



## Diagnosis of subarachnoid hemorrhage in the emergency department

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Headaches are nearly ubiquitous; patients with this complaint account for 1% to 2% of all emergency department (ED) visits [1–3]. Because most of these patients have primary headache disorders, such as migraine or tension and other self-limited processes, extensive urgent evaluation in the ED of the entire group is inappropriate. A small percentage of these patients, however, has far more serious pathology (Box 1) [3,4], where failure to diagnose or a delay in diagnosis may lead to significant morbidity and mortality [1]. Included in this latter category are patients with subarachnoid hemorrhage (SAH). SAH is most commonly caused by trauma; of nontraumatic cases, 80% are caused by ruptured intracranial aneurysms [1].

The incidence of aneurysmal SAH is 6 to 10 per 100,000 persons [5–7]. Approximately 1% of all patients presenting to an ED with headache have SAH [3,8,9]. Furthermore, two studies found that of patients with severe acute-onset headache and a normal neurologic examination, 12% had SAH [10,11]. Early and accurate diagnosis of these patients is critical because prompt treatment leads to improved outcomes [5]. Thus, frontline physicians must distinguish those patients with headache caused by SAH (or other serious causes) from the much larger group of patients whose headaches are benign and self-limited.

Despite the widespread availability of neuroimaging equipment, misdiagnosis remains surprisingly common, occurring in 23% to 53% of patients with SAH on their first physician consultation [1]. Misdiagnosis has been documented in many different settings over the past two decades [12–15]. The list of incorrect diagnoses (Box 2) remains remarkably consistent [1].

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**Box 1. “Cannot miss” causes of headache**

SAH

Meningitis and encephalitis

Cervicocranial artery dissections

Temporal arteritis

Acute narrow angle closure glaucoma

Hypertensive emergencies

Carbon monoxide poisoning

Pseudotumor cerebri

Cerebral venous and dural sinus thrombosis

Acute strokes, hemorrhagic or ischemic

Mass lesions

Tumor

Abscess

Intracranial hematomas (parenchymal, subdural, epidural)

Parameningeal infections

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Diseases or conditions that are treatable and, if untreated, are life, limb, brain, or vision threatening [1].

Emergency physicians (EPs) are thus placed in the problematic position of needing to make rapid decisions about which patients presenting to the ED with the chief complaint of headache to evaluate for SAH or other serious causes of headache, and which to treat symptomatically and

**Box 2. Incorrect diagnoses assigned to patients with SAH**

No diagnosis made, or headache of unknown cause

Primary headache disorders (eg, migraine, tension, and cluster headaches)

Meningitis and encephalitis

Systemic infection (eg, flu, gastroenteritis, viral syndrome)

Stroke or cerebral ischemia

Hypertensive crisis

Cardiovascular diagnosis (rule out myocardial infarction, arrhythmia, or syncope)

Sinus-related headache

Neck problems (eg, cervical disc disease or arthritis)

Psychiatric diagnosis, including malingering and alcohol intoxication

Trauma-related

Back pain

discharge with appropriate follow-up plans. In the general population, migraine headache is approximately 1000 times more common than SAH [16]. Even in an acuity-skewed ED population, patients with migraine are still roughly 50 times more common than those with ruptured cerebral aneurysm. Because of these ratios, and because missed SAH is a common cause of litigation confronting EPs [17], all frontline physicians must develop a strategy to avoid missing this diagnosis.

One potential strategy would be to evaluate every patient with headache for SAH. This would avoid missing the diagnosis in every case. This strategy would also involve using tremendous amounts of time, personnel, and financial resources for cranial CT and lumbar puncture (LP), and involve the morbidity of LP on many more patients than would otherwise undergo that procedure. In addition, a “one size fits all” approach is rarely consistent with good medical practice. Another possible strategy would be to “pass the buck” and consult a specialist on all or most of these patients. This type of policy, too, would suffer from the many of the same problems, including increasing length of stay. More important, it would be anathema to the basic tenets of emergency medicine. Neither of these strategies is recommended.

The other potential strategy is selective evaluation of those patients who might truly benefit from an evaluation beyond patient history and physical examination. Although this has not been validated, the author believes that it is possible in most instances to correctly select which patients presenting to the ED with headache require further evaluations. Patient selection only requires a careful focus on specific elements of patients’ history and physical examination.

In SAH, as with most conditions, there is a bell-shaped curve of presentations, the middle of which represents the classic case. These patients present with a unique and distinctive headache that starts abruptly and is “worst of life” (or 10 of 10) in intensity. The headache typically begins during exertion and is associated with neck pain, nausea, vomiting, and transient loss of consciousness. Physical examination may disclose meningismus, ocular hemorrhages, or any focal or generalized neurologic findings. On the right portion of the bell curve are patients who present with severe symptoms, with localizing neurologic signs or severe alterations of mental status. In both of these groups, the decision to pursue further diagnostic testing, beyond history and physical examination is easy.

