Yield of Catheter Angiography After Computed Tomography Negative, Lumbar Puncture Positive Subarachnoid Hemorrhage

Adam N. Wallace, MD; Jeffrey N. Dines, BS; Gregory J. Zipfel, MD; Colin P. Derdeyn, MD

Background and Purpose—Patients suspected of having aneurysmal subarachnoid hemorrhage (SAH) are initially evaluated with noncontrast head computed tomography. If the computed tomography is negative, but clinical concern for SAH is high, a lumbar puncture with cerebrospinal fluid analysis is typically performed. The purpose of this study was to evaluate the accuracy of cerebrospinal fluid xanthochromia and erythrocytosis for aneurysmal SAH.

Methods—Medical records of all patients who underwent catheter angiography at Barnes Jewish Hospital between July 2002 and April 2012 for clinical suspicion of a ruptured brain aneurysm after a negative computed tomography scan and a lumbar puncture suspicious for SAH were reviewed. The cerebrospinal fluid analysis results, angiographic findings, and outcomes of each case were recorded.

Results—Fifty-seven patients were identified. Two angiographic lesions were identified in patients with xanthochromia (2/24 patients, ie, 8.3%), both of which were confirmed to have ruptured. The diagnostic yield in patients with nonclearing erythrocytosis and no xanthochromia was 6.3% (1/16 patients), although this lesion was not considered the source of SAH.

Conclusions—Catheter angiography should be performed in patients with computed tomography negative but suspicious lumbar puncture, particularly in the presence of xanthochromia. The benefit of angiography in patients with erythrocytosis only is unclear and deserves future study. (Stroke. 2013;44:1729-1731.)

Key Words: aneurysm • angiography • computed tomography • lumbar puncture • subarachnoid hemorrhage

Computed tomography (CT) is 93% sensitive for subarachnoid hemorrhage (SAH) within the first 24 hours, but falls to 50% after 1 week because of resorption of subarachnoid blood.1 Because catheter angiography is invasive and often identifies incidental aneurysms that may not require treatment, lumbar puncture for cerebrospinal fluid (CSF) analysis is typically performed.2 The purpose of this study was to evaluate the accuracy of CSF xanthochromia and erythrocytosis for aneurysmal SAH.

Methods
Institutional review board approval was obtained to review the medical records retrospectively of all patients who underwent catheter angiography at Barnes Jewish Hospital between July 2002 and April 2012. Catheter angiography is obtained for all patients with suspected aneurysmal SAH at our institution, unless moribund or in need of urgent craniotomy for clot evacuation. Included patients had a negative noncontrast head CT at initial assessment at our institution, but a lumbar puncture suspicious for SAH based on the presence of CSF erythrocytosis or visual xanthochromia. CSF samples were centrifuged at 11,000 rpm for 5 minutes and visually inspected for xanthochromia. Nonclearing erythrocytosis was defined as a cell count that decreased <25% during 3 to 4 serial samples of ≈2 mL each. Dictated reports of catheter angiography were reviewed. The images for patients identified with brain aneurysms were reviewed, as well as their hospital course. We attempted to determine whether the aneurysm was responsible for SAH or an incidental finding based on observation at surgery (if operated) or clinical course. The diagnostic yield was calculated for the entire cohort. Subgroups of patients were defined by CSF analysis results, and the diagnostic yield for each was calculated.

Results
Our cohort included 57 patients. The duration between symptom onset and CT scanning could be retrospectively determined for 46 patients (81%; 46/57 patients). Of these, 35% of patients (20/57) were scanned within 24 hours, 49% (28/57) were scanned within 3 days, and 8.8% of patients (5/57) were scanned >1 week after ictus.

Xanthochromia was visualized in 42% of cases (24/57 patients). Patients with CSF samples that were negative (24/57 patients; 42%) or not inspected for xanthochromia (11/57 patients; 19%) went to catheter angiography based on the presence of CSF erythrocytosis. Table 1 summarizes CSF erythrocytosis results. Serial sampling was performed in 44 patients (77%; 44/57 patients). Nonclearing erythrocytosis was observed in 89% of serial samples (16/18) that were negative for xanthochromia.

Angiography identified 3 lesions (5.3%; 3/57 patients; Table 2; Figure). The diagnostic yield in patients with
xanthochromia was 8.3% (2/24 patients). Considering only the subgroup of patients with positive xanthochromia, where serial samples were obtained and nonclearing erythrocytosis was present, the diagnostic yield was 29% (2/7 patients). One patient had a vertebral artery dissection that progressed to a pseudoaneurysm, prompting vertebral artery coil embolization. The second patient had a 2-mm carotid bifurcation aneurysm that was successfully treated with surgical clipping. Yellow-tinged subarachnoid fluid was noted during surgery consistent with SAH. The interval between symptom onset and clinical evaluation was 5 days for both of these patients. Considering only the subgroup of patients with negative xanthochromia, where serial samples were obtained and nonclearing erythrocytosis was present, the diagnostic yield was 6.3% (1/16 patients). This patient was found to have a 1.5-mm anterior communicating artery aneurysm, which was left untreated and remained stable during a 1-year angiographic and 5.5-year clinical follow-up period.

