

Rural Healthcare *Quality* Network  
**Hospital Peer Review**

**March 2011**

*Hospital Peer Review is a monthly newsletter sponsored by the Rural Healthcare Quality Network to alert Critical Access Hospitals regarding findings from the Peer Review Program. Summarized are a few of the key findings and best practices that would be helpful for other critical access hospitals to be knowledgeable about. This newsletter is edited by Myron Bloom, Medical Director and he can be reached at [dmbloom@msn.com](mailto:dmbloom@msn.com).*

**Headaches are such a Headache**

**Part 2: non-traumatic SAH**

Nontraumatic subarachnoid hemorrhage (SAH) is a potentially lethal diagnosis that must be often considered but is rarely found. Most spontaneous SAHs are due to rupture of saccular aneurysms. While the rate of incidental intracranial aneurysm at autopsy is 2% to 3%, rupture of an intracranial aneurysm causing SAH occurs in only 1% of the population causing death in approximately 0.5% of the population. However, the risk of harboring an intracranial aneurysm is double in persons with a first-degree relative who experienced aneurysmal SAH and possibly triple in those with two or more first-degree relatives having had an aneurysmal SAH.

SAH strikes approximately 27,000 Americans annually with a mortality as high as 30% in the first 2 days and 45% in the first 30 days after a rupture. Of patients with headache presenting to the ED, retrospective studies put the rate of SAH generally around 1% (however, one prospective study put that figure as high as 4%). Two prospective studies found that if only patients with “the worst headache” of their lives and a normal neurologic examination were considered, 12% of such patients had subarachnoid hemorrhage. The rate doubled when patients with abnormal examinations were included.

Between 20 and 50% of patients with documented subarachnoid hemorrhage report a distinct, unusually severe headache often with atypical features in the days or weeks before the index episode of bleeding, commonly referred to as a warning headache. The classical thunderclap headaches develop in seconds, achieve maximal intensity within minutes, and may last only hours or go on for days. Nausea and vomiting (75%), transient loss of consciousness (50%), seizure (5%), and buckling of the legs may accompany the headache. The headache may be in any location, may be localized or generalized, may be mild,

may resolve spontaneously or may even be relieved by nonnarcotic analgesics. The physical examination may be normal or just show restlessness. The diagnosis is easier when retinal hemorrhages, nuchal rigidity, altered level of consciousness, or focal neurologic signs are found. Patients with prominent neck pain may be erroneously diagnosed as cervical sprain & arthritis, while blood irritating the lumbar theca may be misdiagnosed as sciatica. Unfortunately, an electrocardiogram with a pattern mimicking myocardial ischemia may result in the erroneous diagnosis of a primary cardiac disorder.

So the first or worst headache ever requires evaluation, as do qualitatively different headaches in patients with established headache patterns, even if the headache is not the “worst ever.” Patients with abnormal clinical findings present little diagnostic difficulty. However, in the absence of such symptoms and signs, clinicians often miss the diagnosis. A study from the University of Toronto, examining the records of 1,603 adults hospitalized for nontraumatic SAH (province-wide patient population and 176 EDs) over a three-year period (2002-2005) identified rates and correlates of missed/delayed diagnosis cases. The total misdiagnosis of SAH was 5.4%. When compared with cases that were not initially missed, patients with missed diagnoses were significantly younger (mean, 54 vs. 58 years), more likely to have a less urgent or non-urgent triage classification (24.7% vs. 5.6%), and were less likely to present to a teaching hospital (12.3% vs. 22.8%). [Vermeulen, M.J., et al, Stroke 38:1216, April 2007] Misdiagnosis stems from three recurring, correctable patterns of diagnostic error: failure to appreciate the spectrum of clinical presentation, failure to understand the limitations of computed tomography (CT), and failure to perform and correctly interpret the results of lumbar puncture (LP).

AVOIDING PITFALLS IN THE DIAGNOSIS OF SUBARACHNOID HEMORRHAGE,  
NEJM 342:1, January 6, 2000

**TABLE 4. REASONS FOR MISDIAGNOSIS OF SUBARACHNOID HEMORRHAGE.**

**Failure to appreciate the spectrum of presentations of subarachnoid hemorrhage**

- Failure to evaluate patients with “warning headaches” (severe, abrupt, unusual headaches)
- Failure to recognize that headache can improve spontaneously or with nonnarcotic analgesic drugs
- Overreliance on the classic presentation, leading to the following incorrect diagnoses:
  - Viral syndrome, viral meningitis, or gastroenteritis
  - Migraine or tension-type headache
  - Sinus-related headache
  - Neck pain (rarely, back pain)
  - Psychiatric disorders
- Focus on secondary head injury (resulting from syncope)
- Focus on electrocardiographic abnormalities
- Focus on high blood pressure
- Lack of knowledge of presentations of unruptured aneurysm

**Failure to understand the limitations of computed tomography**

- Loss of sensitivity with increasing time between onset of headache and scanning
- False negative results in cases of small-volume bleeding (spectrum bias)
- Interpretation factors (e.g., variations in expertise of physician reading the scan)
- Technical factors (e.g., variations in thickness of slices taken at the base of the brain, motion artifact)
- False negative results for blood with a hematocrit of less than 30 percent