The problem arises in those patients who present on the left-hand side of the curve. These patients are mildly affected. They are awake and alert with no neurologic deficits, and are the patients most likely to be misdiagnosed. Paradoxically, they are also the patients who benefit the most from early identification and definitive treatment.

There are three generic causes for the alarming misdiagnosis rate: failure to appreciate the spectrum of clinical presentation, failure to understand the limitations of CT, and failure to perform and correctly interpret the results of LP (Box 3) [1]. Improvements in identifying which patients should be

**Box 3. Reasons for error in diagnosis in SAH***Failure to know the spectrum of presentations of subarachnoid hemorrhage*

Not evaluating patients with unusual (for the patient) headaches

Failure to appreciate that the headache can improve spontaneously or with nonnarcotic analgesics

Overreliance on the classic presentation with misdiagnosis of the following:

Viral syndrome, viral meningitis and gastroenteritis

Migraine and tension-type headache

Sinus-related headache

Neck pain (rarely, back pain)

Psychiatric diagnoses

Focus on the secondary head injury (resulting from syncope)

Focus on the electrocardiographic abnormalities

Focus on the elevated blood pressure

Lack of knowledge of presentations of the unruptured aneurysm

*Failure to understand the limitations of CT scans*

CT scans are less sensitive with increasing time from onset of headache

CT scan can be falsely negative with small-volume bleeds (spectrum bias)

Interpretation factors (expertise of physician reading the scan)

Technical factors (Have thin cuts been taken at the base of the brain? Is there motion artifact?)

CT can be falsely negative for blood at hematocrit levels of less than 30%

*Failure to perform LP and correctly interpret cerebrospinal fluid findings*

Failure to do LP in patients with negative, equivocal, or suboptimal CT scans

Failure to recognize that xanthochromia may be absent very early (< 12 hours) and very late (> 2 weeks)

Failure to realize that visual inspection for xanthochromia is less sensitive than measurement by spectrophotometry

Failure to properly distinguish traumatic tap from true subarachnoid hemorrhage

evaluated for SAH and how that work-up should proceed would likely reduce the frequency of misdiagnosis.

### **Which patients should be evaluated?**

With the understanding that all patients with a classic history or with an abnormal neurologic examination undergo further evaluation, in which headache patients should SAH be considered? By definition, these patients under consideration are awake, alert, and have normal physical examinations. These patients may lack meningismus. In fact, many patients with SAH present atypically [18–20]. The physician must pay careful attention to four aspects of the patient history to best identify this group of patients (Box 4). Whereas the severity of the headache is often considered “worst ever,” many variations exist. Headaches from SAH may improve spontaneously [21], or after administration of narcotic or nonnarcotic analgesics or prochlorperazine [22].

Pain relief, by itself, should not be used as a criterion to rule out an SAH (or other serious neurologic problems) if the patient’s history is otherwise worrisome. In many cases that have come to litigation there is often a brief progress notation that “the patient’s headache has resolved (or substantially improved)” with ketorolac, prochlorperazine, or various narcotic analgesics. The unwary physician or nurse may be misled in his or her perception of the degree of patient improvement, especially when the initial assessment is that the cause of the headache is benign. Care should be taken to distinguish between full pain relief and simply putting a patient to sleep with narcotics and/or sedatives. The pathophysiologic mechanisms that mediate pain in the head are limited [23,24] and interventions that are used to relieve pain do not distinguish benign from serious causes.

The location of the headache is also not a helpful discriminator of benign versus serious causes [1]. Most patients with SAH describe an abrupt onset

#### **Box 4. Aspects of the history and physical examination that help identify SAH**

Onset of the headache—is it abrupt?

Severity of the headache—is it worst ever? Is it 10 of 10 in severity?

Quality of the headache—is it distinct and/or unique for the individual patient? How does it compare with prior headaches

Associated symptoms—is there nausea and/or vomiting, syncope, seizure, or diplopia?

Are there any physical examination abnormalities?

What is the alternative hypothesis?

of pain, though this is not universal. Onset of pain often occurs during exercise or during a valsalva maneuver, but it may begin at any time, not uncommonly during quiet activity or even sleep [25]. Perhaps the most useful historical element is the quality of the pain. Even when patients have frequent headaches of other cause, they describe the pain from SAH as unique. If asked, they will clearly say that this headache is somehow “different” from the others. Last, careful consideration of associated symptoms may provide additional clues. Whereas nausea or vomiting may occur in primary headache disorders, they should, at a minimum, suggest the possibility of intracranial bleeding, especially if vomiting has not occurred with prior headaches. Other associated symptoms, such as syncope, diplopia, and seizure, make SAH far more likely [26].

Information collected by other caregivers often contains important clues about a case. The description of the headache in the prehospital, triage, or nursing note sometimes contradicts what is recorded in the physician’s documentation. These discrepancies are not uncommon, are frequently trivial, and there are often good reasons for their occurrence. When these discrepancies do occur, however, the physician should explicitly document the discrepancy, and what is believed to be the best information and its source. In the medicolegal setting, such discrepancies can be quite damaging. In the medical setting, sorting them out may lead to clinically useful information, which may steer a work-up in another direction.

