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

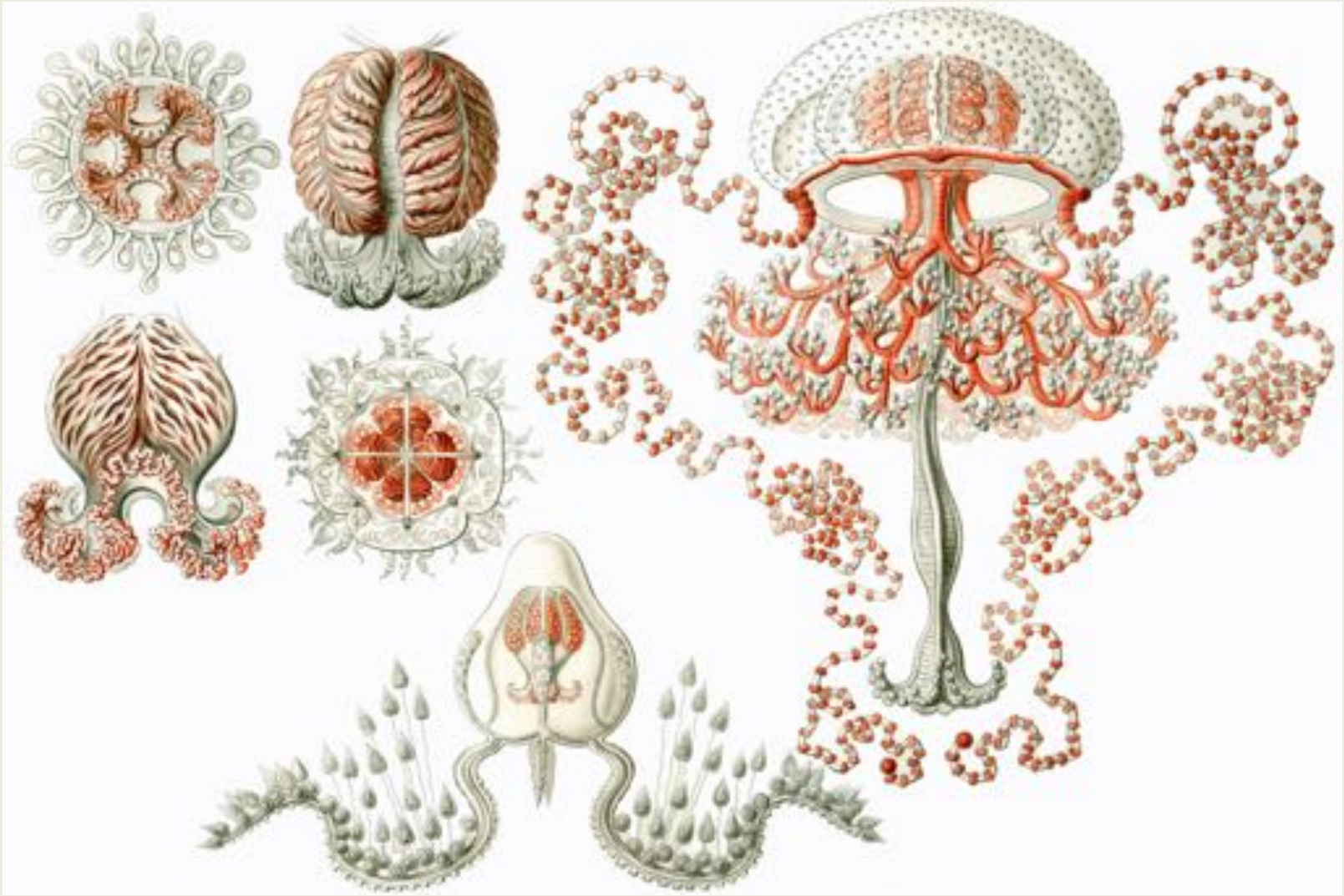
Ms. H.

- 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

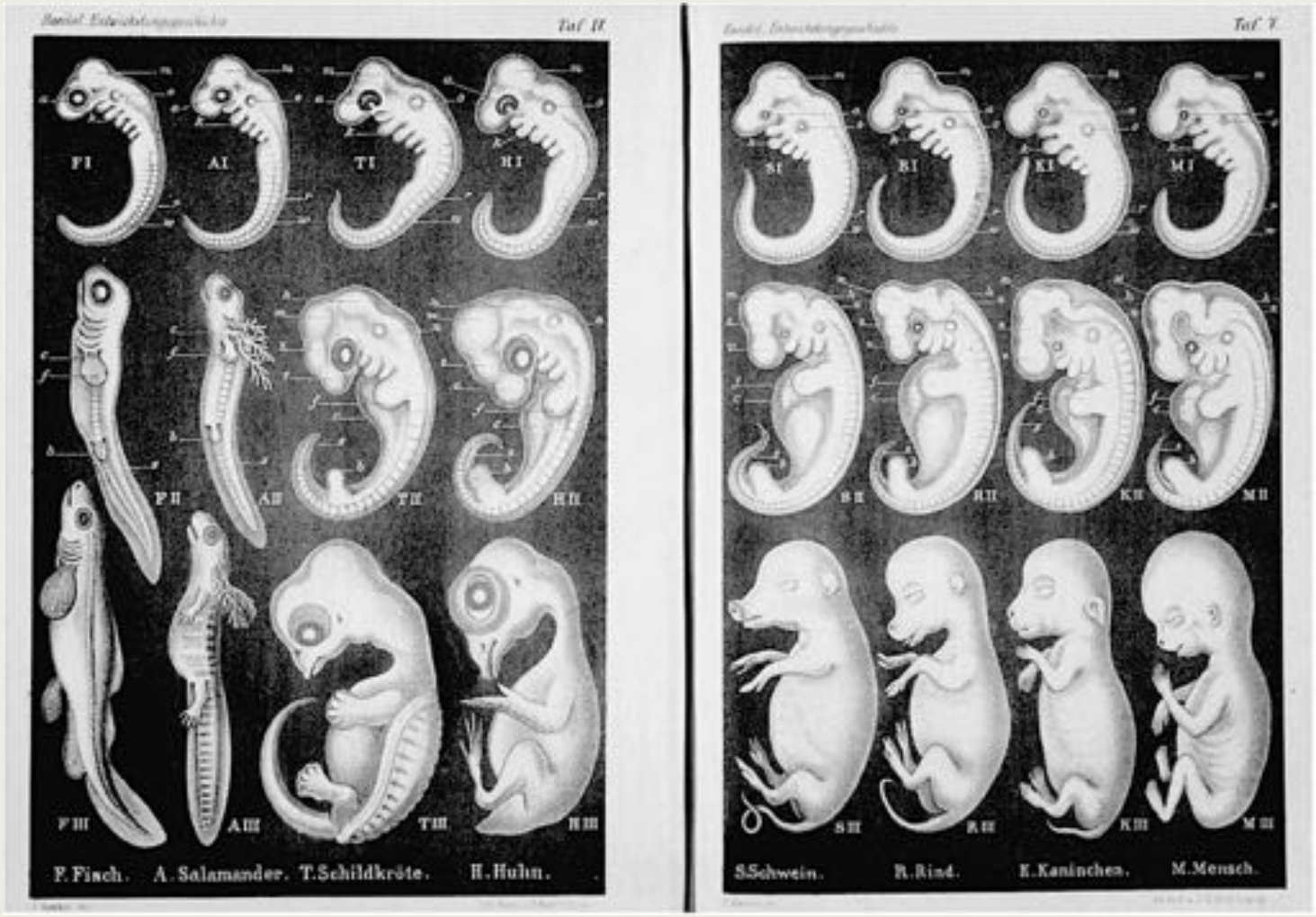
- Abated only slightly, so went to see her G.P. two days later

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)

