

Cluster headache

Author: Doctor Jean-Marc Visy¹ and Professor Marie-Germaine Bousser

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¹Polyclinique Courlancy, 38 bis, rue de Courlancy, 51100 Reims, France. jmvisy@wanadoo.fr

[Abstract](#)

[Keywords](#)

[Name of the disease and synonyms](#)

[Names of excluded diseases](#)

[Diagnostic criteria/Definition](#)

[Comments on the differential diagnosis](#)

[Incidence](#)

[Clinical description](#)

[Management and treatments](#)

[Etiology](#)

[Biological methods of diagnosis](#)

[Genetic counseling](#)

[Unresolved questions and comments](#)

[References](#)

Abstract

Cluster headache mainly affects young adults, predominantly males (M/F sex ratio = 4). Fierce, continuous pain occurs in the orbit and face several times daily as brief attacks over periods of several weeks, separated by attack-free intervals of complete remission. The word attack is used to describe each onset of pain and the word episode or cluster for the period comprised of series painful attacks followed by remission. Diagnostic criteria include A : at least 5 attacks meeting criteria B and D; B : severe unilateral orbital, supraorbital and/or temporal pain lasting 15 to 180 minutes without treatment; C : headache associated with at least one of the following manifestations occurring on the side pain of the conjunctival redness, tearing eyes, nasal congestion, rhinorrhea, sweating of the face and forehead, myosis, ptosis, edema of the eyelid; D : frequency of 1 to 8 attacks per day; E : at least one of the following characteristics : medical history, physical and neurological examinations are not suggestive of any organic disorder; an organic disorder exists but the first cluster headache was temporally independent of its. Prevalence is unknown in France, but is estimated to be 1/10,000 inhabitants based on foreign studies. The first attacks occur between ages 10 and 30 in 2/3 of patients. An underlying genetic factor is probable. The pathophysiology of this disease remains unknown. At present, treatment is only symptomatic. The only two treatments of attacks with proven efficacy are subcutaneous sumatriptan and oxygen inhalation.

Keywords

Contunuous facial pain, vascular algesia of the face headache, attack: onset of pain.

Name of the disease and synonyms

Vascular algesia of the face (VAF);

red migraine;

sphenopalatine neuralgia;

erythroprosopalgia.

Cluster headache (American term), retained in the international classification of headaches, is

much better than the French term (VAF) because it includes the essential characteristic of the disease, which is the occurrence of a volley or 'cluster' of headaches.

Names of excluded diseases

This section corresponds to the differential diagnosis.

Cluster headaches are often confused with migraine essential trigeminal neuralgia and paroxysmal hemicrania.

Diagnostic criteria/Definition

This disease mostly affects young adults and predominantly males (male/female sex ratio = 4). The pain is primarily orbitofacial, continuous, and very sharp. The pain occurs daily in brief attacks during periods of several weeks, separated by attack-free intervals when the remission is complete. We speak of attack or crisis for each painful attack and of episode (or cluster) for each period comprised of series of paroxysmal painful attacks followed by remission.

The diagnostic criteria are: (according to International Headache Society : IHS)

- At least 5 attacks satisfying criteria B and D;
- Severe unilateral orbital, supraorbital or temporal pain, lasting 15-180 minutes without treatment;
- Headache associated with at least one of the following characteristics occurring on the pain-afflicted side:
 - injection of conjunctiva
 - tearing
 - nasal congestion
 - rhinorrhea
 - facial and forehead sweating
 - myosis
 - ptosis
 - palpebral edema;
 - 1-8 attacks per day;
- At least one of the following characteristics:
 - prior history, physical and neurological examinations do not evoke an organic disorder,
 - the possibility of which is eliminated by neuro-imaging or another examination,
 - an organic disorder exists but the first attacks had no temporal association with it.

For episodic cluster headaches

- At least 2 attacks of facial pain correspond to all the criteria of a cluster headache;
- Attacks occurring during periods lasting for 7 days to less than 1 year, separated by remissions of at least 14 days.

For chronic cluster headaches

- The facial pains correspond to all the criteria of a cluster headache;
- No remission during 1 year or more, or remissions lasting for less than 14 days.

