

Expert Opinion

Cluster and Other Nonmigraine Primary Headaches With Aura

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Migraine aura is characterized by focal neurologic features of visual and/or sensory and/or speech disturbance, which precede or accompany a headache attack developing gradually over 5 to 20 minutes with a duration of no longer than 1 hour.¹ In a sample of 163 migraineurs with aura from the general population, visual symptoms were most frequent (99%), followed by sensory (31%), aphasic (18%), and motor (6%) symptoms followed by headache in 93%.² The visual presentation of a migraine aura is varied and scintillating zigzags moving laterally in different quadrants of vision as well as objects surrounded by luminous angles, such as fortifications, hazy spots, shining and flickering star-shaped figures are usually described by patients.²⁻⁴

Cluster headache (CH) is a primary headache well defined in the International Classification of Headache Disorders, second edition, with high specific and sensitive criteria which do not include the presence of aura. The following 2 patients meet episodic CH criteria but also have visual auras.

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CLINICAL HISTORIES

Case One.—A 51-year-old man with a history of episodic cluster headache attacks since the age of 33 years occurring nearly every 2 years with a duration of 6 weeks. The last 4 cluster periods responded well to the use of prednisone for transitional therapy, verapamil for prevention, and injectable sumatriptan (3 mg) for acute attacks.

Since the onset of the current cluster period 14 days prior to presentation, the patient developed black-and-white checkerboard visual hallucinations and/or black-and-white flashing lights, lasting for approximately 20 minutes preceding the most severe attacks. Aura only occurred before a headache in 11 out of 14 days during this time when he experienced a mean frequency of 2 attacks per day.

There was no personal or family history of migraine, cluster headache, or visual disturbances. The patient was a heavy smoker (30-40 cigarettes/day, but had been smoking less than 20 cigarettes/day for nearly 1 year). Alcohol ingestion was infrequent and had triggered cluster attacks in the past. Ophthalmologic and neurologic examinations as well as brain and orbital magnetic resonance imaging scans were normal.

Case Two.—A 46-year-old man with episodic cluster headaches since the age of 29 years presented with shooting black-and-white flashing lights lasting approximately 15 minutes (occurring rarely up to as many as 30 minutes) preceding headache attacks

since the onset and never occurring unrelated to a headache. The cluster periods typically occurred every 1.5 years lasting for 4 weeks with an average daily frequency of 2-3 attacks preceded by the visual symptoms in at least 2 daily attacks.

During the ongoing cluster period, however, which started 7 days prior to presentation and which occurred 5 years after the last with headache features similar to the previous ones, the aura was not present. Neurological examination was normal. The patient responded well to transitional, preventive, and acute therapies.

Questions.—How frequent are auras in cluster headaches? Do auras occur in other nonmigraine primary headaches?

EXPERT OPINION

Auras and Cluster Headaches: 1970s and 1980s.—The frequency of aura with CH is controversial with Ekbom and colleagues stating that, “. . . aura . . . is most likely not a common phenomenon as judged from experience in a representative study population”⁵ and Rozen countering, “studies now have indicated that upwards of 20% of patients with CH may have aura, the same percentage of migraine sufferers who have aura.”⁶ Ekbom reported no aura symptoms in a series of 163 patients with CH in 1970 in Sweden.⁷ Out of 60 CH patients reported by Lance and Anthony in 1971 in Australia, 1 experienced visual spots and 1 visual flashes.⁸ Graham, from the USA, stated in a lecture published in 1972, “Now to our own surprise we were able to establish that in 20 cluster headache patients [out of 100] brief episodes of scintillating scotoma rarely, but occasionally, did precede the cluster headache attack. Several of these were voluntarily presented to us and others we dug out.”⁹ In 1977, Medina and Diamond, in the USA, reported 5 CH with the following auras: 2 visual, 1 contralateral weakness, 1 ipsilateral photopsias, and 1 contralateral paresthesias.¹⁰ In 1988, Guiloff and Fruns in the UK reported CH patients having episodes of limb or body pain in close temporal associated to headaches with 7 as the only additional feature and the following with the additional aura symptoms: 2 with visual, 4 with unilateral paresthesias, and 3 with unilateral weakness.¹¹

Reports in the 2000s.—Silberstein et al¹² in the USA in 2000 reported aura in 6 out of 101 patients with CH, 5 with visual and 1 with an olfactory aura with a duration of 5 to 120 minutes and onset before the headache. In a 2002 study of 554 CH patients in Sweden seen over 3 decades who usually underwent repeated interviews, Ekbom et al found that none of the patients reported aura symptoms in connection with their CH attacks.^{5,13} Although referred to a neurology clinic, they believe that their patients were representative of the general population of patients with CH. In another 2002 study from Spain of 254 CH patients seen in a neurology clinic, Martínez-Fernández and colleagues found aura in 5 (2%), 1 with visual and sensory, 2 with sensory, and 2 with sensory and complaints of weakness auras.¹⁴ In a third 2002 study of 230 CH patients from a specialty clinic and recruited from CH support groups, Bahra et al in the UK found 14% with the following aura symptoms occurring in most either during or within 60 minutes before or after the CH attack: 70% visual, 16% hemimotor, 13% hemisensory, and 1% experienced both visual and hemisensory symptoms.¹⁵ Of those with aura, 36% had a history of migraine with (40%) and without (60%) aura. Considering the occurrence in the total cohort, there was little difference in the frequency of aura between those with episodic (14%) and chronic (15%) CH and between men (13%) and women (18%).