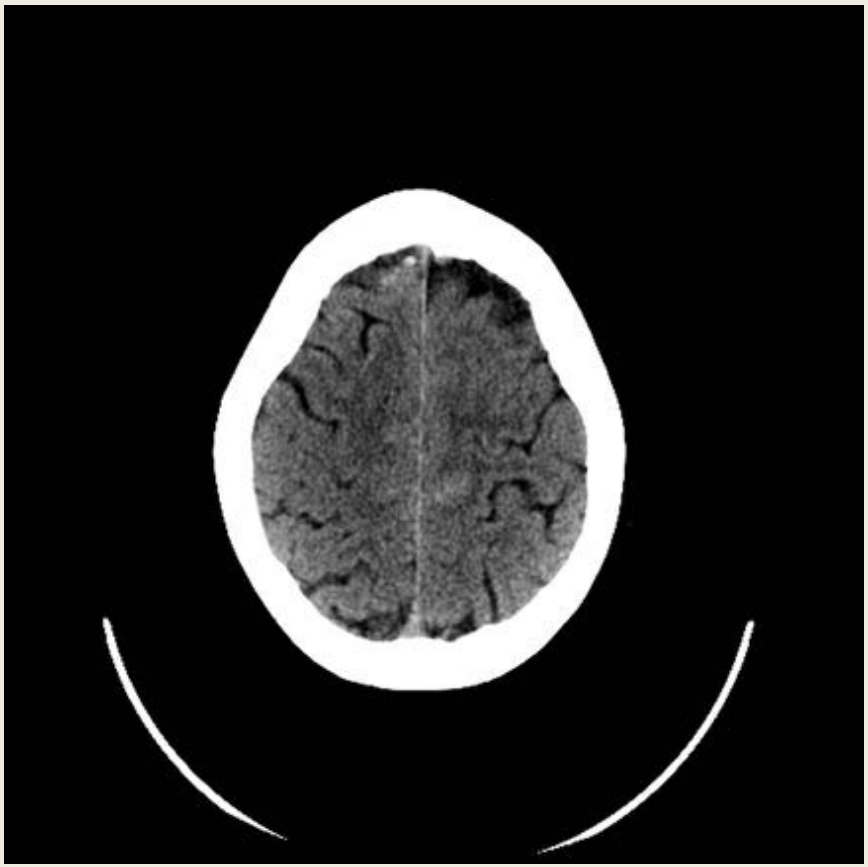
- Neuro exam considered non-focal



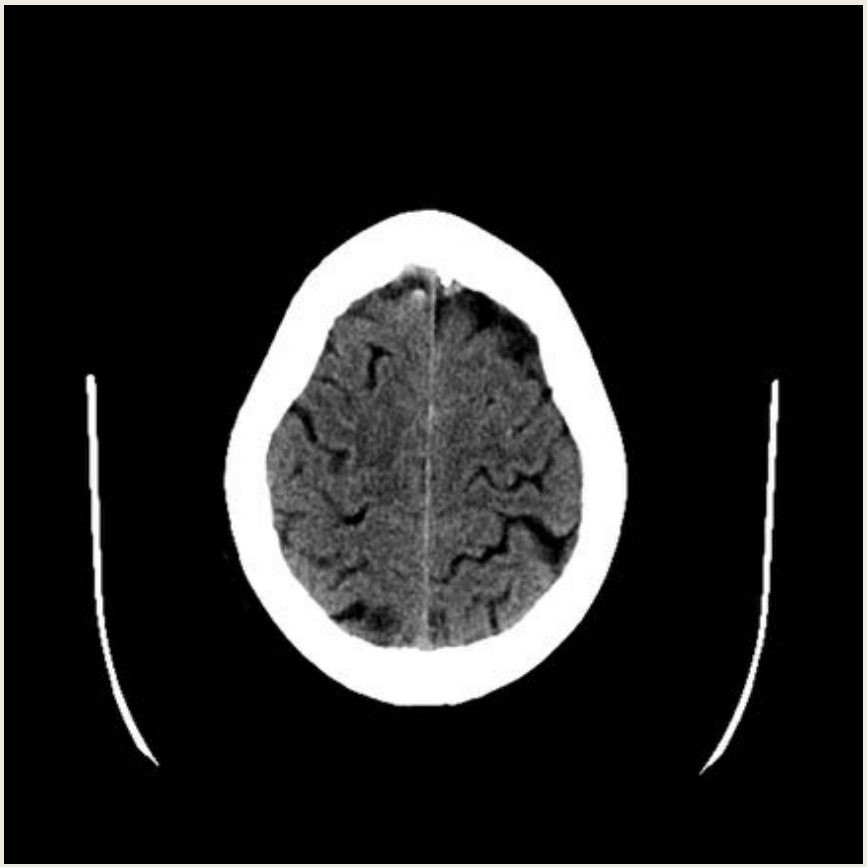
IMAGING – ED VISIT #1

CT – RVH ED

CT #1: 3 days post thunderclap



CT #2: 12 hrs post



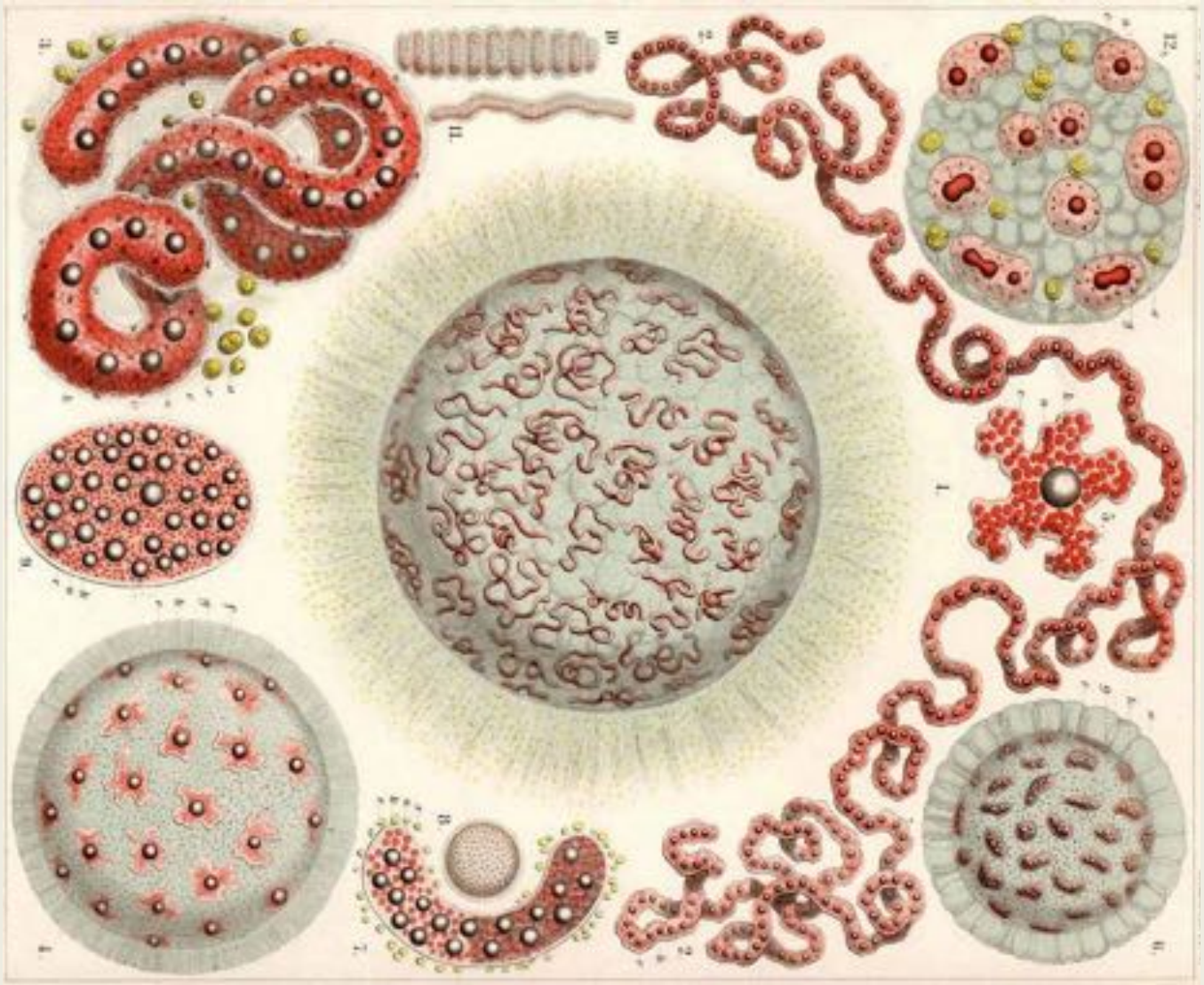
Imaging interpretation

- 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

HPI cont'd – ED visit #2

- 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 <u>10,494 IU/L</u>

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:

