Intracranial hypertension and headache.

Daniel Tibussek, MD

HEINRICH HEINE
UNIVERSITÄT
DÜSSELDORF

Disclosures

- none

Overview

- Case
- Clinical presentation of pediatric PTC
- Nomenclature, Definition
  - What is intracranial hypertension?
  - Diagnostic difficulties
- Epidemiology of headache in PTC
  - Clinical course of headache
  - IIH without papilledema
- Cases continued
- Summary

Case

- 13 yrs, female, obese
- History of intermittend headache, tension-type, for > 1 year

- Blurred vision since 6 wks,
  problems reading black board at school

- Ophthalmology:
  bilateral papilledema, reduced visual acuity, visual fields normal

Case

- LP: CSF OP 21 cm H2O
- prompt improvement of headache
- normalisation of visual disturbances within days post LP, improved papilledema
- No treatment b/o normal CSF OP.

Case con´t

- 2 months later: again blurred vision, vertigo, headache, worse than previously
- CSF OP 24 cm H2O, post LP again rapid improvement of vision
- Put on acetazolamide (20 mg/kg/d)
- Normalisation of papilledema
- Persisting headache, chronic daily
- Furosemide added, increasingly tired, no appetite, persisting headache, misses weeks of school

What is Pseudotumor cererbi in 2016?

Misdiagnosis of Pseudotumor cerebri is common!

Mishra A et al. Eur J Paediatr Neurol 2007 ; 11 : 39 – 42

Colin Kennedy (Editorial) Dev Med Child Neur 2006;48:83-83

PTCS, a headache syndrome?

Are children any different?

Clinical presentation: adults, reviews

- „Headache is the most common symptom of IIH present in 80%-90% of patients“
  Julayanont et al. 2016
- Headache are the predominat feature of the disease, reported by around 75-94%
  Markey et al. 2016
- „Headache is clearly the major symptom“
  Johnston et al. 2007
- Highly heterogenous, migraine-like, often daily headaches,…

Clinical presentation of PTCS in children

PTCS as incidental finding

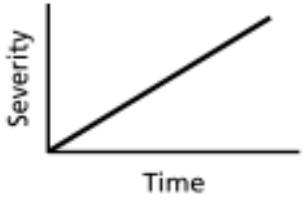
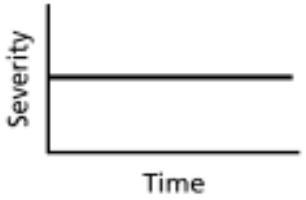
- Germany: 5 out of 61 children
- Düsseldorf: 16 out of 53 children

Literature:

- Lim et al. 3 out of 29
- Bassan et al. 14 out of 45

Tibussek et al. Klin Padiatr. 2013;225:81-5
Tibussek et al. Child Nerv Syst 2010; 26:313-21
Lim et al. Arch Dis Child 2005; 90:206–210
Bassan et al. Acta Neurol Scand. 2008 Oct;118(4):251-5

Headache patterns in PTCS: Duesseldorf

TABLE 2 **Five Temporal Patterns of Headache in Children**		Prepubertal (16/32)	Adolescent (15/21)
Acute headache Single episode of head pain without history of previous events		4/16	6/15
Acute-recurrent headache Pattern of head pain separated by symptom-free intervals		3/16	0
Chronic-progressive headache* Gradual increase in frequency and severity		1/16	3/15
Chronic-nonprogressive (or chronic-daily) headache Frequent or constant headache		8/16	6/15

Lewis DW. Am Fam Physician 2002; 65:625–632

Tibussek et al. Childs Nerv Syst 2010;26:313-21

Definition of…

„seroese Meningitis“
"otitic hydrocephalus"

Benign Intracranial Hypertension

Pseudotumor Cerebri

Idiopathic Intracranial Hypertension

Pseudotumor cerebri Syndrome/complex

Definition of Pseudotumor cerebri syndrome

- A. Papilledema
- B. Normal neurologic examination except for cranial nerve abnormalities
- C. Neuroimaging: Normal brain parenchyma
- D. Normal CSF composition
- E. Elevated lumbar puncture opening pressure

Adapted from: Friedman DI et al. Revised diagnostic criteria for the pseudotumor cerebri syndrome in adults and children. Neurology; 2013;81:1159–1165.

