



Trigemino-Autonomic Headaches

Definition

Cluster headache belongs to a group of idiopathic headaches that all involve activation of trigeminovascular nociceptive pathways along with reflex cranial autonomic activation. The revised version of the classification of the International Headache Society (IHS) outlines this group, known as the trigemino-autonomic cephalgias (TACs). All these headache syndromes have two features in common: short-lasting, unilateral, severe headache attacks and typical autonomic accompanying symptoms. To date, the following syndromes belong to the TACs:

- episodic and chronic cluster headache (CH)
- episodic and chronic paroxysmal hemicrania (PH)
- short-lasting unilateral neuralgiform headache with conjunctival injection and tearing (SUNCT syndrome)

These syndromes differ in the duration, frequency, and rhythm of the attacks and in the intensity of pain and autonomic symptoms, as well as in treatment options. The concept of trigemino-autonomic syndromes is certainly useful for clinicians seeking a pathophysiological understanding of the primary headaches and allows the various treatments aimed at treating or preventing these headaches to be put into context.

Epidemiology

Compared to migraine, cluster headache is relatively rare. CH has a prevalence of less than 1% and mostly affects men. Before 1990, CH was not generally considered an inherited disorder. However, the observation of CH in identical twins and a report on the familial occurrence of CH in 7% of patients underscores the importance of considering genetic factors in the etiology. However, no precise mode of inheritance has yet been found.

One of the most urgent questions patients ask their doctors is whether, as in migraine, the cluster attacks decline with age. Longitudinal data for CH have been anecdotal, and only recently have larger epidemiological studies become available. Taken together, the authors of these studies assume that within the natural course of the condition, the symptoms remit with age.

Pathophysiology

Although the syndrome is well defined from a clinical point of view and has been recognized for more than two centuries, its pathophysiology is still poorly understood. However, the last decade has seen remarkable progress toward unraveling the pathophysiological puzzle. The relapsing-remitting course, the seasonal variation of the syndrome, and the clockwise regularity of single attacks are characteristic and suggest an involvement of the biological clock, namely the hypothalamus, in the origin of the illness. Functional imaging work using positron emission tomography (PET) has confirmed a highly specific activation of the hypothalamic gray in CH attacks, suggesting the involvement in the pain process in a permissive or triggering manner (see the fact sheet on Neuroimaging in Headache).

Clinical Features

The diagnosis of CH is exclusively a clinical task. The International Classification of Headache Disorders uses explicit diagnostic criteria (see the box below). In the episodic form, the relatively short-lived (lasting 15–180 minutes), extremely painful attacks occur daily for some weeks followed by a period of remission. In the chronic form, attacks occur without significant periods of remission. On average, a cluster period lasts 6–12 weeks, while remissions can last up to 12 months.

Cluster Headache Definition

- A:** At least 5 headache attacks fulfilling criteria B–D:
- B:** Severe or very severe unilateral orbital, supraorbital, and/or temporal headache attacks, which last for 15–180 minutes when untreated.
- C:** The headache is accompanied by at least one of the following symptoms ipsilateral to the pain (autonomic symptoms):
1. Reddening of the eye or tearing
 2. Nasal congestion and/or runny nose
 3. Eyelid edema
 4. A sense of restlessness and agitation
- D:** The attacks range in frequency from 1 every other day to 8 per day

Therapy

In general, CH treatment can be divided into acute therapy aimed at aborting individual attacks and prophylactic therapy aimed at preventing recurrent attacks during the cluster period. Nondrug treatment is ineffective in nearly all patients.

Acute Treatment

Inhalation of pure (100%) oxygen via a non-rebreathing facial mask with a flow rate of at least 7 L/min (sometimes more than 10 L/min) is effective in stopping CH attacks. Inhalation should be continued for 20 minutes in an upright seated position. There are no known contraindications for the application of oxygen. About 60% of all CH patients respond to this treatment with a significant reduction in pain within 20–30 minutes.

Oral ergotamine has been used in the treatment of CH attacks for more than 50 years and is effective when given very early in the attack. It has been recommended as an aerosol spray for the treatment of an acute CH attack. Triptans injected subcutaneously or administered as a nasal spray are effective in about 75% of all CH patients (relieving pain within 20 minutes). The absorption and pharmacological actions of oral medications are usually too slow.

Contraindications are cardio- and cerebrovascular disorders and untreated arterial hypertension. The preemptive use of triptans in CH remains controversial.

Preventive Pharmacotherapy

Given that many patients have between one and eight short-lived attacks a day, the importance of an effective preventive regimen cannot be overstated. The primary goal of preventive therapy is to suppress attacks and to maintain the remission over the expected duration of the cluster period. To achieve this goal, an individual therapy regimen has to be designed with the patient. In episodic CH, once the therapy is effective, the medication should be withdrawn when the expected cluster period is over. In chronic CH, the medication should be gradually reduced once every other month, to determine whether it is still necessary.

The cornerstone of medical prophylaxis is verapamil. Regular ECG testing is required. Since verapamil is normally well tolerated, it is also the drug of choice for continuous treatment in chronic CH. Lithium (lithium carbonate) is also very effective; the improvement in chronic CH is reported to be as high as 78%. Regular testing of liver, renal, and thyroid function and of electrolytes is required. The efficacy rates reported for methysergide range between 20% and 73%. However, this drug cannot be used longer than 4 months. Likewise, corticosteroids are clinically very effective, but because of side effects they should only be administered for a few days or weeks in a row.

References

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