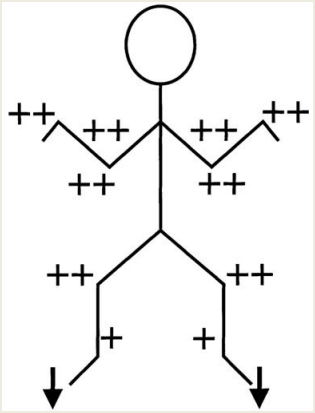
Symmetric 2+ DTR. Plantars downgoing bilaterally.

Sensory:

Normal to LT and temperature.

Gait:

Not assessed.

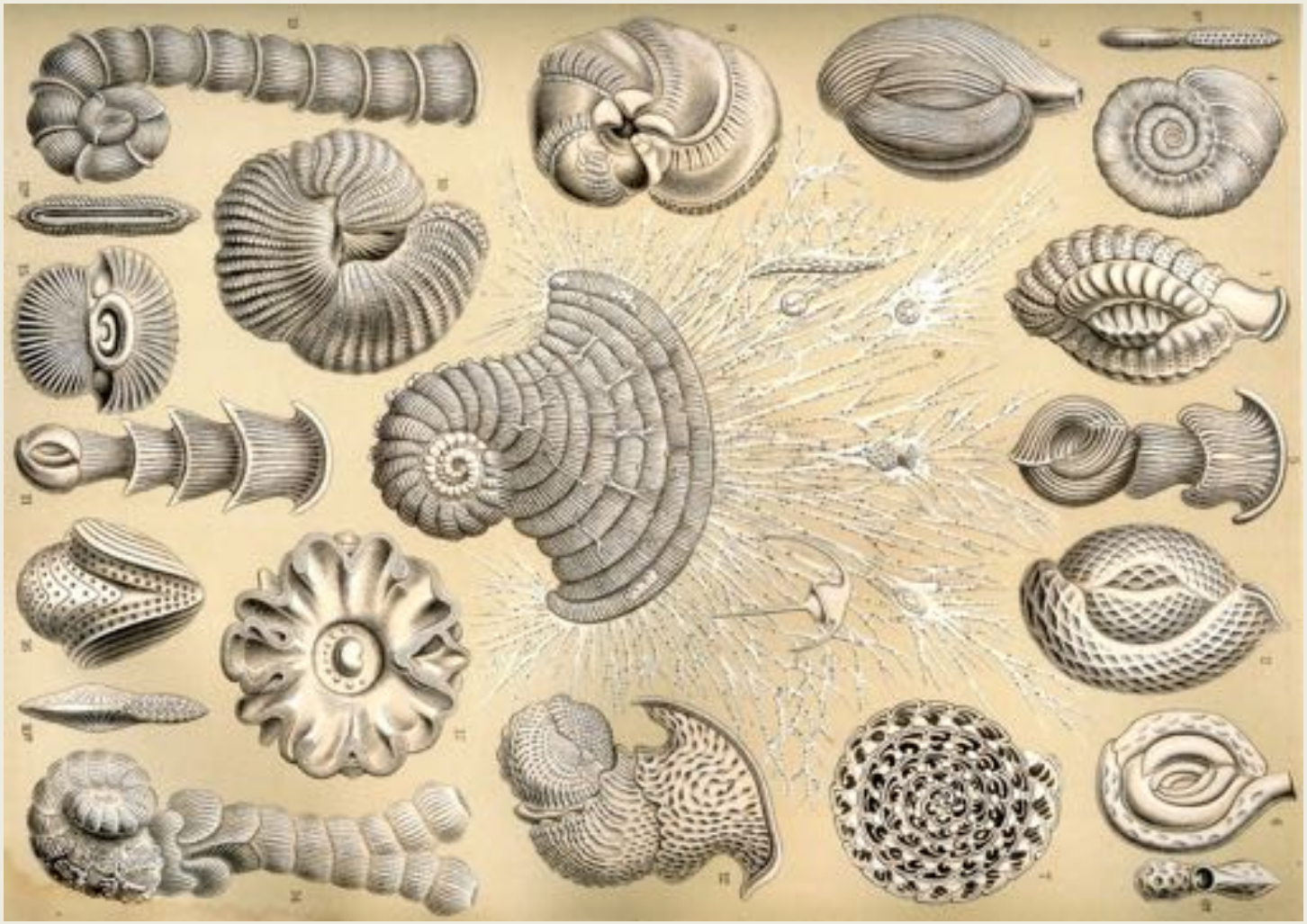


Interim case summary

- 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

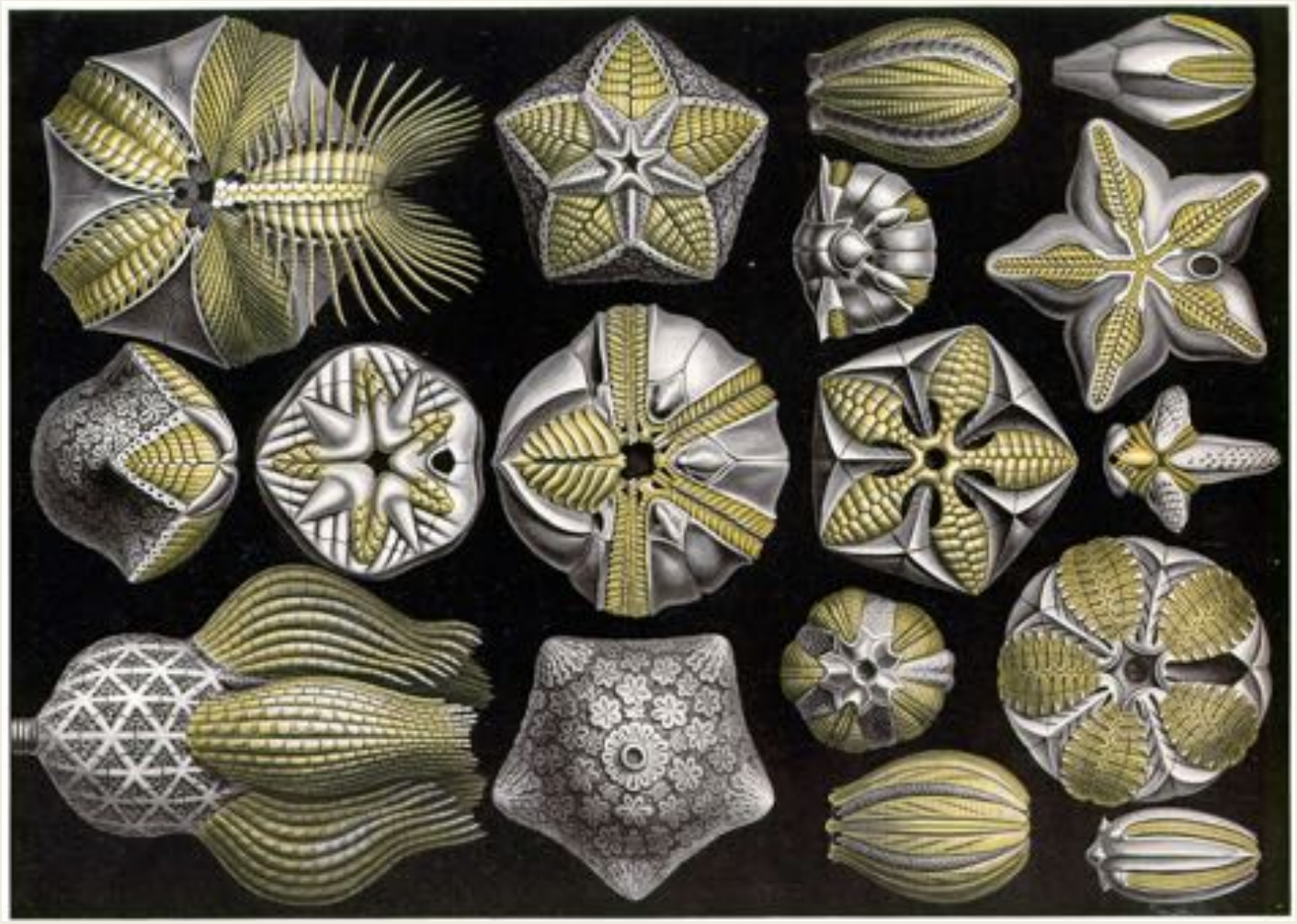
- Patient is newly pregnant, undetermined GA
  - *No ultrasound done at the time*



