DELAYED DIAGNOSIS OF CLUSTER HEADACHE IN AFRICAN-AMERICAN WOMEN

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The male-to-female ratio has fallen in cluster headache over the last several decades and is now 2.1:1. Unfortunately, women still are not diagnosed accurately. This lack of appropriate diagnosis appears related to the misconception that cluster headache rarely occurs in women. Compounding this misconception, there seems to be an ethnic bias. We report cluster headache in five African-American women in whom diagnosis was delayed due to gender, ethnicity, and, most importantly, an inability to make a correct diagnosis of cluster headache.

Cluster headache diagnostic criteria are no different in men or women and have no ethnic boundaries. Clinical features such as disordered chronobiology and abnormal behavior often suggest the diagnosis. Migrainous features occur commonly in cluster headache and, when present, should not exclude the diagnosis. Likewise, neither race nor sex should exclude the diagnosis. The diagnosis of cluster headache is easily made by considering unilateral orbital, supraorbital or temporal location; short duration (15–180 minutes, untreated), and ipsilateral autonomic dysfunction involving the eye or nose. (*J Natl Med Assoc.* 2001;93:31-36.)

Cluster headache is a severe, benign, recurrent headache disorder affecting men more often than women. It is said to be rare, however, we suspect it is more common than appreciated, particularly in African-American women, since the diagnosis is easily missed or delayed. We describe five African-American women with cluster headache in whom delayed diagnosis was associated with gender, ethnicity and, most importantly, a failure to ask the appropriate cluster headache questions. All had episodic cluster headache except Patient 2, who had chronic cluster headache unremitting from onset. The first three cases are presented in detail, all cases are summarized in the tables, and cluster headache clinical features and diagnostic criteria are reviewed.

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CASE REPORTS

Case 1

A 37-year-old African-American woman had an occasional premenstrual tension-type headache until age 34, when she became a hospital administrator. Since that time severe headaches have occurred periodically and begin with left retro-orbital throbbing pain that occasionally radiates to the left occipital and nuchal regions. Ipsilateral lacrimation and eyelid edema occurs. Nausea, sensitivity to light (photophobia), sound (phonophobia), and smell (osmophobia) is typical. The headache is severe for the first 30 minutes, then it is mild and achy for an additional one to two hours. Usually, these headache attacks occur once daily for two to seven days,

then she remains headache-free in a remission period for one to three months before a cluster period returns.

Premonitory symptoms occur one to two days before the headache, typically last 30 to 60 minutes and consist of such visual disturbances as "circles, halos, shadows, rings, and broken mirrors" that are bilateral, possibly greater in the left visual field. Mangoes trigger her headaches. Past medical and family history, general physical and neurological examinations, and brain imaging were non-contributory.

Comment. Episodic cluster headache. This is a "classical" presentation since genuine clustering occurs as a chronobiological or biological clock disturbance. However, despite the name, cluster headache, clustering of attacks is not required for the diagnosis (see Table 1). Migrainous features are present, and a migraine-like aura without headache is experienced during the premonitory or prodromal phase, yet migraine diagnostic criteria are never met (see Tables 2, 3 and 4).

Case 2

A 32-year-old, African-American woman had headaches since age 29, which started several months after bilateral salpingo-oophorectomy for endometriosis. She experiences five headaches weekly, averaging 2.5–3 hours each. However, there are days when she has up to five headaches, each typically lasting 45–60 minutes. Approximately three times monthly, she has headaches of similar quality that last two days. Her headaches typically awaken her from sleep at two in the morning and during the day they are paroxysmal in onset. The headaches are strictly right retro-orbital and temporal, sharp and severe. Ipsilateral conjunctival injection and eyelid edema occurs. Photophobia, phonophobia, kinesophobia (sensitivity to movement), haptephobia (sensitivity to touch), and nausea are noted. She vomits when headaches last two days. She seeks a dark, quiet room, but frequently bangs her head on the floor, headboard or wall, and often moves and paces during the headache.

Her mother has migraine. However, past medical history, physical and neurologic examinations, and brain imaging were non-contributory.

