

# Rebound Intracranial Hypertension Following Treatment of Spinal CSF Leaks

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## Disclosures (past 2 years):

Role	Organization
Advisory Board	Alder BioPharmaceuticals, Amgen, Avanir, Biohaven Pharmaceuticals, electroCore, Eli Lilly, <b>Supernus</b> , Teva, Zosano
Speaker	<b>Allergan</b> , Amgen, Avanir, electroCore, <b>Supernus</b> , Teva
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<b>Board of Directors</b>	American Headache Society, <b>Spinal CSF Leak Foundation</b>
Editorial Board	Headache, Neurology Reviews
Contributing author	Medlink Neurology, Medscape

**Bold** = relevant to content

## Other Disclosures

There are no FDA approved medications indicated for the treatment of (headaches associated with) intracranial hypertension

Due to limited literature on this subject, much of the content is my opinion based on experience treating patients with the pseudotumor cerebri syndrome (idiopathic intracranial hypertension) and those with rebound intracranial hypertension.

# Learning Objectives

- Describe the differential diagnosis of rebound intracranial hypertension
- Develop a rational strategy for headache management in patients with RIH

# Case Presentation

46-year-old woman with orthostatic headaches for 10 years  
Occurred after being upright for 6-7 hours, 7 out of 10  
Top of head, sharp with nuchal aching  
Photophobia, constant tinnitus; pulsatile tinnitus in the AM  
Daily, constant  
Relieved only with sleep and at high altitude  
Also with occipital headaches and interscapular tension and  
burning neck pain

1 year prior she work up two days in a row with a “wet ear” and a halo of blood and clear liquid on the pillowcase