Definition of Pseudotumor cerebri syndrome

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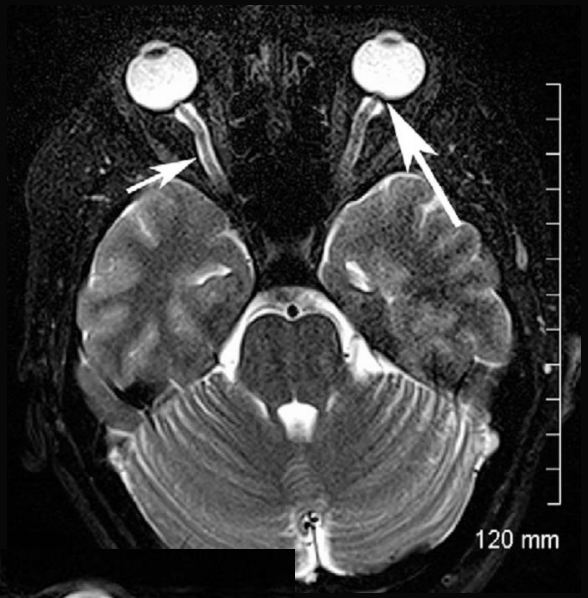
Add Reference Imaging!

Adapted from: Friedman DI et al. Revised diagnostic criteria for the pseudotumor cerebri syndrome in adults and children. Neurology; 2013;81:1159–1165.

partially empty sella

optic nerve sheath distension



flattening of posterior globe

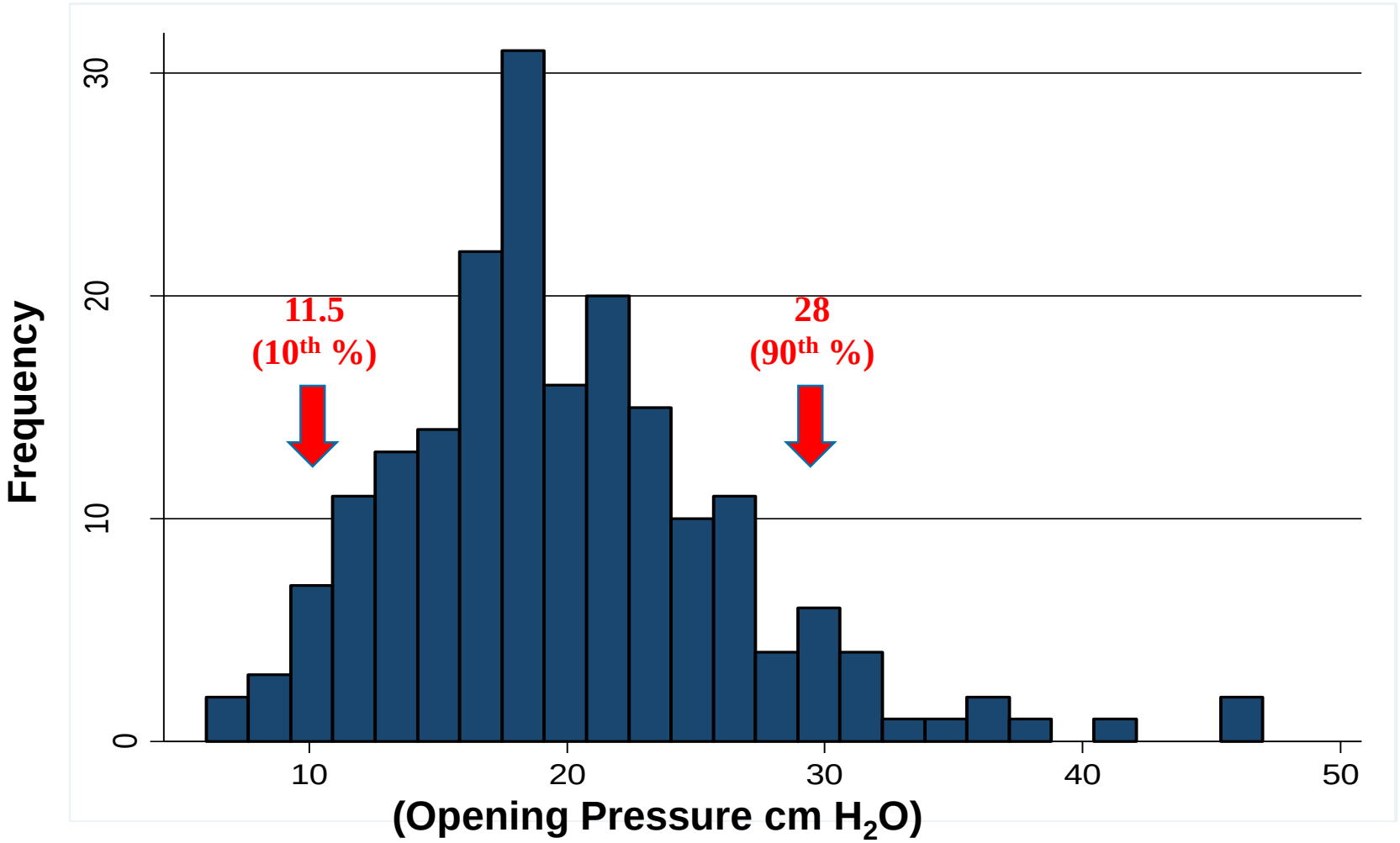
Maralani et al. Clinical Radiology 2012; 67:656-663

Definition of Pseudotumor cerebri

- A. Papilledema
- B. Normal neurologic examination except for cranial nerve abnormalities
- C. Neuroimaging: Normal brain parenchyma
- D. Normal CSF composition
- E. Elevated lumbar puncture opening pressure
- BUT: what is elevated opening pressure?

