Intracranial hypertension and headache.

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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 intermittent 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 cerebri in 2016?
Misdiagnosis of Pseudotumor cerebri is common!

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 predominant 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. Child Nerv Syst 2010; 26:313-21
<table>
<thead>
<tr>
<th>Headache Patterns in PTCS: Duesseldorf</th>
<th>Prepubertal (16/32)</th>
<th>Adolescent (15/21)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acute headache</strong></td>
<td>4/16</td>
<td>6/15</td>
</tr>
<tr>
<td>Single episode of head pain without history of previous events</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Acute-recurrent headache</strong></td>
<td>3/16</td>
<td>0</td>
</tr>
<tr>
<td>Pattern of head pain separated by symptom-free intervals</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Chronic-progressive headache</strong></td>
<td>1/16</td>
<td>3/15</td>
</tr>
<tr>
<td>Gradual increase in frequency and severity</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Chronic-nonprogressive (or chronic-daily) headache</strong></td>
<td>8/16</td>
<td>6/15</td>
</tr>
</tbody>
</table>

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

Definition of Pseudotumor cerebri syndrome

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Definition of Pseudotumor cerebri syndrome

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Add Reference Imaging!
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?

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 ($\geq 250$ mm CSF in adults and $\geq 280$ mm CSF in children)
- [250 mm CSF if the child is not sedated and not obese]
- Our case: $< 25$ mm H2O

CSF opening pressure < 28 cm H$_2$O

- 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

- 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)
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.
   PMID: 22382759 [PubMed - as supplied by publisher]

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, Filorillo C, Bonavita V.
   PMID: 21553736 [PubMed - indexed for MEDLINE]

   De Simone R, Ranieri A, Cardillo G, Bonavita V.
   PMID: 21453557 [PubMed - indexed for MEDLINE]

4. Is idiopathic intracranial hypertension without papilledema a risk factor for migraine progression?
   De Simone R, Ranieri A, Filorillo C, Bito L, Bonavita V.
   PMID: 20702895 [PubMed - indexed for MEDLINE]

5. Bilateral transverse sinus stenosis and idiopathic intracranial hypertension without papilledema in chronic tension-type headache.
   PMID: 18458863 [PubMed - indexed for MEDLINE]

6. Idiopathic intracranial hypertension with and without papilledema in a consecutive series of patients with chronic migraine.
   Vieira DS, Masruha MR, Gonçalves AL, Zukerman E, Senne Soares CA, Naffah-Mazzacorati Md G, Peres MF.
   PMID: 18394415 [PubMed - indexed for MEDLINE]
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

An indication for stenting?

38. JAHRSTAGUNG DER GESELLSCHAFT FÜR NEUROPÄDIATRIE & 9. FORTBILDUNGSAKADEMIE
19. – 22. April 2012 | Münster

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>
<thead>
<tr>
<th>Procedures</th>
<th>Number of studies</th>
<th>Number of cases</th>
<th>Follow-up (months)</th>
<th>Clinical outcomes</th>
<th>Revision rate of procedure (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Headache improvement (range)</td>
<td></td>
</tr>
<tr>
<td>Optic nerve sheath fenestration</td>
<td>8</td>
<td>432</td>
<td>20</td>
<td>26% (13%-90%)</td>
<td>6.5% (5%-21%)</td>
</tr>
<tr>
<td>CSF diversion</td>
<td>7</td>
<td>209</td>
<td>39</td>
<td>55% (21%-92%)</td>
<td>NA</td>
</tr>
<tr>
<td>Cerebral sinus endovascular stent</td>
<td>9</td>
<td>174</td>
<td>23</td>
<td>77% (58%-100%)</td>
<td>44% (8%-85%)</td>
</tr>
</tbody>
</table>

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

**Abbreviations:** CSF, cerebrospinal fluid; NA, not applicable.
Beware of publication bias!
RISKS!!!

- Venous perforation
- 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
  ...

„Patients with PTCS often continue experiencing headache…despite the apparent normalization of their intracranial pressure“

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 unnecessary invasive treatment
Back to the case
Case con´t

• Still normal vision, no papilledema
• Headache still reported
• Follow-up LP, OP 28 cm H²O
• Interpreted as treatment resistance
• 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 resistance
• Clinical deterioration due to medication side effects
• Headache not PTCS related
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 program (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.“

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!

Headache as criteria for success?

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

BUT

Friedman DI, Rausch A. Neurology 2002; 58:1551-1553
Headache as criteria for success?

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BUT

Friedman DI, Rausch A. Neurology 2002; 58:1551-1553
Headache as criteria for success?

„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“

Friedman DI, Rausch A. Neurology 2002; 58:1551-1553
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.
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.
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 loss:
  - Optic nerve sheath decompression (ONSD)
  - High-dose IV steroids and acetazolamide
  - Lumboperitoneal shunt for failed ONSD or intractable headache
  - Bariatric surgery

Always critically question your diagnosis before even considering!
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.

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 necessarily indicate treatment resistance 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.

• „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 successfully as serial LP.