Cluster-Migraine: Does It Exist?

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The nosological boundaries between cluster headache and migraine are sometimes ill-defined. Although the two disorders are distinct clinical entities, patients sometimes present with clinical scenarios having characteristics of both headache types, but either do not fully meet International Classification of Headache Disorders, Second Edition diagnostic criteria for either disorder or have sufficient symptoms and signs to allow both diagnoses to be present. These occasions provide diagnostic challenges and include what is variously described as migraine-cluster, cyclical migraine, clustering episodes of migraine, cluster with aura, or atypical cluster without autonomic symptoms or severe pain. Patients with symptoms overlapping cluster headache and migraine likely reflect the inherent clinical variability in each of these two disorders, rather than distinct diagnostic entities in their own right.

Introduction

Cluster headache (CH), as defined by the International Classification of Headache Disorders, Second Edition (ICHD-2), is characterized by severe, strictly unilateral pain that is orbital, supraorbital, and/or temporal, and lasting 15 to 180 minutes if untreated. The headache also must be accompanied by one of the following: ipsilateral autonomic dysfunction, ipsilateral nasal congestion/rhinorrhea, ipsilateral conjunctival injection, ipsilateral eyelid edema, and/or a sense of restlessness and agitation. Cluster attacks have a frequency of one to eight per day and cannot be attributed to another disorder [1]. Importantly, these criteria do not require the presence of autonomic symptoms if the patient is restless or agitated during an attack.

Migraine without aura, as defined in the ICHD-2, is a recurrent disorder with discernible headache attacks lasting 4 to 72 hours. At least five of the patient's stereotypical headaches must fulfill two of the following criteria: unilateral location, pulsating quality, moderate or severe pain intensity, or aggravation by or causing avoidance of physical activity. During a headache, at least one of the following also must be present: nausea and/or vomiting, or photophobia and phonophobia [1].

CH and migraine headache are thus distinctly codified by ICHD-2 criteria, but the clinical presentations of headache are often not so easily categorized. In some patients, criteria for each disorder are not fully met and a patient is labeled as "probable migraine" or "probable cluster," either of which could have features of the other. Clinical distinctions between CH and migraine sometimes appear to be merely a matter of the degree and severity of the presenting symptoms, and diagnostic dilemmas may arise.

Cyclic Migraine

Case 1

A 63-year-old woman reported headaches that had been occurring intermittently approximately three times per year from her teen years into her 30s. Her headaches then gradually increased in frequency, and over the past 20 years her headaches have developed a recurring pattern of increased and then decreased frequency. She experienced daily headaches for 4 to 5 months at a time before near complete remission from headaches for 1 to 2 years and then recurrence of daily headaches. She thought that her headaches could be triggered by changes in temperature. They usually occurred at night and began retro-orbitally and bilaterally, spreading to involve her lower face. The headaches were mild to moderate in severity, reached maximum severity over an hour, and were treated with 50 mg of sumatriptan, with relief seen within 30 minutes. She denied any prodrome, aura symptoms, agitation, phonophobia, photophobia, nausea, or other autonomic features during the headaches. The headache attacks in this patient have a periodicity suggestive of CH but meet neither the ICHD-2 criteria for CH nor the criteria for migraine. In fact, without regard for their temporal pattern, they would meet ICHD-2 criteria for episodic tension-type headache.

Some individuals experience headache attacks that fit the ICHD-2 criteria for migraine; however, these attacks occur in temporal patterns suggestive of CH. Many CH patients have extended periods of time in which headache attacks recur on a daily basis for weeks to months (cluster periods). These periods are followed by remission periods

of weeks to years, before their headache attacks recur again in a similar cycle. A common pattern, especially in the first few years of CH, is for cluster periods to occur once or twice yearly [2], with seasonal periodicity particularly associated with the months following solstices [3,4].

Patients with migraine may similarly experience frequent headaches during a finite period of time (several weeks to months), recurring during the same season and rarely at other times. The terms cyclic migraine [5] or cyclical migraine [6] have subsequently been used to describe this phenomenon, although this condition is not recognized as a diagnostic entity by ICHD-2 criteria.

