Rigorously Defined Hemicrania Continua Presenting Bilaterally.

Andrew M. Southerland, MD and Ivan S. Login, MD

Department of Neurology, University of Virginia Health System, Charlottesville, VA

*The above authors have no financial agreements to disclose.

Correspondence Information:

Andrew M. Southerland, MD

P.O. Box 800394

Department of Neurology

University of Virginia Health System

Charlottesville, VA 22908

as5ef@virginia.edu

Ivan S. Login, MD

P.O. Box 800394

Department of Neurology

University of Virginia Health System

Charlottesville, VA 22908

Abstract

Background: Hemicrania continua (HC) represents a headache syndrome characterized by continuous, unilateral head pain, autonomic features, and a complete therapeutic response to indomethacin. While HC is classified as a unique entity among primary headache disorders, it clearly shares features with other primary headaches including trigeminal autonomic cephalalgias and chronic daily headaches, such as chronic migraine and chronic tension-type headache. Additionally, the diagnosis is often delayed secondary to a relatively low incidence and the occurrence of some phenotypic variability as found in previous case series.
Case: A 62 year-old woman presented with five months of unremitting, bilateral headache with significant autonomic symptoms during exacerbations of pain. Neurological exam and imaging studies were normal. After failure to respond to numerous prior therapeutic medicines and interventions, she experienced complete resolution following administration of indomethacin and eventual remission on sustained treatment.
Conclusion: This case demonstrates that hemicrania continua with requisite autonomic features can occur in a purely bilateral form. While the definitive aspects of HC continue to evolve, a bilateral headache meeting the current criteria warrants a therapeutic trial of indomethacin.

Introduction

Hemicrania continua (HC) was once thought to be rare with only 18 patients identified in the first seven years after the initial report.[1,2] However, more concerted recognition and a clarified definition have highlighted many more cases in recent years. As more examples of HC have been appreciated, the clinical spectrum of HC has widened and the true nosology has elicited scrutiny and debate.[3,4]

HC is characterized with most certainty by constancy and commonly, but not always, some degree of cranial autonomic symptoms (CAS). The continuous, unremitting pattern of HC draws an association, and sometimes overlap, with other chronic daily headaches (CDH) such as new daily persistent headache (NDPH), chronic tension-type headache, and transformed migraine.[5] While unilaterality characterizes HC in the literature, several case reports have declared "bilateral hemicrania continua,"[2,6] though some consider this term "oxymoronic."[7] The distinguishing feature in these reports is usually the exquisite therapeutic response to indomethacin, prompting others to propose the "indotest" as a better way to stratify.[8] By this distinction, HC is linked to the lineage of the indomethacin responsive paroxysmal hemicranias, in which CAS are also a defining characteristic. Several of these entities fit under the rubric of trigeminal autonomic cephalgias (TAC), which are non-constant headaches but exhibit variable frequencies that a patient may

relate as constant. Since chronic paroxysmal hemicrania may be reported as constant if not carefully questioned, CAS symptoms require thorough discussion about this constancy to avoid mislabeling the headache type, even if both HC and CPH are "indotest" positive. Evans reported the first ever case of "bilateral paroxysmal hemicrania with autonomic symptoms" treated successfully with indomethacin.[9] To our knowledge, there has not previously been reported a rigorous example of indomethacin-responsive hemicrania continua with the requisite autonomic features presenting bilaterally. We submit one here.

Case Report

A 62 year-old right-handed woman was referred to the emergency department with a severe exacerbation of a bilateral "pressure" headache that had been present without remission for five months. Her headache was associated with photophobia and nausea, but no significant phonophobia, positional component, or worsening with Valsalva. While bilateral pain was always present to some degree, exacerbations of severe pain had become daily and typically lasted several hours. Both the chronic underlying headache and severe exacerbations were bilateral and symmetric without side-alteration. During peak episodes of pain she and her family reported striking reddening of her eyes, swelling of her eyelids, tearing, nasal drainage, flushing of her face, diffuse sweating of her scalp, and associated restlessness and agitation. Her face and scalp were affected bilaterally and equally by these autonomic symptoms. Her daughter, a healthcare worker, had noticed dilation of her pupils on more than one occasion during the height of the pain. At various doses and treatment duration, she had no benefit from daily amitriptyline, topiramate, and valproic acid, or from abortive therapies including non-steroidal anti-inflammatrories, antiemetics, sumatriptan, and oral methylprednisolone, or physiotherapy and acupuncture.

On direct questioning, she denied any other recent or remote history of headaches or head pain of any kind. Her other past medical history was significant for two cervical foraminotomies, and chronic left leg thrombophlebitis treated with warfarin secondary to venous thrombosis during pregnancy. There was no family history of headaches known to her or her accompanying family members on direct questioning.

