Learn the latest treatment strategies and multidisciplinary management options for patients with acute and chronic pain.
Interesting Cases in Headache Medicine

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PAIN MEDICINE FOR THE NON-PAIN SPECIALIST
FEBRUARY 16-18, 2017
Disclosures

• **Relevant financial disclosures**
  • None in association with this presentation.

• **FDA labels**
  • All treatments discussed are off label.
Objectives

• Share a series of interesting head/face pain cases

• Give emphasis during discussion to key diagnostic clues and therapeutic interventions
• 53 F developed intermittent right face pain a few days after routine dental cleaning.

• Pain described as intermittent, sudden onset, severe immediately, electric/shock-like. Starts pre-auricular and spreads to ipsilateral maxilla and upper lip/gum. Lasts 5 seconds but can come one after another and when very active can have residual mild dull pain for variable time but is not constant. No numbness face or mouth.

• Shock-like pain triggered by touching the face, eating, brushing teeth, wind blowing in face, or moving jaw.

• Carbamazepine effective but not tolerated.

• 53 F developed intermittent right face pain a few days after routine dental cleaning.

• Pain described as **intermittent, sudden onset, severe immediately, electric/shock-like**. Starts pre-auricular and spreads to ipsilateral maxilla and upper lip/gum. Lasts 5 **seconds** but can come one after another and when very active can have residual mild dull pain for variable time but is not constant. **No numbness** face or mouth.

• Shock-like pain **triggered** by touching the face, eating, brushing teeth, wind blowing in face, or moving jaw.

• **Carbamazepine effective** but not tolerated.

• Normal dental exam. Normal brain MRI elsewhere (not available). **Normal neuro exam**.
CN V just
Distal to root entry
Zone with slight
Indentation from
Adjacent vascular loop

Arterial loop
(likely from SCA)
Trigeminal neuralgia

- Initial treatment usually medical with single 1st line agent (carbamazepine or oxcarbazepine)
  - Baclofen also likely to be beneficial
  - Insufficient data: gabapentin, pregabalin, phenytoin
- Consider surgery if adequate trial of 1st line agent at maximum tolerable dose has failed
  - Microvascular decompression
  - Non-percutaneous destructive neurosurgical techniques (stereotactic radiosurgery)
  - Percutaneous destructive neurosurgical techniques (radiofrequency thermocoagulation, glycerol rhizolysis, and balloon compression)

Zarkzewska JM. *BMJ* 2015;350:h1238
• 72 M referred for trigeminal neuralgia. One year prior developed left upper lip numbness, gradually spreading to left maxilla. Two months before seen developed constant dull pain in same areas, gradually spreading to left retro-orbital region. Has superimposed “lightning strikes”: brief sharp pains left eye for seconds, multiple times a day, without triggers. No fever or weight loss.

• Outside normal head MRI and CTA. Negative dental evaluation.

• Neuro exam: decreased superficial pain sensation left V2. Symmetrically hypoactive deep tendon reflexes. Otherwise normal.
Most likely diagnosis?

A. Primary stabbing headache
B. Painful trigeminal neuropathy
C. Left V2 trigeminal neuralgia
D. Left maxillary sinusitis
E. “Atypical face pain” (now Persistent Idiopathic Face Pain)
F. Somatic symptom disorder
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• Neuro exam: **decreased superficial pain sensation left V2**. Symmetrically hypoactive deep tendon reflexes. Otherwise normal.
Trigeminal neuropathy

Trauma
- Accidental, surgical, dental (especially at 3rd molar), chemical (glycerol rhizotomy), radiation

Inflammatory/autoimmune
- Undifferentiated and mixed connective tissue disease
- Progressive systemic scleroderma, Sjögren’s syndrome, sarcoidosis, multiple sclerosis

Vascular
- Pontomedullary ischemia or hemorrhage (CNS mimic)
- Vascular malformation

Neoplastic
- Intra- or extra-cranial compression (meningioma, trigeminal or vestibular schwannoma, nasopharyngeal carcinoma)
- Perineural spread (adenoid cystic carcinoma, squamous cell carcinoma, lymphoma)
- Metastasis (breast and lung carcinoma, melanoma)
- Carcinomatous meningitis (breast and lung carcinoma, melanoma, lymphoma)

Infectious
- Leprosy, viruses (varicella zoster virus, herpes simplex virus), Lyme disease, syphilis, fungi (actinomycosis)