Other epidemiologic risk factors should be sought. Alcohol (especially a recent binge), cigarette smoking, and hypertension are risk factors for SAH. Past or family history of SAH are other strong risk factors. A variety of other connective tissue disorders have been associated with SAH as well [1].

The physical examination must include a diligent search for the cause of the patient’s symptoms. Fever or an extremely high blood pressure may be clues to the correct diagnosis (SAH and others). For headache, not only is a careful head, ears, eyes, nose and throat (HEENT) examination important, but in individuals older than 60, the temporal arteries should be examined for evidence of temporal arteritis. The eyes may show signs of narrow angle closure glaucoma. The sinus examination may show evidence of sinusitis, although physicians should be cautious of making this diagnosis (or any other benign one) if the history of the headache or the physical examination otherwise suggests intracranial pathology.

In patients with SAH, physical examination may disclose nuchal rigidity, cranial neuropathy, retinal or vitreous bleeding, or any other focal or generalized neurologic finding. Nuchal rigidity occurs in approximately 70% of cases. The third cranial nerve contains fibers innervating four of the six extraocular muscles and the pupillary constrictor fibers. Therefore, eye movement is limited and the eye is frequently described as “down and out” in patients with a third nerve palsy. In general, roughly 40% of third nerve palsies are caused by microvascular infarct, in which cases, the pupil is spared because the fibers that innervate the muscles are central within the

nerve, which is the portion most affected by ischemia. In the classic aneurysmal third nerve palsy (also referred to as a “surgical third nerve”), the pupil is dilated. This is because the pupillary constrictor fibers’ peripheral location in the nerve makes them more susceptible to external compression. Third nerve palsy only occurs in 10% to 15% of cases of SAH, however [27,28]. Unruptured aneurysms can also cause a third nerve palsy or they can present with headache, seizure, or symptoms of ischemia. Fundoscopy is helpful to look for retinal hemorrhage (which may be the only sign of SAH in comatose patients) and papilledema (which may suggest benign intracranial hypertension or tumor).

In patients with abnormal examinations, the decision to proceed with further evaluation is clear-cut. Physical examination may be entirely normal, however, and it is in this scenario that the diagnosis is sometimes missed. Of ED patients with acute severe headache and normal neurologic examination, roughly 12%, or one in eight, have SAH [10,11]. After the history and physical examination, the physician must decide if further evaluation is necessary. If there is no plausible alternative hypothesis, the physician and patient are well served to proceed with further testing. A first severe headache cannot be confidently diagnosed as tension or migraine, both of which diagnoses require multiple episodes before they can be definitively established [29]. Whereas all patients with these primary headache disorders must have their first episode at some point in time, they usually do not show up in the ED for them. Even if they do, physicians cannot definitively make these diagnoses on the first episode by history and physical examination alone.

Several specific misdiagnoses merit mention. Occasionally, the neck symptoms overshadow the head symptoms. Severe neck pain and stiffness is a well-described variant that leads clinicians to diagnose cervical strain or arthritis [12,13,15,30]. Patients with low-grade fever, neck stiffness, or back pain may be incorrectly diagnosed with viral meningitis or viral syndrome [12–15]. Those with prominent nausea and vomiting may be labeled as having gastroenteritis [12–14]. Because isolated nausea and vomiting can occur in several high-risk diagnoses (eg, acute myocardial infarction), physicians should always question the diagnosis of gastroenteritis in the absence of diarrhea. High blood pressure or abnormalities on electrocardiography may suggest a cardiovascular diagnosis [7,12,13]. Although uncommon [31], some patients are in a confused state, which leads to a psychiatric diagnosis [12–15]. Compulsive focus on the aforementioned historical details usually identifies those patients requiring evaluation. In awake and alert patients, headache or severe posterior neck pain is almost always the chief complaint.

## **Evaluation for SAH**

Once the decision to pursue the diagnosis of SAH is made, the current standard evaluation is straightforward (Fig. 1). The first test is the