In a series of articles written between 1977 and 1982 [5–8], Medina and Diamond described a series of 27 patients with so-called cyclical migraine. These patients experienced headache attacks occurring in periods of 2 weeks or longer, separated by headache-free periods. The average headache period lasted 6 weeks. Nine of the patients reported particular seasonal occurrence of their headache periods, but the mean number of periods was five per year across the patient series. Individual headache attacks ranged in duration from 1 hour to 72 hours, with a mean duration in excess of 6 hours. The headaches could be bilateral or unilateral, with side-shifting sometimes reported within a headache period. The headaches were typically throbbing, severe, and associated with nausea and often photophobia or phonophobia. Nasal congestion, tearing, or Horner's syndrome was also reported in several patients. Eleven of 27 patients reported visual or other migraine aura symptoms. The presence or absence of restlessness or agitation was not recorded for these patients. Notably, of 22 of these patients treated with lithium carbonate, 19 reported partial or complete resolution of headache periods—typically within 1 week of initiation of therapy. Lithium is widely appreciated as a standard prophylactic therapy for CH [9]. In summary, Medina and Diamond described a cohort of patients that would likely have met ICHD-2 criteria for migraine with or without aura had they been studied today, but whose headaches additionally demonstrated one or both of two features strongly associated with CH—headaches clustered into cyclic periods and response to lithium carbonate.

CH with Migrainous features

Whereas "cyclical migraine" might be considered as a description of migraine patients with additional symptoms typical of CH, other patients have been described with otherwise typical CH who have concurrent symptoms typical of migraine. A prospective study of the clinical and epidemiologic characteristics of CH sufferers by Bahra et al. [2] noted 14% with aura symptoms. Silberstein et al. [10] studied 101 CH patients retrospectively and found six with aura (five visual and one olfactory). The auras always occurred with, or were followed by, a severe CH attack. Medina and Diamond [7] described five patients with CH-like attacks preceded by scotomata, paresthesias, and in one instance, hemiparesis contralateral to the pain. Recently, Schürks et al. [11•] reported a large cohort of CH patients, almost 25% of whom described typical migrainous aura symptoms preceding CH attacks.

Nausea, photophobia, phonophobia, and osmophobia also are more prevalent in CH than is commonly appreciated. Bahra et al. [2] found that 50% of CH patients experienced nausea during an acute attack; other symptoms included photophobia (56%), phonophobia (43%), and osmophobia (36%). Schürks et al. [11•] reported photophobia or phonophobia in 61.2% of CH patients, as well as nausea and emesis in 27.8%. Vingen et al. [12] also reported that photophobia and phonophobia were significant features of CH. Sjaastad [13] wrote that "photophobia seems to be one of the most frequently occurring accompaniments of attacks." Some patients with CH also report a variety of triggers for their attacks, such as certain foods, chocolate, and strong odors, which are also known to precipitate migraine attacks [14].

Atypical CH

Case 2

A 30-year-old man developed abrupt onset of daily headaches during the spring. The headaches spontaneously remitted 3 weeks later, and he remained free of headache until two springs later (age 32 years) when they returned. His headaches were present upon awakening, and he described them as sharp, of mild to moderate severity, pulsating, and with a ring-like pattern like "a hat that is too tight." The headaches reached maximum severity over minutes and lasted up to an hour, with the most severe pain lasting for 15 to 30 minutes. They were associated with bilateral increased lacrimation, nasal congestion, and nasal stuffiness. He also reported "numbness" of the legs and muscle tenderness in his back. Ptosis or miosis was not noted. When experiencing the attacks, the patient preferred to lie still and avoid movement. He denied any aura but did notice particular triggers for headache attacks, including loud noises, exercise, changes in posture, or too little or too much sleep. The features suggestive of migraine in this patient include the pulsatile nature of the pain, phonophobia, and photophobia. The short duration of the attacks, the symptoms of increased nasal congestion, lacrimation, and the spring-time periodicity suggest CH; however, the absence of severe headache is atypical. The possibility of "bilateral paroxysmal cephalalgia" [15] is raised in this case, but the presence of cranial autonomic features argues against this entity, and it is unknown whether this patient's headache attacks would have responded to indomethacin.