Comments on the differential diagnosis

Cluster headache is a poorly understood disease. Very often, sinus, dental, nasal or temporomandibular joint lesions are wrongly incriminated in the clinical picture of cluster headache and are sometimes at the origin of self-mutilation. In a personal study of 76 cases of cluster headache (18), we showed that several years passed before the diagnosis was made. The patients had consulted ophthalmologists (30%), ear, nose and throat specialists (46%), stomatologists (40%), gastroenterologists (6%), without counting the number of patients wrongly treated for facial neuralgia. Other paroxysmal headaches and unilateral facial algeias included the following principal diagnoses.

Migraine (5)

The headaches are more prolonged (4- 72 hours), less localized, less severe, associated with: Photophobia, phonophobia, digestive signs, nausea, vomiting. Sometimes a neurological aura precedes the onset of the headache. In comparison with a cluster headache, the vasomotor component, centered on the eye and nose, is weaker. The evolution over time does not include cluster attacks. The patient's behavior is different: seeking rest for a migraine, being agitated during a cluster headache.

Essential trigeminal neuralgia

This entity affects subjects over 60 years old, which constitutes the major element of its differential diagnosis. The facial pain is unilateral, either episodic or chronic. The pain is of much shorter duration (in flashes and electric shocks of several seconds) than that of cluster headaches and is repeated in 1- or 2-minute volleys. These volleys are repeated several times per 24 hours. The site of the pain in the trigeminal region differs in the two entities. There is a trigger zone and usually no neurovegetative signs are associated.

Sometimes, trigeminal neuralgia can be associated with cluster headaches, giving rise to a 'cluster tic' (19).

Paroxysmal chronic hemicrania

This rare disease was described in 1974 by Sjaastad and Dale (12). It occurs in women in 80-90% of the cases and starts between 20 and 60 years of age (range: 11-81 years) (3).

The symptomatology of the attacks is the same as that for cluster headaches, but the volleys are briefer, lasting several minutes and more frequent (10-30/day) and disappear under indomethacin.

Unilateral headaches caused by lesions

- Raeder's paratrigeminal syndrome (10) : it associates unilateral and continuous orbital pain with an incomplete Claude Bernard-Horner syndrome and hypoesthesia in the ophthalmic nerve region (V1). An organic pathology should be sought in the cavernous sinus (tumor, aneurysm).
- Unilateral pain of a dissected carotid (4) : a dissected carotid can be manifested by pain in the eye and a Claude Bernard-Horner sign mimicking a first attack of cluster headache. Doppler ultrasonography of the vessels of the neck should be performed without hesitation when confronted with these symptoms, when the evolutive character by crises is not known.
- Acute glaucoma : its pattern of evolution is very different from that of cluster headaches.
- Horton's (giant-cell) arteritis : the region, associated signs and permanent character of the pain differ from those of cluster headaches.

Incidence

Cluster headache is a rare disease, 100 times less frequent than migraine. Its prevalence is poorly known in France. It is estimated at approximately 1/10,000 inhabitants, based on studies in other countries.

The first attacks occur between the ages of 10 and 30 years in 2/3 patients (5), but a range of 1-73 years has been observed. There is a clear-cut male predominance, with 85-92.6% of cluster headaches occurring in men.

Clinical description

The pain (5,8)

The pain is strictly unilateral in 60-80% of the patients, in the ocular or periocular region. It can radiate towards the forehead, temple, cheek bone, cheek, upper gums. More rarely, it can extend to the lower gums, palate, mandible, affecting in this case the entire side of the face. It can spread to the neck or even the shoulder.

In 15-20% of the patients, pain is maximal in the temple (15) but, even in this situation, the presence of ocular pain is constant.

The pain remains unilateral for the entire duration of the attack. During the course of the volleys, the pain can change sides, but such an event is highly unusual (9). It occurs on the same side of the face in 91% of the cases.

The pain is atrocious, readily described as a blunt knife piercing the eye and being twisted.

The attack lasts between 15 and 180 minutes, with a median around 90 minutes.

The cluster is repeated 1-8 times a day, often at the same time, usually at night, with the pain

presenting the same characteristics and the same duration.

Symptoms associated with the pain (5, 6, 8)

The manifestations are almost constant and located on the same side as the pain:

- Claude Bernard-Horner syndrome (homolateral myosis and ptosis, 20%) with tearing (50-80%), conjunctival redness (27-84%);
- Congestion with nasal obstruction (one-third of the cases);
- More rarely, nausea, with or without vomiting; protuberance of the temporal artery; hypersensitivity to touch, light and sound; periorbital edema, painful hyperesthesia of the face that persists for several hours after the attack.

