Pediatric Headache: exclude the malignant, manage the benign

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Disclosures:
none
Learning objectives

1. Recognizing malignant headaches

2. Headache syndromes
   A. Benign Intracranial Hypertension
   B. Migraine
   C. Uncommon headache syndromes
   D. Tension

3. Treatment:
   1. Acute: Outpt / ER / Inpt
   2. Prophylaxis
Headaches are common

• 4% of MD visits
• 24% of pediatric neurology office visits
• HA Prevalence in adolescence
  – Boys 54%
  – Girls 77%
• Migraine prevalence
  – Boys 3.8%
  – Girls 6.6%

Wober-Bingol Curr HA report 2013 17:341
Abu-Arefeh et al. BMJ. 1994;309:765-9
Moore and Shevell, JCN 2004 26:365-8
Malignant headache is uncommon

- Pediatric brain tumors = 3.3 / 100K / yr
- Pediatric aneurysm ~ 0.5 / 100k / yr
- Pediatric symptomatic AVM ~ 0.2 / 100K / yr
- Moyamoya 0.1 / 100K / year
- Total = 1 / 15 years of average pediatric practice

*NCI Fact Sheet 2011
Malignant headaches: features

Table 1 Red flags in the diagnosis of headache

<table>
<thead>
<tr>
<th>Red flag</th>
<th>Consider</th>
<th>Possible investigation(s)</th>
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<tbody>
<tr>
<td>Sudden-onset headache</td>
<td>Subarachnoid hemorrhage, bleed into a mass or AVM, mass lesion (especially posterior fossa)</td>
<td>Neuroimaging; lumbar puncture (after neuroimaging evaluation)</td>
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Malignant headaches: subarachnoid hemorrhage

- Very rare in children
- Sudden severe headache < 5 min to max
- CT + LP: xanthochromia by 6 hours (bilirubin)
  - MRI + SWI ~ CT (check)
- Aneurysm > AVM > Cavernoma
- Rebleeding:
  - 15% 1 day
  - 40% 1 month
  - Then 3% / year
- Triggered by HV or with deficits: moyamoya

Al-Shahi et al. *BMJ* 2006;33: 235-240
Malignant headaches: brain tumors

![Graph showing frequency of symptoms in children with brain tumors]

Figure 1 Relative frequency of symptoms in 200 children with brain tumors.

Figure 3 Box and whisker plot of relation between symptom interval and presenting symptom or sign in children with brain tumors (n = 175).

Malignant headaches: brain tumors

- NS: Severity, location, response to NSAIDs
- NS: Pattern of HA (migraine vs chronic)
- 1/3 Pedi brain tumors 1st Dx = migraine or tension HA

- Duration < 3 months
  - Increase < 3 months & no prior image
- Nocturnal or on waking
- Vomiting (frequent)
- Neurological deficit: vision ataxia school LOC Sz
- Papilledema

Malignant headache: triage guidelines

• First sudden / severe headache
  – Sudden = 5 minutes to maximum

• Worsening headache
  – 3 months

• Headache + other symptoms / signs
  – Fever, meningismus
  – VII palsy (Lyme)
  – Focal deficits

• Nocturnal / waking
Malignant Headache: exclusion

- Tiny masses don’t cause headache
- Fast MRI better than CT for tumor, not SAH
  - Radiation
  - Scan time ~ 2 minutes
  - Better resolution, especially posterior fossa re:
    - Medulloblastoma
    - Ependymoma
    - Brainstem glioma
Unusual headache syndromes I.

- Pediatric Cluster headache
  - Unilateral / periorbital
  - Thunderclap onset, severe
  - < 3 hours
  - Cluster frequency up to 8 / day x week(s)
  - Ipsilateral autonomic features:
    - Conjunctival injection, lacrimation, nasal congestion, rhinorrhea, lid edema, facial sweating, miosis, ptosis
  - $R_X$ sumatriptan, $O_2$
Unusual headache syndromes II.

• Hemicrania
  – Paroxysmal: < 30-minute attacks, multiple / day
  – Continuous: unilateral HA + autonomic features
  – Uniquely responsive to indomethacin

• Valsalva and exertional headache
  – Sudden onset, respond to indomethacin

• Trigeminal and hypoglossal neuralgia
  – Facial pain < 2 min, triggered by touch; tic douloureux
  – Check MRI for Arnold-Chiari, posterior fossa tumors
  – T<sub>x</sub> AEDs

Unusual headache syndromes III.

