Cluster Headache and Chronic Paroxysmal Hemicrania

Old synonyms - Raeder syndrome, Horton cephalalgia, histamine cephalalgia, sphenopalatine neuralgia.

PATHOPHYSIOLOGY

- not fully determined.

Theories

A) circadian pacemaker alterations (due to hypothalamic dysfunction).
   • attacks increase following beginning and end of daylight savings time.
   • there is loss of circadian rhythm (for blood pressure, temperature, hormones - prolactin, melatonin, cortisol, beta endorphins).
   • recently, functional neuroimaging have identified posterior hypothalamic grey matter as key area for basic defect.
   • pain is generated at PERICAROTID / CAVERNOUS SINUS COMPLEX.

B) neurogenic inflammation

C) carotid body chemoreceptor dysfunction

D) central parasympathetic & sympathetic imbalance

E) increased responsiveness to histamine.

EPIDEMIOLOGY

PREVALENCE 0.01-1.5% (≈ 0.3%)
- higher in men (male : female ≈ 6-8:1) and in blacks.
- family history is rare.

ONSET - any age (generally - in late twenties).
- ≈ 10% patients develop cluster in their sixties.
Peptic ulcer disease is only known associated medical disorder.
  - strong associations with smoking, alcohol use, and previous head / face trauma.
  - certain personality and physical characteristics have been associated with cluster headache (e.g. tall and rugged-looking body, leonine facial appearance, multifurrowed and thickened skin with prominent folds, broad chin, vertical forehead creases, nasal telangiectasias).

**CLINICAL FEATURES**

A. **EPISODIC** cluster headache - remission periods lasting ≥ 14 days (usually 6 months ÷ 2 years).
B. **CHRONIC** cluster headache (≈ 10%) - no remissions or remissions last < 14 days; headache is occurring for > 1 year.

Either type may transform into other! (in 4-13% patients, episodic CH transforms into chronic CH)

Multiple episodes of headache:
1) pain begins without warning.
2) severe – pain rapidly increases (within 5-15 minutes) to excruciating levels.
3) short-lived – if left untreated, attacks usually last 80-90 minutes (15-180 minutes).
4) strictly unilateral*, periorbital (orbital / supraorbital / temporal) – distribution of 1st or 2nd divisions of trigeminal nerve. *usually affects same side in subsequent months
5) may radiate to forehead, temples, jaws, nostrils, ears, neck, or shoulder.
6) pain is deep, constant (not throbbing), boring, piercing, burning, explosive.
7) at least one symptom of unilateral (ipsilateral) autonomic dysfunction:
   a) conjunctival injection (“red eye”)
   b) lacrimation
   c) miosis
   d) ptosis
   e) eyelid edema
   f) nasal congestion
   g) rhinorrhea
   h) facial sweating
   – in variant of cluster headache, full Horner’s syndrome can be seen.
8) patients feel agitated or restless with need to isolate themselves and move around (most sufferers assume upright position to relieve discomfort!); patients have been known to become violent or bang their heads against wall.
9) GI symptoms uncommon.

Attack frequency varies (8 attacks per day ÷ 1 attack every 2 days).

**PERIODICITY is hallmark of cluster headache!** - attributed to hypothalamic (particularly suprachiasmatic nuclei) hormonal influences

- attacks often occur at same time each day ("alarm clock headache"); onset is nocturnal in 50% cases (may awaken patients from sleep).
- attacks occur in CLUSTER periods that last 1 week ÷ 1 year (usually 1-3 months) separated by periods of headache-free remission.
- cluster episodes often appear at characteristic times of year (particularly around vernal and autumnal equinoxes).
- attacks may cease during pregnancy (but attacks seldom correlate with menses).
DIFFERENTIAL DIAGNOSIS

1. Secondary cluster-like headache (due to structural lesions near cavernous sinuses).
2. Chronic paroxysmal hemicrania
3. Migraine
4. Trigeminal neuralgia
5. Temporal arteritis
6. Raeder paratrigeminal syndrome - pain is constant (no distinct attacks)
7. Tolosa-Hunt syndrome
8. Sinusitis
9. Glaucoma

EVALUATION

- strictly clinical diagnosis - careful history is all that is needed.
- MRI is justified only in atypical cases or abnormal neurological examination (except when abnormality is Horner's syndrome!).

ABORTIVE THERAPY

Oral preparations are not recommended - absorbed too slowly.