**Failure to perform lumbar puncture and correctly interpret cerebrospinal fluid findings**

- Failure to perform lumbar puncture in patients with negative, equivocal, or suboptimal results on computed tomography
- Failure to recognize that xanthochromia may be absent very early (<12 hours after hemorrhage) and very late (>2 weeks after hemorrhage)
- Failure to realize that visual inspection for the presence of xanthochromia is less sensitive than spectrophotometry
- Failure to distinguish properly between “traumatic tap” and true subarachnoid Hemorrhage

The 1996 Clinical Policy on Headache as determined by the American College of Emergency Physicians is a noncontrast head computed tomography (CT) followed by diagnostic lumbar puncture (LP) to exclude SAH. However, the guideline does not consider pretest probability of SAH or the generation of CT scanner in determining which patients require LP.

In the International Cooperative Study of the Timing of Aneurysm Surgery, over 3500 patients with aneurysmal subarachnoid hemorrhage underwent scanning with the type of CT equipment in use between 1980 and 1983. Ninety-two percent of the scans were positive on the day of rupture, but diagnostic sensitivity declined to 86% one day later, 76% two days later, and 58% five days later. A modern noncontrast CT scan will pick up an SAH in up to 98% of cases within 12 hours after the onset of symptoms declining significantly to 93% at 24 hours, and dropping to 85% at 5 days, 50% at one week, and to 30% by 2 weeks as extravasated blood becomes increasingly isodense over time. Sensitivity is probably lower in alert, neurologically intact patients because the extravasation might be too small to be initially seen and the small amount of blood or “minor leak” might disappear too fast to be detected on a delayed CT. Because the increased density of blood on CT is a function of the hemoglobin concentration, a hemoglobin concentration below 10 g per deciliter may appear isodense. Therefore, lumbar puncture should be performed in any patient with suspected SAH and a delayed negative or equivocal result CT scan.

After aneurysmal hemorrhage, RBCs distribute throughout the subarachnoid space, where they may persist for days or weeks and are gradually lysed. Released hemoglobin is metabolized to the pigmented molecule oxyhemoglobin (reddish pink) and then bilirubin (yellow), resulting in xanthochromia. The formation of bilirubin, is an enzyme-dependent process requiring up to 12 hours, and is diagnostically more specific than just finding blood cells. When an LP is performed between 12 hours and 2 weeks from headache onset, it is highly diagnostic for acute SAH because both blood cells and xanthochromia will be present. A too early LP might be falsely negative for blood in the first couple hours and for xanthochromia in the first 12 hours. Besides properly timing the LP, the handling of the CSF is important: the cerebrospinal fluid should be examined for RBCs and centrifuged promptly, so that RBCs resulting from a bloody tap do not have time to undergo lysis producing bilirubin xanthochromia from oxyhemoglobin degradation.

However the disadvantages of delaying lumbar puncture for 12 hours are both logistic (prolongation of a patient's ED stay) and the potential for an early rebleeding.

Five hundred ninety-two patients (including 61 with subarachnoid hemorrhage) were enrolled at 2 tertiary care EDs in Ottawa, Ontario, Canada over 3 years, to test the recommended practice of getting a head CT and LP to rule out SAH in acute headache patients. Patients were followed up with a structured telephone questionnaire 6 to 36 months after their ED visit and electronic hospital records review to ensure no missed SAH cases. One patient without SAH was subsequently diagnosed with cerebral aneurysm, requiring surgery. They calculated SAH sensitivity, specificity, and positive and negative likelihood ratios for diagnosis of subarachnoid hemorrhage or aneurysm at 98%, 67%, 2.98, and 0.02 respectively. [Perry JJ, et al, "Is the combination of negative computed tomography result and negative lumbar puncture result sufficient to rule out subarachnoid hemorrhage?" *Ann Emerg Med.* 2008 Jun; 51(6):707-13.]

CT accuracy has increased with evolving technology such that it is debatable whether an LP after a negative scan continues to be necessary. A retrospective review was performed identifying all patients who presented to a tertiary care academic ED from August 1, 2001, to December 31, 2004, with nontraumatic SAH to determine whether patients were diagnosed by cranial CT or lumbar puncture, the presence of headache and level of consciousness at ED presentation, and whether or not they had an aneurysm or arteriovenous malformation. Noncontrast CT scan diagnosed 139 patients, but 10 were diagnosed by lumbar puncture for an overall CT scan sensitivity of 93%. Of the 67 patients presenting with headache and normal mental status who had a SAH and either aneurysm or arteriovenous malformation, the sensitivity of cranial CT scan was 91%. Their conclusion was that noncontrast CT imaging exhibits inadequate sensitivity to serve as a sole diagnostic modality in detecting spontaneous subarachnoid hemorrhage caused by aneurysm or arteriovenous malformation. [Byyny RL, et al, Sensitivity of noncontrast cranial computed tomography for the emergency department diagnosis of subarachnoid hemorrhage. *Ann Emerg Med.* 2008 Jun; 51(6):697-703.]