• Tolosa Hunt:
  – Unilateral orbital pain (esp with eye movement)
  – Unilateral CN III / IV / V / VI palsies
    • Cavernous sinus / orbital apex
  – Responds to steroids in 72 hours
  – MRI:
    • Cavernous sinus granuloma
    • 30% normal
  – Exclude: tumors, vasculitis, infection, sarcoid
  – 90% recover completely
Idiopathic Intracranial Hypertension

- AM HA ↑ with Valsalva / recumbency; floaters, rushing noises
- Papilledema
- Associations:
  - Obesity
  - Anemia
  - Acne $T_X$ (tetracylines, retinoic acid)
  - Steroid withdrawal
  - Growth hormone ($3/10,000 T_X$ yrs)
  - (Lyme)
  - (Venous sinus thrombosis: OCPs, smoking, CA, SLE)
- MRI negative
- ICP > 28 cm water, normal CSF
- Treatment:
  - LP
  - Acetazolamide, furosemide (or bumetanide)
  - LP shunt, optic nerve fenestration
- Visual field testing every 6 months til 21 yo

Standridge Pediatr Neurol 2010;43:377-90
Avery, Neurology 2011;76;1658
**Post LP headache**

- **Prevention: Non-cutting needle**
  - incidence 20 → 8%
  - duration 4 days → 1 day

- **Prevention: medical**
  - ACTH (Cosyntropin IV), epidural morphine, IV aminophylline
  - NS: caffeine, dexamethasone, indomethacin

- **Fluids, bedrest:** NS prevent, good to treat

- **Tx:**
  - Caffeine, gabapentin, hydrocortisone, theophylline
  - Blood patch OR .04-.18 (small studies)


- Migraine with or without aura
- Recurrent (>4) attacks lasting 1–72 h.
- Typical characteristics:
  - Unilateral pulsating moderate-or-severe
  - Bilateral more common in pediatrics
  - Aggravation by routine physical activity (allodynia)
  - Nausea, photophobia, and phonophobia.
- Not attributed to another disorder
- Useful non ICHD:
  - Relieved by sleep
  - Family history
- Genetics:
  - GWAS - low risks, clinic subjects
- Pathophysiology: not yet

Ferrari Lancet Neurol 2015, 14:65-80
J Neurosci:
Visual auras: monochromic (not colored), scintillating, fortification (not spherical), absolute
Complicated migraine: nonvisual neurological deficit

• Language, sensation, motor
• Precedes headache by 1 - 60 minutes
• Progression over *many minutes* along homunculus
  – differentiate from stroke
• Ophthalmoplegic migraine
  – III IV VI palsy + MRI enhancement
  – HA precedes ↓EOM; steroids help
  – vs. Tolosa-Hunt syndrome: granuloma
• Retinal migraine
  – Monocular aura
• Basilar or vestibular migraine
  – Vertigo, nystagmus
• Confusional: Alice in Wonderland
Hemiplegic migraine

- Prevalence 10 / 100,000
- Recurrent attacks of hemiplegia
- Onset over 5 minutes
- Duration < 24 hours
- Mono or hemiplegia but not bilateral
- Associated: fever, seizures, confusion, coma, intellectual disability, ataxia
- Interictal: epilepsy; episodic blindness
- DDX: basilar migraine, stroke, Todd’s paralysis, infxn
- Familial: CACNA1A, ATP1A2 (glial), and SCN1A (Dravet)
  - (v Alternating Hemiplegia of Childhood: ATP1A3 - neuronal)
- Tx acetazolamide, lamotrigine; triptans off-off-label

Russel Lancet Neurol. 2011;10:457-70
Ferrari Lancet Neurol 2015; 14: 65-80
Migraine: Differential D\textsubscript{x}

- **Occipital epilepsy**
  - + visual symptoms: colors, round, may be formed; shorter duration
  - EEG +
  - Respond to “migraine” AEDs (VPA, topiramate)

- **Panayiotopoulos Syndrome**
  - Prolonged (hours), variable LOC, very infrequent
  - Autonomic sx (syncope, sphincters, emesis)
  - May have + visual S\textsubscript{x} (formed)

- **Acute pathologies: D\textsubscript{x} MRI with diffusion**
  - **Stroke**
    - Onset rapid or stuttering vs. gradual onset of migrainous hemiplegia
    - Dissection: Pain often inferior, non-throbbing; Horner’s
  - **Hemorrhage (vs 1\textsuperscript{st} migraine)**
    - Deficits and reduced LOC more common
  - **Infections**
    - Acute; fever, meningismus
    - Sinusitis, empyema, abscess
  - **Neoplasia**
    - Hemorrhage, acute CSF block
Patent foramen ovale, migraine & stroke

- Migraine with aura: RR 2.2 for stroke
  - Still low (25 / 100k / year) even in young women
- PFO twice as common in migraine with aura
- Retrospective: Migraine resolves in 50% after PFO closure
- Prospective (MIST 2008): 5% resolution = sham
- PFO closure complication rate 3-8%
  - Tamponade, PE, Afib, hematoma