**Discussion**

Xanthochromia is produced by hemolysis of subarachnoid erythrocytes, which releases oxyhemoglobin that is gradually converted into bilirubin by macrophages and other cells in the leptomeninges.³ Xanthochromia becomes apparent ≈12 hours after SAH and persists for ≥2 weeks.⁴ Aneurysms were identified in 8.3% of patients (2/24) with xanthochromia, both of which were proven to have ruptured. These findings suggest that CSF xanthochromia warrants further evaluation with catheter angiography to exclude a ruptured aneurysm.

Many institutions use nonclearing erythrocytosis in addition to, or instead of, xanthochromia to determine whether further evaluation for a ruptured aneurysm is necessary. Considering only the subgroup of patients with positive xanthochromia, where serial samples were obtained, and nonclearing erythrocytosis was present, the diagnostic yield was 29% (2/7). These findings suggest that patients with xanthochromia and nonclearing erythrocytosis are at greatest risk for having a ruptured aneurysm. Within our subgroup of 16 patients with negative xanthochromia, where serial samples were obtained and nonclearing erythrocytosis was present, 1 aneurysm (6.2%) was identified which was most likely incidental. Thus, the value of angiography in these patients may be limited.

Only one other study has addressed the prevalence of angiographic lesions in patients with negative CT, but positive lumbar puncture for SAH. Horstman et al⁵ reported an overall diagnostic yield of 53% (16/30). The lower yield in our study likely reflects multiple factors. First, 59% of our patients (35/59) were diagnosed with SAH based on the presence of CSF erythrocytosis alone. In contrast, Horstman’s cohort only included patients with CSF xanthochromia. Second, although xanthochromia was identified visually in our study, Horstman et al⁵ identified xanthochromia using spectrophotometry. Spectrophotometry is more specific for SAH because it can differentiate between in vivo blood degradation products and in vitro lysis of erythrocytes following a traumatic tap,³ but is seldom available in the United States. Finally, 93% of Horstman’s cohort (28/30) presented >3 days after ictus compared with 51% of patients (29/57) in our study. Both of our patients with proven aneurysms presented 5 days after the onset of symptoms.

There are several limitations to this study. This study is small and retrospective. Data collection regarding presence of xanthochromia is incomplete. This analysis was limited to imaging and laboratory aspects of presentation. Patients with severe neurological injury and a poor prognosis, or large parenchymal hematomas, and acute neurological decline may not undergo catheter angiography at our institution, thus, introducing selection bias into the data. However, neither of these groups of patients is likely to be CT negative.

**Table 2. Clinical Features and CSF Analysis Results of Patients With Positive Angiograms**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Time to Presentation</th>
<th>Xanthochromia</th>
<th>Serial Sampling Erythrocyte Cell Count</th>
<th>Angiography</th>
<th>Rupture Confirmed?</th>
</tr>
</thead>
<tbody>
<tr>
<td>37/M</td>
<td>5 d</td>
<td>+</td>
<td>First Tube: 1118, Last Tube: 3268</td>
<td>Distal VA dissection</td>
<td>Y</td>
</tr>
<tr>
<td>23/W</td>
<td>&lt;24 h</td>
<td>–</td>
<td>First Tube: 27, Last Tube: 163</td>
<td>1.5-mm Acomm aneurysm</td>
<td>N</td>
</tr>
<tr>
<td>51/W</td>
<td>5 d</td>
<td>+</td>
<td>First Tube: 13378, Last Tube: 13289</td>
<td>2-mm ICA bifurcation aneurysm</td>
<td>Y</td>
</tr>
</tbody>
</table>

Acomm indicates anterior communicating artery; CSF, cerebrospinal fluid; ICA, internal carotid artery; and VA, vertebral artery.
Conclusions

Catheter angiography should be performed in patients with CT negative but suspicious lumbar puncture, particularly in the presence of xanthochromia. The benefit of angiography in patients with erythrocytosis only is unclear and deserves future study.

Disclosures

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References

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An erratum has been published regarding this article. Please see the attached page for:
/content/45/1/e10.full.pdf
The version of the article, “Yield of Catheter Angiography After Computed Tomography Negative, Lumbar Puncture Positive Subarachnoid Hemorrhage” by Wallace et al (Stroke. 2013;44:1729–1731) that published online ahead-of-print on April 25, 2013 contained an error in the title. The correct title is “Yield of Catheter Angiography After Computed Tomography Negative, Lumbar Puncture Positive Subarachnoid Hemorrhage”. This has been corrected in the online version of the article.