Headaches worsened after this

Evaluation for skull base CSF leak was negative

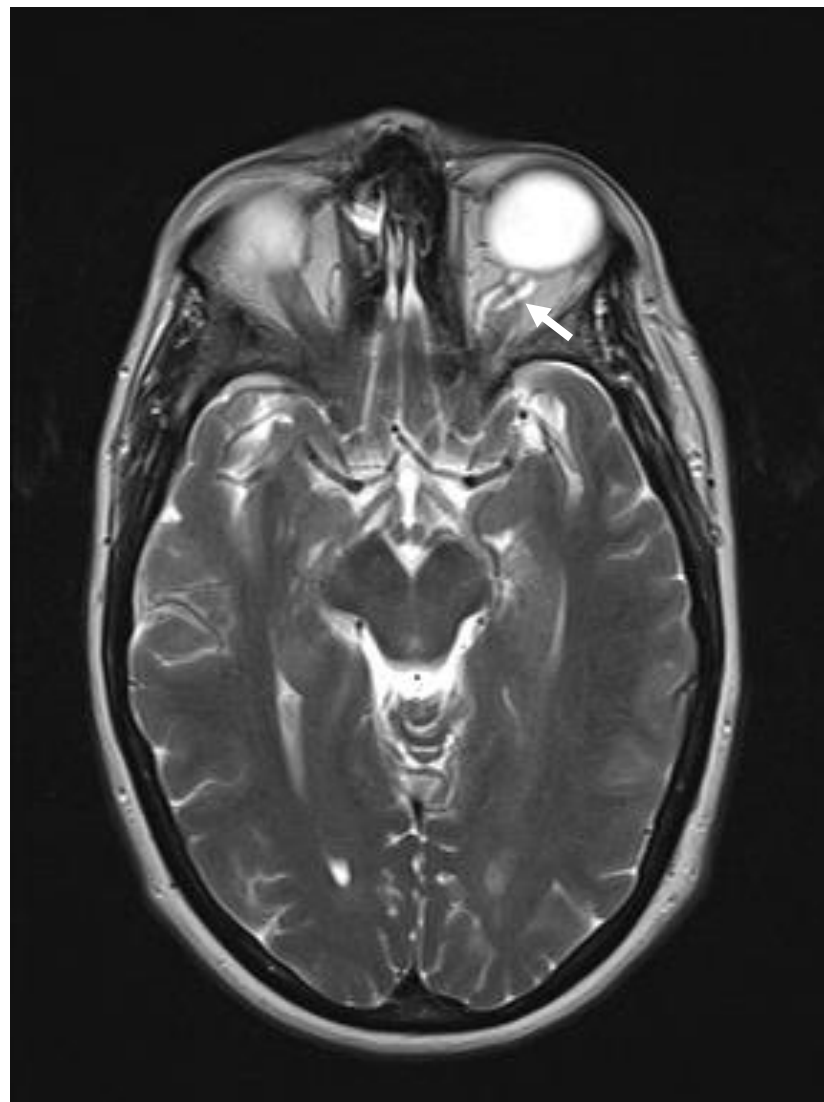
Started on topiramate 100 mg daily

LP 5 years prior for possible IIH showed OP 150 mm CSF

CT myelogram showed multiple perineural cysts but no leak

Headaches improved for 1 month after non-targeted blood patch

# Imaging 2 years prior



PMHx: Ehlers Danlos syndrome

Exam: BMI 28 kg/m<sup>2</sup>

Normal optic nerves with spontaneous venous pulsations

Normal neuro exam

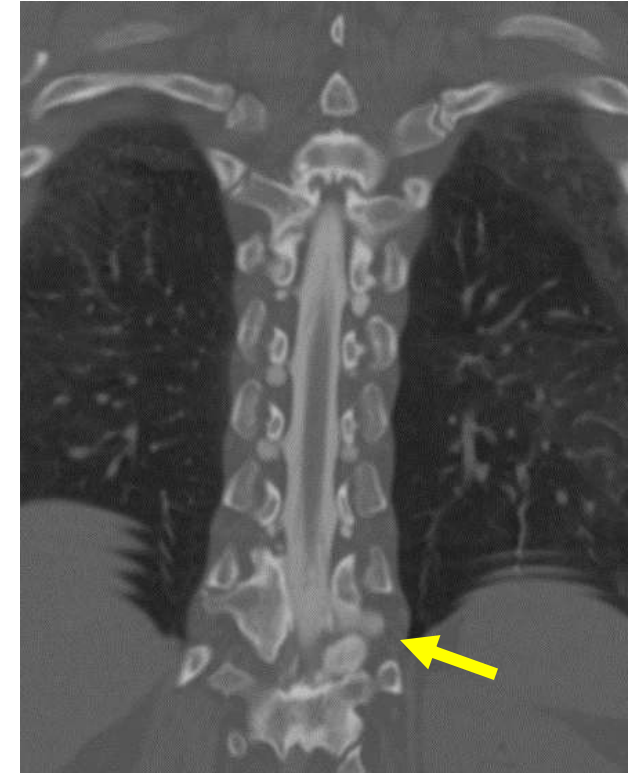
Trendelenburg test: 7 → 5 out of 10 in 10 minutes



Targeted blood patch of perineural cyst at T10-11 gave short-lived relief

Topiramate discontinued for possible exacerbation of intracranial hypotension

Subsequent blood patches with relief for 5-9 weeks.



Developed a different headache 10 days after her last blood patch

Worse when lying flat

Awakened with headache that resolved 10-15 minutes of being upright, then the previous orthostatic headache began 4 hours later

More history....

Gained 30 pounds after stopping topiramate

“Life long” history of transient visual obscurations when standing



# Characteristics of Rebound Intracranial Hypertension (RIH) Headaches

Usually occur within hours to days of epidural blood patch (or surgery)

Headache phenotype is completely different than SIH headache

- Location (often frontal or retro-orbital)
- Orthostatic component disappears
- May be worse upon awakening
- Patients may be unable to sleep flat

# Why Does RIH Occur?

1. Overcorrection of SIH (mechanism uncertain)
  - Disrupted spinal CSF absorption from blood patch
  - Upregulation of CSF production (unlikely)
2. The primary problem was unrecognized intracranial hypertension
  - “Self decompression” via spinal CSF leak
  - (Optic nerve sheath, sella, skull base leak, spinal leak)

# High Pressure Headaches in IIH: IIHTT Headache Characteristics at Baseline (n=165)

HA present in 84% at baseline (70 ACZ, 69 PBO)

Locations of headache:

Frontal 68%

Ocular 47% (usually bilateral)

Nuchal 47%

Posterior 39%

Unilateral 30%

Global 36%

Characterization of pain:

Pressure-like 47%

Throbbing 42%

Stabbing 5%

Wall M et al. JAMA 2014;311:1641-51  
Friedman DI et al. Headache 2017;57:1195-1205  
Yunisova G et al. Headache 2017;57:1152-3

ACZ = Acetazolamide, PBO = placebo

## IIH-related symptoms

Constant visual loss (34%)

Transient visual obscurations (68%)

Diplopia (22%)

Dizziness (53%)

Headache with none of the above (14%)

Migraine associated symptoms were common (86%):

Photophobia (70%), phonophobia (52%), nausea (47%), vomiting (17%), worsened with routine physical activity (50%)