Comment. Chronic cluster headache, unremitting from onset and migraine without aura (see Tables 1–4). Chronic cluster headache is characterized by at least one year of continued headache attacks that are not associated with remission periods in excess of two consecutive weeks. Chronic cluster headache can evolve from episodic cluster headache, previously termed chronic secondary cluster headache, or be unremitting from onset, previously known as chronic primary cluster headache. Chronobiological disturbances are illustrated by the early morning awakenings. Head banging and pacing manifests abnormal behavior typical of cluster headache. This combination of bizarre features in a headache sufferer is highly suggestive of a diagnosis of cluster headache.

Case 3

A 15-year-old, African-American girl rarely had headaches until age 13 when she had the onset of daily headaches lasting for two months. These remitted until age 14 when daily headache recurred. They typically last 30 minutes, although occasionally 45 minutes. They occur on awakening in the morning, and often return when she arrives home from school in the late afternoon. They are strictly right temporal and retro-orbital, and can radiate into her face. They start as a "pinch," but peak in five minutes with sharp excruciating pain. Ipsilateral lacrimation, conjunctival injection, ptosis, and nasal congestion occur. Photophobia, phonophobia, and kinesophobia are present. She seeks a dark, quiet room and rests. There are no specific headache triggers. Her mother had migraine in her teens.

General physical and neurologic examinations were unremarkable except for mild right ptosis and conjunctival injection that was evident only during a cluster headache. Brain imaging was non-contributory.

Comment. Episodic cluster headache. This is not chronic cluster headache because a year of continued headache attacks with remission periods of no more than two consecutive weeks is required for this diagnosis (see Tables 1 and 4). Some migrainous features are present and are not uncommon (see Tables 2, 3). Chronobiological abnormalities are noted in that periodicity is defined by headache occurrence at similar times during the day.

DISCUSSION

Cluster headache is a benign, recurrent primary headache disorder predominately affecting men, and affecting women less, but surprisingly more

often than usually thought. The prevalence of cluster headache varies between 15.6 per 100,000 in Olmsted County, MN and 69 per 100,000 in San Marino.[1,2] Older studies indicate that men with cluster headache outnumber women 6.2:1. However, recent evidence suggests that women are now affected to a greater extent than previously thought and the male to female ratio has fallen to 2.1 to 1.[3,4] The widespread misconception of marked male preponderance in cluster headache readily biases against this diagnosis in women. Additionally, most male and female headache patients believe that cluster headache rarely, if ever, occurs in women. Cluster headache occurs in African-American men, but in headache clinic populations it is not as frequent as in white men. Nevertheless, it appears more frequent than in African-American women. Unfortunately, few population-based prevalence studies have been done and there are no good statistics on cluster headache in various ethnic populations. However, Lovshin[5] suggested an overrepresentation of cluster headache in African Americans, but these data are biased since these patients were derived from specialty clinic populations.

Cluster headache is characterized by:

1. Severe, strictly unilateral, short duration orbital-temporal pain.
2. Autonomic dysfunction involving eye or nose ipsilateral to the headache.
3. Chronobiological disturbances.
4. Behavioral features.

The headache is strictly unilateral, involving the orbital, supraorbital or temporal regions, and it is excruciatingly severe. The pain is reported as having sharp, knife, stabbing, boring, sticking, jabbing, dagger, arrow or hot poker qualities, but these descriptions are neither invariable nor specific. Clearly, the headache is associated with activation of the trigeminal vascular system with a marked elevation in calcitonin gene-related peptide in jugular venous blood ipsilateral to the headache.[6]

Ipsilateral autonomic dysfunction represents activation of the parasympathetic system, and a marked rise in vasoactive intestinal peptide has been shown in jugular venous blood ipsilateral to the cluster headache.[7] Parasympathetic activation is accompanied by such clinical features as ipsilateral conjunctival injection, lacrimation, nasal congestion, rhinorrhea, forehead and facial sweating, miosis, ptosis, and eyelid edema. Moreover, at least one of these symptoms or signs is required for the diagnosis of cluster headache.