In Lin et al's study of 140 episodic CH patients in Taiwan in 2004, only one had a visual aura.¹⁶ Fattah and Cutrer, in 2006, described the unusual case of a 72-year-old woman with a 30-year history of episodic CH preceded 50% of the time by a single visual aura lasting seconds to 3 minutes occurring 3 days to 1 week before the onset signaling the beginning of a new cluster period.¹⁷ In Schürks et al's 2006 cohort of 246 clinic- and nonclinic-based CH patients in Germany, 23% reported an aura prior to the onset (fortifications, tunnel vision, hemiparesis, hemisensory symptoms, dysarthria, and/or dysphasia) with no difference between men and women and episodic and chronic CH.¹⁸ Donnet et al, in 2007, reported 109 chronic CH patients (82% men) seen in specialty clinics and reported the following types of auras in 20% (3 woman): visual, 18 patients (positive in 11 and

negative in 7); paresthetic, 9 patients, and/or aphasic in 1 patient.¹⁹

Rozen and Rishman performed a large US survey in 2008 of 1134 (816 men and 318 women) email and internet respondents with CH who reported visual, sensory, or language/speech auras in 21% and in the following percentages among these groups: men, 22%; women, 19%; chronic CH, 23%; and episodic CH, 20%.^{6,20} Ninety-two percent of auras lasted less than 25 minutes, 55% lasting less than 10 minutes, and 25% less than 5 minutes. Women's aura typically lasted 5 minutes or less while men had average auras lasting 6-10 minutes. In Wöber and Knopf's 2009 Austrian survey of 76 CH patients, aura occurred in 28% with visual symptoms in 20%.

Why the Disparity? Pathophysiology.—This is a curious situation to find such a great disparity in the frequency of CH aura across the multinational reports of so many notable headache researchers. As Tfelt-Hansen elaborates,²¹ historically, it is of interest that Horton, who reported seeing 1176 patients with histaminic cephalgia,²² and Kudrow, who describes 495 CH patients in his book,²³ did not mention any with aura yet Graham reported 20%. Ekblom, with a special interest in aura, personally interviewed 427 patients, and found none with aura, and yet others are finding about 20%. Tfelt-Hansen states, "These differences demonstrate that the method of registering 'so-called aura' must have varied considerably," and concludes, "In my opinion, aura must be rare among cluster headache patients." (Krymchantowski contributed the 2 cases for the expert opinion from his specialty clinic in Brazil where 6-7% of his 181 CH patients have reported aura while Evans, in the USA, cannot recall seeing any CH patients with aura in 29 years although, like many neurologists, may not have specifically asked about the presence of aura symptoms which may lead to underreporting.)

Are there other explanations and are the descriptions accurate? What to make of Rozen and Rishman's finding of 25% of auras lasting less than 5 minutes? Although arbitrary, what is the minimum duration of an aura to be considered an aura, is it seconds or minutes or 5 minutes? Migraineurs may have a brief period of perturbed vision without posi-

tive or negative phenomena before the visual aura.²⁴ Does this occur before aura in CH and does the duration count towards the total duration of the aura? Is blurred vision alone an aura? CH patients may remember poorly their symptoms and not know the actual duration of the auras. If occurring during a cluster headache, hyperventilation syndrome, which might be provoked by pain, can produce unilateral paresthesias and blurred vision.²⁵

There is no definitive explanation for the aura in cluster patients but its presence suggests cortical spreading depression as in migraine aura. The aura would not originate from the suprachiasmatic nucleus of the hypothalamus, which is the presumed generator for cluster periods.²⁶⁻²⁸ Rozen suggests a hypothetical link that cortical spreading depression may modulate the hypothalamus (directly and have an effect on orexin A) and also leads to nitric oxide production (nitric oxide may be a main contributor to CH pathogenesis).⁶

Chronic Paroxysmal Hemicrania, Hemicrania Continua, and New Daily Persistent Headache.—Auras may also be present in other nonmigraine primary headaches. There is a report of a 60-year-old man with no prior history of headache who developed chronic paroxysmal hemicrania 3 days after sustaining a minor head injury without loss of consciousness. The resultant headaches were associated with an aura of tingling and mild-to-marked weakness of the ipsilateral upper extremity with resolution on indomethacin, recurrence off, and resolution on again.²⁹ A second report exists of a 17-year-old boy with a history of prior migraine without aura and visual aura without headache with probable episodic paroxysmal hemicrania (only 1 attack period lasting longer than 7 days) who had 4 visual auras followed by attacks of paroxysmal hemicrania.³⁰

Aura may be associated with hemicrania continua (HC) as well. Peres and Rosen reported 4 patients with visual aura preceding or accompanying headache exacerbations lasting 5-15 minutes.³¹ Peres et al reported 2 patients with HC with side shifting and visual aura lasting 15-20 minutes.³² Kuhn et al described a single patient with the remitting form of HC with an olfactory aura during episodes of exacerbation.

Finally, in a study of 56 patients with new daily persistent headaches meeting Silberstein's criteria, visual photopsias were reported by 9% and seeing zigzag lines by 5%.³³ In another study, 1/31 patients who met International Classification of Headache Disorders second edition criteria for new daily persistent headaches had a visual aura lasting 5-10 minutes during painful exacerbations.

CONCLUSION

Although of a somewhat controversial frequency in CH, auras present a fascinating association with CH and other nonmigraine primary headaches of uncertain pathophysiology. Consequently, they should be studied further. When aura or other migrainous symptoms are present, they might lead to diagnostic confusion with migraine and contribute to the diagnostic delay of CH, which continues to be a significant problem. Rozen and Fishman's large survey found the average time to correct diagnosis was less than 1 year for only 25% but 10 or more years for 22%.²⁰

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