Diagnosis of Subarachnoid Hemorrhage (SAH) and Non-Aneurysmal Causes

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Disclosures

I have no disclosures
Course Objectives

- Review significance and differential diagnosis of thunderclap headache
- Review diagnosis of subarachnoid hemorrhage (SAH)
- Review causes of non-aneurysmal subarachnoid hemorrhage (SAH)
Case

65 y/o gentleman presents with the following history:

• 3 months ago he had a sudden onset, thunderclap HA that was associated with a stiff neck
• He never sought immediate medical attention because he was out of town
• The pain persisted and was very localized to the posterior R side of the head
• Later his saw his PCP who prescribed indomethacin
• He had a CT of the head over a month later that didn’t show much
• He is healthy, and has no significant PMHx

What test should I order to work up this thunderclap HA?
Thunderclap Headache

**Definition:**
- sudden severe headache
- “worst headache of my life”
- A headache that reaches maximal intensity very quickly.
  - Research studies have used a “one hour” cut off

**Differential diagnosis:**
- Subarachnoid hemorrhage (SAH)
- Thunderclap headaches NOT associated with SAH
  - Arterial dissection
  - Cerebral venous sinus thrombosis
  - Reversible cerebral vasoconstriction syndrome
  - Retroclival tumor
  - Post coital headache
  - Intracranial hypotension
  - Meningitis
  - Migraine
  - Benign thunderclap headache
- Patients with thunderclap HA and no SAH need further imaging (arterial & venous imaging) even if head CT and CSF studies are normal
What Percentage of Patients Presenting with Thundercalp Headache have SAH?

Study out of the Netherlands was published in 1994

- Lancet 1994; 344(8922): 590-3

148 patients with thunderclap headache

- Subarachnoid hemorrhage: 25%
  - Out of the patients with SAH, 57% of these had a cerebral aneurysm
- Other serious cause of HA, but no SAH: 12%
- Benign: 63%
Symptoms associated with SAH

Patient have sudden severe headache

But they may also have ......
   Brief loss of consciousness (LOC) or decreased LOC
   Meningismus
   Nausea, emesis
   Seizures
   Focal neurological symptoms
What is a Sentinel Bleed

Sentinel bleed refers to leaking of an aneurysm prior to rupture

Approximately 40% of patients with SAH report a sentinel headache prior to the development of SAH

Left untreated, a ruptured aneurysm can rebleed within days to weeks. Ruptured aneurysms are associated with significant morbidity and mortality

Misdiagnosis of SAH is not uncommon and has been shown to be associated with worse outcomes

*JAMA* 2004; 291(7): 866-69: 12% patients were initially misdiagnosed

*Stroke* 1996; 27: 1558-64: 25% patients were initially misdiagnosed
SAH Diagnosis

Once you suspect SAH, the next decision is what tests to order.

The standard of care has been to order head CT and if this test is negative, to then perform a lumbar puncture to look for RBCs and/or xanthochromia in the CSF next.

The timing of the tests is important
Is the Combination of Negative Computed Tomography Result and Negative Lumbar Puncture Result Sufficient to Rule Out Subarachnoid Hemorrhage?

Study published in 2008 in Annals of Emergency Medicine

Review of patients ages 15 and older in an ED

Abrupt onset (maximal intensity within 1 hour) non-traumatic HA, HA started within 14 days of arrival to ED

Patients had to have GCS of 15 and non-focal neurological examination

Outcome measured was SAH defined by one or more of the following:

- SAH on CT report
- + xanthochromia on CSF centrifuged supernatant
- **RBCs in final tube of CSF > 5 x 10^6 RBCs** (basically > 5 RBCs) with aneurysm on angiography
- autopsy confirming SAH

Annals Emer Med 2008; 51(6): 707
Results

- Most common diagnoses were
  - Benign headache
  - Migraine headache
- 10.3% had SAH
- 11.7% had “serious headache”
  - SAH, ICH, ischemic stroke, tumor, bacterial meningitis
- 19.6% were not reachable by phone after the study for follow up
  - 10% lost to follow up
  - 9% had received care in the same system and had no death or aneurysm treatment
  - None of the 19% had been seen in any of the regional neurosurgical centers for aneurysm treatment

Follow up was at least 6 months later after ED visit

Annals Emer Med 2008; 51(6): 707
Conclusion

Patients presenting to the ED with a prevalence of SAH ~ 10% (patients similar to those studied in this research study), if the head CT and lumbar puncture are negative, such patients have a post test probability of SAH of 0.0001%

Because presence of RBCs of $>5 \times 10^6$ in last CSF tube, specificity was lower.