A contrary conclusion was reached by Danish authors who retrospectively evaluated the diagnostic accuracy of CT scanning in 499 admitted patients referred for suspected or documented SAH from 2000 through 2005. The range of CT scanners that were employed reflected available technological upgrades, to include the current standard of 64-slice multi-detector. The diagnosis of SAH was excluded based on a negative CT scan and a negative LP in 40.7% of the patients. The CT scan was positive in 295 of the 296 patients with documented SAH. In the remaining patient, the diagnosis was based on a positive LP on day six. The sensitivity and specificity of CT scanning for SAH were each 100% from day one to day five, and the overall sensitivity and specificity when later presentations were included were 99.7% and 100%. The rate of post-dural

puncture headache of sufficient severity to prompt readmission or prolonged hospitalization was 7.4%. The authors suggest that current CT scanning technology has excellent sensitivity and specificity for SAH up to three days after symptom onset, and that LP might not be necessary if the CT scan is negative during this time period. [Cortnum, S., et al, Determining the sensitivity of computed tomography scanning in early detection of Subarachnoid Hemorrhage, Neurosurgery 66(5):900, May 2010]

Is doing CTA after a negative noncontrast CT a safe alternative to LP? Because a study comparing the equivalence of CT&LP and CT&CTA would require several thousand subjects, a mathematical probability model was constructed to determine the posttest probability of excluding SAH by a CT/CTA strategy. The investigators conservatively set the prevalence of SAH in ED headache patients at 15%, and used a sensitivity for SAH of 91% and sensitivity of CTA for aneurysm to be 97%. Based on the data and construct assumptions, the posttest probability of excluding aneurysmal SAH after a negative CT/CTA was calculated to be 99.43%. Thus the authors concluded that CT followed by CTA can exclude SAH with a greater than 99% posttest probability. In ED patients complaining of acute-onset headache without significant SAH risk factors, CT/CTA may offer an alternative diagnostic paradigm. [McCormack RF, et al, "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 Apr; 17(4):444-51.]

It has been suggested that spectrophotometry is more sensitive than visual inspection for the identification of CSF xanthochromia as an indicator for SAH. Experts argue whether visual inspection for xanthochromia is adequate or not. The following two paragraphs give contradictory evidence.

Investigators from Los Angeles County / USC Medical Center retrospectively reviewed the records of 1,323 patients with an imaging study confirming the diagnosis of SAH from 1993 to 2005. Only 19 of those patients fulfilled study entry criteria of documentation of visual inspection for xanthochromia of CSF collected between 12 hours and 2 weeks after headache onset. Xanthochromia was apparent on visual inspection in fewer than half of these patients (9/19), representing a sensitivity of only 47.3% (95% CI 24.4-71.1%). Their conclusion was that visual inspection of CSF for xanthochromia appeared to be an unreliable indicator of SAH. 16 references [Arora, S., et al, Evaluating the sensitivity of visual xanthochromia in patients with Subarachnoid Hemorrhage, J Emerg Med 39(1):13, July 2010]

A prospective study, from the University of Ottawa, compared visual inspection and spectrophotometry for the detection of xanthochromia in 220 neurologically intact adults presenting with headache and undergoing LP for possible SAH. SAH was ultimately diagnosed in two patients (0.9%) and both were identified by CSF cell count and visual inspection. The specificity of visual inspection of CSF

for xanthochromia was 97%, while that of spectrophotometric xanthochromia, using four different definitions of "positive," ranged between 29% and 89%. Angiography was actually performed in 5.9% of the patients in the series. Reliance on visual CSF inspection for xanthochromia to select patients for angiography would have decreased its use by 85%, while reliance on spectrophotometric analysis would have increased this by 185% to 1208%. The use of spectrophotometry to identify xanthochromia in CSF had a high false-positive rate in this study, and its routine use would be anticipated to produce a marked increase in the unnecessary performance of cerebral angiography. A highly sensitive test applied to a low prevalence problem finds many more false positives. [Perry, J.J., et al, Should spectrophotometry be used to identify xanthochromia in the cerebral spinal fluid of alert patients suspected of having subarachnoid hemorrhage? Stroke 37:2467, October 2006]

Lastly, Does the response to medication lower the risk of a serious problem?  
...No.

Authors, from Beth Israel Deaconess Medical Center in Boston, examined the findings of 18 published articles (128 patients) concerning the relationship between the response to analgesics (seven articles) or triptans (eleven articles) and a serious underlying headache etiology. Almost half of the 103 patients (44%) experienced a positive response to analgesics, but the articles reported serious causes of headache (e.g., SAH, meningitis, cerebral venous sinus thrombosis, brain tumors) in patients responding to analgesics, with a diagnostic delay of hours to weeks in seven patients. The eleven articles (ten case reports) involving treatment of 25 patients with sumatriptan reported various serious underlying causes of headache (e.g., carotid artery dissection, carbon monoxide exposure, tumor), with a delay in diagnosis by hours to weeks in ten patients. A reduction in pain from analgesics or triptans does not exclude a serious underlying cause of headache. [Pope, J.V., et al, Favorable response to analgesics does not predict a benign etiology of headache, Headache 48:944, June 2008]