Adapted from: Friedman DI et al. Revised diagnostic criteria for the pseudotumor cerebri syndrome in adults and children. Neurology; 2013;81:1159–1165.

Opening Pressure Distribution (N = 197)



Avery et al. N Engl J Med 363;891-3

Still, this is not the final answer..

Diagnostic Criteria for Pseudotumor Cerebri Syndrome

- Elevated lumbar puncture opening pressure (≥250 mm CSF in adults and ≥280 mm CSF in children)
- **[250 mm CSF if the child is not sedated and not obese])**

- **Our case: < 25 mm H2O**

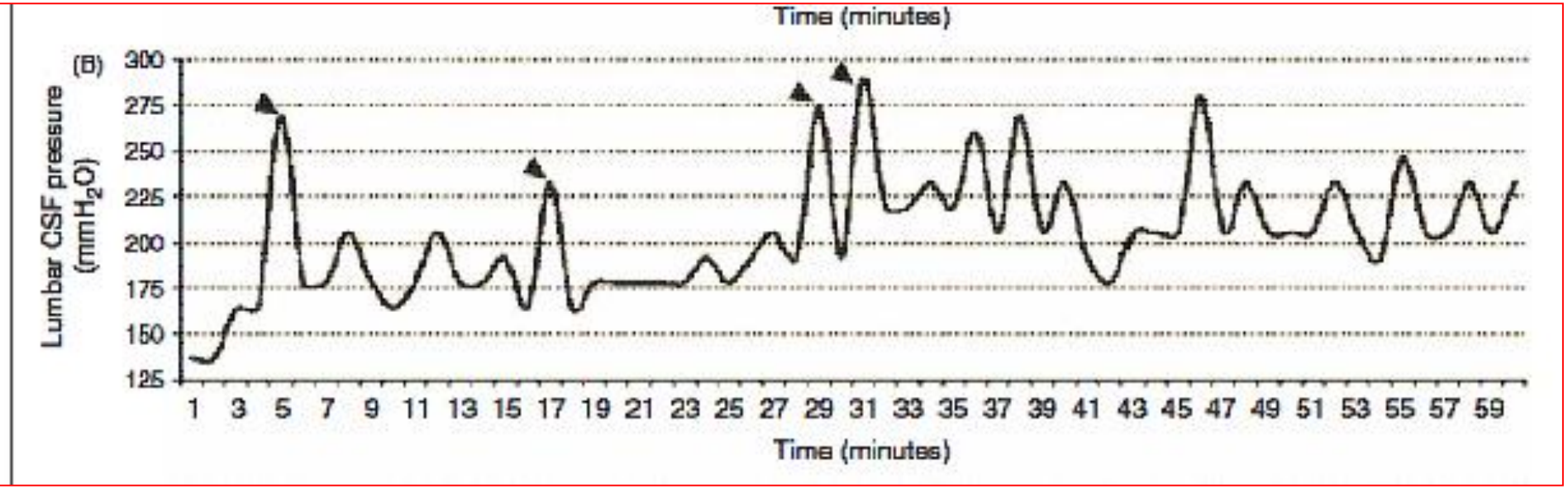
Friedman DI et al. Revised diagnostic criteria for the pseudotumor cerebri syndrome in adults and children. Neurology; 2013;81:1159–1165.

CSF opening pressure < 28 cm H_2O

- Germany: 13/61 PTCS pediatrics patients
- Duesseldorf: 14/75 PTCS pediatric patients
- **This represents 18% of the total pediatric PTCS study population**
- PTCS diagnosis possible with OP < 28 cm
- There is NO *cutoff value* for normal CSF opening pressure

Tibussek et al. Eur J Paediatr Neurol. Under revision.
Friedman DI et al. Revised diagnostic criteria for the pseudotumor cerebri syndrome in adults and children. Neurology; 2013;81:1159–1165.

!Pressure variability in 1 h!