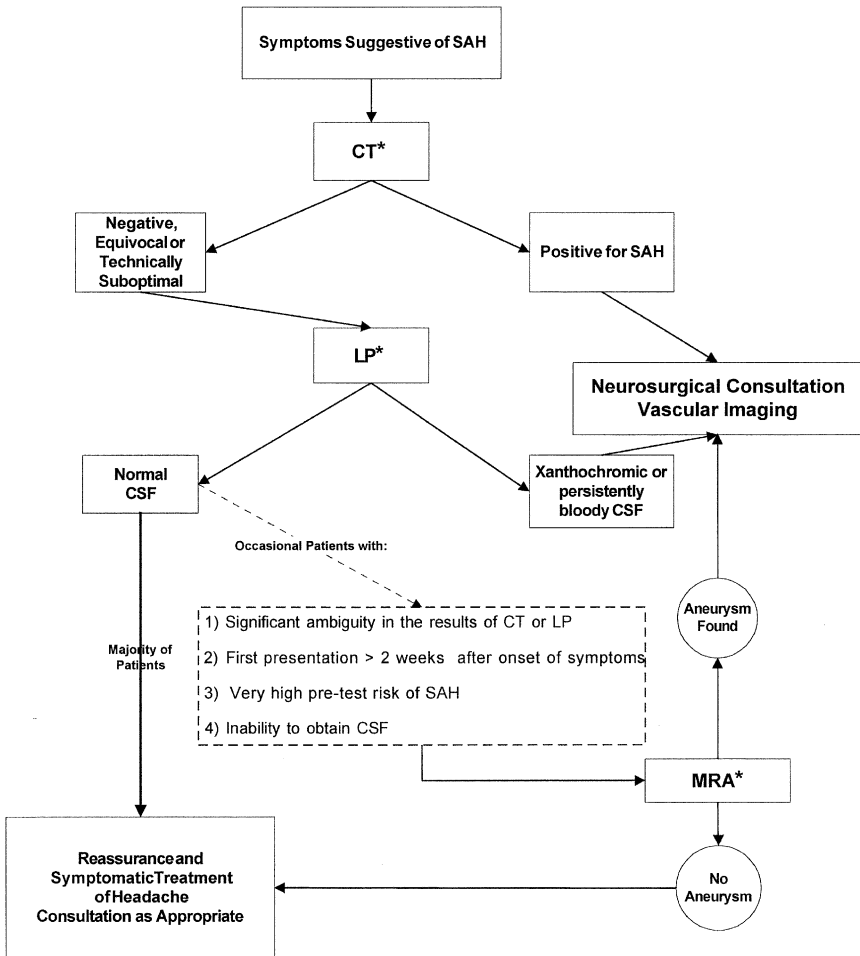


Fig. 1. Diagnostic algorithm for evaluation of patients with possible subarachnoid hemorrhage (SAH). CSF, cerebrospinal fluid; CT, noncontrast computed tomography of the brain; LP, lumbar puncture; MRA, magnetic resonance angiography. \*Each of these diagnostic tests may also show other serious brain disorders, which must be evaluated and treated appropriately.

unenhanced cranial CT. Whereas this test has revolutionized the diagnosis of SAH, it has several limitations that clinicians must understand well (see Box 3). Spectrum bias occurs in patients with smaller bleeds, who are more likely to be conscious and well appearing, and more likely have normal scans [32]. In addition, errors in interpretation inevitably occur, especially in this group of patients with mild symptoms, who may have suffered from small-volume bleeds. The sensitivity of CT decays rapidly with time. Even in the first 12 hours after the ictus, when CT displays excellent sensitivity, the confidence intervals are sufficiently wide that further testing is

recommended, even when the CT is normal in these early-presenting patients [33,34]. By day 3, only 85% of patients with SAH have abnormal CT scans and by 1 week out, this figure drops to 50%. Last, anemic patients and those in whom the scan was suboptimal, because of motion artifact or other technical factors, may have falsely normal scans [1].

In patients with mild symptoms who present early, the factors that influence the CT sensitivity are pulled in opposite directions. Early-presenting patients are much more likely to have positive scans whereas patients with mild symptoms are more likely to have normal scans. The author believes, from the literature and his experience, that in this group of patients (early presentation and mild symptoms), their scans are usually abnormal and the “early presentation” factor trumps the “mild symptoms” factor. The literature, however, does not provide clinicians with a definitive answer on this point. In the absence of such data, routinely performing an LP is the best way to avoid misdiagnosis in patients with normal scans [33–35].

In patients with head injury, subarachnoid blood on the CT scan may be traumatic in origin; however, the possibility that a ruptured aneurysm caused the trauma must be considered [36,37]. Location of the blood on the CT may be a clue to this situation because the blood from traumatic SAH usually appears higher on the cerebral convexities, whereas that from a ruptured aneurysm is more likely to be in the basal cisterns.

False-positive CTs are unusual, but may occur in the setting of intravenous contrast neurotoxicity [38], purulent meningitis [39], and isodense subdural hematoma [40]. In each of these settings, the next diagnostic steps, LP and/or specialist consultation, are the same as for patients with true SAH. Therefore, for patients with positive CT scans, immediate consultation with a neurologist or neurosurgeon is indicated. If meningitis is a serious consideration, intravenous antibiotics should be administered as soon as possible. For patients with negative, equivocal, or suboptimal scans, LP is indicated [1].