Headache periodicity, clustering, and certain diurnal and hormonal variations manifest chronobiological or biological clock disturbances in cluster headache. Cluster headache is often periodic and can strike or attack at the same time during the day, week, month, season or year. A predominance of attacks occurs two weeks following the longest and shortest days of the year in July and January. Headache attacks typically awaken sufferers from sleep in the middle of the night, often between two and four in the morning. They often occur in "clusters," wherein multiple attacks occur for days to weeks to months, followed by pain-free cluster remission periods of weeks, months, years, or decades, then recurrence. The pattern can imitate Cheyne-Stokes respirations in that there is a build-up in severity with each headache more severe than the previous headache, finally peaking and then waning in severity followed by a quiet remission period characterized by freedom from headache. This disturbed chronobiology most likely reflects hypothalamic dysfunction and Goadsby's group[8] has reported evidence for a cluster headache "generator" localized to the hypothalamus.

Behavioral features are common in benign primary headache disorders although migraine and cluster headache behaviors differ dramatically. The migraine sufferer typically seeks a dark, quiet room, quickly assumes their special preferred position and lies motionless. Migraine sufferers are overwhelmed by such sensations as light, sound, smell and touch. However, the pain usually overwhelms cluster headache sufferers. They are agitated, frustrated and angry because of the pain. They sit, recline or rock, rather than lie flat. They repeatedly change positions, even when flat, often prefer to sit, and when up they are restless or pace. It is not uncommon for the cluster headache sufferer to strike or bang the wall, bed or floor with their fists, feet or head. Nor is it uncommon for them to rub, pound, pat or slap their heads. Often this counter-irritation produces a brief respite from the cluster pain. Even if they do not perform these activities, they often think about them. When these aggressive, hyperactive behavioral features occur in the setting of a benign headache, the diagnosis of cluster headache must be entertained.

International Headache Society (IHS) diagnostic

Table 1. IHS Cluster Headache Diagnostic Criteria

Criterion	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
A. At least five attacks fulfilling B-D	Yes	Yes	Yes	Yes	Yes
B. Severe unilateral orbital and/or temporal pain lasting 15–180 minutes (untreated)	Yes	Yes	Yes	Yes	Yes
C. Associated with at least one of the following on pain side:	Yes	Yes	Yes	Yes	Yes
1. Conjunctival injection	No	Yes	Yes	No	Yes
2. Lacrimation	Yes	No	Yes	Yes	Yes
3. Nasal congestion	No	No	Yes	No	No
4. Rhinorrhea	No	No	No	No	No
5. Forehead and facial sweating	No	No	No	No	No
6. Miosis	No	No	No	No	No
7. Ptosis	No	No	No	Yes	Yes
8. Eyelid edema	Yes	Yes	No	No	No
D. Attack frequency: 1 every other day to 8/day	Yes	Yes	Yes	Yes	Yes

IHS = International Headache Society.

Table 2. IHS Migraine Diagnostic Criteria

Criterion	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
A. At least five attacks fulfilling B-D	No	Yes	No	No	Yes
B. Headache attacks lasting 4–72 hours	No	Yes	No	No	Yes
C. Headache has at least two of the following:	Yes	Yes	Yes	Yes	Yes
1. Unilateral	Yes	Yes	Yes	Yes	Yes
2. Pulsating quality	No	No	Yes	Yes	Yes
3. Moderate or severe intensity	Yes	Yes	Yes	Yes	Yes
4. Aggravation by walking stairs or similar routine physical activity	Yes	Yes	No	Yes	Yes
D. During headache at least one of the following:	Yes	Yes	Yes	No	Yes
1. Nausea and/or vomiting	No	Yes	Yes	No	No
2. Photophobia and phonophobia	Yes	Yes	Yes	No	Yes

IHS = International Headache Society.

criteria for cluster headache and migraine are illustrated in Tables 1 and 2[9] for these five patients, and the clinical features of their cluster headaches are described in Table 3. Cluster headache is defined as a severe, strictly unilateral, orbital-temporal headache of short duration (15–180 minutes, untreated) associated with ipsilateral ocular and nasal parasympathetic dysfunction characterized by conjunctival injection, lacrimation, nasal congestion, rhinorrhea, forehead and facial sweating, miosis, ptosis, and eyelid edema. It can be episodic or chronic (Table 4) and more than four individual headache attacks must have been experienced. During a cluster period, cluster attacks occur as frequently as eight per day or as infrequently as one headache attack every other day.