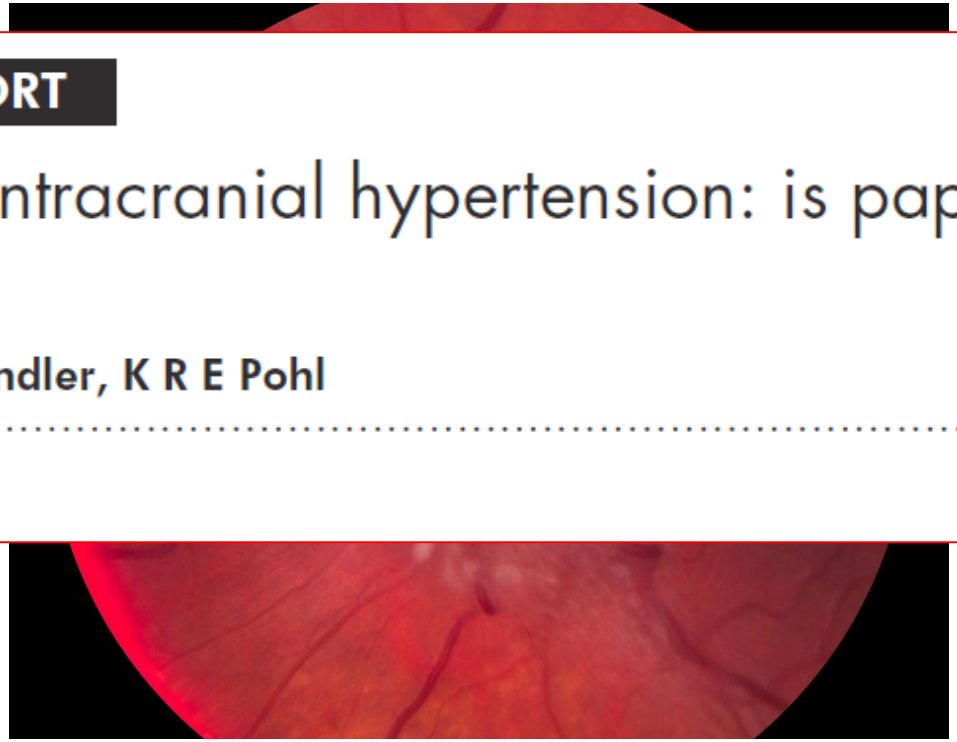


- Bilateral transverse sinus stenosis
- Initial LP Opening pressure < 20cm

Cephalalgia 2010 30:1419-25

IIWHOP

IIHWOP: Does it exist?



SHORT REPORT

Idiopathic intracranial hypertension: is papilloedema inevitable?

E Wraige, C Chandler, K R E Pohl

Arch Dis Child 2002;**87**:223–224

„idiopathic intracranial hypertension (IIH) without Papilloedema“ (**IIHWOP**)

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1. Sinus Venous Stenosis-Associated Idiopathic Intracranial Hypertension Without Papilledema as a Powerful Risk Factor for Progression and Refractoriness of Headache.
De Simone R, Ranieri A, Montella S, Marchese M, Bonavita V.
Curr Pain Headache Rep. 2012 Mar 1. [Epub ahead of print]
PMID: 22382759 [PubMed - as supplied by publisher]
Related citations

2. Sinus venous stenosis-associated **IIHWOP** is a powerful risk factor for progression and refractoriness of pain in primary headache patients: a review of supporting evidences.
De Simone R, Ranieri A, Montella S, Erro R, Fiorillo C, Bonavita V.
Neurol Sci. 2011 May;32 Suppl 1:S169-71. Review.
PMID: 21533738 [PubMed - indexed for MEDLINE]
Related citations

3. High prevalence of bilateral transverse sinus stenosis-associated **IIHWOP** in unresponsive chronic headache sufferers: pathogenetic implications in primary headache progression.
De Simone R, Ranieri A, Cardillo G, Bonavita V.
Cephalalgia. 2011 Apr;31(6):763-5. No abstract available.
PMID: 21493643 [PubMed - indexed for MEDLINE]
Related citations

4. Is idiopathic intracranial hypertension without papilledema a risk factor for migraine progression?
De Simone R, Ranieri A, Fiorillo C, Bilo L, Bonavita V.
Neurol Sci. 2010 Aug;31(4):411-5. Epub 2010 Feb 25. Review.
PMID: 20182895 [PubMed - indexed for MEDLINE]
Related citations

5. Bilateral transverse sinus stenosis and idiopathic intracranial hypertension without papilledema in chronic tension-type headache.
Bono F, Messina D, Giliberto C, Cristiano D, Broussard G, D'Asero S, Condino F, Mangone L, Mastrandrea C, Fera F, Quattrone A.
J Neurol. 2008 Jun;255(6):807-12. Epub 2008 May 6.
PMID: 18458863 [PubMed - indexed for MEDLINE]
Related citations

6. Idiopathic intracranial hypertension with and without papilloedema in a consecutive series of patients with chronic migraine.
Vieira DS, Masruha MR, Gonçalves AL, Zukerman E, Senne Soares CA, Naffah-Mazzacoratti Mda G, Peres MF.
Cephalalgia. 2008 Jun;28(6):609-13. Epub 2008 Mar 31.
PMID: 18384415 [PubMed - indexed for MEDLINE]