Clinicians must also be cognizant of the limitations of LP, the most significant of which is failure to perform one in the first place [1]. Performing the LP also avoids missing the occasional patient with an atypical presentation of meningitis, usually of a nonbacterial cause, and other intracranial pathology. Careful attention to technique may reduce the likelihood of traumatic puncture. Measuring the opening pressure is helpful to distinguish traumatic puncture from true SAH (where two thirds of cases show elevated pressure) and to provide clues to other potential diagnoses, such as benign intracranial hypertension and cerebral venous thrombosis [1]. The cerebrospinal fluid (CSF) may contain erythrocytes and/or show xanthochromia, the yellow discoloration caused by hemoglobin breakdown products—oxyhemoglobin and bilirubin. Again, details are important because the presence of either varies as a function of timing and method of measurement. Red blood cells could be absent in LPs done in the first

minutes after SAH but should be abundant in the ensuing hours. In Walton's classic study [28], all 21 of 21 patients tapped in the first 4 hours after the ictus were positive for blood (including 4 patients inside of 2 hours). Rare case reports from the pre-CT era have documented patients with SAH whose lumbar theca were devoid of blood [41,42] from aneurysmal rupture directly intraparenchymal [43] or into the subdural space, or from tonsillar herniation with CSF block. In each of these rare instances, CT scanning would be expected to be diagnostic. On average, erythrocytes gradually disappear over the course of 7 to 14 days [28,44], although exceptions on either end exist and the disappearance of blood in the CSF has been reported as soon as 24 hours after the ictus [28].

There is no specific threshold of red blood cells in the CSF below which SAH is excluded. Anecdotally, SAH has been reported in a patient with "a couple of hundred" red cells in the CSF [45], but this low number is probably very unusual. Most patients will have many thousands of cells, but the time interval between the LP and the onset of the headache must be factored into this analysis. Oxyhemoglobin can develop within hours whereas bilirubin formation is an enzyme-dependent *in vivo* process that requires time to develop [46,47]. Xanthochromia can be either assessed visually or by spectrophotometry [1]. Some authorities recommend a delay of 12 hours before performing LP, because xanthochromia as measured by spectrophotometry may not be present until this time [48,49]. The study on which this recommendation is based, however, has certain flaws [50]. First, an entry criterion for the study was a positive CT scan. The patients in whom physicians really need to understand the significance of xanthochromia are those with negative CT scans. Thus, it is unknown whether this study's findings apply to the population of patients with negative scans. Second, this study did not perform any LPs prior to 12 hours after the ictus; therefore, it was not designed to evaluate the utility of the early LP.

Last, that study used spectrophotometry to assess for xanthochromia. A recent survey of hospitals in North America found that this method was used in only 1% of hospital laboratories [51]. Another survey of about 2500 hospital laboratories also found that over 99% use visual inspection [52]. It is unnecessary to wait for 12 hours if the clinical laboratory in that hospital uses visual inspection to measure xanthochromia. In addition, many patients do, in fact, have early xanthochromia, even when measured visually. In Walton's [28] series, which used visual inspection, 1 patient had xanthochromia within 4 hours of the ictus, and, of patients seen within 4 to 6 hours, 57% (16 of 28 patients) had xanthochromia [28]. In patients presenting between 6 to 12 hours after the ictus, this figure rose to 65% (26 of 40 patients), which does not include 10 (of the 40) additional patients for whom the presence or absence of xanthochromia was not recorded. Thus, xanthochromia can occur very early, probably from oxyhemoglobin. Blood was present in all of these early-presenting cases. For these reasons, and

because of the possibility of ultra-early rebleeding, other authors do not recommend delaying the LP by 12 hours [1,53].

### **Other diagnostic issues**

Some authors have advocated an LP-first strategy in carefully selected patients with acute-onset severe headache who have normal physical examinations, including vital signs and no stiff neck, arguing that this would speed ED throughput, decrease total resource utilization, and force physicians to do the LP [54], which otherwise is frequently omitted in practice [11]. Most of the studies addressing this issue were done some 20 years ago, in an era when there was less access to CT scanning. Although CT first is clearly the standard of practice, the data on LP-first strategy are worth reviewing.

Some investigators have found performing LP first to be safe, even in grade 2 and 3 patients, who have meningismus and may be drowsy [55,56]. These investigators observed that another reason to perform LP is to not miss bacterial meningitis. Others contend that this practice is unsafe, because collecting CSF in those patients who have a ruptured aneurysm may precipitate rebleeding or herniation from an unrecognized intracranial hematoma [57,58], which can occur in the absence of localizing neurologic findings [55,58]. Most of the patients who deteriorated in these latter two studies had neck stiffness and were Hunt and Hess grades 1 to 3 (primarily grade 2). One patient was documented to have no neck stiffness [58].

The justification for an LP-first strategy comes from mathematical modeling, not from clinical trials. At present, whereas this practice may well be safe in very carefully selected patients, there are insufficient data to recommend a routine LP-first strategy in these patients. If a physician were to use this strategy, he or she would be well advised to compulsively select patients who fit the entry criteria, perform a very careful neurologic examination, clearly spell out his or her decision making in the chart and to the patient, and measure the opening pressure when performing the LP. Last, he or she should understand and address the issues mentioned previously regarding how xanthochromia is being assessed at their hospital lab.