We initially observed the patient in the emergency department (ED) during a severe exacerbation and noted profound bilateral scalp and facial diaphoresis, flushing, lacrimation, and rhinorrhea. The remainder of the neurological exam was normal. MRI/MRA/MRV with contrast were non-diagnostic. She initially

received intranasal oxygen, prochlorperazine, and fentanyl in the ED with little effect. Her clinical presentation led us to consider the possibility of bilateral HC. We proceeded to treat with one dose of oral indomethacin 25 milligrams (mg.), and she experienced remarkable resolution of her headache within one hour. She received two more doses at eight-hour intervals, and after one day of treatment her headache disappeared for the first time in five months.

There were no further headaches while in the hospital on continued treatment, but a few days later at home nocturnal headaches returned. The pain was less severe than prior to indomethacin treatment and an additional indomethacin dose at bedtime brought relief. Her indomethacin dose was slowly titrated up to 50 mg. three times daily with an additional 25 mg. at night. She remained under excellent control and was able to taper off indomethacin four months later. Now over two years after diagnosis of bilateral HC, she remains essentially headache free, but occasionally has a bilateral breakthrough headache with autonomic features (similar to her pre-indomethacin headache) that responds completely to a single dose (25mg.) of indomethacin.

Discussion

There have been a limited number of patients reported under the rubric of bilateral hemicrania continua responsive to indomethacin, but none have had both bilateral headache plus bilateral autonomic signs concurrently, as required. One case clearly displayed autonomic features, but the localization of pain was predominantly unilateral with the contralateral side only becoming affected to a lesser degree at the height of pain.[10] An excellent recent series by Cittadini and Goadsby reported 39 HC cases. Several patients had bilateral headache in the setting of medication overuse including indomethacin, raising the possibility of a subgroup of HC patients that may be genetically prone to bilateral pain syndromes. The same series also highlighted the prevalence of side-alternating attacks in HC, prompting a proposed revision to the diagnostic criteria.[4] Our patient suffered with chronic bilateral pain from onset, non-lateralizing pain exacerbations, and clearly symmetric autonomic disturbance, rigorously meeting criteria for HC bilaterally.

While autonomic symptomatology in trigeminal autonomic cephalalgias (TACs) is thought to stem from a predominant parasympathetic output,[11] our patient demonstrated mydriasis rather than miosis at the height of pain, which was also observed in 2 cases in the Cittadini series.[4] This sign, while exceptional, might

indicate a reflex sympathetic response to the initial parasympathetic preponderance, or perhaps suggests both a relative imbalance in the entire cervicocephalic autonomic system plus a unique threshold for such imbalance in each patient.[11] Restlessness and agitation during pain exacerbations occurs in other TACs such as SUNCT and cluster headache, and may be an association consistent with hypothalamic activation in the family of autonomic headaches.[4] Additionally, our patient suffered significant nausea and photophobia at the height of pain, similar to the high association of migrainous symptoms observed in the aforementioned series, although our patient reported no personal or family history of migraine.[4]

This case demonstrates that when faced with a daily or continuous headache with autonomic symptoms at the height of pain, the absence of a strictly unilateral pattern should not preclude a diagnosis of HC or trial of indomethacin. HC appears to demonstrate a propensity for a wide range of phenotypes such as bilaterality, absence of autonomic symptoms, indomethacin resistance,[12] pain that alternates sides,[4,13,14,15] a remitting time course, and apparent evolution from another headache variant or chronic disease.[16] The Cittadini series highlighted the variations in time course that can be seen in HC, with primary chronic forms being most prevalant.[4] While chronic HC can evolve into a secondary episodic form spontaneously, our case demonstrated this transition following indomethacin, with episodes remaining exquisitely responsive to treatment during remission.

Another interesting aspect of our case related to the circadian nature of pain exacerbations both during the primary chronic state, and with her recurrent episodic headaches following treatment. While nocturnal attacks are more typical of cluster headache, 63% of HC patients in the Cittadini series reported some history of nightly exacerbations with a high degree of variability.[4] Although this notion promotes a linkage between HC and cluster headaches as a subgroup of TACs, a review has questioned this association based on a number of distinguishing features, not least of which is the general lack of indomethacin response in cluster headache. An alignment between HC and the paroxysmal hemicranias as a subgroup seems more plausible.[17]

Our patient clearly exemplified the dynamic nature of the hemicrania spectrum with bilateral and symmetric presentation, nocturnal exacerbations, and transition to a more episodic nocturnal pattern following an initial absolute response to indomethacin. Unquestionably, as the diagnostic criteria for HC evolve it remains ever important to recognize a clinical opportunity for a novel and effective treatment.

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