There were many false positives.
Timing of CT Scan & Sensitivity for SAH Diagnosis

Initial test of choice: CT head without contrast should be done on all patients with a new thunderclap headache

- Hallmark sign of SAH is blood within the sulci
- Blood may additionally be seen in the: ventricular system, subdural space, and intraparenchymal space

How does timing of the CT scan affect the sensitivity of CT head?

- Within 24 hours of onset of symptoms: CT is ~ 92% sensitive
- Within 5 days of onset of symptoms: CT is ~ 58% sensitive
- 3 weeks: ~ 0%
Timing of CT scan & Sensitivity for SAH Diagnosis

Prospective study of 3132 patients in Canada presenting to the ED with worst HA of their life was published in BMJ in 2011

Headache intensity peaked within 1 hour of onset, ages 15 and older, GCS 15
Excluded if onset of HA was > 14 days ago
Study used same methods of dx of SAH: + CT head, or abnormal CSF with xanthochromia or > 5 x 10^5 RBCs in final tube
Patient follow up for 6 months

<table>
<thead>
<tr>
<th>Time from headache onset to scan</th>
<th>No of patients</th>
<th>% Sensitivity (95% CI)</th>
<th>% Specificity (95% CI)</th>
<th>Likelihood ratio (95% CI)</th>
<th>Predictive value (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Positive</td>
<td>Negative</td>
</tr>
<tr>
<td>All patients</td>
<td>3132</td>
<td>92.9 (89.0 to 95.5)</td>
<td>100 (99.9 to 100)</td>
<td>Infinity 0.07 (0.05 to 0.11)</td>
<td>100 (98.3 to 100) 99.4 (99.1 to 99.6)</td>
</tr>
<tr>
<td>≤6 hours</td>
<td>953</td>
<td>100 (97.0 to 100.0)</td>
<td>100 (99.5 to 100)</td>
<td>Infinity 0.00 (0.00 to 0.02)</td>
<td>100 (96.9 to 100) 100 (99.5 to 100)</td>
</tr>
<tr>
<td>&gt;6 hours</td>
<td>2179</td>
<td>85.7 (78.3 to 90.9)</td>
<td>100 (99.8 to 100)</td>
<td>Infinity 0.14 (0.14 to 0.17)</td>
<td>100 (96.3 to 100) 99.2 (98.7 to 99.5)</td>
</tr>
</tbody>
</table>
Timing of Lumbar Puncture & Sensitivity for SAH Diagnosis

Historical Article published in J Neurol Neurosurg Psychiatry in 1989
Reviewed records and CSF from 111 patients who had been admitted with SAH. They were all admitted within 3 days of onset

All had SAH on CT head

All patients underwent lumbar puncture
   111 had CSF testing between 12 hours to 7 days after onset
   32 patients had CSF testing after 2 weeks
   22 patients had CSF testing after 3 weeks
   14 had CSF testing after 4 weeks

Xanthochromia was measured by spectrophotometry

J Neurol Neurosurg Psychiatry 1989; 52: 826-8
**What is Xanthochromia?**

Xanthochromia is a finding seen in CSF after SAH. It is caused by lysis of the RBCs in the CSF which leads to oxyhemoglobin and bilirubin.

It takes at least 2 hours to see xanthochromia in the CSF.

There are 2 ways to measure xanthochromia:

- **Naked eye**: place a white sheet of paper behind the CSF tube and look for yellowish discoloration of the CSF. This is not very sensitive.

- **Spectrophotometry**: CSF is centrifuged, and then supernatant is examined with spectrophotometry. + xanthochromia is seen when the peak absorption curve is 450-460nm or when the extinctions exceeding 0.023 at wavelength 415nm.
Timing of Lumbar Puncture & Sensitivity for SAH Diagnosis

Results published in 1989

<table>
<thead>
<tr>
<th>Timing after onset of SAH</th>
<th># of patients where CSF was tested for xanthochromia</th>
<th># of patients positive for xanthochromia</th>
<th>% of patients tested positive for xanthochromia</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 hours to 1 week</td>
<td>111</td>
<td>111</td>
<td>100%</td>
</tr>
<tr>
<td>1 Week to 2 Weeks</td>
<td>32</td>
<td>32</td>
<td>100%</td>
</tr>
<tr>
<td>After 3 Weeks</td>
<td>22</td>
<td>20</td>
<td>91%</td>
</tr>
<tr>
<td>After 4 Weeks</td>
<td>14</td>
<td>10</td>
<td>71%</td>
</tr>
</tbody>
</table>

J Neurol Neurosurg Psychiatry 1989; 52: 826-8
Timing of Lumbar Puncture & Sensitivity for SAH Diagnosis

Conclusions

Xanthochromia is very sensitive for SAH if tested between 12 hours and 2 weeks of onset of symptoms

The sensitivity of xanthochromia diminishes with time, especially after 2 weeks

**If CSF is tested within first 12 hours of symptoms**, previous studies showed that xanthochromia may not have developed yet, and so one could get a false negative

*J Neurol Neurosurg Psychiatry 1989; 52: 826-8*
Is MRI useful in the diagnosis of SAH?