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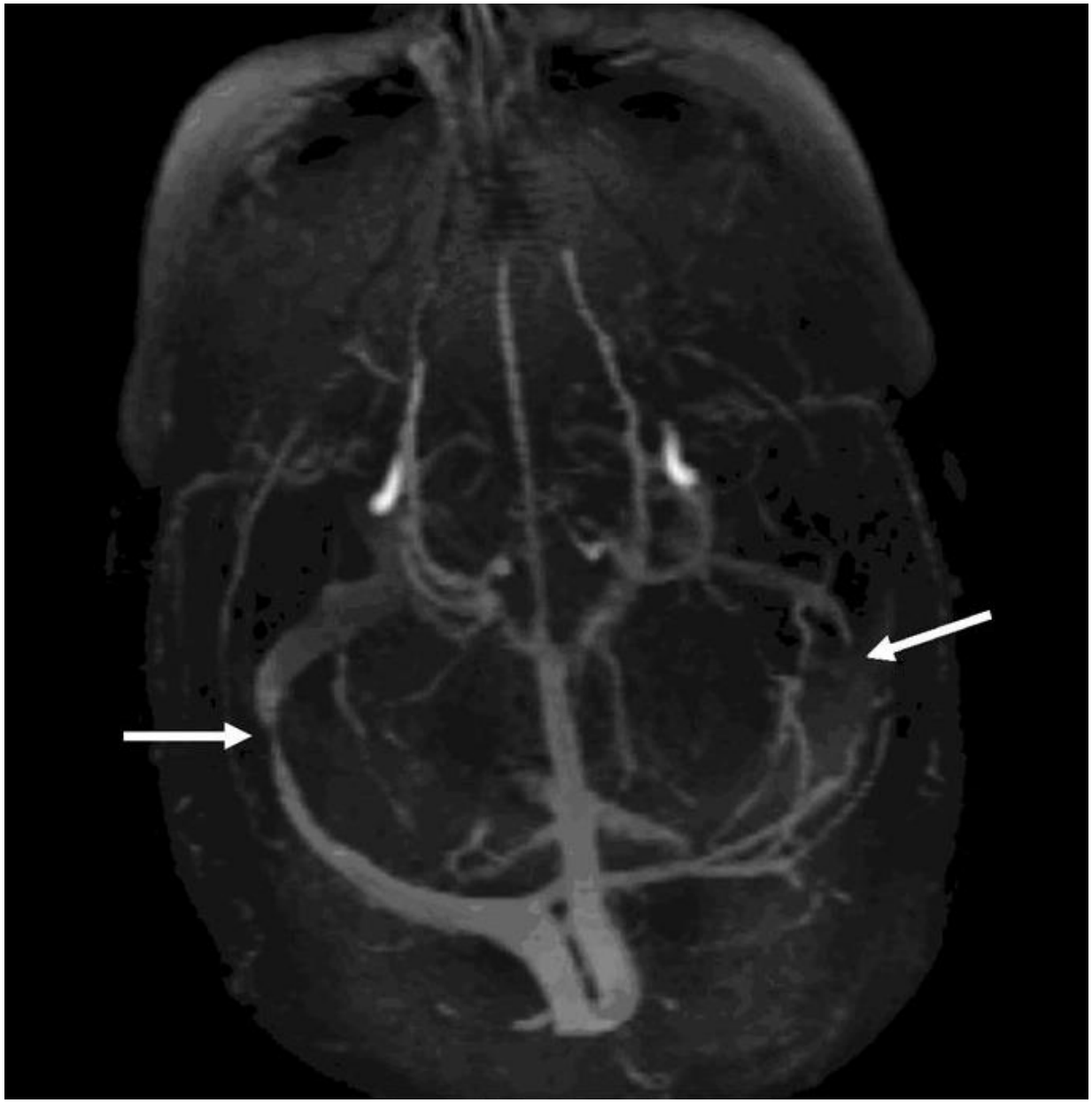


Kelly et al. Clin Neurol Neurosurg. 2013 Aug; 115(8): 1215–1219. .

Chronic migraine and PTCS

- Has been linked to PTCS in adults
- Has been linked to transverse sinus stenosis
- Has been linked to IIH without papilledema

Transverse sinus stenosis (TSS) in PTCS patients

- Is almost always bilateral!
- Degree of stenosis does NOT correlate with the clinical course
- Clinical features, not the degree of TSS, should be used to determine management in IIH /PTCS

Riggeal et al. Neurology. 2013;80:289-295

An indication for stenting?

PS14-01

Idiopathische intrakranielle Hypertension (IIH, Pseudotumor cerebri) - Stufentherapie und endovaskuläre Behandlung bei Kindern und Jugendlichen

Wörle H. (Stuttgart), Marquard K., Henkes H., Keimer R.

To stent or not to stent?