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

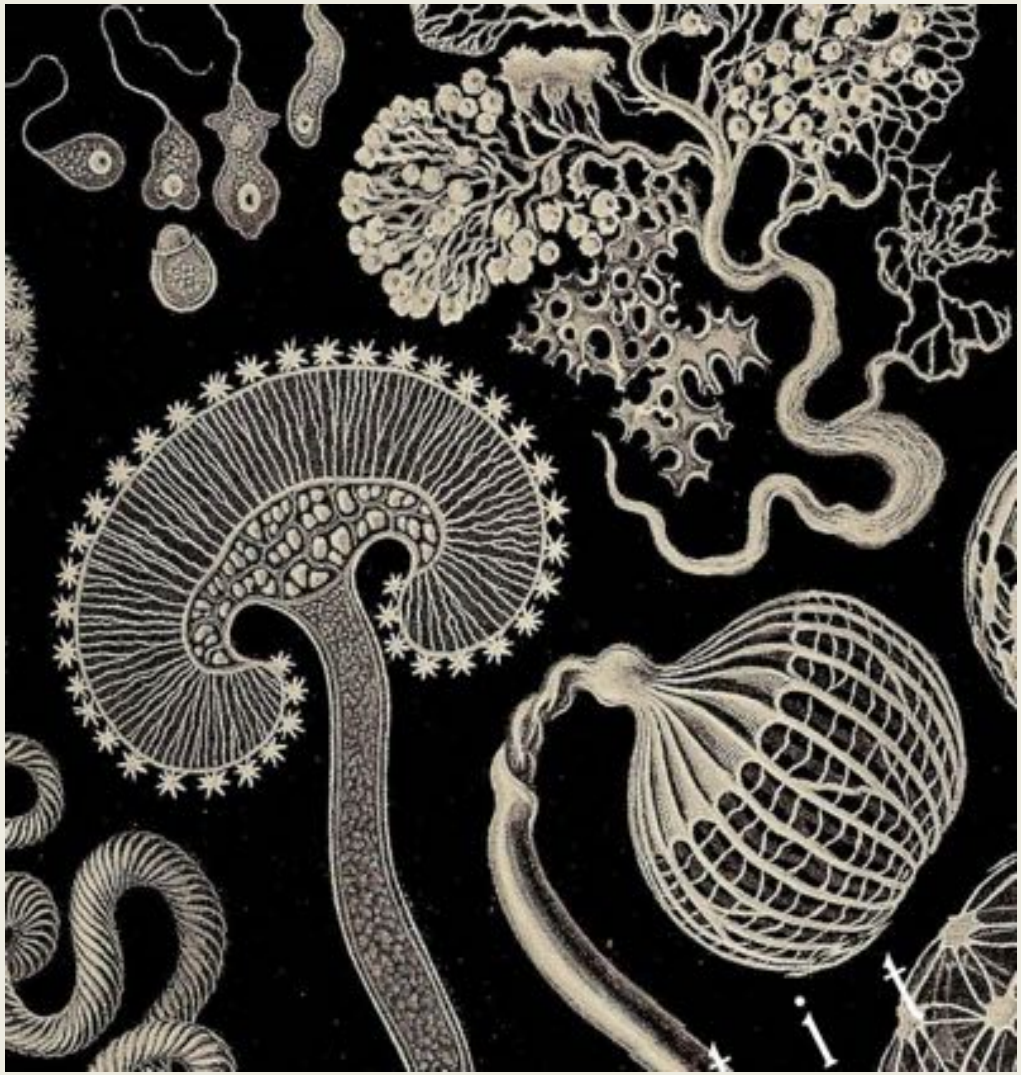
HPI cont'd – ED visit #2

- 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

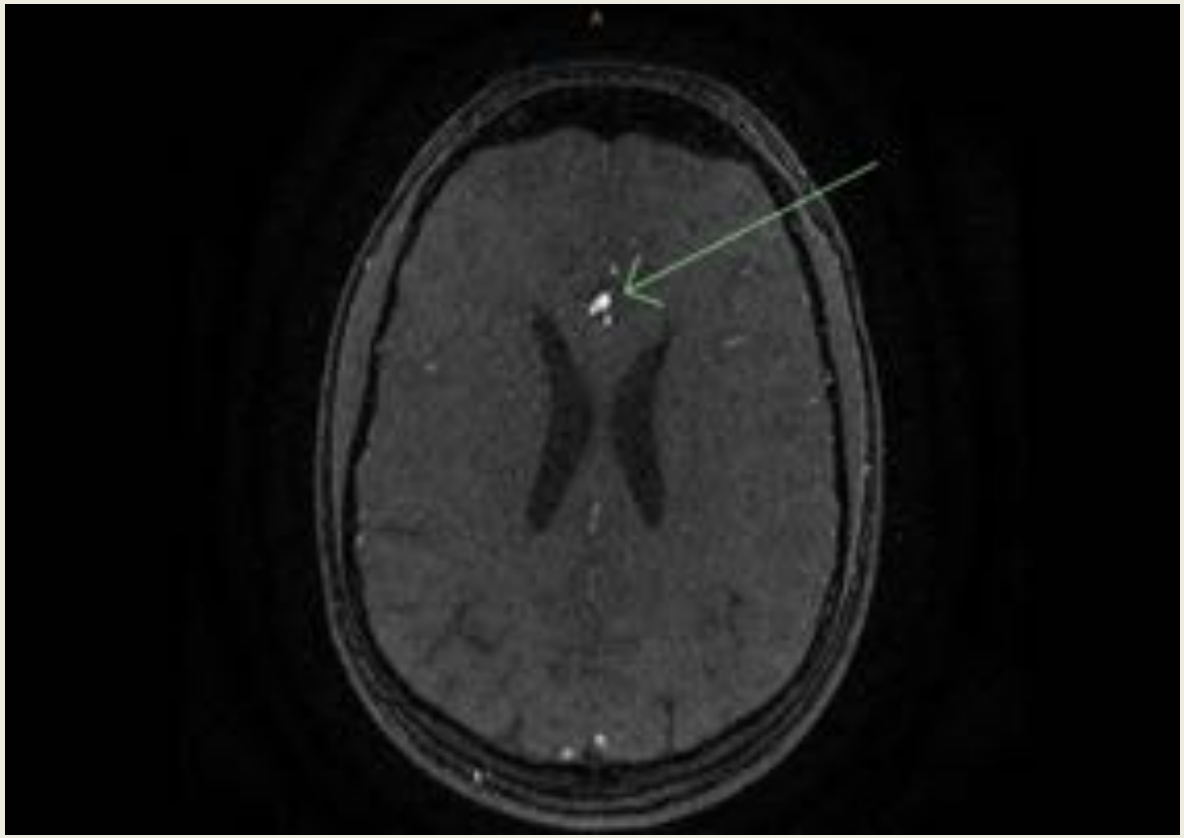
- Examination unchanged, except mild nuchal rigidity that is **new**