Study published in 2001 compared looking at patients with SAH diagnosed by CT +/- lumbar puncture. Patients underwent MRI and radiologists were blinded to CT findings.

Findings consistent with SAH:
- T1 & FLAIR: high signal seen in the subarachnoid space
- Gradient echo T2*: loss of signal with blooming artifact in the subarachnoid space

Limitations on T2* is near the skull base where there is artifact.

* J Neurol Neurosurg Psychiatry 2001; 70: 205-11
MRI in the diagnosis of SAH

Conclusions of the MRI study:

• < 4 days: T2* and FLAIR images are ~ 94% sensitive

• 4-14 days: T2* and FLAIR are ~ 100% sensitive

Later study published in 2006 also concluded that MRI, especially FLAIR, is very sensitive for SAH in the acute and subacute phase

J Comput Assit Tomogr 2006; 30:295-303

MRI can be useful in patients with suspected SAH and negative head CT who cannot undergo lumbar puncture, but at this point it is not considered a replacement for the CT-LP diagnostic work up

• MRI is helpful in the subacute phase of SAH when sensitivity of CT diminishes

• It is especially helpful in convexity & low grade SAH where to sensitivity of CT is less

• It is not helpful in interhemispheric SAH

J Neurol Neurosurg Psych 2001; 70: 205-11
What about CTA and MRA?

While these studies are very sensitive in looking for aneurysms, if the patient has an aneurysm, they do not tell you whether or not the patient has had subarachnoid hemorrhage.

For patients with thunderclap headache, CTA, MRA/MRV are useful in screening for other causes of thunderclap headache such as arterial dissection and cerebral venous sinus thrombosis.
Etiologies of Non-Traumatic SAH

If you find SAH, what are the causes?
## Etiologies of Non-Traumatic SAH

<table>
<thead>
<tr>
<th>Base of the skull SAH</th>
<th>Cath angio not helpful</th>
<th>Cath angio +/- spine helpful</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ruptured cerebral aneurysm: most common cause</td>
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<tr>
<td>Perimesencephalic non-aneurysmal SAH</td>
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<tr>
<td>Intracranial arterial dissection</td>
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<tr>
<td>Pituitary apoplexy</td>
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<tr>
<td>Cortical SAH at the convexities (&quot;cSAH&quot;)</td>
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<tr>
<td>Mycotic aneurysm</td>
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<tr>
<td>Other vascular malformation: AVM, dural AVF, spinal dural AVF</td>
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</tr>
<tr>
<td>• Up to 10% of spinal dural AVFs can present with SAH</td>
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<tr>
<td>Cerebral venous sinus thrombosis or cortical venous sinus thrombosis</td>
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<tr>
<td>Reversible Cerebral Vasocostriction Syndrome (RCVS)</td>
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<tr>
<td>Posterior Reversible Encephalopathy Syndrome (PRES)</td>
<td></td>
<td></td>
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<tr>
<td>Moyamoya</td>
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<td></td>
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<tr>
<td>Cerebral amyloid angiopathy (CAA)</td>
<td></td>
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</tr>
<tr>
<td>Vasculitis</td>
<td></td>
<td></td>
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<tr>
<td>Cocaine use</td>
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</tbody>
</table>
Perimesencephalic Non-aneurysmal SAH

Definition:

Blood in the subarachnoid space limited to the following regions:
- Prepontine cistern
- Interpeduncular cistern
- Posterior supracellular cistern

Blood should not extend past the proximal Sylvian fissure or into the interhemispheric fissure.

Some blood may settle into the occipital horns of the lateral ventricles, but there should not be frank IVH.
Perimesencephalic Non-aneurysmal SAH

Aneurysm is not identified in the majority of cases of perimesencephalic hemorrhage

Theory of etiology
  • Venous bleeding

Prognosis is good compared to the prognosis associated with ruptured cerebral aneurysm
  • Re-bleeding is rare
  • Vasospasm is rare
Both intracranial carotid and vertebrobasilar dissections can be associated with SAH
- Anterior circulation are more common in children
- Posterior circulation are more common in adults, especially V4 segment of the vertebral artery near PICA take-off

Intracranial dissections can be associated with:
- Headache
- Symptoms of cerebral ischemia
- SAH → occurs when the tear in the arterial wall extends through the adventitia. More rare occurrence
In a case series of patients with intracranial arterial dissections:
  • 35/37 of the patients who presented with SAH had rebleeding with a mean interval of 4.8 days

*Stroke* 2013; 44: 126-131

Anticoagulation is not recommended in patients with intracranial arterial dissection, especially if they present with symptoms of SAH

Endovascular treatments reported:
  - Proximal occlusion/sacrafice of the vessel
  - Wrapping
  - Endovascular coiling
Cerebral Amyloid Angiopathy

Case series of 38 patients with histopathological proven CAA were reviewed. Their T2* MRI images were reviewed for presence of superficial siderosis.

