Hemicrania continua is not that rare

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Article abstract—*Background:* Hemicrania continua is an indomethacin-responsive headache disorder characterized by a continuous, moderate to severe, unilateral headache. More than 90 cases of hemicrania continua have been reported, but there is still uncertainty about its clinical features. *Methods:* The authors compared 34 new cases (24 women, 10 men) with previously reported cases. All the patients met Goadsby and Lipton's proposed criteria. The authors compared baseline (continuous background headache) and exacerbation (attacks of severe periods of headaches). *Results:* The baseline headache was typically mild to moderate in intensity and usually not associated with severe disability. In contrast, the headache exacerbations were severe and associated with photophobia, phonophobia, nausea, and disability. At least one autonomic symptom was present in 25 patients (74%). Jabs and jolts were present in 14 patients (41%). The mean indomethacin dose was 136.7 ± 60 mg (range 25 to 225 mg). Twenty-four patients (70.6%) met International Headache Society criteria for migraine in their exacerbation period. Occipital tenderness was observed in 23 patients (67.6%). The temporal pattern was remitting in four patients (11.8%), continuous from onset in 18 (52.9%), and continuous evolving from remitting in 12 (35.3%). *Conclusion:* Hemicrania continua is not a rare disorder. All cases of chronic unilateral daily headaches should receive an indomethacin trial early if not first in treatment.

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Hemicrania continua (HC) is an indomethacin-responsive headache disorder characterized by a continuous, unilateral headache that varies in intensity, waxing and waning without disappearing completely. The continuous baseline headache is frequently associated with exacerbations of more severe pain and is often associated with autonomic disturbances, such as ptosis, miosis, tearing, and sweating. HC is commonly associated with jabs and jolts (idiopathic stabbing headache). HC is not triggered by neck movements, but tender spots in the neck may be present. Some patients have photophobia, phonophobia, and nausea.

HC almost invariably has a prompt and enduring response to indomethacin. However, the requirement of a therapeutic response is problematic because it excludes the diagnosis of HC in patients who were never administered or who failed to respond to indomethacin. Cases have been described that did not respond to indomethacin but meet the phenotype.[1,2] For this reason Goadsby and Lipton have provided an alternate means of diagnosis (table 1).[3]

HC exists in continuous and remitting forms. In the remitting variety, distinct headache phases last weeks to months, with prolonged pain-free remissions.[4] In the continuous variety, headaches occur on a daily, continuous basis, sometimes for years. They can be continuous from onset or can evolve from remitting.[5,6]

HC takes precedence over the diagnosis of other types of chronic daily headache (CDH). CDH refers to the broad group of people with very frequent headache (15 or more days a month; duration greater than 4 hours). The major CDH subtypes are chronic (transformed) migraine (CM), HC, chronic tension-type headache (CTTH), and new daily persistent headache (NDPH).

HC was first described by Sjaastad and Spierings in 1984.[7] They reported two patients, a woman 63 years of age and a man 53 years of age, who developed strictly unilateral headache, continuous from onset, absolutely responsive to indomethacin. The man had associated autonomic features: redness, lacrimation, and sensitivity to light; the woman had superimposed jabs and jolts. Ninety-three cases of HC have been reported, but there is still uncertainty about its clinical features. Atypical features, including bilaterality,[8] side shifting,[9,10] and unresponsiveness to indomethacin,[1,2] have been described. Ten secondary cases, eight posttraumatic,[11] one with a

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Table 1 *Proposed criteria for hemicrania continua*[3]

A.	Headache present for at least 1 month
B.	Strictly unilateral headache
C.	Pain exhibits the following three features:
	1. Is continuous but fluctuating
	2. Is moderate in severity, at least some of the time
	3. Lacks precipitating mechanisms
D1.	Absolute response to indomethacin, or
D2.	One of the following autonomic features is present with severe pain exacerbation*:
	Conjunctival infection
	Lacrimation
	Nasal congestion
	Rhinorrhea
	Ptosis
	Eyelid edema
E.	May have associated stabbing headaches
F.	At least one of the following
	1. There is no suggestion of one of the disorders listed in groups 5 to 11.
	2. Such a disorder is suggested but is ruled out by appropriate investigations.
	3. Such a disorder is present, but first headache attacks do not occur in close temporal relation to the disorder.