Degenerative
- Kennedy’s disease

Toxic-metabolic
- Stilbamidine, trichloroethylene, oxaliplatin, diabetes mellitus

Congenital
- Congenital trigeminal anesthesia with or without Goldenhar-Gorlin syndrome or Möbius syndrome
- Skull base anomalies

Idiopathic trigeminal neuropathy

Other
- Amyloidosis, pseudotumor cerebri
Patient presenting with facial/intraoral pain, numbness and/or masticatory weakness

Clinical history and physical examination

Electrophysiologic confirmation if no clinical deficit

Normal study

Repeat clinical evaluation in 6 months

Trigeminal sensory or motor deficit

History of trauma or malignancy

CT of the skull base +/- MRI of the head/face

No history of trauma or malignancy

MRI of the head +/- cervical spine + laboratory evaluation, including connective tissue/nuclear autoantibodies

Lip biopsy in seronegative patients with suspicion for Sjögren’s

Normal diagnostic evaluation

Ongoing surveillance for malignancy and connective tissue disease

Abnormally large and asymmetrically enhancing V2

From: David F. Black, MD
Abnormally large and asymmetrically enhancing V2

From: David F. Black, MD
Left V2- abnormal enhancement continues into the pterygopalatine Fossa where.
See different sizes of V2 within the right and left foramen rotundum

From: David F. Black, MD
Contiguous
Soft tissue mass
in the left pterygopalatine fossa
Enhancing soft Tissue mass
Left sided soft tissue/soft palate mass
Possibly representing the primary tumor

Associated osseus destruction of hard palate on CT
FDG avid biopsy-proven adenoid cystic carcinoma of the left palate with perineural extension without evidence of distant metastatic disease.
Painful Trigeminal Neuropathy (“Anesthesia dolorosa”)

• Pain treatment strategies based on pain type

• **Neuropathic**-often burning, more constant, frequently accompanied by allodynia, dysesthesia, and hyperesthesia
  • amitriptyline
  • gabapentin
  • duloxetine
  • pregabalin

• **Neuralgiform**-brief, shock-like, often triggered
  • As in trigeminal neuralgia

New widespread metastatic disease including multiple osteolytic skeletal metastases, two hepatic metastases, and a pulmonary metastasis.
46 M, previously healthy. Working outside had the sudden onset of severe headache, neck pain, nausea and vomiting.
Thunderclap Headache (TCH) = a severe headache of instantaneous onset (1 min at most)

• Acutely, evaluate with urgent unenhanced head CT followed by lumbar puncture if CT normal (looking for xanthochromia)

• Subarachnoid hemorrhage (SAH)
  • One of most common causes
  • Found in 11-25% of patients presenting with TCH

• Multiple other causes

Ducros A. BMJ 2012;345:e8557
21 F, history of infrequent tension-type headaches. Developed a single TCH at vertex and occiput. Normal neuro exam.

- Axial FLAIR without contrast shows fluid–fluid level consistent with layering of blood by-products within a pituitary cystic lesion suspicious for an adenoma.

35 M, 2 weeks after fall snowboarding developed transient sudden onset severe bilateral temporal headache. Followed by daily headache, severe standing, gone when recumbent. Head CT and LP normal. No opening pressure measured. Neuro exam normal.
• 31 F, history of infrequent tension-type headache, seen for different headaches.

• Reported that about a year prior to visit, throughout 7 months had recurrent TCH 2/month. Negative brain MRI/A/V, Neck MRA. These resolved when got pregnant and later delivered child in setting of preeclampsia.

• Since delivery 2 weeks before seen, having intermittent, mild, bilateral temporal, featureless headaches. But also every 1-2 days a TCH, bilateral temporal, with photo/phonophobia, and occasional nausea. Tapering off labetalol, just had negative head CT/CTA/CTV and neck CTA. TCH getting less frequent. Normal neuro exam. BP 140s/80s.
What would you do next?