Findings:
- CAA patients: 60.5% had evidence of superficial siderosis on T2* MRI
- Control patients who had h/o ICH but no CAA: none had superficial siderosis

Neurology 2010; 74(17): 1346-50

Focal SAH on CT that can be seen with CAA

Multifocal superficial siderosis from prior SAH that can be seen on MRI
Reversible Cerebral Vasoconstriction Syndrome

Definition:
- Condition associated with reversible constriction of the cerebral arteries
- Patients typically present with thunderclap headache and can also have SAH and ischemic stroke
- Often associated with drugs (antidepressants, pseudoephed, cocaine, amphetamines, triptans) or pregnancy

Imaging findings:
- Vasoconstriction: smooth tapering of vessels with poststenotic dilation, called “sausage on a string”
- SAH, cortical/convexal, similar to what is seen in CAA
- Vasogenic edema
- Ischemic stroke

SAH seen in the R frontal convexity on FLAIR images
Spinal Dural AVFs Presenting as SAH

- In a large case series of spinal aneurysms with or without AVMs, 32.6% had SAH on imaging
  - Most common location of the cerebral SAH was posterior fossa
  - The most common location of the spinal aneurysms was cervical region

- Many patients with spinal aneurysms had presented with headache +/- backache

- Patients who p/w SAH of the posterior fossa and/or fourth ventricle and have negative cerebral catheter angiograms should have spinal angiogram to look for a spinal aneurysm +/- AVM

In Conclusion........
Thunderclap HA

No Evidence of SAH
- MRI brain w/ w/o CTA or MRA H/N MRV
- Imaging is normal: Benign Causes
  - Post coital HA
  - Benign thunderclap HA
  - Migraine
- Structural Pathology associated with non-SAH Thundercalp HA
  - Meningitis
  - CVST
  - RCVS
  - Arterial dissection without SAH
  - Intracranial hypotension
  - Retroclival tumor

Evidence of SAH
- Head CT and if negative lumbar puncture
- Other tests to consider
  - MRI brain with gradient echo/SWI, Urine tox, Spinal angiogram
- Angiogram
- Aneurysmal SAH
- MRI brain with gradient echo/SWI, Urine tox, Spinal angiogram
- Angiogram

Non-aneurysmal SAH
- Perimesencephalic
- Intracranial arterial dissection
- Pituitary apoplexy
- Mycotic aneurysm, other vascular malformation: AVM, dural AVF, spinal dural AVF
- Cerebral venous sinus thrombosis or cortical venous sinus thrombosis
- Rversible Cerebral Vasocostriction Syndrome (RCVS)
- Posterior Reversible Encephalopathy Syndrome (PRES)
- Moyamoya
- Cerebral amyloid angiopathy (CAA)
- Vasculitis
- Cocaine use
Diagnosis of SAH

**Onset of SAH**

- **6 hrs**: CT Head most sensitive in 1st 6 hrs, reported at 100% (but small bleeds could be missed), can assess > 5 RBCs in 4th tube of CSF, early for xanthochromia.
- **12 hrs**: CT Head most sensitive, can assess for RBCs in CSF. Xanthochromia is reliable at 12 hrs to 2 weeks after onset.
- **24 hrs**: CT Head is about 92% sensitive within 24 hrs onset, Xanthochromia is up to 100% sensitive 12 hrs to 2 weeks after onset.
- **<4 days**: MR FLAIR and T2* are ~ 94% sensitive.
- **2 weeks**: CT unhelpful for SAH if it is negative. Xanthochromia is up to 100% sensitive 12 hrs to 2 weeks after onset.
- **4 weeks**: CT is unhelpful. Xanthochromia may still be seen at this time, but sensitivity is low. MRI T2* images may be helpful.

**Time**
Back to My Clinic Case

- I ordered a MRI brain with SWAN images

- MRI showed numerous cerebral microbleeds, evidence of prior SAH in the posterior R temporal occipital region and intraparenchymal bleed in the L occipital region

- Diagnosis is probable cerebral amyloid angiopathy
Thank you