Neurologic or neurosurgical consultation and vascular imaging (magnetic resonance angiography [MRA], CT, or conventional cerebral angiography) are the final diagnostic steps. All patients with positive CT scans and persistently bloody or xanthochromic CSF should undergo vascular imaging [1]. In addition, vascular imaging should be performed in patients whose other tests are ambiguous (eg, early-presenting patients with bloody CSF but no xanthochromia and patients who present more than 2 weeks beyond the original ictus whose CSF findings may have normalized) [1]. In addition, clinicians should consider vascular imaging in patients with

an extremely high likelihood of SAH and those in whom CSF cannot be obtained (see Fig. 1). Whereas MRA and CT angiography are continually improving, the gold standard remains catheter angiography. One recent report highlighted this by reviewing two cases of false-negative MRAs in patients with symptomatic aneurysms. In both of these cases, experienced neuroradiologists who were aware of the clinical concern for an aneurysm were unable to see aneurysms, despite having technically high-quality studies [59].

Some patients have been reported with symptoms of acute headache caused by an expanding, thrombosed, or dissecting cerebral aneurysm [60,61], but without SAH. This situation must be rare because there are four studies that specifically demonstrate good outcomes of patients with severe abrupt-onset headache who have a normal CT and normal CSF. In a retrospective analysis of 71 such patients, observed for an average of 3.3 years, none later developed SAH or died suddenly [62]. In three prospective studies of 117 other patients, this same finding was reproduced [10,63,64]. It is important to distinguish between normal fluid (zero cells and no xanthochromia) from slightly abnormal fluid that is “probably” from a traumatic tap. Methods for distinguishing traumatic tap from true SAH have been recently reviewed [65]. Therefore, in the vast majority of patients presenting with severe, acute headache and with normal CT and LP, reassurance and symptomatic treatment for other causes of headache is a safe practice.

Providing the patient with clear follow-up instructions and trying to organize post-ED care is important. Patients diagnosed with migraine, tension headache, sinusitis, and other such diagnoses should be told to urgently seek follow-up medical attention if they develop new neurologic or ophthalmologic symptoms or fever, or if the headache or other associated symptoms worsen.

## **Summary**

To decide which patients with headache ought to be evaluated for SAH, physicians should focus on specific elements of the patient history, such as onset, severity, and quality of the headache and associated symptoms. These questions should be asked and the responses documented for every patient with a headache. The physical examination should be compulsive with regard to vital signs, HEENT, and neurologic signs. Then, the physician should form an explicit differential diagnosis and have reasons for diagnosing migraine, tension, or sinus headache and other benign causes.

If there is no clear-cut alternative hypothesis, the patient should be evaluated by CT and LP (if the CT is negative, equivocal, or technically inadequate). Physicians should understand the limitations of this diagnostic algorithm. In addition, the CSF should be carefully analyzed, including

measuring the opening pressure. In patients whose CT scans and CSF analyses are normal, further testing is rarely indicated.