* Silberstein et al.[15] criteria lack these features.

Table 2 *Demographics of 34 patients with hemicrania continua*

Characteristic	Value
Age, mean (range) y	49.3 ± 12.5 (19–73)
Sex, n	
F	24
M	10
Age at onset, mean (range) y	28 ± 17.9 (5–67)
Smokers, n (%)	5 (14.7)
Alcohol use, n (%)	
None	21 (61.7)
Occasional	11 (32.3)
Moderate	2 (6)
Family history of headache, n (%)	13 (38)
Jabs and jolts syndrome, n (%)	14 (41)

Headache type	Baseline, n (%)	Exacerbation, n (%)
Throbbing	8 (23.5)	18 (52.9)
Stabbing	5 (14.7)	14 (41.1)
Dull	12 (35.3)	2 (5.9)
Pressure	13 (38.3)	8 (23.5)
Ache	9 (26.4)	1 (2.9)

mesenchymal tumor,[12] and another with HIV[13] have been reported. HC can also be aggravated by a C7 root irritation caused by a disc herniation.[14] We report 34 new cases, present their clinical features, and compare them with the previously reported cases. (See supplemental data available at www.neurology.org)

Patients and methods. Patients were diagnosed using the criteria of a strictly unilateral continuous headache that was absolutely responsive to indomethacin.[15] All the patients met Goadsby and Lipton's[3] proposed criteria (see table 1). The following were ascertained: family history, age at headache onset, smoking and alcohol habits, pain intensity (0 to 10 scale) for the baseline and exacerbation, function (normal, slightly decreased, severely decreased, or totally bedridden) for the baseline and any exacerbation, temporal pattern (remitting, continuous, or continuous evolving from remitting), headache location, quality of pain, associated symptoms, autonomic symptoms, triggers, presence of nocturnal attacks, occipital tenderness, depression (Beck Depression Inventory-II scores), and indomethacin dose required. Baseline headache was defined as the background continuous pain, and exacerbations were considered episodes of more intense pain.

Results. Thirty-four patients (24 women, 10 men; table 2) were identified over 3 years. The baseline headache was unilateral, typically mild to moderate in intensity, and usually not associated with severe disability. It was not usually associated with photophobia, phonophobia, nausea, vomiting, or autonomic symptoms. The pain was typically dull, achy, or pressure-type. In contrast, the headache exacerbations were severe and associated with photophobia, phonophobia, nausea, and disability. Autonomic symptoms (tearing, ptosis, conjunctival injection, nasal congestion, rhinorrhea, and edema) were often associated with pain exacerbations. The severe headache was typically throbbing or stabbing.

Pain intensity (scale 0 to 10) was 4.7 ± 1.6 for the baseline headache and 9.3 ± 1.0 for the exacerbations. Baseline function was normal in 14 patients (41.1%), slightly decreased in 14 patients (41.1%), and severely decreased in 6 patients (18.9%). No patient was totally disabled. During periods of exacerbation, function was slightly decreased in nine patients (26.4%), severely decreased in 12 patients (35.3%), and totally disabling in 13 patients (38.3%). All patients had decreased function with exacerbation. Autonomic and associated symptoms are listed in table 3. All patients met parts A, B, C and D1 of Goadsby and Lipton's[3] proposed criteria (see table 1), 73.5% met part D2 (at least one autonomic symptom), 41% met part E (may have stabbing pain), and all met part F (not attributable to another disorder).