- Radiology again paged to expedite MRI
  - MR eventually done at 20h30 (nearly 36 hours after arrival to ED)

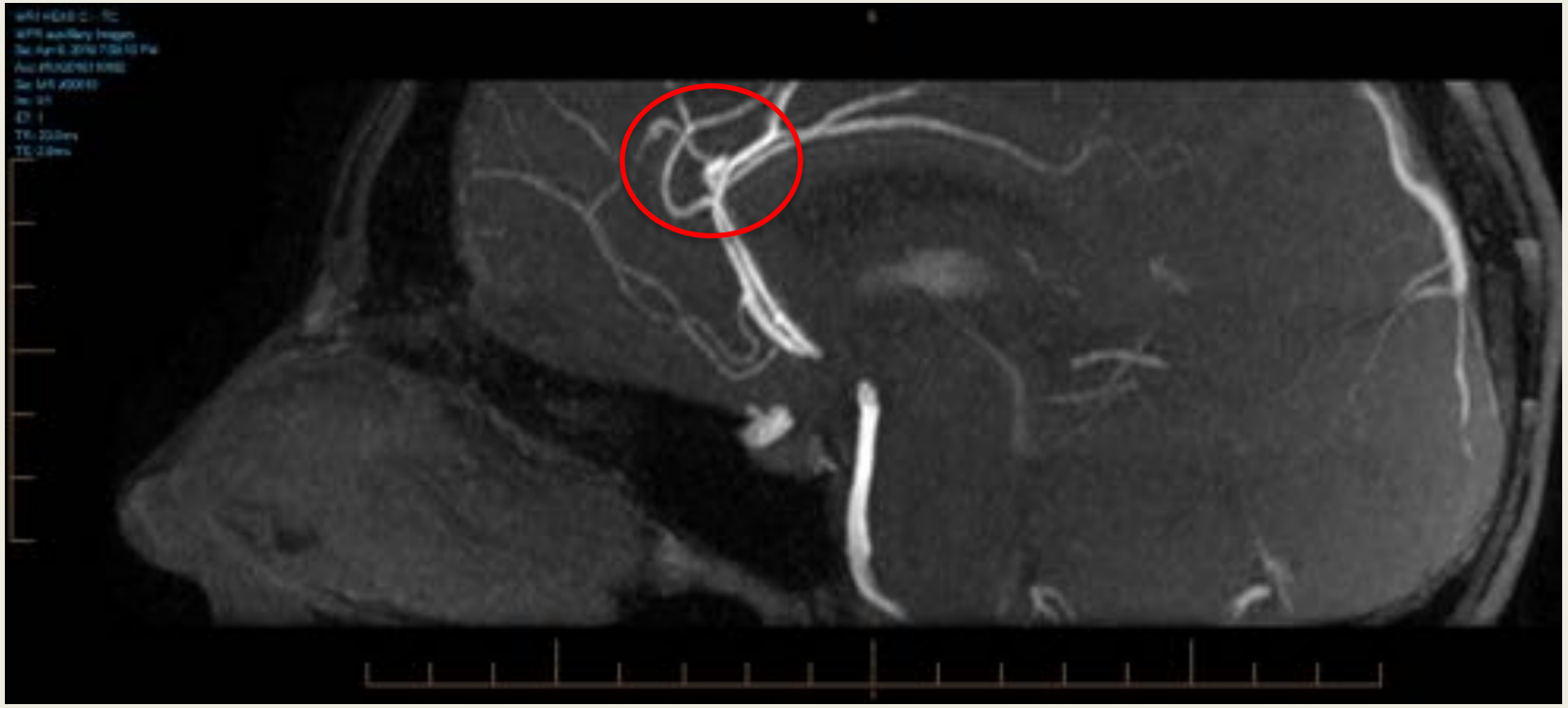


IMAGING – ED VISIT #2

MRI/MRA



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

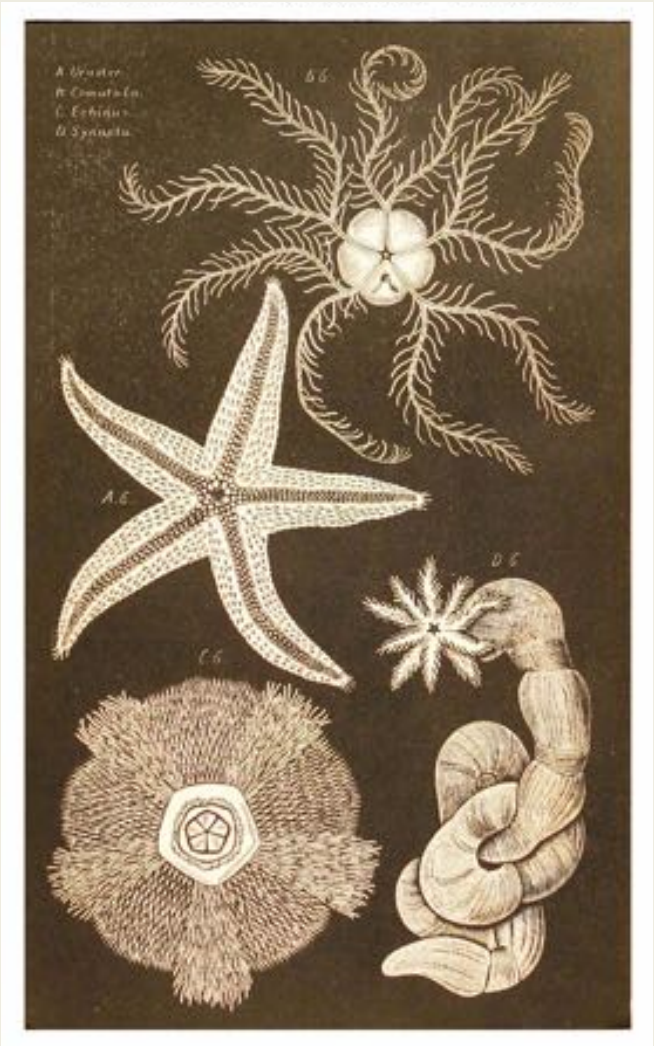
- Represents approximately 3% of all strokes in US
  - More likely to affect women
  - More likely to affect African Americans than caucasians
- Incidence increases with age
  - Mean age of onset ~50 years old
- 80% of non-traumatic SAH is due to a ruptured aneurysm
  - Remaining made up of AVMs, vasculitis, 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

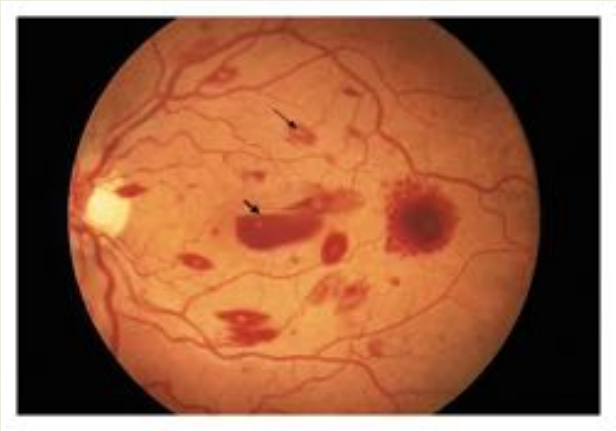
- **Non-modifiable:**
  - Family History
    - Aneurysm in 1◦ relatives
  - Genetic risk
    - Polycystic kidney disease
    - Ehlers-Danlos Syndrome
    - Other connective tissue dx