A. Lumbar puncture for routine studies and opening CSF pressure
B. Cerebral angiogram
C. ESR, CRP, ANA, ENA, rheumatoid factor
D. Urine metanephrines/catecholamines
E. Escalate in antihypertensives
F. MRI/A/V head and MRA neck
G. Other
Multiple TCHs return.......
<table>
<thead>
<tr>
<th></th>
<th>Value</th>
<th>Unit</th>
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<tbody>
<tr>
<td>Collectn Durat.</td>
<td>24</td>
<td>h</td>
</tr>
<tr>
<td>Urine Volume</td>
<td>3178</td>
<td>mL</td>
</tr>
<tr>
<td>Norepinephrine</td>
<td>200</td>
<td>mcg/24 h</td>
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<tr>
<td>Epinephrine</td>
<td>118</td>
<td>mcg/24 h</td>
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<tr>
<td>Dopamine.</td>
<td>203</td>
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<tr>
<td>Metanephrine</td>
<td>2015</td>
<td>mcg/24 h</td>
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<tr>
<td>Normetanephrine</td>
<td>1602</td>
<td>mcg/24 h</td>
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<tr>
<td>Total Metanephrine</td>
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<td>mcg/24 h</td>
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Head MRA-focal zones of mild narrowing

Supraclinoid left internal carotid artery

Proximal A2 segments bilaterally
Head MRA-focal zones of mild narrowing

Proximal right M1 segment

Right P1 and P2 segments
3.6 x 3.5 x 3.8 cm complex solid and cystic mass
Over the next few days……

- Labetalol changed to verapamil
- Resistant hypertension
  - Phenoxybenzamine (adrenergic antagonist specifically blocking alpha receptors) added
- Still TCH intermittently
- To urgent care with chest pain and tachycardia
  - Unclear if cardiac ischemia, propranolol added by cardiologist
Reversible Cerebral Vasoconstrictive Syndrome (RCVS)

- Likely accounts for most “benign TCHs”
- Characterized by severe headaches, and diffuse segmental cerebral arterial vasoconstriction that resolves within 3 months
- Half occur during postpartum or after exposure to serotoninergic agents, adrenergic substances, or cannabis.
- Most have multiple TCH that recur every day or so for a few days to 4 weeks. Sexual activity, emotion, exertion, coughing, straining, urination, bathing, and showering are common triggers.

Ducros A. *BMJ* 2012;345:e8557
Reversible Cerebral Vasoconstrictive Syndrome (RCVS)

- 1 in 4 patients has a convexity subarachnoid hemorrhage—usually mild
- Hemorrhagic and ischemic stroke can occur
- MRA, CTA, cerebral angiography may be normal up to 6 or 7 days after headache onset
- There is no evidence-based treatment
- All vasoactive substances should be removed and avoided even after vasoconstriction resolves
- Nimodipine mostly used, despite scarce evidence
- Outcome usually good

Ducros A. *BMJ* 2012;345:e8557
Thunderclap Headache (TCH)

**Common causes**
- Subarachnoid hemorrhage (SAH)
- Reversible Cerebral vasoconstriction syndrome (RCVS)
  - Suspect if multiple recurrent TCH

**Uncommon causes**
- Cerebral venous sinus thrombosis
- Cervical arterial dissection
- Ischemic Stroke
- 3rd ventricle colloid cyst
- Pheochromocytoma
- Acute Sinusitis
- PRES
- Spontaneous CSF leak
- Pituitary apoplexy
- Others (see references)

Ducros A. *BMJ* 2012;345:e8557
Heo YE. *Cephalalgia* 2009;29:388-90.
Thunderclap Headache (TCH)

Key points

• Any TCH must be considered secondary
  • Still debatable if primary TCH exists
• Should always be evaluated urgently
• Absence of associated symptoms and presence of normal neuro exam does not exclude serious cause

Ducros A. BMJ 2012;345:e8557
The 35 M, snowboarder who had a TCH followed by orthostatic headache
Which one is an acquired Chiari from spontaneous CSF leak?

25 M with cough induced headache
23 F with cough induced headache
• 24 F, history of infrequent tension-type headache since 14. For last 5 years, constant and daily headache, slightly worse if exercising or laughing. Briefly worse upon standing but laying down does not improve them. Normal MRI and CTA head with contrast. Normal neurologic exam.