Nocturnal attacks were present in 10 patients (29.4%). The indomethacin dose ranged from 25 to 225 mg, mode 150 mg, mean 136.7 ± 60 mg. Twenty-four patients (70.6%) met International Headache Society criteria for migraine during an exacerbation. Occipital tenderness was present in 23 patients (67.6%); in 15 (44.1%) it was ipsilateral to the pain side, and in eight (23.5%) it was bilateral. HC was remitting in four patients (11.8%), continuous in 18 (52.9%), and continuous evolving from remitting in 12 (35.3%). The mean Beck Depression Inventory-II score was

Table 3 *Autonomic and accompanying symptoms in hemicrania continua*

Symptoms	Baseline	Exacerbation	Literature, 41 cases
Autonomic symptoms			
Conjunctival injection	—	4 (11.7)	13 (31.7)
Nasal stuffiness	3 (8.8)	7 (20.6)	6 (14.6)
Tearing	4 (11.7)	18 (52.9)	15 (36.5)
Ptosis	—	6 (17.8)	11 (26.8)
Rhinorrhea	—	4 (11.7)	4 (9.7)
Miosis	—	—	1 (2.4)
Edema	—	1 (2.9)	—
At least one autonomic symptom	—	25 (73.5)	26 (63)
Associated symptoms			
Photophobia	—	20 (58.8)	17 (36.9)
Phonophobia	—	20 (58.8)	13 (28.2)
Nausea	1 (2.9)	18 (52.9)	18 (39.1)
Vomiting	—	8 (23.5)	6 (13.0)

Data expressed as n (%).

11.3 ± 8.8, ranging from 0 to 33. Six patients (17.6%) had a score greater than 21 (indicative of depression).[16]

Discussion. HC, a unilateral, continuous, indomethacin-responsive headache with periodic exacerbations, was believed to be a rare disorder. We found 34 new cases and suggest that HC may be more common than has been appreciated. This was probably due to the systematic use of indomethacin in all patients with unilateral CDH; we believe that indomethacin should be administered early if not first in treatment. The number of patients with unilateral CDH who respond to indomethacin is unknown; we did not systematically look for this. A prospective study of the indomethacin response in this group of patients would address this issue.

Sixty-three of the 93 previously reported patients were typical indomethacin-responsive cases. Of these, 53 (84%) were continuous (approximately two-thirds continuous from onset), and 10 were remitting (16%). Our patients were similar: 30 patients (88.2%) had the continuous form, 18 (52.9%) from onset and 12 (35.3%) transformed from remitting; four (11.8%) had the remitting form.

Thirty patients had atypical features, including headaches that alternated sides,[9] bilateral pain,[8] unresponsiveness to indomethacin,[1,2] posttraumatic headache,[11] association with hemiplegic migraine,[17] and HC evolving from cluster headache.[18] Two secondary cases have been reported, one with a mesenchymal tumor[12] and another with HIV.[13] The four bilateral reported cases were either remitting (two patients) or had transformed from remitting (two patients). They represent 16% of this subgroup. No bilateral or side-shifting cases of HC were found in our clinic. They may have been undiagnosed because we did not consider HC in these patients and would not have tried indomethacin. Bilateral cases of CDH responsive to indomethacin have been called bilateral HC. Perhaps a trial of indomethacin should be conducted in patients with bilateral CDH to assess its effectiveness.

A preponderance of women (5:1) was present in the first 18 reported cases;[19] the gender ratio decreased as more cases were reported (1.8:1).[20] Summarizing all the cases for which gender data are available, there are 61 women and 22 men, with a 2.8:1 woman to man ratio. The sex ratio in our patients was similar (2.4:1).

Exacerbations are common features of HC, occurring in 74% of reported cases and in all our patients. Nocturnal exacerbations occur and could result in a mistaken diagnosis of cluster or hypnic headache. Thirty percent of the reported cases had nocturnal exacerbations that usually lasted 1 to 2 hours, whereas 29.4% of our patients had nocturnal exacerbations.