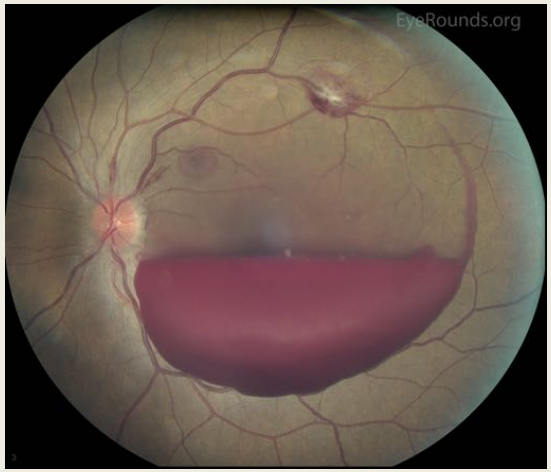
Suarez, Continuum, 2015

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

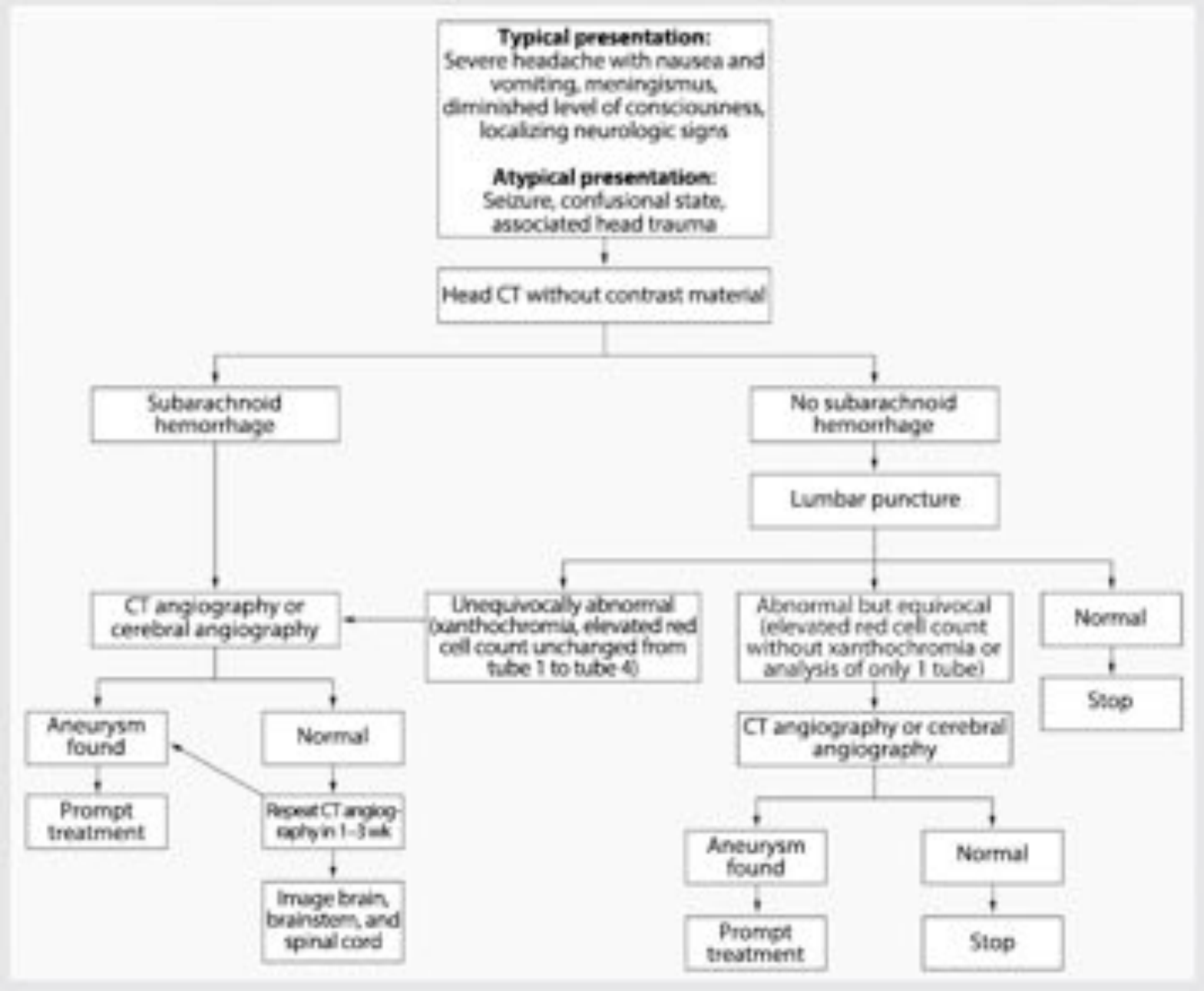
- The differential for these includes:
  - SAH
  - Acute expansion, dissection, or thrombosis of unruptured aneurysms
  - Cerebral venous sinus thrombosis
  - Orgasmic h/a

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%

Suarez, Continuum, 2015



Suarez, Continuum, 2015

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

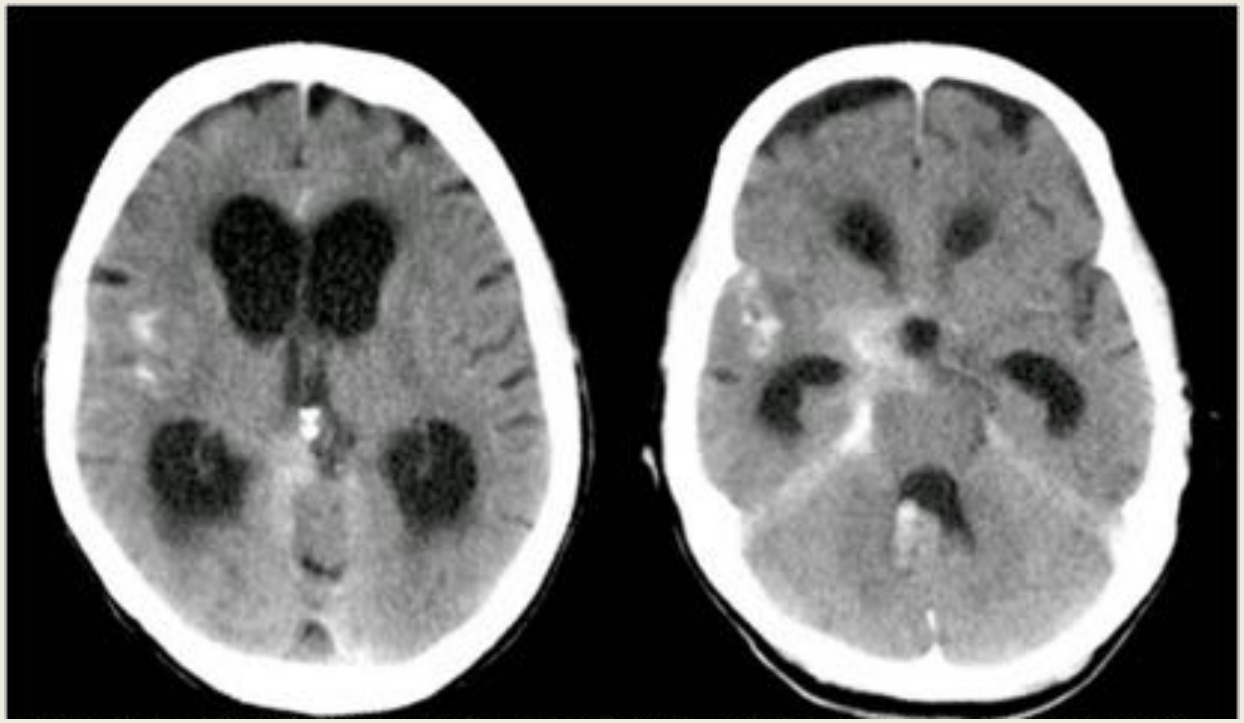
- Tight glucose control
  - Some evidence to suggest that this improves outcomes (level 2B)
- Blood pressure control
  - Aim for sBP < 160 mmHg, or MAP < 100 mmHg to reduce the risk of rebleeding (level 1B)
- DVT prophylaxis
  - Yes
- Vasospasm
  - Nimodipine is standard preventative therapy