### Headache phenotype (ICHD -3 beta)

Migraine 52%

Tension-type 22%

Not classifiable 7%

Probable migraine 16%

Probable tension-type 4%



# Why Does IAH Cause Headaches?

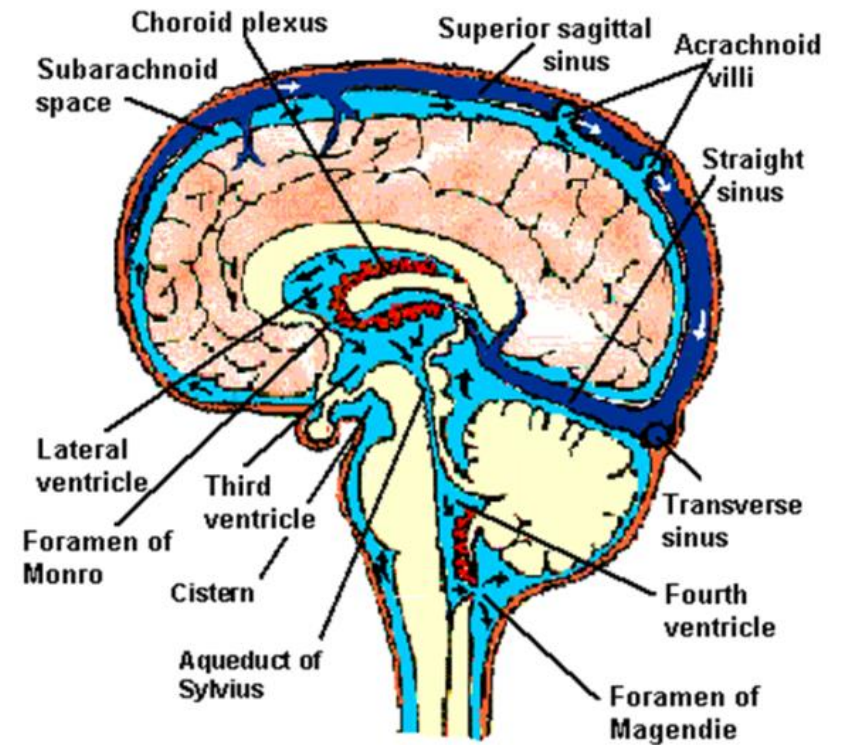
Pain sensitive structures in the brain

- Meninges
- Veins

Increased central venous pressure

Venous sinus stenosis

Central sensitization?



# Was IIH the Initial Problem? Clues on History and Exam

Prior diagnosis of IIH/PTCS

Obesity or recent weight gain

Other risk factors for IIH (cyclines, vitamin A, etc.)

Undiagnosed/untreated sleep apnea

History (or symptoms of) prior skull base leak

CSF rhinorrhea or otorrhea

Other IIH symptoms in the past

Pulsatile tinnitus

Previous imaging signs of increased ICP

The opposite of what is seen in SIH:

Empty sella

Expanded perioptic subarachnoid space

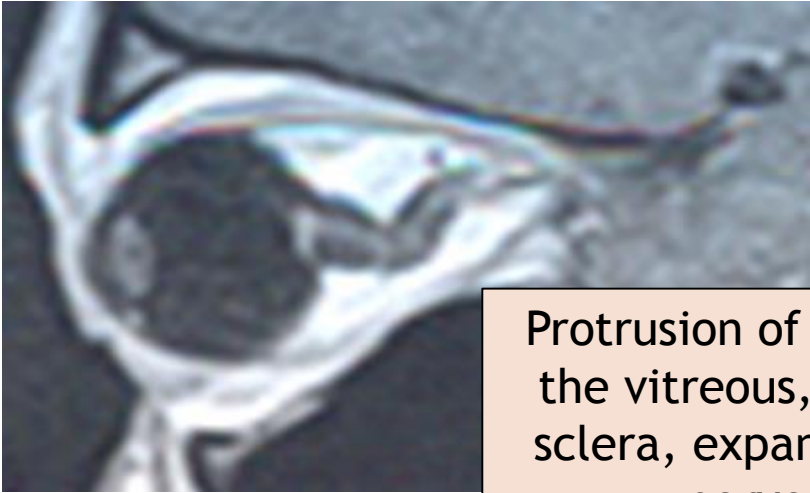
Tortuous optic nerve

Venous sinus stenosis

Tonsillar descent can occur with high or low pressure

No other evidence of brain sag

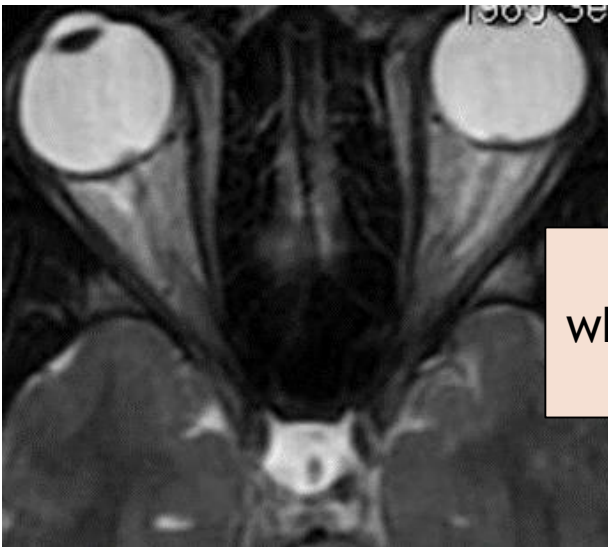
# Imaging Abnormalities\*



Protrusion of optic nerve papilla into the vitreous, flattening of posterior sclera, expanded and tortuous optic nerve sheath complex



