erythrocytes in the cerebrospinal
fluid of patients with suspect J Clin Pathol Vol. 47 no. 11 pp. 986-9
1994 Nov

AIM--To assess the diagnostic value of cerebrospinal fluid (CSF) spectrophotometry, cytology, ferritin, and D-dimer measurements in the investigation of suspected subarachnoid haemorrhage in patients with negative or equivocal computed tomography (CT) scans. METHODS--CSF specimens submitted for assessment of xanthochromia were examined for erythrocytes using a cytospin preparation stained with Wright's stain, for ferritin using the Ciba-Corning Magic IRMA assay, D-dimers using the Dimertest 2 latex agglutination slide test, and for bilirubin by scanning spectrophotometry. The patients were divided into three groups for data analysis and the results compared with the existing methods, CT, and angiogram results. Final diagnoses were reviewed by a consultant neurologist. RESULTS--Thirty six patients were recruited. In those patients with confirmed subarachnoid haemorrhage CSF cytology had a low sensitivity and there were false negative results with both the D-dimer and ferritin assays. Eleven patients with a negative or equivocal CT scan underwent angiography, but only one aneurysm and no arterio-venous malformations or bleeding points were identified. In the patient with the aneurysm there was no laboratory evidence of subarachnoid haemorrhage. Six patients had CSF abnormalities detected by the special tests only and in none of these cases was subarachnoid haemorrhage confirmed. All results were normal in four out of five cases of traumatic tap. CONCLUSIONS--This is a small study, but it shows that, depending on the timing of the lumbar puncture, false negative results can occur with both ferritin and D-dimer measurements. It suggests that neither of these tests adds significantly to the information provided by CT, visualisation of CSF, and spectrophotometry and confirms that, despite the use of spectrophotometry, D-dimer and ferritin assays in selecting

patients for angiography, the proportion of patients with negative CT scans and colourless CSF with demonstrable vascular lesions remains low.

(5)

Yurdakok M, Kocabas CN

CSF erythrocyte volume analysis: a simple method for the diagnosis of traumatic tap in newborn infants.

Pediatr Neurosurg 1991-92;17(4):199

An objective method to evaluate the erythrocytes in cerebrospinal fluid (CSF) in traumatic tap is described. In newborn infants with intracranial bleeding the CSF mean corpuscular volume (MCV) values are lower than the peripheral blood MCV, but in patients with traumatic tap, the CSF and blood MCV values are similar.

> I recently saw a normotensive, nondiabetic young female pt who presented about
> one hour after the sudden onset of neck pain >> headache and photophobia. I
> did a fairly extensive neurological exam which was totally normal. The rest
> of the physical exam and history were unremarkable. I then did an LP which
> demonstrated gross blood. A subsequent CT confirmed the diagnosis of SAH
> without evidence of increased ICP. She subsequently had angiography and a
> PCA aneurysm was clipped and treated surgically. Despite the good outcome,
> some have questioned doing the LP prior to a CT (to "ensure" a safe tap).
> I am interested if someone knows the incidence of herniation in this kind
> of presentation and from the more academic types in the audience I was
> wondering what the current guidelines were from ACEP... when I trained a CT
> in this circumstance was considered unnecessary and less sensitive for
> SAH.
>

We had a discussion about this several months ago. At that time I cited a recommendation from the AHA that "Patients suspected of having SAH or meningitis whose neurological examinations, including gait are normal and who will not be hospitalized if their CSF were clear should have a lumbar puncture in the physician's office or emergency ward. In this circumstance, CT is a low yield procedure and can probably be omitted unless the CSF is bloody or xanthochromic." (1).

Admittedly this is a rather old reference. In the interests of saving time I have reproduced a previous post with references below:

"As I indicated recently the option of performing an LP prior to CT scanning is a viable one in the patient with a non-focal exam who is not obtunded (1). Only one study found a high rate of deterioration in patients with SAH who underwent LP (2). [this latter study found a high rate of herniation due to the presence of intracerebral clot--aneurysms can rupture either intracerebrally, subarachnoid or both]. By contrast, others have found it to be safe (3,4).

On the other hand, limiting LP to patients who have a negative CT, limits the number of invasive procedures (by a small amount) that eventually need to be performed. It's also much easier to justify a CT scan which demonstrates the presence of intracerebral clot than to explain why one missed the subtle focal findings that would have contraindicated the LP."

At the present time I see no rationale in performing an LP before SAH is ruled out by CT unless a CT scan is not available. By contrast if the working diagnosis is meningitis then several studies have found that proceeding directly to LP is safe if focal findings or signs of increased ICP are absent. In those circumstances, CT is a waste of time and money. It's too late at night to dig out those latter references, so let me know if you need them.

H. Louzon MD

(1) Caplan LR, Flamm ES, Mohr JP, Toole J, Plum F, Fisher CM, Drake CG, Peerless SJ Lumbar puncture and stroke. A statement for physicians by a Committee of the Stroke Council, American Heart Association. Circulation 1987 Feb;75(2):505A-507A

(2) Duffy Lumbar Puncture in Spontaneous Subarachnoid Hemorrhage. BMJ 1982;285:1163-1164

(3) French et.al. Lumbar Puncture in Subarachnoid Hemorrhage: yes or no? New Z J Med 1985;98:383-384

(4) Patel et.al. Lumbar Puncture and Subarachnoid Hemorrhage. Post Med J 1986;62:1021-1024