A young woman with a splitting headache

Medical Grand Rounds
December 13, 2016
Alby Richard & Dr. Colin Chalk
Neither of the presenters have conflicts of interest to report
Outline

1. Case presentation

2. Clinical evolution
   – Associated imaging findings

3. Teaching interlude

4. Back to the patient
Ms. H.

- 31F, RHD
- Neurology consulted because of a second visit to ED in 2 weeks for HA
Patient profile

- Known for migraines
  - Typically retro-orbital, unilateral, pulsatile pain
  - Sonophobia, osmophobia, photophobia
  - Usually resolves with ibuprofen
  - Frequency ~ 2-3 year
  - FamHx negative for migraines or other significant neurological dx

- Rx
  - Ibuprofen PRN

- SocHx
  - Bank manager, married
  - Habits negative (non-smoker, no drug use)
ED VISIT #1 (2 WEEKS PRIOR)
History of presenting illness – ED visit #1

- Two weeks ago the patient had a new, sudden onset headache that started at the time of orgasm
  - Onset to peak intensity within 30 seconds to 1 minute
  - 10/10 pain

- Did not ‘feel like’ her typical migraines
  - More intense, sharper quality of pain
  - Bilateral localization with pain at the vertex

- Abated only slightly, so went to see her G.P. two days later
HPI cont’d – ED visit #1

• G.P. sent the patient directly to the RVH ED for urgent assessment in order to rule out subarachnoid hemorrhage

• On arrival to ED:
  – Vitals stable, afebrile
  – Main labs including Chem7, CBC normal
  – HA pain down to 5/10 from 10/10 the day preceding
  – Patient still describes that it’s not like her usual migraines, though does have some features in common (light sensitivity, nausea)

• Neuro exam considered non-focal
IMAGING – ED VISIT #1
CT – RVH ED

CT #1: 3 days post thunderclap

CT #2: 12 hrs post
Imaging interpretation

- There is a [stable] small, focal, well-defined hyperdensity over the anterior surface of the right frontal lobe, in keeping with a cortical vein.

- No acute intracranial abnormalities, particularly no evidence of hemorrhage.
HPI cont’d – ED visit #1

- Patient discharged home with diagnosis of orgasmic headache

- Neurology not consulted, no other investigations
  - No neurology follow up established

- CTA not done

- Lumbar puncture not done
ED VISIT #2
HPI – ED visit #2

- 2 weeks later, patient awoke and felt normal in the morning

- Went jogging, then sudden onset severe headache
  - Peak pain reached within 30 seconds
  - Witnessed loss of consciousness, wakes up with vomiting
  - Urgence Santé called, patient brought directly to RVH ED ~10h00

- Seen by ED physician, treated again as migraine
  - Maxeran 10 mg IV x2 → no effect
  - Ibuprofen → no effect

- ~17h30, Neurology consulted
Patient describes ongoing severe headache, between 8/10 and 10/10 throughout the day
  - Unresponsive to migraine treatment
  - Has had recurrent nausea and vomiting

Describes that the pain is constant, bilateral, and holocephalic
  - Associated sonophobia, photophobia
  - No positional component, denies any visual changes
  - Still ‘feels different’ from usual migraines

Labs within normal limits, except...β-HCG elevated 10,494 IU/L
Neurological examination

General:
Appears uncomfortable. Lights dimmed. No meningismus.

VS:
Within normal limits. Afebrile.

MS:
No confusion. Able to provide accurate history. Digit span 5.

CN:
VF full. PERL. Fundi well visualized. No facial asymmetry. EOM N.

Motor:
No drift. Tone normal. Power normal.

Reflexes:
Symmetric 2+ DTR. Plantars downgoing bilaterally.

Sensory:
Normal to LT and temperature.

Gait:
Not assessed.
Interim case summary

• 31y F, known migraineur, second thunderclap headache in 14d period
  – Exam non-focal
  – Not responding to standard migraine treatment

• CT (x2) done 2 weeks ago was considered normal

• Patient is newly pregnant, undetermined GA
  – *No ultrasound done at the time*
DIFFERENTIAL THOUGHTS?
DDx

- SAH
- Reversible cerebral vasospasm (RCVS)
- Venous sinus thrombosis
- Carotid or vertebral artery dissection
- Pituitary apoplexy
- ...Migraine?
WHAT WOULD YOU DO?
HPI cont’d – ED visit #2

• MRI/MRA with MRV requested to r/o SAH and VST
  – Radiology paged x2 with no answer

• Patient treated for migraine
  – Solumedrol, Maxeran, NSAIDs

• Observation overnight

• LP deferred while waiting for imaging
HPI cont’d – ED visit #2

- Patient spent the night in the waiting room

- Assessed by Neurology consult team the following morning:
  - Headache improved to 4/10 with migraine treatment
  - Nausea subsided with Maxeran
  - Headache continued to improve throughout the day

- Examination unchanged, except mild nuchal rigidity that is **new**

- Radiology again paged to expedite MRI
  - MR eventually done at 20h30 (nearly 36 hours after arrival to ED)
IMAGING – ED VISIT #2
MRI/MRA
Imaging summary

- There is a focal bulge of the anterior aspect of the left pericallosal artery, measuring 4 x 4 x 5 mm.