Expanded/empty sella



Flattening of posterior sclerae where optic nerve leaves the globe

\*in the appropriate clinical context

# Neuro-Ophthalmic Symptoms and Signs

Transient obscurations of vision

Blurred vision

Visual field defects

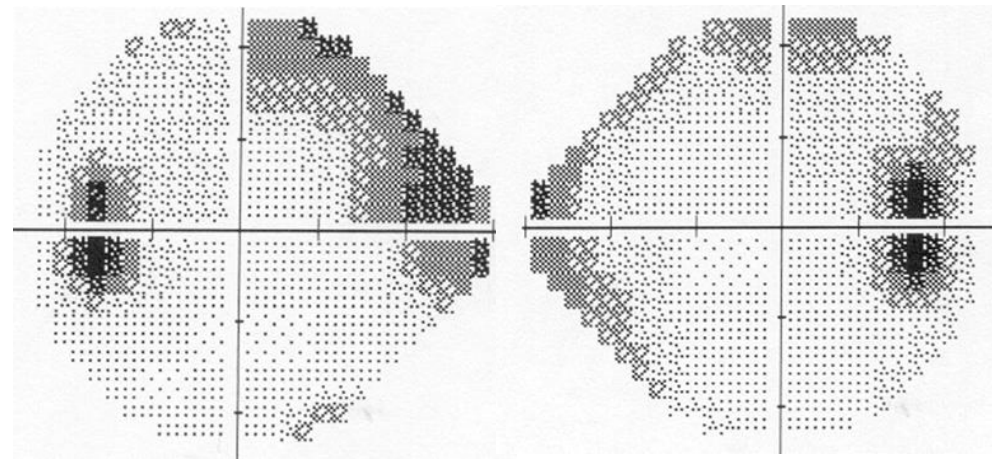
Binocular diplopia

Usually horizontal

Abducens palsy

Loss of previously present spontaneous venous pulsations

Papilledema

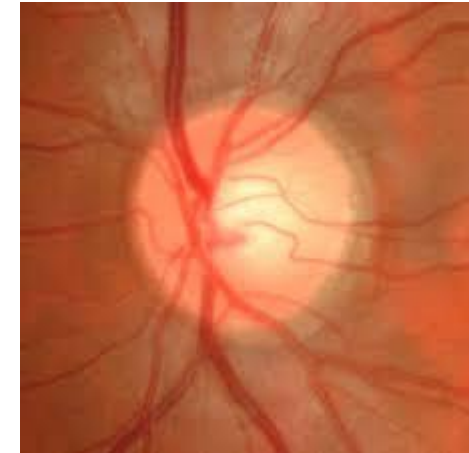


# Papilledema

Helpful:

Disc elevation, obliteration of optic cup  
Peripapillary halo, obscuration of vessels  
crossing the disc margin

Normal



Grade 2



Grade 3



Grade 4



Grade 5



# Treatments

Discontinue caffeine

Low sodium diet

Sleep reclining or sitting, elevate head of bed

Sleep apnea evaluation/treatment as indicated

Therapeutic lumbar puncture

Medical management

CSF pressure-lowering agents (oral; IV glycerol helpful in one case report of RIH)

Management of IIH (e.g., weight loss)

Procedural options

# Medical Management of CSF Pressure

**First choice:** Acetazolamide

Starting dose (adults) 500 mg BID

Titrate up to 2000 mg BID as tolerated

**Second choice:** Methazolamide

Starting dose 25 mg BID

Titrate up to 100-200 mg BID as tolerated (not renally excreted)

**Third choice:** Furosemide or bumetanide

**Fourth choice:** You choose

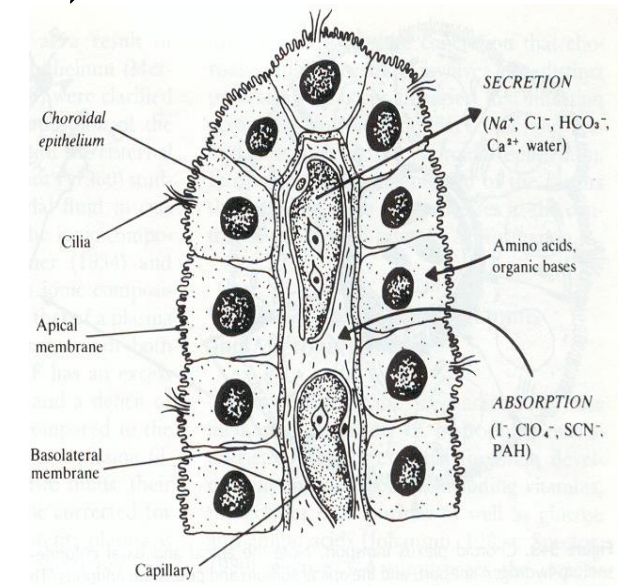
**Allergic patient (no cross reaction with sulfa antibiotics):**