Migraine Equivalents

- Benign paroxysmal vertigo (40% of ME)
  - < 5 minutes, school-age, perceived function
- Cyclic vomiting (20% of ME)
  - 40% migraine, 40% +FHx, 30% anxiety / depression
  - 10 episodes / year, 4 days / episode
  - 70% respond to amitriptyline or propranolol
- Benign paroxysmal torticollis (10% of ME)
  - 2 months - 3 years old
  - + FHx migraine
  - Alternating, present during sleep, ± vomiting, irritable
  - Attack lasts < 1 week, recurs weeks – months
- Acephalgic migraine (Dx of exclusion!) (30% of ME)

Rosman, J Child Neurol. 2009 24:155
Lee, Eur J Gastroenterol Hepatol. 2012 24:1001
Chronic headaches

• Tension headache
  – Steady; afternoon / early evening
    • Waking component: rebound from yesterday’s Tx?
    • AM component: school (learning) problems?
  – Few related symptoms e.g. N/V
  – Strong relation to tension
    • Weekends
    • Summer
    • Shared custody

• Post concussive
• Transformed migraine
• Chronic daily headache: > 15 days / mo x 3 mo
Chronic Headache: natural history

1st 2 years: 50% / year resolution with any Tx

Wang et al. Neurology 2009 73:416
Chronic headache: post-concussive

- Longest-lasting postconcussive symptom
- HA as major complaint after injury:
  - 10% at 3 months
  - 75% at 6 months
  - 100% at 1 year
- Risk factors:
  - LOC
  - Pre-existing HA (50%)
- 50% migraine, 50% tension pattern

Chronic headache:
Early recognition of comorbidities

- Somatization: nonorganic $S_x$ for $> 1$ year
  - not malingering / factitious (conscious)
- Anxiety
  - Sleep / panic
- Depression
  - Appetite / weight / sleep / activity / anger
- Reasons to recognize:
  - Improve family’s confidence
  - Explain comorbid presentations:
    - Irritability
    - Fatigue
  - Suicide and self harm in major depressive disorder
  - Treatment may improve HA
- Plan = psychiatry, CBT, antidepressants
Chronic headache: Rebound = medication overuse

• ~ 20% of pediatric HA clinic patients
• IHC criteria:
  – 3 month duration
  – Tx ≥ 15 days / month
    • Ergots
    • Triptans
    • Opioids
    • NSAIDs (not asa)
    • (Butalbital / other barbiturates)
  – HA worsening
• Periodic, predictable exacerbation between doses
• Increasing refractoriness to $T_X$
• 75% respond to taper in 2 weeks; use neuroleptics or nasal DHE; ± steroids

J Saper CNS Drugs 2013
Acute headache management: Outpatient NSAIDs

- **Acute headache**
  - PRN Ibuprofen (suspension)
    - 7.5 – 10 mg / kg max 800 mg
  - Aspirin
    - 10 mg / kg or 975 mg Q6H
    - Combination T\textsubscript{\text{X}} (e.g. Excedrin asa/acet/caffeine)
    - Reyes – hold ASA for febrile URIs, < 12 yo
  - Frequency < 3 / week

- **Rebound headache**
  - Stop medication

Lewis Headache 2002; 120:390-2
Werder Headache 1984; 24:122-6
Acute headache management: Outpatient migraine RX

- Nasal inhalers and autoinjectors
  - Avoid reductions in GI absorption
  - Nasal sumatriptan = only effective acute TX > placebo

- PO & SL Triptans
  - Give prior to nausea; best for classic migraine
  - Avoid for complicated migraine (preceding deficit)
  - Sumatriptan PO: generic, covered by all insurances
    - Efficacy ~ NSAIDs in trials (but useful when NSAIDs fail)
    - Dose = 25 mg PO > 6 yo; repeat in 30 min PRN x1; max 3 days / week
  - Sublingual preps easier to take, but absorbed via GI
    - E.g. Maxalt MLT (rizatriptan) 5mg FDA approved for >= 6 yo

- Sumatriptan + naproxen (Trexima – vs single tx)

Treatment costs 2012

- Rizatriptan 5 mg SL = $39 / dose
- Sumatriptan 25 mg generic = $17 / dose
- Sumatriptan 4mg injectable = $54 / dose
- Zolmitriptan 10 mg nasal spray = $48 / dose
- Treximet = $31 / adult dose
  - 85 mg sumatriptan
  - 500 mg naproxen
- Compazine 10 mg $4
  - (use with Benadryl)
- Compare to ER visit!
Acute headache management: Emergency Room

Δ Pain - amount

2 hour Δ pain - any

Relative risk, vs placebo

Sumatriptan  Toradol  Neuroleptic

Acute Migraine Treatment in Emergency Settings
Comparative Effectiveness Review #84, 2012
Agency for Healthcare Research and Quality
**Acute HA management: inpatient prior to admission**