- Evidence of subarachnoid blood on SWI sequence

- The findings are consistent with a saccular aneurysm with residual mainly superior scattered subarachnoid hemorrhage

- Suggestion of a developing communicating hydrocephalus
Teaching interlude – subarachnoid hemorrhage

- Presentation
- Diagnosis
- Management
- Complications
Things to know about SAH

- Represents approximately 3% of all strokes in US
  - More likely to affect women
  - More likely to affect African Americans than caucasians

- Incidence increases with age
  - Mean age of onset ~50 years old

- 80% of non-traumatic SAH is due to a ruptured aneurysm
  - Remaining made up of AVMs, vasculitis, or idiopathic

- Associated with high morbidity and mortality
  - Median mortality ~30% in US

Suarez, Continuum, 2015
SAH – Risk factors

• **Modifiable:**
  – Cigarette smoking (#1 preventable)
  – Hypertension
  – Alcohol
  – Sympathomimetic drugs

• **Non-modifiable:**
  – Family History
    • Aneurysm in 1° relatives
  – Genetic risk
    • Polycystic kidney disease
    • Ehlers-Danlos Syndrome
    • Other connective tissue dx

Suarez, Continuum, 2015
Physical exam pearls of SAH

• Retinal or vitreous hemorrhage
  – Terson syndrome

• Meningismus

• Decreased LOC

• Focal neuro signs
  – CN III palsy – PCoA, SCA
  – CN VI palsy – raised ICP
  – bilateral leg weakness – ACA
Diagnosis of SAH

- Typical features on presentation:
  - “Worst headache of my life”, thunderclap onset (peak within 1 minute)
  - Lateralized 30% of the time
  - Nausea, vomiting, photophobia, neck pain, and loss of consciousness

- Atypically:
  - Seizures, acute encephalopathy, subdural hematoma, trauma

- Sentinel headache
  - Often occur days to weeks prior to aneurysmal SAH
  - May represent small leak that self-limits/tamponades
The importance of ‘sentinel’ headaches

- 20-50% of patients with documented SAH report a distinct, unusually severe headache in the days or weeks preceding

- Warning headaches are commonly misdiagnosed as migraine, tension type headache, or sinus-related headache

- The differential for these includes:
  - SAH
  - Acute expansion, dissection, or thrombosis of unruptured aneurysms
  - Cerebral venous sinus thrombosis
  - Orgasmic h/a

Edlow & Caplan, NEJM, 2000
Diagnosis of SAH

• Plain CT is sensitive for subarachnoid blood
  – Within 12 hours: 98%
  – Within 24 hours: 93%
  – 7 days: down to <50% (~10% per day rule)

• MRI is thought to be as sensitive in the acute phase
  – SWI and FLAIR sequences more sensitive than CT at 7 days

• LP: recommended whenever CT is negative or equivocal

• CT angiogram to identify source of bleed
  – Sensitivity 90-97%, specificity 93-100%
Misdiagnosis of SAH

Common sources of error include:

1. Failure to recognize spectrum of clinical presentation

2. Failure to appreciate the limitations of plain CT
   – Sensitivity decreases with increasing time from HA onset
   – False negative results for small volume bleeds

3. Failure to perform lumbar puncture
Common pitfalls regarding LP

• Failure to perform LP with negative, equivocal, or suboptimal results on CT

• Failure to recognize traumatic tap (20% of LPs) from SAH
  – Look for xanthochromia; the “4 tube” method is unreliable

• What is xanthochromia?
  – Yellowish discoloration of CSF produced by breakdown products of erythrocytes (oxyhemoglobin and bilirubin)
  – Spectrophotometry is more sensitive than visual inspection, but visual inspection is more reliably performed
  – Can be absent very early (i.e. <12 hours) or very late (i.e. >2 weeks)

Edlow & Caplan, NEJM, 2000
Management pearls for SAH

• Tight glucose control
  – Some evidence to suggest that this improves outcomes (level 2B)

• Blood pressure control
  – Aim for sBP < 160 mmHg, or MAP < 100 mmHg to reduce the risk of rebleeding (level 1B)

• DVT prophylaxis
  – Yes

• Vasospasm
  – Nimodipine is standard preventative therapy

Suarez et al., NEJM, 2006
COMMON COMPLICATIONS
Hydrocephalus

- Occurs in ~20% of patients with SAH, usually within a few days
  - Look for decreased LOC, impaired up-gaze, hypertension

Suarez et al., NEJM, 2006
Delayed cerebral ischemia

• What is it?
  – Any neurologic deterioration (focal or global) presumed secondary to cerebral ischemia that persists for more than 1 hour
  – Involves cerebral vasospasm, microcirculatory constriction, micro-thrombosis, and delayed cellular apoptosis
  – Occurs in ~30% of SAH patients, usually within 4-14 days from onset
  – Transcranial doppler for diagnosis (mean velocity >120 cm/s)

• How to treat?
  – We give milrinone at the MNI
  – Everywhere else they give nimodipine (21d course, strong evidence [level 1A])

Lannes et al., 2012; Suarez, Continuum, 2015
What about radiation exposure in pregnancy?