The associated symptoms of HC can be divided into three main categories: autonomic symptoms, "jabs and jolts," and migrainous features. Autonomic symptoms (conjunctival injection, tearing, rhinorrhea, nasal stuffiness, eyelid edema, and forehead sweatiness) are not so prominent in HC as in cluster headache or chronic paroxysmal hemicrania and can be absent. They occurred in 63% of 41 cases with available description and in 73.5% of our patients during exacerbations but not with baseline headache (see table 3). The most common symptom in both our series and the literature was tearing; conjunctival injection and ptosis were slightly more frequent in the literature than we observed.

Jabs and jolts syndrome is defined as a sharp pain that lasts less than 1 minute. It occurs in patients with tension-type headache, migraine, cluster headache, and in headache-free individuals and often responds to indomethacin. It occurs in HC more frequently in the exacerbation periods. Jabs and jolts syndrome was described in 26% of the cases in the literature and in 41% of our patients. Its prevalence in the general population is reported to be 30%.[21] Because of its low sensitivity and specificity, it should not be part of the diagnostic criteria for HC.

Migrainous features were common. Twenty-four (70.6%) of our patients met International Headache Society criteria for migraine in the exacerbation period, but none did in the baseline period. This diagnostic criteria for migraine could not be applied to previously reported cases because of lack of information. Nevertheless, 23 patients (50%) had at least one migrainous feature, either nausea, vomiting, photophobia, or phonophobia.

HC is one of the indomethacin-responsive headaches; others are chronic and episodic paroxysmal hemicrania, exertional headaches, and some cases of migraine and cluster headache. The reported effec-

tive dose of indomethacin for HC ranged from 50 to 300 mg a day. Our most common dose was 150 mg a day (range 25 to 225 mg). Drugs other than indomethacin reported to be effective in HC include ibuprofen (800 mg tid),[22] piroxicam beta-cyclodextrin (20 to 40 mg a day),[23] and rofecoxib.[24] Other classes of drugs, including sumatriptan, have not been successful in controlling HC.[25] Injectable indomethacin 50 mg IM ("indotest") has been used as a diagnostic test for HC.[24] Complete pain relief was reported to occur within 2 hours. Six patients who met HC phenotype but were not responsive to indomethacin were reported.[1,2] Whether these patients have HC is uncertain.

The long-term outcome of indomethacin response was investigated in five men and four women.[26] Follow-up was possible in eight patients. Indomethacin could be discontinued after 3, 7, and 15 months and patients remained pain-free. Three patients discontinued treatment because of side effects and had headache recurrence; two had relief with aspirin. Two other patients continue to take indomethacin with partial relief. Symptomatic cases of HC in which the response to indomethacin faded have also been reported.[12] These cases suggest that escalating doses or loss of indomethacin's efficacy should be treated with suspicion and that the patient should be reevaluated.

HC is one type of primary CDH; others include CM, CTTH, and NDPH. CTTH is characterized by a relative lack of autonomic and migrainous symptoms (including nausea, vomiting, and photophonophobia). It is usually bilateral and is not associated with exacerbations. CM typically evolves out of episodic migraine headache and retains many migrainous features, as do many cases of HC. CM and HC are both associated with acute medication overuse. NDPH is a new headache of subacute onset that occurs without a clear prior history of migraine; however, it often has migrainous features. Depression is more common in patients with migraine than in nonmigraine control subjects. Because CM evolves from migraine, one would expect to find psychiatric comorbidity in CM. In fact, depression occurs in 80% of patients with CM.[15] Using the Beck Depression Inventory scores, only six of our patients (17.6%) were depressed; perhaps depression is not so common in HC as in CM.

CTTH, TM, NDPH, and HC may all be unilateral. The only feature that separates HC is indomethacin responsiveness, which is not unique to HC. We used absolute responsiveness to indomethacin to define the presence of the disorder. It is uncertain whether nonresponsive patients have the same biology as indomethacin responsive patients do. Hemicrania continua is not a rare disorder. All cases of chronic unilateral daily headaches should receive an indomethacin trial early if not first in treatment.

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