Diagnostic difficulties may appear if clinical features in the known constellation of diagnostic signs and

symptoms are missing. Sjaastad et al. [16] recognized this in 1988, in an article describing three men with cases of "mild" CH. All three patients had unilateral headache with tearing but were uncharacteristically able to carry out their daily work. The authors suggested that these cases may represent "the left-side slope of a Gaussian severity distribution scale" and possibly experience less severe pain associated with cluster. Vigl et al. [17] reported a case of episodic, unilateral, periorbital, severe headache without autonomic symptoms. This patient's attacks were noted to be recurrent, short-duration, and associated with motor hyperactivity, with periods separated in time by 4 years. He was diagnosed with CH; however, the ICHD criteria in effect at the time of the report did not include the presence of agitation or motor symptoms, but only autonomic symptoms.

Migraine-cluster Syndrome

Migraine-cluster syndrome is a term often avoided by clinicians because of the confusion it engenders. For instance, some clinicians use it when elements of migraine headache occur simultaneously in patients suffering with CH [18], whereas others may apply it to episodes of migraine that occur in clusters without any of the features of CH [19]. The term cluster migraine has even been used synonymously with CH [20].

Solomon et al. [21] sought to determine whether a distinct diagnostic entity of migraine-cluster exists. They studied patients with migraine and CH to determine the prevalence of cases in which several symptoms of the two conditions coexist. Over a 2-year span, 1081 patients were diagnosed as having either migraine, CH, or both using diagnostic criteria that predated the ICHD-2. Because some symptoms of CH occur during migraine, and vice versa, a tentative set of diagnostic criteria for migraine-cluster syndrome was proposed. These criteria required one major distinguishing feature of CH occurring in a patient with migraine or vice versa (eg, episodes of migraine occurring in clusters or scintillating scotoma occurring with stereotypical CH). If one, two, or three other symptoms (as opposed to major distinguishing features) of one type of headache were noted in the other, the diagnosis of cluster-migraine was not thought to be warranted. In four patients, they found signs and symptoms of migraine and CH blended in such a way that neither diagnosis predominated. These were labeled migraine-cluster. In addition, nine of the 923 patients with migraine had four or more features of CH, and five of 154 patients with CH had four or more characteristics of migraine. The analysis of Solomon et al. [21] reflects the inherent individuality of symptoms of both CH and migraine in particular patients.

Evolution of Migraine to Cluster

Ekbom [22] reported five patients with migraine and CH, noting an additional interesting relationship between the two entities. Four of these patients had migraine with aura (classic migraine), and the other patient had migraine without aura (common migraine). In four patients, the migraine started before the onset of CH, and in three cases it ceased in conjunction with the appearance of CH symptoms. One such case was a 24-year-old man who developed headache between age 17 and 20 years. His headaches were associated with nausea, vomiting, photophobia, and phonophobia. They lasted for 3 to 4 hours and alternated sides. At age 22 years, he had the onset of a different type of headache. This was characterized by a splitting, unilateral, orbital headache with associated autonomic features. These headaches lasted 45 to 60 minutes and occurred for periods of 4 weeks, roughly once a year.

Solomon and Cappa [23] reported that in 14 of 16 patients in whom CH and migraine co-occurred, CH followed the onset of migraine. A review of the literature revealed 50 of 53 cases with a similar sequence. Although the age-related incidence of migraine is more common than CH in the first decade of life, the age of onset thereafter is relatively similar. Therefore, it seems likely that progression of age is not the major factor in the development of cluster in migraine headache patients. The overall prevalence of migraine in patients with CH is comparable to that seen in the general population [24].

Conclusions

Although migraine and CH have been shown to have distinctly different heritability patterns [25], imaging patterns [26], and neurochemical signatures [9,27], the clinical presentations of these disorders can often overlap in individual patients, and certain medications may be therapeutic for both disorders (eg, sumatriptan, verapamil [28]). The similarities between CH and migraine may merely reflect the inherent individuality of clinical presentations for protean disorders or may reflect shared pathogenetic mechanisms to be further defined [29].

Graham [30] eloquently stated the following:

> "…in any event, I should like to suggest for your consideration that the difference between cluster headache and classical and common migraine may be matters of timing and intensity. The physiological phenomena, the reactions to drugs, the relations to life situations, unilaterality, location, the stimuli—all are the same, and the areas of difference, which at first seemed black, this is family history, the lack of prodromata, the sharp clustering, the complete remissions—all begin to fade a little into gray, as more transitional forms in each group are seen."

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