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

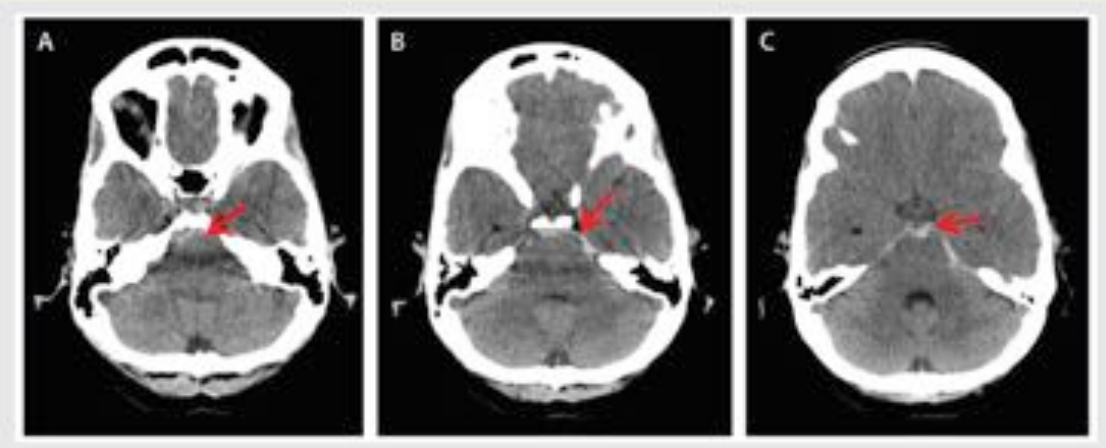
- No clear consensus, but fetal risk depends largely on gestational age
  - Risk of miscarriage, congenital malformations, and growth retardation are highest with exposure in 1st trimester (8-15 weeks)