Triamterene

Spironolactone (also good for PCOS)

Ethacrynic acid

***Be careful if combining diuretics!***





# Considerations for Headache Treatment

## Headache Phenotype - ICHD classification

Location, character of pain, duration, associated features (nausea, photophobia, phonophobia, etc.)

Migraine

Tension-type

Hemicrania continua

# Symptomatic Treatment of Headache

Naproxen

Acetaminophen

Other NSAIDs

Indomethacin may lower ICP

Triptans, dihydroergotamine (migraine phenotype or previous history of migraine)

Avoid butalbital, caffeine

Avoid opioids if possible although may be needed short-term

Antiemetics as needed

# Preventive Medications

Headaches at least once a week

Symptomatic medications  $\geq 3$  days weekly

Start low, go slow

Leverage possible side effects - **many cause weight gain**

Silberstein SD et al. Neurology 2012;78:1335-45  
Holland S et al. Neurology 2012;78:1346-53

Medications	Advantages	Disadvantages	Comments
Topiramate Zonisamide	Weight loss pCSF lowering effect	Tolerability Renal stones Pregnancy	
TCAs (low dose)	Sleep disturbance	Weight gain with higher doses	No adverse effect on weight loss in IIHTT
Indomethacin	May lower pCSF	Tolerability	
Naproxen			
OnabotulinumtoxinA	No systemic AEs		CM phenotype
SSRI/SNRI	Co-morbid depression	Possible weight gain	
Calcium channel blockers		Peripheral edema	
Beta blockers		Worsen depression Exercise intolerance	

Medications	Advantages	Disadvantages	Comments
Gabapentin		Weight gain	
Riboflavin			

Unknown:

Devices (neuromodulation)

GCRP targeted treatments

Cannabinoids

# Shunting for Headaches in IIH - JHMI

(n=115 procedures)

1 procedure 46%

2 procedures 24%

3-5 procedures 19%

≥6 procedures 12%

95% had HA improvement at one month

Recurrent headache in 48% at 36 months

Revision more common with LP shunts

# Transverse Sinus Stenting For IIH (any reason)

Literature Review of 19 studies (207 individuals)

- Inconsistent criteria used for stenting (not all had papilledema)
- Headache and ICP were only universal findings
- Gradients varied and were not always measured

192 patients presented with headache (duration weeks to years)

Headache after stenting

- Complete resolution in 72 (38%)
- Improvement in 83 (43%)
- No change in 35 (18%)
- Worse in 2 (1%)

Long term durability not reported

# Summary: Headache and ICP

Feature	IIH	SIH	Primary HA
Location	Often frontal	Often posterior	Anywhere
Postural component	Usually none	Often worse when upright	Depends on HA type
Timing	Morning or no fluctuation	Latter part of day	Patterns vary by HA type
Nocturnal awakening	Yes	Yes	Possible
Worse with Valsalva, exertion, bending	Yes	Yes	Yes
Migrainous associated symptoms	Yes	Yes	Yes
Effect of caffeine	None or worse	Improvement	Either
Effect of high altitude	Worsens	Improves	Often worse
Trendelenburg	No effect	Often improves	No
Pulsatile tinnitus	Common	Uncommon	Uncommon



# Summary: Other features

Feature	IIH	SIH	Primary HA
Pulsatile tinnitus	Common	Rare (not pulsatile)	May be present
TVOs	Common	No	No (or > seconds and not postural)
Body habitus	Usually obese	Often slim or normal	All
Joint hypermobility	Uncommon	Common	Uncommon
Sex	Usually female	Male or female	Male or female
Neck or back pain	Common	Common	Common
Radicular pain	Yes	No	No
Papilledema	Usually present	No	No
Venous pulsations	Absent	Usually present	Usually present