## References

- [1] Edlow JA, Caplan LR. Avoiding pitfalls in the diagnosis of subarachnoid hemorrhage. *N Engl J Med* 2000;342:29–36.
- [2] Evans R. Diagnostic testing for the evaluation of headaches. *Neurol Clin* 1996;14:1–26.
- [3] Ramirez-Lassepas M, Espinosa CE, Cicero JJ, et al. Predictors of intracranial pathologic findings in patients who seek emergency care because of headache. *Arch Neurol* 1997; 54:1506–9.
- [4] Frishberg BM. The utility of neuroimaging in the evaluation of headache in patients with normal neurologic examinations. *Neurology* 1994;44:1191–7.
- [5] Schievink WI. Intracranial aneurysms [published erratum appears in *N Engl J Med* 1997;336:1267]. *N Engl J Med* 1997;336:28–40.
- [6] Linn FH, Rinkel GJ, Algra A, van Gijn J. Incidence of subarachnoid hemorrhage: role of region, year, and rate of computed tomography: a meta-analysis. *Stroke* 1996;27: 625–9.
- [7] Mayberg MR, Batjer HH, Dacey R, et al. Guidelines for the management of aneurysmal subarachnoid hemorrhage. *Stroke* 1994;25:2315–28.
- [8] Dhopes V, Anwar R, Herring C. A retrospective assessment of emergency department patients with complaints of headache. *Headache* 1979;19:37–42.
- [9] Leicht M. Non-traumatic headache in the emergency department. *Ann Emerg Med* 1980; 9:404–9.
- [10] Linn FH, Wijdicks EF, van der Graaf Y, et al. Prospective study of sentinel headache in aneurysmal subarachnoid haemorrhage. *Lancet* 1994;344:590–3.
- [11] Morgenstern L, Luna-Gonzales H, Huber J, et al. Worst headache and subarachnoid hemorrhage: prospective computed tomography and spinal fluid analysis. *Ann Emerg Med* 1998;32:297–304.
- [12] Adams HP Jr, Jergenson DD, Kassell NF, Sahs AL. Pitfalls in the recognition of subarachnoid hemorrhage. *JAMA* 1980;244:794–6.
- [13] Kassell N, Kongable G, Torner J, et al. Delay in referral of patients with ruptured aneurysms to neurosurgical attention. *Stroke* 1985;16:587–90.
- [14] Mayer PL, Awad IA, Todor R, et al. Misdiagnosis of symptomatic cerebral aneurysm: prevalence and correlation with outcome at four institutions. *Stroke* 1996;27:1558–63.
- [15] Neil-Dwyer G, Lang D. “Brain attack”—aneurysmal subarachnoid haemorrhage: death due to delayed diagnosis. *J R Coll Physicians Lond* 1997;31:49–52.
- [16] Stewart WF, Lipton RB, Celentano DD, Reed ML. Prevalence of migraine headache in the United States. Relation to age, income, race, and other sociodemographic factors. *JAMA* 1992;267:64–9.
- [17] Karcz A, Holbrook J, Burke M, et al. Massachusetts emergency medicine closed malpractice claims: 1988–1990. *Ann Emerg Med* 1993;22:553–9.
- [18] Hunt WE, Hess RM. Surgical risk as related to time of intervention in the repair of intracranial aneurysms. *J Neurosurg* 1968;28:14–20.
- [19] Rosenorn J, Eskesen V, Schmidt K, et al. Clinical features and outcome in 1076 patients with ruptured intracranial saccular aneurysms: a prospective consecutive study. *Br J Neurosurg* 1987;1:33–46.
- [20] Weir B. Headaches from aneurysms. *Cephalgia* 1993;14:79–87.
- [21] Liedo A, Calandre L, Martinez-Menendez B, et al. Acute headache of recent onset and subarachnoid hemorrhage: a prospective study. *Headache* 1994;34:172–4.
- [22] Seymour JJ, Moscati RM, Jehle D. Response of headache to nonnarcotic analgesics resulting in missed intracranial hemorrhage. *Am J Emerg Med* 1995;13:43–5.

- [23] Limmroth V, Cutrer FM, Moskowitz MA. Neurotransmitters and neuropeptides in headache. *Curr Opin Neurol* 1996;9:206–10.
- [24] Moskowitz MA, Henrikson BM, Markowitz S. Experimental studies on the sensory innervation of the cerebral blood vessels. *Cephalgia* 1986;6:63–6.
- [25] Schievink WI, Karemaker JM, Hageman LM, van der Werf DJM. Circumstances surrounding aneurysmal subarachnoid hemorrhage. *Surg Neurol* 1989;32:266–72.
- [26] Linn F, Rinkel G, Algra A, van Gijn J. Headache characteristics in subarachnoid hemorrhage and benign thunderclap headache. *J Neurol Neurosurg Psychiatry* 1998;65:791–93.
- [27] Sarnier M, Rose F. Clinical presentation of ruptured intracranial aneurysm. *J Neurol Neurosurg Psychiatry* 1967;30:67–70.
- [28] Walton J. Subarachnoid hemorrhage. Edinburgh: E & S Livingstone; 1956.
- [29] Anonymous. Classification and diagnostic criteria for headache disorders, cranial neuralgias and facial pain. *Cephalgia* 1988;8(Suppl):1–73.
- [30] Schattner A. Pain in the neck [letter]. *Lancet* 1996;348:411–2.
- [31] Reijneveld JC, Wermer M, Boonman Z, et al. Acute confusional state as presenting feature in aneurysmal subarachnoid hemorrhage: frequency and characteristics. *J Neurol* 2000;247:112–6.
- [32] Kassell NF, Torner JC, Haley EC Jr, et al. The International Cooperative Study on the Timing of Aneurysm Surgery. Part 1: overall management results. *J Neurosurg* 1990;73:18–36.
- [33] Edlow JA, Wyer PC. Feedback: computed tomography for subarachnoid hemorrhage. Which review should we believe regarding the diagnostic power of computed tomography for ruling out subarachnoid hemorrhage? *Ann Emerg Med* 2001;37:679–80; discussion, 680–5.
- [34] Edlow JA, Wyer PC. How good is a negative cranial computed tomographic scan result in excluding subarachnoid hemorrhage? *Ann Emerg Med* 2000;36:507–16.
- [35] Hoffman JR. Computed tomography for subarachnoid hemorrhage: what should we make of the “evidence”? *Ann Emerg Med* 2001;37:345–9.
- [36] Sakas DE, Dias LS, Beale D. Subarachnoid haemorrhage presenting as head injury. *BMJ* 1995;310:1186–7.
- [37] Vos PE, Zwienenberg M, O’Hannian KL, Muizelaar JP. Subarachnoid haemorrhage following rupture of an ophthalmic artery aneurysm presenting as traumatic brain injury. *Clin Neurol Neurosurg* 2000;102:29–32.
- [38] Sharp S, Stone J, Beach R. Contrast agent neurotoxicity presenting as subarachnoid hemorrhage. *Neurology* 1999;52:1503–5.
- [39] Mendelsohn DB, Moss ML, Chason DP, et al. Acute purulent leptomeningitis mimicking subarachnoid hemorrhage on CT. *J Comput Assist Tomogr* 1994;18:126–8.
- [40] Huang D, Abe T, Ochiai S, et al. False positive appearance of subarachnoid hemorrhage on CT with bilateral subdural hematomas. *Radiat Med* 1999;17:439–42.
- [41] Voris H. Subarachnoid hemorrhage. *Illinois Med J* 1949;95:160–7.
- [42] Wolfe H. Spontaneous subarachnoid hemorrhage. *Br J Surg* 1955;50:319–25.
- [43] Roberston E. Cerebral lesions due to intracranial aneurysms. *Brain* 1949;72:150–85.
- [44] Richardson J, Hyland H. Intracranial aneurysms. *Medicine (Baltimore)* 1941;20:1–83.
- [45] Weir B. Diagnostic aspects of subarachnoid hemorrhage. In: Weir B, editor. *Subarachnoid hemorrhage: causes and cures*. New York: Oxford University Press; 1998. p. 144–76.
- [46] Fishman R. Composition of the cerebrospinal fluid. In: *Cerebrospinal fluid in diseases of the central nervous system*. Philadelphia: WB Saunders; 1992. p. 183–252.
- [47] Roost KT, Pimstone NR, Diamond I, Schmid R. The formation of cerebrospinal fluid xanthochromia after subarachnoid hemorrhage. *Neurology* 1972;22:973–7.
- [48] van Gijn J. Slip-ups in diagnosis of subarachnoid haemorrhage. *Lancet* 1997;349:1492.
- [49] Vermeulen M. Subarachnoid haemorrhage: diagnosis and treatment. *J Neurol* 1996;243:496–501.