Patient's behavior

The patient's behavior is highly evocative. It is opposite to that of a person suffering from a migraine. A patient with a cluster headache cannot stand still, "he is like a bear in a cage", "he wants to bang his head against the wall" or "to rip out the painful eye".

Periodicity of the attacks (5, 8, 9)

- Episodic cluster headaches (18)

For 90% of the patients, the attacks occur in periods of 3-16 weeks, separated by attack-free intervals lasting from several months to 2 decades. Most often, the patients have 1 or 2 episodes per year, usually in the fall or spring.

- Chronic cluster headaches

For 10% of the patients, the attacks occur daily over several months or even several years without remission. Cluster headaches can be chronic from the start or be preceded by an episodic type of evolution. However, chronic disease can revert to the episodic form.

Management and treatments

Treatments of attacks

The only two treatments proven effective by controlled trials versus placebo are:

- inhalation of normobaric oxygen with a mask (7 liters/minute for 15 minutes)
- sumatriptan (6 mg subcutaneously).

In addition, despite the lack of controlled trials versus placebo, the efficacies of dihydroergotamine (inhalation, subcutaneous, intramuscular, intravenous) and ergotamine tartrate (oral, suppository) have been observed.

Symptomatic treatment of episodic cluster headaches

These therapies have not been subjected to controlled trials versus placebo:

- ergotamine tartrate (2-mg/day, per os)
- methysergide (3-18 mg/day)
- pizotifen (2-3 mg/day)
- verapamil (120-80 mg/day)
- prednisone (40 mg/day for 5 days then 10-20 mg/day).

Treatment of chronic cluster headaches

These therapies have not been tested by controlled trials:

- verapamil (120-480 mg/day)
- lithium (blood lithium concentrations < 0.9 mmole/liter).

Etiology

The pathophysiology of the disease remains obscure, but the involvement of the trigeminal-vascular system on the one hand, and the autonomic nervous system on the other, is highly probable. Histamine and serotonin are the neuromediators that have been studied the most. Increased histamine and serotonin metabolism during cluster headaches has been reported (2).

Data concerning vasomotor modifications are contradictory: concentric diminution of the arterial diameter secondary to parietal edema or a spasm but not followed by a perturbation of the blood flow.

Neurovegetative modifications reflect sympathetic hypoactivity (ptosis, myosis, nasal obstruction, conjunctival redness) and parasympathetic hyperactivity (sweating, tearing, rhinorrhea, myosis).

The circadian periodicity oriented research towards a dysregulation of the organism's internal clock. A lower level of nocturnal melatonin was observed during attacks.

According to recent segregation studies, the existence of a genetic factor is probable.

Biological methods of diagnosis

This approach is justified only in atypical forms, with Doppler ultrasonography of the vessels of the neck, arteriography to eliminate carotid dissection, computed tomography scan, magnetic resonance imaging.

Genetic counseling

Several observations raise the possibility of a genetic factor in cluster headaches. But the data remain preliminary:

- Familial incidence in 5% of the cases (1);
- Cluster headaches observed in 3 pairs of homozygous male twins;
- Families with cluster headaches over several generations (Sprierings' family: paternal grandfather, father, affected children) (14);

- Kudrow (7) studied 405 men and 90 women with cluster headaches: 38% of the men and 58% of the women had a first-degree relative who suffered from migraines, thus giving rise to the hypothesis of a common genetic susceptibility for the 2 entities;
- Russell *et al* (11) studied 421 probands with cluster headaches by analyzing the questionnaires they filled out concerning the presence of cluster headaches in their respective families. By comparing them to the general population; Russell *et al*. found a relative risk of 14.1% for first-degree relatives and 2.3% for second-degree relatives, thus suggesting a strong genetic predisposition;
- In an ongoing investigation based on 130 subjects, our group identified 12 families with at least one first-degree relative affected, which seems to confirm the existence of a genetic factor.

Unresolved questions and comments

- The pathophysiology of this disease remains unknown.
- No epidemiological study in France has been undertaken.
- The natural history of cluster headaches is still poorly understood.
- Treatment at present is symptomatic; no curative therapy exists.
- With the exception of sumatriptan and oxygen inhalation for attacks, no other treatment has been subjected to randomized controlled trials and most treatments prescribed are outside the indications authorized.

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