The IHS classification and diagnostic criteria do not consider or recognize any of the chronobiological or behavioral phenomena associated with cluster headache as necessary criteria for the diagnosis. Nevertheless, disordered chronobiology and abnormal behavior are frequent and can often allow clues to the identification and appropriate diagnosis of cluster headache.

Migraine is a chronic, recurrent primary headache disorder. Headache attacks typically last four to 72 hours and are characterized by: unilaterality (33%–40% are bilateral), a pulsatile quality, mod-

Table 3. Cluster Headache Clinical Characteristics

Parameter	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Gender	F	F	F	F	F
Age (age onset), years	37 (34)	32 (29)	15 (13)	54 (48)	37(12)
Severe orbital-temporal pain	+	+	+	+	+
Ipsilateral autonomic symptoms (number)	2	2	4	5	3
Attack duration (minutes)	90–150	45–180	30–45	60	90–180
Attack frequency (per day)	1	.7–5	2–3	1–2	1–2
Cluster period duration (months)	25	—	9-10	1	.75

Table 4. Cluster Headache Definitions

	Definition
1. Cluster attack	The individual cluster headache attacks
2. Cluster period	The period of time during which cluster attacks occur.
3. Cluster remission period	The period of time during which cluster attacks do not occur.
4. Episodic cluster headache	Cluster attacks that occur in cluster periods lasting seven days to one year and are separated by pain free periods (cluster remission periods) lasting 14 days or more.
5. Chronic cluster headache	Cluster periods lasting one year or more with cluster remission periods lasting less than 14 days.
6. Chronic cluster headache unremitting from onset	Chronic cluster headache that is not associated with cluster remission periods of 14 days or more from the beginning.
7. Chronic cluster headache evolved from episodic	Chronic cluster headache starting as episodic cluster headache with at least one cluster remission period lasting 14 days or more within one year after onset and evolved or transformed over time by an unremitting course for at least one year.

erate or severe intensity, aggravation by walking up stairs or other similar routine physical activities (at least two of these four features) and nausea and/or vomiting *or* photophobia and phonophobia (at least one of these two features).

The patients presented herein were most often misdiagnosed as having migraine headache. This is understandable if historical details are absent or incomplete. However, this is not acceptable since appropriate treatment requires accurate diagnosis. Two patients did have migraine (Patients 2 and 5, Table 2) in addition to cluster headache, both experienced migraine first, and subsequently developed cluster headache several years later. In Patient 2, migraine continues to occur. In Patient 1, migraine aura without headache was present and served as a cluster premonitory or prodromal symptom.

Migrainous features are well described and are common in cluster headache. Nappi et al[10] reported such migrainous features as photophobia (55.8%), nausea (40.6%), and vomiting (23.9%) in a series of 251 consecutive cluster headache patients. Unfortunately, migrainous features are not widely recognized to occur in cluster headache and their presence often results in a diagnosis of migraine even though the clinical and diagnostic criteria are not met or are incompatible. All of the patients reported experienced migrainous features in combination with their cluster headaches. Photophobia and phonophobia were present in four patients, aggravation by walking stairs or similar routine physical activity in four, a pulsatile quality in three, and nausea and/or vomiting was present in two. Thus, if the diagnosis of cluster headache is excluded based on the presence of these migrainous features, erroneous diagnosis is likely.

CONCLUSION

The cluster diagnostic features that seem to have a high degree of reliability and predictability, in our experience, include short headache duration and the presence of ipsilateral parasympathetic dysfunction involving the eye or nose. Short headache duration seems to be the single best discriminator

between migraine and cluster headache since migraine with cluster features can occur and seems to represent a migraine-cluster overlap syndrome or variant defined by the presence of ipsilateral parasympathetic dysfunction in IHS migraine.[11]

The diagnosis of cluster headache was delayed in these African-American women not just because of their gender and ethnicity, but because of the failure to ask the appropriate cluster headache questions. This last point cannot be overemphasized since successful diagnosis in all patients relies heavily on an accurate history. Finally, the diagnosis of cluster headache is easily made by considering: unilateral orbital, supraorbital or temporal location, short duration (15–180 minutes, untreated), and ipsilateral autonomic dysfunction involving the eye or nose.

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