- **Criteria:**
  - No pain response, or unable to PO in ER (3 - 7%)
  - Medication Overuse Headache: Inpatient taper

- **Clarify objective endpoints**
  - Typical length of stay = 3 days
  - Improvement of pain not reliable
  - Sufficient improvement for outpt $T_X$ vs normalization
  - RN documentation of
    - Emesis
    - PO intake
    - Sleep

- **Discuss psychiatry consult:**
  - Somatization
  - Depression
  - Anxiety disorder
Acute HA management: inpatient pharmacology

1. Neuroleptic
   - e.g. Prochlorperazone (Compazine) 0.15 mg / kg IV Q8H
     • Diphenhydramine prevents dystonia, not akathisia
   - Alternatives = metaclopramide, ondansetron

2. IV Ketorolac 0.5 mg / kg Q6H (max 30 mg / dose, 80 mg /day)

1. IV DHE: 0.1 – 0.2 mg Q6H

2. IV VPA 15 mg / kg then 5 mg /kg Q8H

3. IV Solumedrol 1 mg / kg Q12H

*Headache* 2002 Jun;42(6):519
*Pediatric Annals* 2005 34:466
*Headache* 2013;53:491
$T_x$ of chronic post concussive headache

- 14 year old pts, 2:1 female: male
- 64% response may reflect natural Hx

Kuczynski et al. *DMCN* 2013 55:636
Initial headache management: what to do while waiting for regression back toward mean

- **Headache log**
  - iheadache app (free)

- **Diet**
  - (Diet log)
  - Hydration
  - Breakfast, lunch

- **SLEEP!**
  - Sleep latency
  - Number of AM rousals
  - Weekend sleep deficit
  - No electronics in bedroom

- **School:**
  - ADHD, LD in 25% HA pts
Headache prophylaxis

• Sufficient headache severity & frequency
  – Migraine or tension or daily headache
  – School absences >= 2 / month
    • Or sufficient to put advancement at risk
  – Interfering with QOL in other spheres
  – Headache diary

• Placebo effect 30 - 40%
  – HA frequency: regression toward mean

Nonmedical headache prophylaxis

- PT: trapezius & paracervical muscle stretching
- Biofeedback
  - Challenge = finding a practitioner
- Yoga
- Weight loss
- Acupuncture
  - Sustained > 9 months
  - > Medical prophylaxis, less side effects
  - Needle placement not important

Headache. 2007 47:654-61
Pain. 2007 128:111-27
Cochrane Database Syst Rev. 2009
Pediatric headache prophylaxis

- **cyproheptidinedine**
  - 2 - 4 mg QHS – TID (32 mg max)
  - Drowsiness
  - Weight gain

- **Effective in 1 study each:**
  - Propranolol 20 mg TID < 35kg, 40 mg TID > 35kg
    - Ineffective in 2 subsequent studies
  - Flunarizine, but not any US Ca channel blockers

- **Probably effective:**
  - Valproate
  - Topiramate (100 mg / day)
  - Gabapentin

- **Most trials too small to determine inefficacy**
Amitriptyline prophylaxis

- > 10 years: 10 mg PO QHS
  - 10% of antidepressant dosage
- < 10 years: start at 5 mg PO QHS
- EKG if
  - dosage > 0.25 mg / kg / day (used up to 1 mg /kg/day)
  - cardiac history
- 6 week therapeutic latency
- Drowsiness >> dry mouth
- Sleep effects may lead to rapid improvement
- Efficacy ~ 80% in small unblinded series
- Cardiac toxicity in overdose

Botulinum toxin treatment

- Chronic migraine (not effective in chronic tension HA or MOH)
  - >15 HA days / month
  - 8 migraine days / month
  - 3 month duration
- 31 injections in 7 head/neck muscles q 12 weeks

PREEMPT trial
Aurora SK
Headache 2011
Future migraine therapies

• Calcitonin gene-related peptide R: vasodilator, peripheral pain
  – antagonists for acute migraine: 66% vs 50% placebo
  – Telcagepant: ↑ LFTs
  – Development halted: Olcegepant, Rimegepant
  – Prevention? Monoclonal Ab: ALD403, LY2951742

• Sumatriptan
  – iontophoretic patch, OptiNose powder, Sumavel needleless transdermal

• DHE inhaler

• Not so far:
  – NMDA, GABA, TRPV1, NO, 5HT1D/B
  – Lasmiditan: 5HT1F agonist; more selective than triptans; 55% vs 45% placebo

• Stimulators
  – Occipital, Vagal – modest to no effects
  – Transcranial Cranial Magnetic stimulation – acute: maybe

Deiner Lancet Neurol 2015 14:1010-22