Brent, 2006; Robba et al., 2016

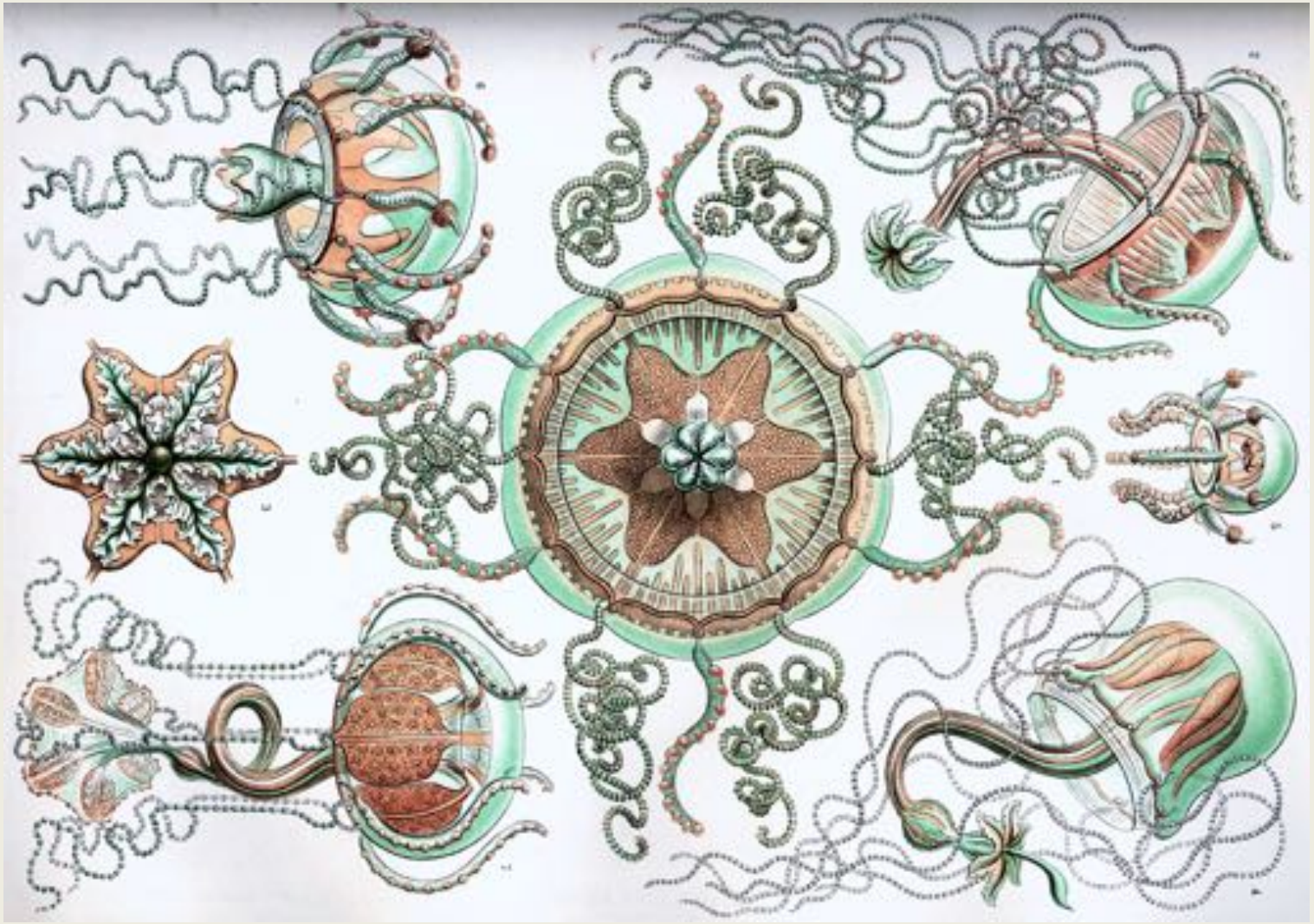
Perimesencephalic hemorrhage

- 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

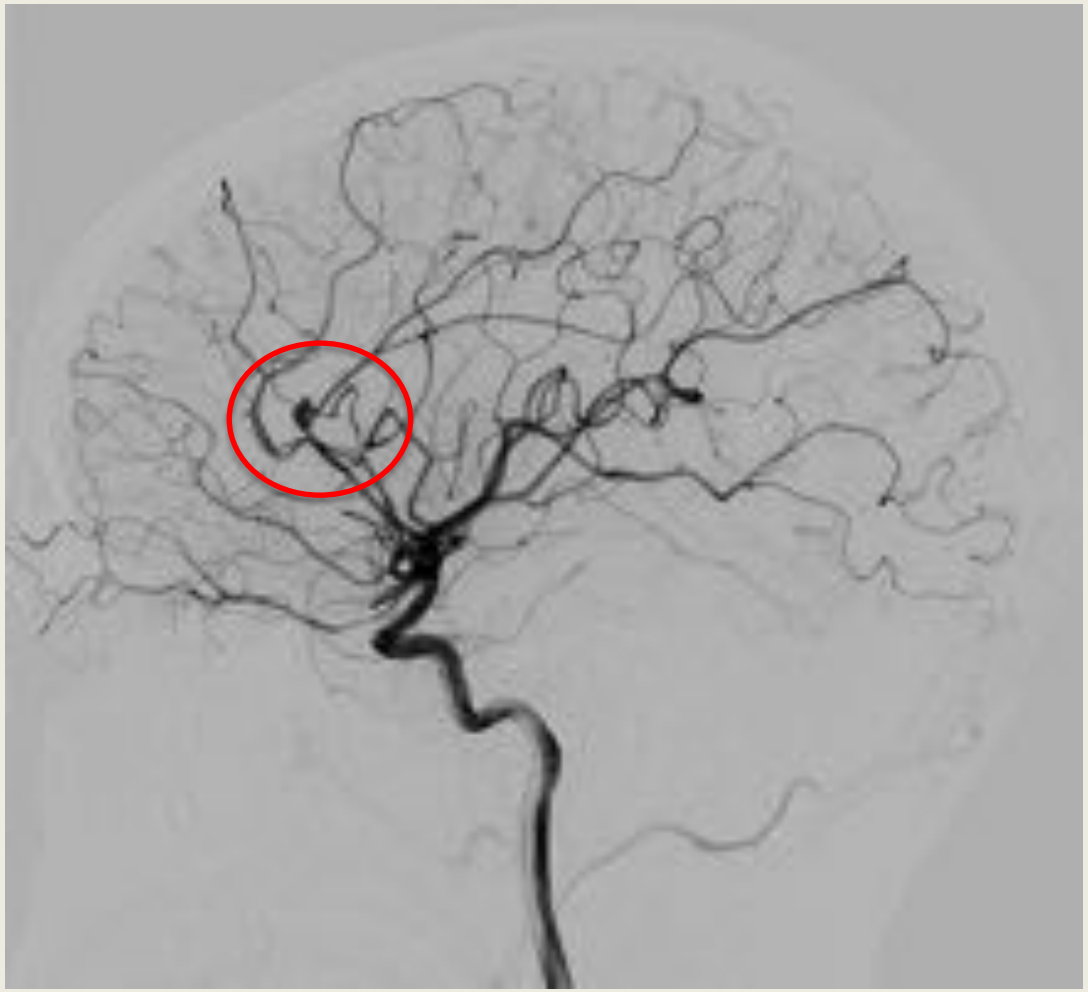


Suarez, Continuum, 2015



BACK TO OUR PATIENT…

Urgent transfer to MNH – Angiogram done



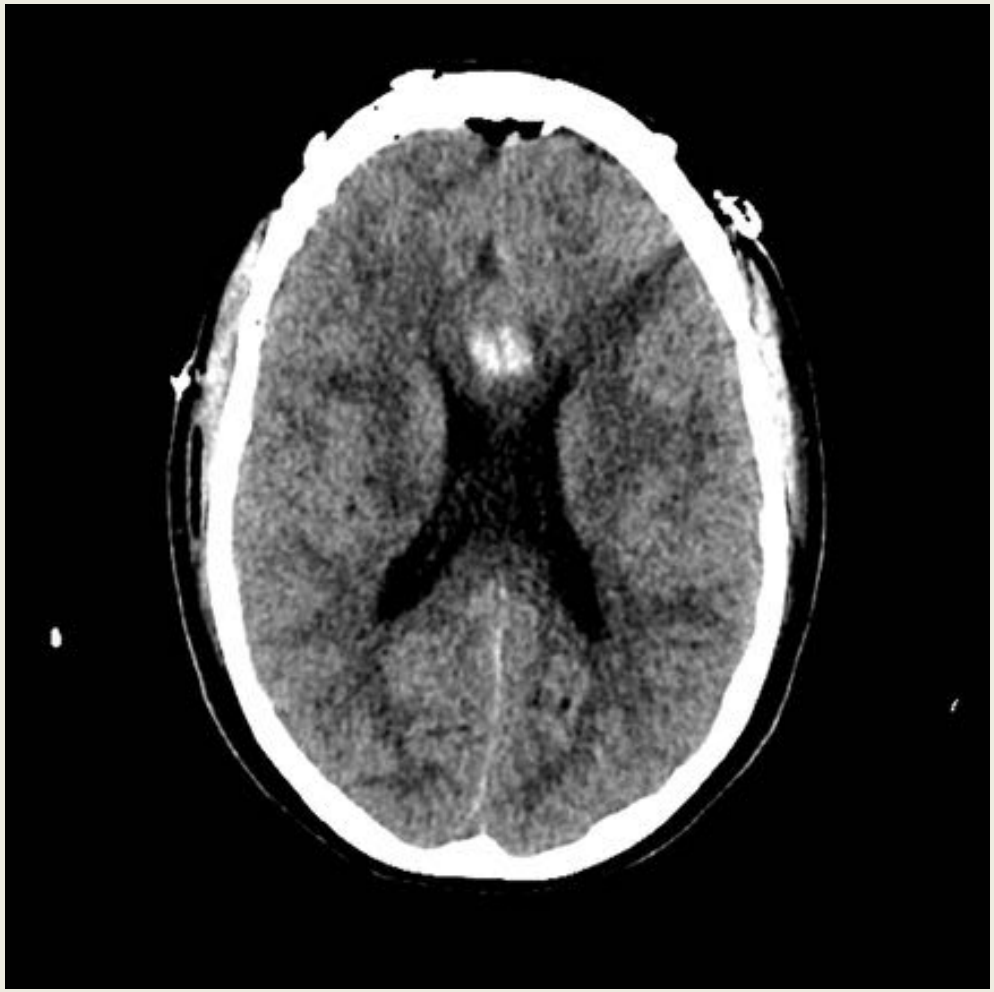
Imaging summary – MNH

- 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
- Brent RL. Counseling patients exposed to ionizing radiation during pregnancy. *Rev Panam Salud Publica* 2006; 20:198-204.
- Edlow JA, Caplan LR. Avoiding pitfalls in the diagnosis of subarachnoid hemorrhage. *N Engl J Med* 2000; 342: 29–36.
- Lannes M, Teitelbaum J, et al. Milrinone and homeostasis to treat cerebral vasospasm associated with subarachnoid hemorrhage: the Montreal Neurological Hospital protocol. *Neurocrit Care* 2012; 16(3): 354-62.
- Robba C, Bacigaluppi S, et al. Aneurysmal Subarachnoid Hemorrhage in Pregnancy-Case Series, Review, and Pooled Data Analysis. *World Neurosurg* 2016; 88:383-98.
- Suarez JI, Tarr RW, Selman WR. Aneurysmal subarachnoid hemorrhage. *N Engl J Med* 2006; 354(4):387-396.
- Suarez JI. Diagnosis and management of subarachnoid hemorrhage. *Continuum (AAN)* 2015; 21(5):1263–1287.

Clinical and Radiologic scales for SAH

Table 1. Clinical and Radiologic Grading Scales for Subarachnoid Hemorrhage.

Clinical Grading Scale of the World Federation of Neurological Surgeons*			Head CT Grading Scale†		
Grade	Score on Glasgow Coma Scale‡	Clinical Appearance	Grade	Subarachnoid Hemorrhage	Intraventricular Hemorrhage
1	15	No motor deficit	0	Absent	Absent
2	13–14	No motor deficit	1	Minimal	Absent in both lateral ventricles
3	13–14	Motor deficit	2	Minimal	Present in both lateral ventricles
4	7–12	With or without motor deficit	3	Thick§	Absent in both lateral ventricles
5	3–6	With or without motor deficit	4	Thick§	Present in both lateral ventricles

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 (eg, cocaine)
▶ **Other**
Certain genetic disorders (eg, 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

Suarez, Continuum, 2015