Table 5 Long-term outcomes of the intervention to visual function and headache when follow-up >1 year

Procedures	Number of studies	Number of cases	Follow-up (months)	Clinical outcomes				
				Headache improvement (range)	Visual acuity improvement (range)	Visual field improvement (range)	Papilledema improvement (range)	Revision rate of procedure (range)
Optic nerve sheath fenestration	8	432	20	26% (13%–90%)	42% (17%–100%)	72% (48%–100%)	92% (79%–100%)	6.5% (5%–21%)
CSF diversion	7	209	39	55% (21%–92%)	56% (40%–93%)	77% (64%–100%)	70% (56%–87%)	44% (8%–85%)
Cerebral sinus endovascular stent	9	174	23	77% (58%–100%)	89% (69%–100%)	79% (77%–79%)	93% (50%–100%)	NA

Abbreviations: CSF, cerebrospinal fluid; NA, not applicable.

Julayanont et al. Journal of Pain Research 2016:9 87-99

Beware of publication bias!

RISKS!!!

- Venous peforation
- Subdural hemorrhage
- Stent migration
- In-stent thrombosis
- Recurrent stenosis
- Long-term antithrombotic treatment
- …

Headache in treated PTCS

- N=82
- 68% developed subsequent headache

Episodic tension type	30
Migraine w/o aura	20
Chronic tension type	10
Analgesic overuse headache	8

…

Friedman D, Rausch E. Neurology. 2002 May 28;58(10):1551-3.

„Patients with PTCS often continue experiencing headache

…despite the apparent normalization of their intracranial pressure“

Friedman D, Rausch E. Neurology. 2002 May 28;58(10):1551-3.

An indication for stenting?

„We do not usually recommend surgical treatment or venous stenting for patients with isolated chronic headaches and mild to moderate papilloedema without visual loss“

„because of high prevalence of associated primary headache disorders and the frequent development of chronic headache unrelated to raised ICP make the success … too unpredictable“

Anne Ducros and Valerie Biousse in Lancet Neur 2015;14:655-68

Therapy

What are our treatment goals?

1) Maintain/regain normal visual function

2) Relief headaches

3) prevent unneccesary invasive treatment

Back to the case

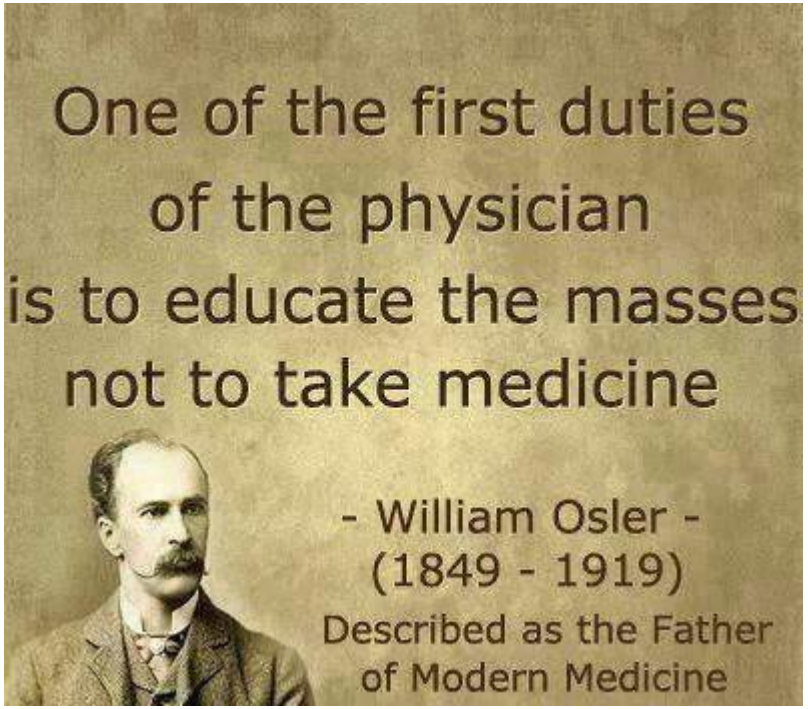
Case con´t

- Still normal vision, no papilledema
- Headache still reported
- Follow-up LP, OP 28 cm H^2O
- Interpreted as treatment resistence
- Scheduled for VP-shunt

Interpretation and recommendation

- „probable PTCS“ (OP <25 cm H2O)
- Response to LP very suggestive of PTCS
- Good response to treatment (Vision)
- f/u LP with increased OP falsely interpreted as treatment resistence
- Clinical deterioration due to medication side effects
- Headache not PTCS related

Therapy



Sir William Osler, 1st Baronet (born July 12, 1849 – December 29, 1919) was a Canadian physician and one of the four founding professors of Johns Hopkins Hospital (Wikipedia).