# Summary: Diagnostic Tests

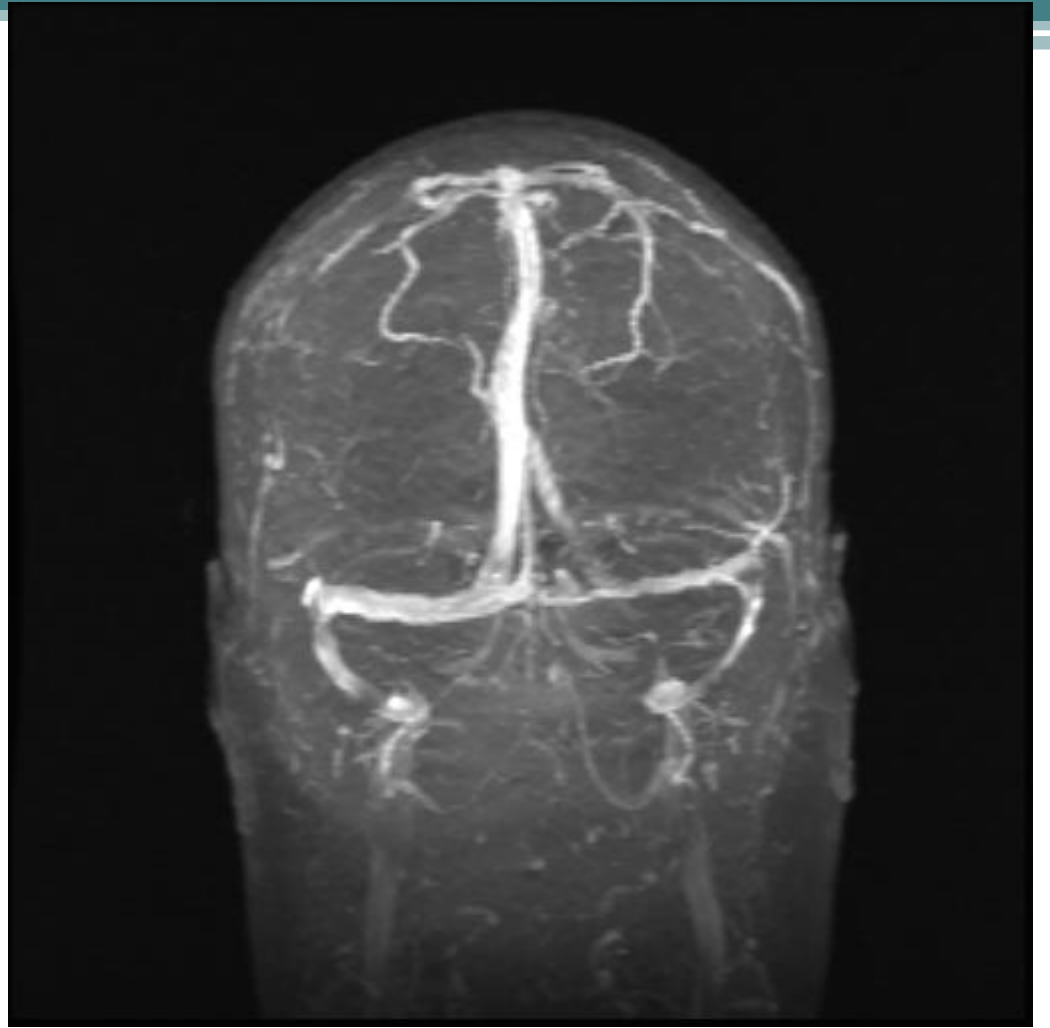
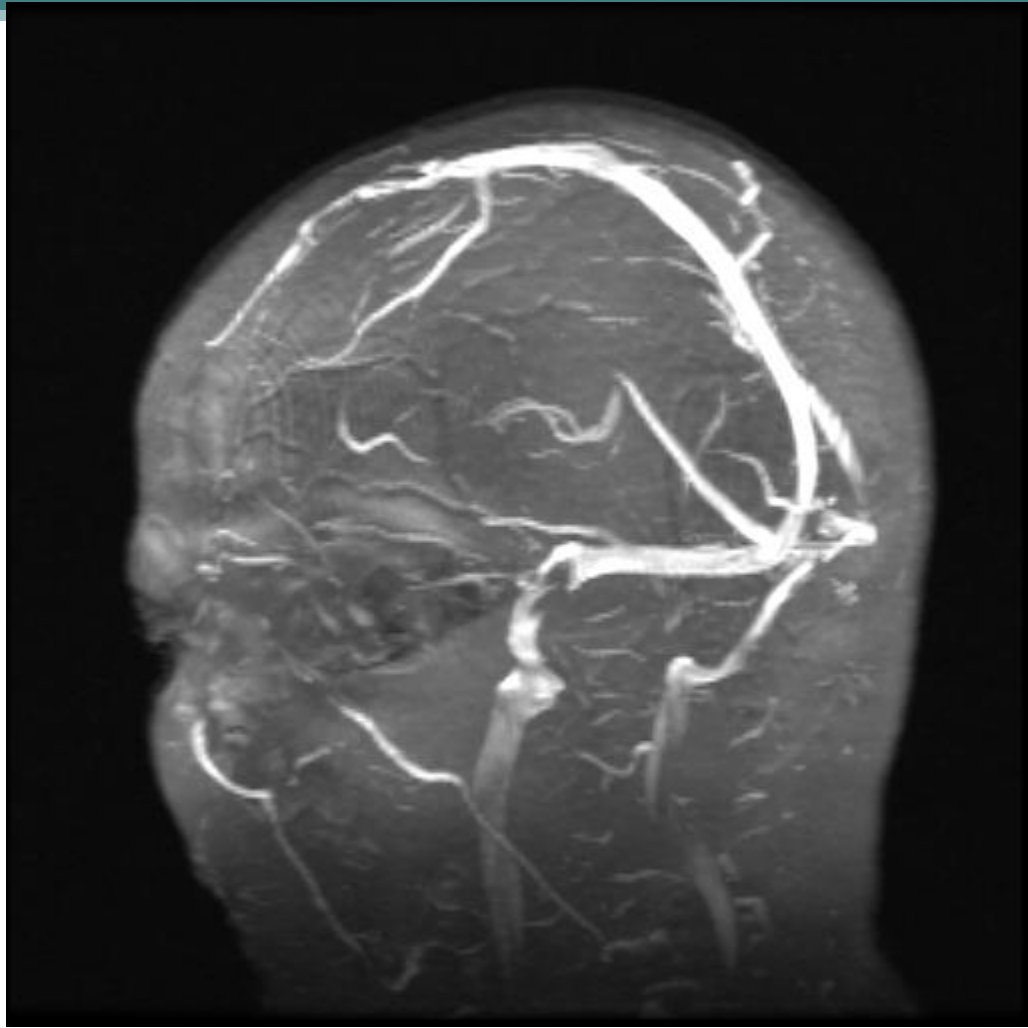
Feature	IIH	SIH	Primary HA
Sella / Pituitary	Empty sella	Enlarged pituitary	Sometimes empty; pituitary enlarges in pregnancy
Ventricular size	Normal	Normal	Normal
Tonsillar descent	Possible	Common	Possible
Flat posterior sclera	Common	No	No
Distended optic nerve sheath complex	Common	No	Rare
Flat anterior pons	No	Yes	No
LP opening pressure	High	Low, normal or high	Anything
Post LP headache?	Possible	Possible	Possible
Improvement of headache with LP?	Often	No	Possible