• Trial with amitriptyline off hydrocodone did not help.
“IMPRESSION: Prominent ventral extradural CSF collection extends from C3 into the thoracic spinal canal. Interestingly, there is no intracranial stigmata of CSF hypotension.”
Diagnostic Studies

Radioisotope Cisternography (RICG)

- May also help answer whether leak exists in doubtful cases
- Uncommonly finds leak site

Images from: Kranz PG. AJR 2016;206:8-19
Diagnostic Studies
Myelographic Techniques

- Best tests to show leak site
- CT myelogram (CTM) often 1st
  - fast leaks
  - slow leaks
  - no leak
- Other techniques
  - Dynamic/ultrafast CTM
  - Digital subtraction
  - Conventional MRI with heavy T2
  - MR myelography with intrathecal gadolinium

Fig. 5B — 56-year-old man with low-flow CSF leak.
B, Coronal CTM image shows CSF leak (arrowhead) in neural foramen at same level, without significant epidural pooling of fluid in spinal canal.

Image from: Kranz PG. AJR 2016;206:8-19
Treatment

• No guideline available
• Approach not straightforward and varies
• Some may improve without therapy

• 1st line
  • Caffeine, rest, hydration

• 2nd line. Epidural blood patch
  • Lumbar if site unknown
  • Targeted if site known or suspected

• 3rd line
  • Epidural blood patch with fibrin glue
  • Multilevel epidural blood patch
  • Surgery-if leak site identified
• 29 F, history of infrequent left or right hemicranial migraine, 1 month ago developed new near daily bilateral occipital headache and intermittent “blurred vision” and “whooshing noises”. This followed a 50 pound weight gain in the 2 previous months. Routine eye exam by MCHS ophthalmologist noted papilledema, called for guidance on next steps.
Partial empty sella

Bilateral transverse sinuses are attenuated most marked at the junction with the sigmoid sinuses.

Mild prominence of CSF around the optic nerves, “string sign”
• Lumbar puncture CSF opening pressure 34 cmH$_2$O

• Normal CSF formula
  • Protein 25 mg/dL
  • Glucose 66 mg/dL
  • 6 erythrocytes
  • 1 total nucleated cell count
  • Clear appearance

• Headache transiently improved after lumbar puncture.

• Idiopathic intracranial hypertension (IIH) confirmed
# Idiopathic Intracranial Hypertension (IIH)

<table>
<thead>
<tr>
<th>Table</th>
<th>Idiopathic Intracranial Hypertension Treatment Trial Modified Dandy Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Signs and symptoms of increased intracranial pressure</td>
</tr>
<tr>
<td>2.</td>
<td>Absence of localizing findings on neurologic examination</td>
</tr>
<tr>
<td>3.</td>
<td>Absence of deformity, displacement, or obstruction of the ventricular system and otherwise normal neurodiagnostic studies, except for evidence of increased CSF pressure (&gt;200 mm water); abnormal neuroimaging except for empty sella turcica, optic nerve sheath with filled out CSF spaces, and smooth-walled non-flow-related venous sinus stenosis or collapse should lead to another diagnosis</td>
</tr>
<tr>
<td>4.</td>
<td>Awake and alert</td>
</tr>
<tr>
<td>5.</td>
<td>No other cause of increased intracranial pressure present</td>
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</tbody>
</table>

For CSF opening pressure of 200-250 mm water required at least one of the following:

- Pulse synchronous tinnitus
- VI palsy
- Frisen grade II papilledema
- Echography for drusen-negative and no other disc anomalies mimicking disc edema present
- Magnetic resonance venography with lateral sinus collapse/stenosis preferably using auto-triggered elliptic centric-ordered technique
- Partially empty sella on coronal or sagittal views and optic nerve sheaths with filled out CSF spaces next to the globe on T2-weighted axial scans
Frequent overdiagnosis of IIH

• 34/86 (39.5%) seen for IIH in neuro-ophthalmology tertiary center did not have it

• Most common reasons for overdiagnosis
  • Inability to perform accurate ocular fundus examination
  • Intuitive presumption that obese young women with headache must have IIH (and difficulty deviating from this suspected diagnosis)

• Less common reasons for overdiagnosis
  • Isolated radiologic findings
  • Moderately elevated CSF opening pressure in the absence of papilledema or CNVI palsies
Normal disc

Papilledema in 22 year-old female with IIH

1. From James A. Garrity, MD
2. From Jacqueline A. Leavitt, MD
Pseudopapilledema

- Exposed drusen
- Buried drusen
- Congenital blurred disc
- Tilted disc
- Structurally full disc

- Presence of spontaneous venous pulsations favors congenital disc anomaly
- Absence of spontaneous venous pulsations not helpful
• IIH managed with acetazolamide 500mg BID and weight loss. Papilledema gradually resolved and vision fields were normal even off acetazolamide. She, however, continues to have daily headache, using daily ________, ibuprofen, or tramadol. She also is on gabapentin 300mg TID.

