Hemicrania Continua: A Question and Answer Review

A headache specialist explores the incidence, diagnosis, and treatment of this frequently misdiagnosed headache type.

BY RANDOLPH W. EVANS, MD

There are four primary types of chronic daily headache with a duration of four hours or more daily which include hemicrania continua (HC), chronic migraine, chronic tension-type headache, and new daily persistent headache. Probably first described as a cluster variant responsive to indomethacin in 1981,[1] the term "HC" was proposed in 1984.[2] Since then, more than 100 cases of HC have been reported.[3]

WHAT ARE THE DIAGNOSTIC CRITERIA FOR HC? WHAT ARE THE SYMPTOMS?

The International Classification of Headache Disorders 2nd edition diagnostic criteria[4] are as follows:

- Headache for more than three months fulfilling criteria B through D
- All of the following characteristics:
  - Unilateral pain without side-shift
  - Daily and continuous, without pain-free periods
  - Moderate intensity, but with exacerbations of severe pain
- At least one of the following autonomic features occurs during exacerbations and ipsilateral to the side of pain:
  - Conjunctival injection and/or lacrimation
  - Nasal congestion and/or rhinorrhea
  - Ptosis and/or miosiz
- Complete response to therapeutic doses of indomethacin
- Not attributed to another disorder.

> "HC is more common in females than males (1.6:1). The onset is often during the third decade of life, with a range from the first to seventh decade."

HC is a unilateral headache with varying intensity that is rarely bilateral or alternates sides.[5] In Cittadini and Goadsby's study of 39 patients, the pain was reported in the following locations: temporal, 82 percent; orbital, 67 percent; frontal, 64 percent; retro-orbital, 59 percent; occipital and parietal, 54 percent; vertex and periorbital, 51 percent; neck, 33 percent; maxillary and ear, 30 percent; upper teeth, 20 percent; shoulder, 18 percent; nose, 15 percent; jaw, 15 percent; eyebrow and lower teeth, 10 percent; retro-auricular area, eight percent; and upper and lower gum, two percent.[5]

The pain was described by the following percentages: throbbing, 69 percent; sharp, 43 percent; constant/continuous, 41 percent; pressure, 30 percent; dull, 26 percent; burning sensation, 15 percent; aching, 15 percent; stabbing, 13 percent; boring, 10 percent. Exacerbations of pain

could occur spontaneously or after triggers by the following percentages: stress, 51 percent; alcohol, 38 percent; irregular sleep, 38 percent; bright lights, 36 percent; exercise, 31 percent; warm environment, 28 percent; skipping meal, 23 percent; strong smell, 15 percent; coughing, 15 percent; weather change, 13 percent; tiredness, 13 percent; period, 10 percent. Fifty three percent of patients reported exacerbations during the nighttime. During severe pain, 69 percent of patients were agitated or restless or both, and 28 percent were verbally aggressive. Twenty three percent of patients had abnormal findings on neurological examination, which were mainly ipsilateral sensory changes such as decreased sensation of the face.

HC can be labeled chronic when daily and continuous without pain-free periods for a minimum of one year and episodic when there are pain-free intervals of at least a day without treatment. In one series, 82 percent of cases had chronic (unremitting) HC which was chronic from the onset in 69 percent.[5] Evolution from the episodic form occurred in 28 percent after a latency of 7.9 years (range of two weeks to 26 years). Some of the patients with the initial episodic form had headaches that were not daily initially and one patient had about 10 headache days per month. Fifteen percent of patients had the episodic form, which was episodic from the onset in 33 percent and evolved from the chronic form in 66 percent

Seventy-five percent have exacerbations of severe throbbing or stabbing pain lasting 20 minutesto several days which can be associated with photophobia (59 percent), phonophobia (59 percent) [often unilateral], nausea (53 percent), and vomiting (24 percent). A visual aura can rarely occur.[6] Exacerbations can last from 20 minutes to several days with pain awakening one-third of patients. Cranial autonomic features are present in up to 75 percent with tearing and then conjunctival injection the most common. Primary stabbing headache or jabs and jolts are reported by 41 percent especially in exacerbations. Some report a feeling of sand in the eye.

HC is often misdiagnosed. In a study of 25 patients with HC seen at a headache center, 85 percent were assessed by physicians within six months of the onset of symptoms, but the mean latency of diagnosis was five years, with the average number of physicians seen before the headache was correctly diagnosed at 4.6.[7]

WHAT IS THE EPIDEMIOLOGY AND PATHOPHYSIOLOGY?