Case: Follow-up

- After cessation of furosemid prompt clinical improvement
- Back to school
- Referral to headache progam (multimodal therapy)
- Gradually improving headache
- Still remission, normal eye exam
- No neurosurgery

Therapy-Escalation: When and Why?

„treatment decisions should **not** rest on … the severity of papilledema, or CSF opening or closing pressure.“

„Instead, the modern management of pseudotumor cerebri is **based largely upon the level of visual loss**.“

Aus: Liu et al.: Neuro-Ophthalmology. Diagnosis and Management. Second edition. 2010

What about headache?

Headache and QOL

- N=24, female adults with PTCS
- Quality of life is significantly reduced in PTCS patients
- Headache was the only clinical outcome that correlates with enhanced QOL
- **Effective headache management is required to improve QOL in PTCS!**

Mulla et al. J Headache Pain. 2015;16:521.

Headache as criteria for success?

- A „classical“ patient shows rapid headache relief after LP

BUT

Bruce BB, Biousse V, Newman NJ. Am J Ophthalmol 2011;152:163-169
Friedman DI, Rausch A. Neurology 2002; 58:1551-1553

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Friedman DI, Rausch A. Neurology 2002; 58:1551-1553

Headache as criteria for success?

- E

„Many IIH patients have persistent headaches,

even after normalization of the intracranial pressure“

„Patients with IIH frequently have headaches **not necessarily related to increased intracranial pressure**“

Bruce BB, Biousse V, Newman NJ. Am J Ophthalmol 2011;152:163-169
Friedman DI, Rausch A. Neurology 2002; 58:1551-1553

Therapy, little evidence

Update 2015:
Although the two included RCTs showed modest benefits for acetazolamide for some outcomes, there is insufficient evidence to recommend or reject the efficacy of this intervention, or any other treatments currently available, for treating people with IIH.

Original Investigation

Effect of Acetazolamide on Visual Function in Patients With Idiopathic Intracranial Hypertension and Mild Visual Loss

The Idiopathic Intracranial Hypertension Treatment Trial

The NORDIC Idiopathic Intracranial Hypertension Study Group Writing Committee

the use of acetazolamide with a low-sodium weight reduction diet, compared with diet alone, **resulted in modest improvement in visual field function**.

No significant treatment effects were noted with respect to **headache** disability

JAMA. 2014;311(16):1641-1651

Step-wise approach

Step 3: No visual loss:

- Symptomatic headache (migraine) therapy

Step 4: Mild visual loss:

- Acetazolamide
- Furosemide
- (Topiramate)
- Weight reduction, if necessary

Liu et al. 2011 in: Neuro-Ophthalmology, Diagnosis and Management, Saunders, Elsevier

Step-wise approach

Step 3: No visual loss:

- Symptomatic headache (migraine) therapy
- weight loss

Although plausible, no evidence that topiramate is superior when headache is predominant complaint

