Diagnostic dilemmas and subarachnoid subtleties: What to do when the evidence gives you a headache

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Mann's article[1] in this issue of *CJEM* (see page 102) illustrates some of the problems encountered in the emergency department (ED) assessment of suspected subarachnoid hemorrhage and addresses the role of lumbar puncture (LP) and imaging modalities in rural Canada.

Mann describes two cases. In the first, a 68-year-old woman with minimal clinical findings undergoes LP shortly after the abrupt onset of her worst-ever headache. The LP results are negative, but 3 hours later she deteriorates, requiring emergent intubation and transfer. An intracerebral hematoma is subsequently evacuated and the patient recovers with permanent neurological deficits. In the second case, a 19-year-old woman presents with a vague history of gradual-onset headache and constitutional symptoms. Her exam is normal apart from "slight" meningismus. Despite observation and rehydration, her headache and meningismus persist. An LP is done, and a diagnosis of subarachnoid hemorrhage (SAH) is made based on red blood cells and xanthochromia in her cerebrospinal fluid (CSF). She is transferred, treated appropriately and recovers uneventfully.

As an urban emergency physician, what are most striking about these cases are not the differences, but the similarities between small town and tertiary care practice. Mann's discussion highlights dilemmas facing all practitioners fearful of missing a subtle SAH and helps underscore the paucity of evidence surrounding SAH diagnosis. Indeed, there are several fundamental questions that are answered poorly by current literature.

What is the sensitivity of computed tomography for diagnosing SAH?

Mann suggests that computed tomography (CT) sensitivity peaks at 24 hours; however, most references suggest that sensitivity is highest immediately after the bleed (i.e., less than 12 hours), then falls rapidly as blood in the CSF is broken down.[2,3] To provide a more useful answer to the sensitivity question, several factors should be considered. First, how much blood is in the CSF? Not surprisingly, patients with major neurological findings tend to have larger bleeds than those with headache alone. CT is, therefore, very sensitive in clinically obvious cases and less sensitive in subtle cases — the very ones where we need the most help with diagnosis. Many studies have combined patients with different grades of SAH, and the relatively high sensitivities reported in these studies cannot necessarily be generalized to patients with subtle clinical findings.

The second factor involves the timing of the bleed. Blood is most radio-dense immediately after it enters the CSF. The longer the CT is delayed, the more red blood cells (RBCs) break down and the less likely they are to be seen on CT. The third critical factor is who interprets the CT. Studies suggest that neuroradiologists are more accurate than other radiologists,[2] who, in turn, are likely more accurate than tired emergency physicians, particularly at 3 am.

What is clear is that no adequately-powered prospective study of CT in suspected SAH in the ED has demonstrated 100% sensitivity for SAH, even within 12 hours of headache onset; hence, we cannot rely on CT alone to rule-out SAH. This is especially true in patients with minimal findings or headache alone (who likely have small bleeds), or in patients with delayed presentations (where most RBCs may already be broken down).

What constitutes a positive LP?

In the setting of suspected SAH, 2 CSF parameters — the RBC count and xanthochromia — are used to determine whether the LP is positive. Mann suggests threshold RBC

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counts to guide the interpretation of the LP; however, there are no good studies that have addressed this question and there are no widely accepted thresholds to determine when an LP becomes positive. Further, the dogma that a falling RBC count (from the first to the last tube) rules out SAH is unreliable[2] and there is no agreement on how much the RBC count must drop. If the count is 100/mm^3 in tube 1 and 25/mm^3 in tube 4, this 75% drop might suggest a traumatic tap. But can we draw the same conclusion with a fall from 10 000/mm^3 to 2500/mm^3? Or, is there a threshold above which the RBC count in tube 1 alone is sufficient to consider the LP positive? No one knows. Practically speaking, we still need to interpret our LPs even without good evidence, and Mann is probably correct in suggesting that a RBC count of <10 cells/mm^3 is negative for SAH, so long as there is no xanthochromia.

Most experts consider xanthochromia in the CSF supernatant the most important finding.[2,3] Xanthochromia develops over a period of 4 to 12 hours as RBCs break down into bilirubin and oxyhemoglobin. It is thought that even small amounts of blood, which might not be visible on CT scan, are sufficient to produce xanthochromia. Since spinal fluid is examined immediately after an LP, any CSF xanthochromia must reflect the presence of blood that has been degrading in the CSF over several hours; it cannot be the result of a traumatic tap. The absence of xanthochromia in a delayed tap is therefore reassuring, even in the setting of questionable RBC counts.

What is the optimal timing for an LP?

This question is controversial and poorly studied. The few studies that are available suggest that xanthochromia can take up to 12 hours to develop, hence some authors (including this one) suggest waiting 12 hours after the onset of headache before carrying out an LP, regardless of when the CT is performed. Others[2] argue that this delay may make it harder to identify RBCs in the CSF, and hence might lead to a false-negative results.

What about doing an LP as the first test?

As Mann suggests, the "LP First" approach is an option for some patients and may be particularly appealing in rural areas. However, some caveats apply. This approach should be limited to carefully selected patients with normal vital signs, level of consciousness and neurologic exam, including the absence of neck stiffness. Both cases described by Mann had "slight" meningismus and might not, in my opinion, have been optimal for an LP First approach. The importance of neck stiffness as a predictor of LP sequelae comes from one report documenting 4 patients who suffered complications after LP (in a series of 283 with SAH). All 4 were in Hunt–Hess Scale grades 1 to 3 and had neck stiffness. Although it is unclear from the study, some of these patients may have had neck stiffness as their only physical finding.[4] The second caveat concerns the detection method for CSF xanthochromia. Naked-eye exam is associated with up to 50% false-negative rate, alarmingly high for such a deadly disease. Sadly, most hospitals lack spectrophotometers to assess xanthochromia. In such circumstances, 2 imperfect tests (CT plus naked-eye LP) may be preferable to one.

What's the bottom line?

The best evidence about how and when to use LP in cases of suspected SAH is poor and provides only limited guidance. Existing research plus expert opinion suggest that

- patients with nothing more than a bad headache can have subarachnoid bleeding;
- a CT scan cannot rule out a sentinel bleed, therefore, in cases of suspected SAH, an LP is warranted following a negative CT;
- when interpreting the LP, both the RBC count and xanthochromia are helpful in distinguishing positive, negative and traumatic taps. When LP results are indeterminate, patients need further assessment; and finally,
- the LP First strategy should be limited to carefully selected patients.

Subarachnoid hemorrhages are often subtle. They have humbled many experienced clinicians and crippled their unlucky patients. Physicians should not focus on what constitutes the ideal diagnostic strategy but on which patients need investigation for this silent killer.

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