HC is a rare disorder that may have a prevalence of up to one percent of the population.[8] HC is more common in females than males (1.6:1). The onset is often during the third decade of life, with a range from the first to seventh decade.[9]

The pathophysiology of HC is unknown. However, a PET study of seven patients with HC showed activation of the contralateral posterior hypothalamus and ipsilateral rostral pons during baseline pain which was blocked by administration of intramuscular indomethacin.[10]

WHAT IS THE DIFFERENTIAL DIAGNOSIS?

Secondary causes reported include the following: mesenchymal tumor of the sphenoid, lung malignancy, HIV (causal association unclear), C7 root irritation reported to aggravate, left lateral medullary infarction with left vertebral artery occlusion on MRI and MR angiography (head pain contralateral to infarction), internal carotid artery dissection, unruptured cavernous internal carotid artery aneurysm, prolactinoma (headache exacerbation with dopamine agonists), venous malformation of the right masseter; sphenoid sinusitis, osteoid osteoma of ethmoid sinus, post-traumatic, and cerebellopontine angle epidermoid.[11]

Other chronic daily headaches of long duration can be unilateral, including chronic migraine, tension-type, and new daily persistent headache. An indomethacin trial should be considered in all patients with strictly unilateral daily headaches to exclude HC since the clinical features can be the same. The issue of transformed migraine is not entirely clear but if the initial frequency before becoming daily was less than 10 days per month, then the odds are great that the patient has chronic migraine. If 10 days or greater per month, then the patient may have evolved from episodic to chronic HC and a trial of indomethacin is indicated.

Trigeminal autonomic cephalalgias are also unilateral but of shorter duration. Chronic paroxysmal hemicrania has a duration of two to 45 minutes with a frequency of attacks of five or more per day and associated cranial autonomic symptoms. Cluster headache has a duration of 30 to 180 minutes with up to eight attacks per day.

WHAT IS THE TREATMENT?

Absolute response with headache freedom has been reported on indomethacin 50-300mg per day in divided doses, usually 150mg/d or less. One regimen is the following: 25mg three times a day for five to seven days, subsequently increasing, if ineffective, to 50mg three times a day for a further five to seven days and then, if ineffective, to 75mg three times per day for two weeks (Peter Goadsby, personal communication). There are rare reports of response at 300mg/d. Side effects occur in 75 percent of patients with this regimen.[5] This extended titration schedule has been used so the occasional patient with HC who is a slow responder will not be missed. However, most patients may respond quickly. In a prospective study of 12 patients who discontinued indomethacin until HC recurred, complete pain relief was

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B) All of the following characteristics:
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- Moderate intensity, but with exacerbations of severe pain

C) At least one of the following autonomic features occurs during exacerbations and ipsilateral to the side of pain:
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D) Complete response to therapeutic doses of indomethacin

E) Not attributed to another disorder

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obtained within eight to 48 hours.[12] Based on this, Rozen has suggested a trial of three days at each dose.[13]

The lowest effective dose of indomethacin should be used because of the risk of side effects including abdominal pain, dizziness, nausea and/or vomiting, diarrhea, ulcer disease, renal impairment, and association with adverse cardiovascular thrombotic events. Some patients may respond to doses as low as 25-50mg daily. One study found benefit from a median dose of 61mg daily when patients were asked to taper the doses down to lowest effective after six months of treatment.[14] Because of the risk of gastroduodenal mucosal injury, indomethacin is typically taken with a proton pump inhibitor. Some patients may respond to other NSAIDS such as ibuprofen and COX-2 inhibitors (celecoxib).

Some patients may have contraindications to indomethacin or not able to tolerate use. There are other options, which, unfortunately, are not nearly as effective. In a recent series,[5] greater occipital nerve block and intravenous dihydroergotamine were effective as a short-term treatments in 35 percent and 33 percent, respectively; topiramate was effective in 41 percent for prevention. Occipital nerve stimulation is a promising treatment where larger series for confirmation will be of interest.[15] Melatonin 6-12mg hs, botulinum toxin, verapamil, gabapentin, and intravenous methylprednisolone have been reported as effective in case reports.

WHAT IS THE PROGNOSIS?

One small study suggests that some patients may remain pain-free after initial treatment with indomethacin for three to 15 months.[16]

WHAT IS THE "TAKE-AWAY"?

HC is a unilateral headache with daily and continuous mild to moderate pain which can be anywhere in the head, face or the neck. Most have severe exacerbations often brought on by triggers and usually with cranial autonomic symptoms and migraine features. HC can easily be mistaken for unilateral chronic migraine or new daily persistent headache. Secondary headaches should be excluded especially early on. HC is completely responsive to indomethacin which makes the diagnosis and is the treatment. Topiramate helps about 40 percent of patients. Gabapentin may be effective. Occipital nerve blocks and intravenous dihydroergotamine may temporarily be of benefit. Occipital nerve stimulation is a promising treatment which requires confirmation in further studies. ■

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