- Weight reduction, if necessary

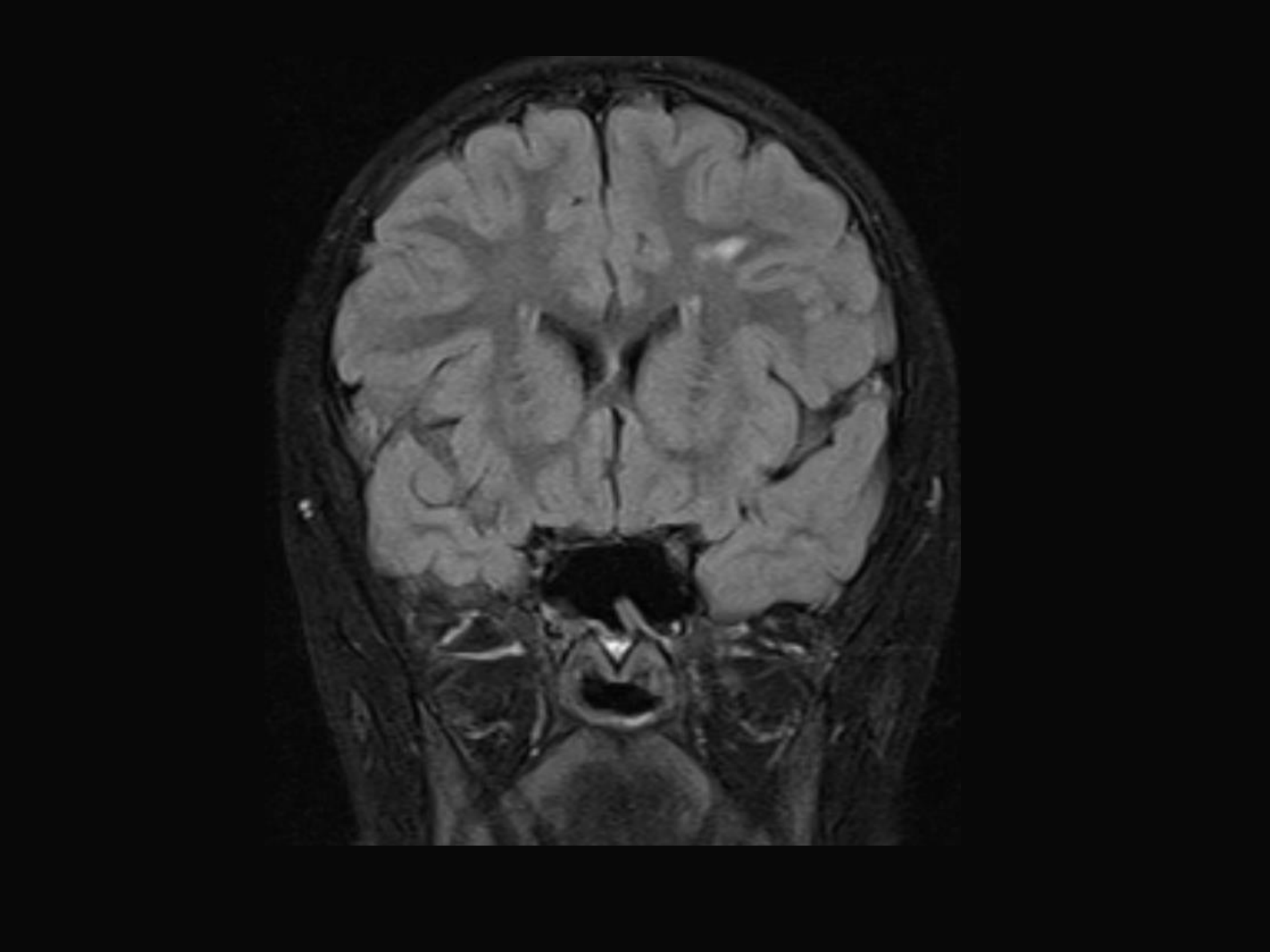
Liu et al. 2011 in: Neuro-Ophthalmology, Diagnosis and Management, Saunders, Elsevier

Invasive therapy

- Step 5: Severe, or progression of visual

Always critically question your diagnosis before even considering!

- High-dose IV steroids and acetazolamide
- Lumboperitoneal shunt for failed ONSD or intractable headache
- Bariatric surgery



Do not forget: Differential diagnoses

Elevated CSF opening pressure in Pediatric Demyelinating Disease Cohort:

„Almost 1/3 of children with inflammatory demyelinating disease have an elevated CSF opening pressure“

Pediatric Neurology 2015;52:446-449

Interdisciplinary decision!

- Optimal management of IIH requires good communications between specialties to protect the patient from unnecessary lumbar punctures and CSF diversion surgery on the one hand and avoidable visual loss on the other.

Standridge SM. Idiopathic intracranial hypertension in children: A review and algorithm. Pediatr Neurol 2010;43:377-390.

Take home message

- The doubtless diagnosis of PTCS is difficult!
- Exclusion of papilledema should always be part of headache work-up
- Beware of pseudopapilledema!
- If MRI appears indicated do high quality MRV
- Relevance of transverse sinus stenosis in children unclear.
- However, bilateral TSS suggestive of PTCS
- Frequency of IIHWOP in children is unknown

Take Home Messages

- Headache may or may not improve after LP even in proven PTCS cases
- Headache may or may not respond to pressure lowering medication on follow-up
- Headache is **not** a good monitoring instrument
- Persisting headache after treated PTCS is common in children and adults
- Persisting headache does not neccesarily indicate treatment resistence of PTCS
- Beware of medication induced headache

Take home messages

- Critically question diagnosis BEFORE invasive treatment.
- PTCS needs to be treated in a multidisciplinary fashion

- PTCS should usually not be considered a surgical problem

Lost? Questions?

Intracranial pressure monitoring. Solution?

- Lumbar Puncture Opening Pressure Is Not a Reliable Measure of Intracranial Pressure in Children.

  Journal of Child Neurology 2015, Vol. 30(2) 170-173.
- „Lumbar puncture therefore significantly overestimates the intracranial pressure in children.”

Step-wise approach

- Step 1: correct potentially causal factors (medication, anaemia, hypothyroidism, ..)

- Step 2: LP with CSF drainage to lower pressure >> measure post punctional pressure („closing pressure“)

Pressure release as the only therapy

„Interestingly, **it is not uncommon** to observe a lasting clinical remission after a single lumbar puncture in some IIH patients“

Germany study

- **14/61 Patients** got LP pressure as the only treatment. In 1 case succesfully as serial LP.

Bruce BB, Biousse V, Newman NJ. Update on Idiopathic Intracranial Hypertension. Am J Opthalmol 2011;152:163-169