• What should be the next step in headache management?
What should be the next step in headache management?

A. Lumboperitoneal (LP) CSF shunt
B. Optic Nerve Sheath Fenestration
C. Venous Sinus Stenting
D. Ventriculoperitoneal (VP) CSF shunt
E. None of the above
IIH
Surgical procedures

• Indications
  • Progressive visual loss despite maximal tolerated medical therapy
  • Severe visual loss at presentation

• Options
  • Optic Nerve Sheath Fenestration (ONSF)
  • CSF Shunting
  • Venous Sinus Stenting (VSS)
• 68 F seen for left face pain

• At age 55 had left V2 trigeminal neuralgia. Did not tolerate medications so Gasserian ganglionectomy performed. Pain resolved and had expected left hemifacial anesthesia. Days later, developed left hemifacial mild–moderate, constant, ‘difficult to describe’ pain and severe itching. Over the next years, experienced left forehead and periorbital erythematous lesions and a false sense of airflow obstruction in left nasal airway. She frequently manipulated attempting to relieve this ‘blockage’, which led to nasal septum erosion. By age 67 started to feel intermittent, brief (seconds), painful ‘bug bites’ in the left nasolabial fold, intranasal cavity and periorbital region. If she pressed with her fingers, the intensity would diminish. A constant ocular foreign body sensation and severe neuralgic pain eventually developed too. Opiates, topiramate, pregabalin, nortriptyline, amitriptyline, clonazepam and oxcarbazepine failed. Gabapentin 2400 mg/day gave partial relief. On examination, she had left hemifacial anesthesia and absent corneal reflex.
Her inferior nasal septum and complete nose columella were absent. Multiple skin ulcerations and annular erosions were seen in her left scalp, lateral nose and medial eyebrow. The largest ulceration was at the left nasal ala.
Trigeminal Trophic Syndrome

- Rare result of lesion to trigeminal nerve or its nuclei
- Classical clinical manifestations are those of painful trigeminal neuropathy, persistent/recurrent facial ulcerations and neuropathic itch.
- Skin lesions commonly involve the ala nasi but other trigeminal distributions can be affected less commonly
- Latency from onset days to years
- Patients may be unaware of self-manipulation which causes or worsen skin lesions
- Must rule out other dermatologic disorders
- Management is multidisciplinary.

Garza I. Cephalalgia 2008;28(9):980-5
• 62 M with 2 year history of headaches, intermittent, precipitated by cough, sneeze, strain. Cough the worst. Moderate-severe, peak intensity immediately, lasting 1 second or so at a time. LP normal opening pressure, normal CSF formula. Brain MRI/A/V, heat CT all normal. Multiple medications failed but indomethacin 50mg BID helps the most. Normal neurologic exam.

• Diagnosed with primary cough headache.
• T-spine MRI- tiny nerve root cyst arises from the exiting T10 nerve root on the right.

• CT myelogram- extrathecal contrast right T12 - L1 neural foramen suspicious for CSF leak. Could not confirm leak.

• Epidural blood patches
  • T12-L1 no benefit
  • T12-L1 blood/fibrin glue no benefit
  • L2-3 x 3 transient relief for weeks
  • Other, multiple. Variable results
CSF to paraspinal vein fistula

• Can explain some cases “without leak” on myelography

(B) Axial intrathecal gadolinium-enhanced T1 magnetic resonance myelography image in case 2 shows contrast in the right T12-L1 foramen (arrow) draining into paravertebral veins (dotted arrows).

Image from: Kumar N. Neurology 2016;86:2310-2312
• 53 F seen for bilateral face pain.

• 5 months prior developed intermittent left upper deep gum pain. Starts with 3-5 seconds of “tingle” followed by sudden onset, severe, sharp, stabbing pain towards left side of nose with peak intensity immediately. Happens 2-25 times a day. Doesn’t wake her up. No obvious triggers except perhaps drinking hot soup or breathing cold air. About 2-3 months after all started developed identical symptoms on right side.

• No fever or weight loss. Denied prior face surgery or trauma. On low dose gabapentin and amitriptyline without improvement.

• Multiple specialties without cause found. Normal neuro exam, normal MRI head/face.
Midpupillary line location of the supraorbital, infraorbital, and mental nerves
Questions & Discussion