• Amount depends on the test:
  – CT plain involves exposure of 1.1-2.5 mSv
  – CTA typically involves 3.57-5.73 mSv
  – Conventional angiography involves ~10.5 mSv
    • Above are whole body doses of radiation, and do not necessarily reflect fetus exposure

• Comparison: NY to Tokyo flight would be ~0.06 mSv, or ~2 CXRs

• No clear consensus, but fetal risk depends largely on gestational age
  – Risk of miscarriage, congenital malformations, and growth retardation are highest with exposure in 1st trimester (8-15 weeks)

Brent, 2006; Robba et al., 2016
Perimesencephalic hemorrhage

- Represents 5-10% of spontaneous SAH
  - In 95% of cases, thought to represent venous bleed (not aneurysm)
  - Rebleed and delayed cerebral ischemia rate very low

- Hemorrhage centered anteriorly to the pons and midbrain, which can extend into basal cisterns

Suarez, Continuum, 2015
BACK TO OUR PATIENT...
Urgent transfer to MNH – Angiogram done
Imaging summary – MNH

- Evidence of a small, multi-lobed aneurysm at the A3 segment of the left ICA

- Aneurysm measuring approximately 5 x 2.3 x 2.5 mm
  - Aside: MRI measurement was 5 x 4 x 4 mm

- There is increased venous angle indicating hydrocephalus, stable post-operatively
Continued course at the MNH

• Patient underwent successful surgical clipping of aneurysm
  – No complications

• Post-operative course complicated by flattened affect, likely attributable to frontal vasospasm
  – Transcranial dopplers showed stable moderate vasospasm of the MCAs bilaterally (L>R)

• Slow recovery, but eventually discharged home 10 days after surgery in stable condition
Post-operative CT
Final thoughts

• We will see these cases – recognition is paramount due to high morbidity and mortality
  – Important to identify since therapeutic options exist

• A large proportion of SAH have unrecognized warning headaches

• Would you have done anything differently in this case?
  – CT right away in this newly pregnant female?
  – LP?
Thank you for your attention!

- Artwork by Ernst Haeckel
Clinical and Radiologic scales for SAH

<table>
<thead>
<tr>
<th>Grade</th>
<th>Score on Glasgow Coma Scale</th>
<th>Clinical Appearance</th>
<th>Clinical Grading Scale</th>
<th>Subarachnoid Hemorrhage</th>
<th>Intraventricular Hemorrhage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>15</td>
<td>No motor deficit</td>
<td>Grade 0</td>
<td>Absent</td>
<td>Absent</td>
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<tr>
<td>2</td>
<td>13–14</td>
<td>No motor deficit</td>
<td>Grade 1</td>
<td>Minimal</td>
<td>Absent in both lateral ventricles</td>
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<td>3</td>
<td>13–14</td>
<td>Motor deficit</td>
<td>Grade 2</td>
<td>Minimal</td>
<td>Present in both lateral ventricles</td>
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<td>4</td>
<td>7–12</td>
<td>With or without motor deficit</td>
<td>Grade 3</td>
<td>Thick</td>
<td>Absent in both lateral ventricles</td>
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<td>5</td>
<td>3–6</td>
<td>With or without motor deficit</td>
<td>Grade 4</td>
<td>Thick</td>
<td>Present in both lateral ventricles</td>
</tr>
</tbody>
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Suarez et al., NEJM, 2006
### TABLE 1-1 Risk Factors for Subarachnoid Hemorrhage

#### Nonmodifiable Risk Factors
- Age
- Female sex
- Prior history of aneurysmal subarachnoid hemorrhage
- Family history of subarachnoid hemorrhage
- History of aneurysm in first-degree relatives (especially in two or more relatives)

#### Modifiable Risk Factors
- Hypertension
- Cigarette smoking
- Heavy alcohol use
- Sympathomimetic drug use (e.g., cocaine)

#### Other
- Certain genetic disorders (e.g., autosomal dominant polycystic kidney disease, type IV Ehlers-Danlos syndrome)
- Anterior circulation aneurysms are more likely to rupture in patients who are younger than 55 years of age
- Posterior circulation aneurysms are more likely to rupture in men
- Significant financial or legal problems within the past 30 days
- Cerebral aneurysms of more than 7 mm in diameter