## Back to the Case

- Acetazolamide started was poorly tolerated at the dose needed to help headache (had to take it in the middle of the night) - severe cognitive effects
- Changed to methazolamide, better tolerated but did not work as well
- Added furosemide without benefit
- Several therapeutic LPs helped only briefly
- Patient distraught

## Considered options:

- VP shunt
- Optic nerve sheath fenestration
- Stenting



Vision good and not felt to be a good candidate for ONSF

Agreed to avoid shunt because of EDS

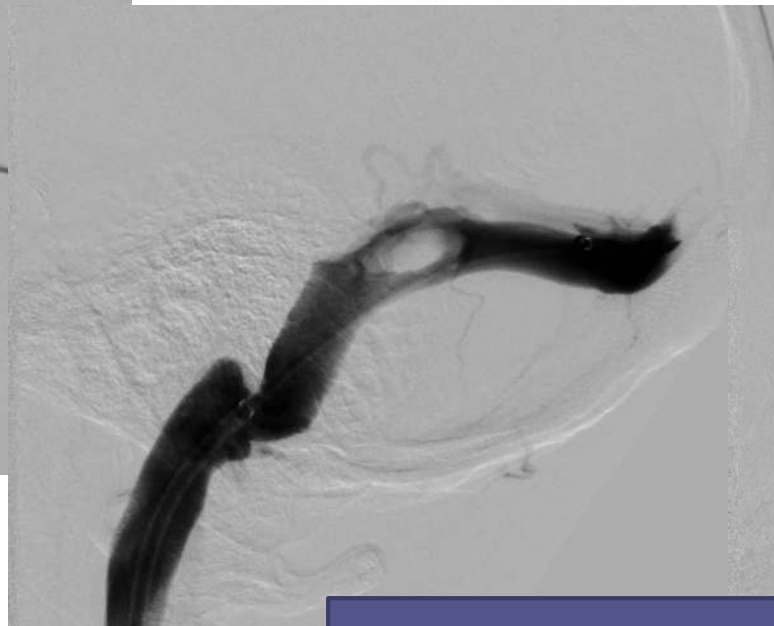
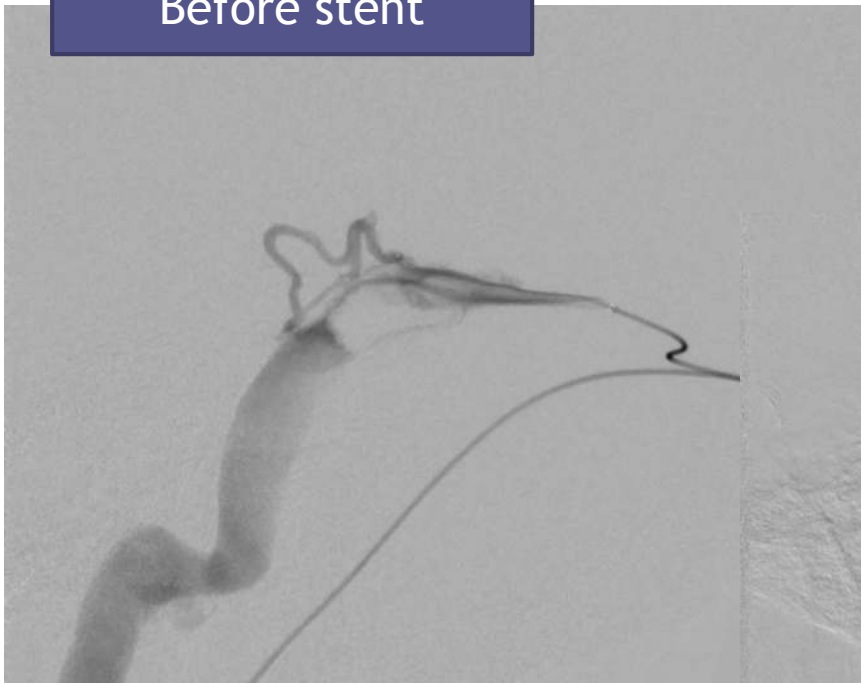
Evaluated for a stent and had procedure done

Right transverse sinus stented (and through to be fenestrated rather than having arachnoid granulation)

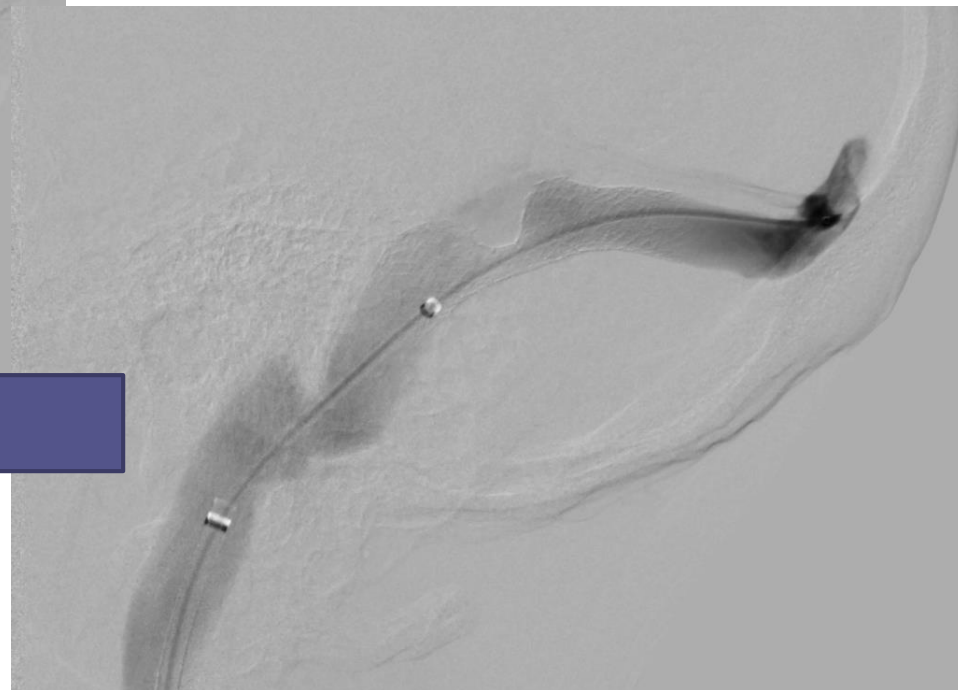
Pre-procedure gradient 21 mm Hg across stenosis

Post-procedure gradient <5 mm Hg stenosis

Before stent



After stent



# Take Home Points

- RIH headache is different than SIH headache and usually begins within hours to days of blood patches
- Therapeutic LP may be enough to relieve symptoms
- First line for medical treatment: acetazolamide or methazolamide
- It is possible for patient with primary IIH to develop cranial and spinal CSF leaks - evaluate patient for evidence of pre-existing IIH
- Headaches are usually self-limited although may take months to resolve
- Surgery is the last option to treat headache alone



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