1. Inhaled high-flow **OXYGEN** (12 L/min 100% by mask for full 15 minutes following headache onset) - treatment of first choice (70-80% effective); postulated mechanism – O₂ is vasoconstrictor and increases serotonin synthesis.
2. Parenteral **SUMATRIPTAN** 6 mg s/c
3. Parenteral **DHE**
4. Topical (intranasal) **local anesthetics** (2-4% LIDOCAINE) - to most caudal aspect of inferior nasal turbinate (patient in supine position) - can deliver **sphenopalatine ganglion block** - remarkably effective!
5. Parenteral **narcotics**
6. **Sphenopalatine ganglion stimulation** with implantable system
   - at 15 minutes following stimulation, 55% of treatment group had pain relief compared with 6% in sham treatment group (P < .0001); pain relief was maintained to 90 minutes (50% pain relief for treatment group vs 13% for sham). [http://www.medscape.com/viewarticle/807281](http://www.medscape.com/viewarticle/807281)

PREVENTIVE THERAPY

- required for almost all patients!:
  - attacks are too short and too severe to treat with only abortive medication;
  - prophylactic treatment is most effective among all primary headache disorders! (except **chronic CH** - notoriously resistant to standard prophylactic agents)
- avoid **alcohol** and **nitroglycerin**.
  Alcohol provokes attacks in 70% patients but has no effect when cluster bout remits (“on-off vulnerability to alcohol” - pathognomonic of cluster headache!!!).
- **Peripheral Nerve Blocks** see p. S24 >>

In order of preference (begin early in cluster period and continue until headache-free for at least 2 weeks):

1) **ERGOTAMINE** (orally 2 mg × 2/d) - classic treatment - most effective when given 1-2 hours before expected attack (for patients with single nocturnal episode, 1 mg suppository at bedtime may be all that is necessary)
   - Educate regarding early symptoms of ergotism (limb claudication) when ergotamine is used daily (H: weekly limit of 14 mg).
2) **VERAPAMIL**
3) METHYSERGIDE (no longer available in USA)
4) LITHIUM (300 mg bid or tid titrated according to serum lithium level) – esp. useful in chronic cluster headache!
5) PREDNISONE (10-day course, beginning at 60 mg/d for 7 days and rapidly tapering); long-term use not recommended.
6) DIVALPROEX
7) CAPSAICIN drops to ipsilateral nostril - induces substance P release (principal mediator of pain); after repeated applications, depletes neuron of substance P.
8) INDOMETHACIN

N.B. PROPRANOLOL and AMITRIPTYLINE are largely ineffective!
- new approach: in refractory CCH + low risk for anticoagulant-related hemorrhagic complications, low-intensity anticoagulation with WARFARIN (to achieve INR 1.5–1.9) is associated with significantly higher incidence of remission lasting ≥ 4 weeks, as well as significantly less impact of headache on patients' quality of life as compared to placebo.

Surgical therapy:
1) new promising approach - DBS into posterior inferior hypothalamus.
2) surgical intervention (for strictly unilateral chronic cluster) - ablation of sensory input of trigeminal nerve and autonomic pathways (e.g. percutaneous RF trigeminal gangliorhizolysis, rhizotomy) - effective in 75%.
3) SRS – methodology as for trigeminal neuralgia but results not as good (no sustained pain relief beyond 2 years F/U); some authors tried to add 8 mm shot to sphenopalatine ganglion (Pollock BE & Kondziolka D. J Neurosurg 87:450-453, 1997).

PROGNOSIS
- chronic headache that may last for patient’s life.
- drug therapy may convert from chronic to episodic cluster.
- prolonged, spontaneous remissions have been described in up to 12% patients.

CHRONIC PAROXYSMAL HEMICRANIA
- as CLUSTER HEADACHE (2% prevalence of cluster headache) with following differences:
  - dramatic response to INDOMETHACIN – diagnostic criterion!
  - women > men (7:1)
  - shorter headache duration ≈ 13 (5-30) minutes.
  - headaches occur ≈ 5-11 times/day.
  - 10% attacks may be triggered by flexing / rotating / pressing upper portion of neck.
  - typically, no remissions! (rarely, episodic paroxysmal hemicrania with remissions lasting weeks or months).
  - MRI / CT should be undertaken to exclude symptomatic causes.
  - treatment of choice - INDOMETHACIN (up to 200 mg/d); aspirin may also be beneficial, but relief is usually not complete.
  - prognosis - may last indefinitely (with frequently reduced indomethacin requirement); spontaneous cures have been described.
HEMICRANIA CONTINUA

- exclusively 1-sided, constant moderate ÷ severe headache exquisitely responsive to INDOMETHACIN.

BIBLIOGRAPHY see p. S24 >>