- [50] Vermeulen M, Hasan D, Blijenberg BG, et al. Xanthochromia after subarachnoid haemorrhage needs no revisitation. *J Neurol Neurosurg Psychiatry* 1989;52:826–8.
- [51] Judge B. Laboratory analysis of xanthochromia in patients with suspected subarachnoid hemorrhage: a national survey [abstract]. Presented at the Scientific Assembly, American College of Emergency Physicians. Philadelphia, October 23, 2000.
- [52] Edlow JA, Bruner KS, Horowitz GL. Xanthochromia. *Arch Pathol Lab Med* 2002; 126:413–5.
- [53] Gerber CJ, Crawford P, Mendelow AD, et al. Lumbar puncture should not be delayed in subarachnoid haemorrhage [letter]. *BMJ* 1998;317:148.
- [54] Schull M. Lumbar puncture first: an alternative model for the investigation of lone acute sudden headache. *Acad Emerg Med* 1999;6:131–6.
- [55] French JK, Glasgow GL. Lumbar puncture in subarachnoid haemorrhage: yes or no? *N Z Med J* 1985;98:383–4.
- [56] Patel MK, Clarke MA. Lumbar puncture and subarachnoid haemorrhage. *Postgrad Med J* 1986;62:1021–4.
- [57] Duffy GP. Lumbar puncture in spontaneous subarachnoid hemorrhage. *BMJ* 1982; 285:1163–6.
- [58] Hillman J. Should computed tomography scanning replace lumbar puncture in the diagnostic process in suspected subarachnoid hemorrhage? *Surg Neurol* 1986;26:547–50.
- [59] Johnson MR, Good CD, Penny WD, et al. Lesson of the week: playing the odds in clinical decision making: lessons from berry aneurysms undetected by magnetic resonance angiography. *BMJ* 2001;322:1347–9.
- [60] Day JW, Raskin NH. Thunderclap headache: symptom of unruptured cerebral aneurysm. *Lancet* 1986;ii:1247–8.
- [61] Raps EC, Rogers JD, Galetta SL, et al. The clinical spectrum of unruptured intracranial aneurysm. *Arch Neurol* 1993;50:265–8.
- [62] Wijdicks EFM, Kerkhoff H, vanGijn J. Long-term follow-up of 71 patients with thunderclap headache mimicking subarachnoid hemorrhage. *Lancet* 1988;ii:68–9.
- [63] Harling DW, Peatfield RC, van Hille PT, Abbot RJ. Thunderclap headache: is it migraine? *Cephalgia* 1989;9:87–90.
- [64] Markus HS. A prospective follow-up of thunderclap headache mimicking subarachnoid hemorrhage. *J Neurol Neurosurg Psychiatry* 1991;54:1117–25.
- [65] Shah KH, Edlow JA. Distinguishing traumatic lumbar puncture from true subarachnoid hemorrhage. *Journal of Emergency Medicine* 2002;23(1):67–74.