122

Cluster Headache and Other Trigeminal Autonomic Cephalalgias

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Introduction

Trigeminal autonomic cephalalagias (TACs) are a group of primary headache disorders that share many clinical features, but differ in the epidemiology, duration and frequency of the pain attacks as well as their response to treatment [1, 2].

Cluster headache is the most common TAC. Pain attacks are short but excruciating. Pain is unilateral and accompanied by autonomic signs and symptoms. Another important feature is the presence of restlessness or agitation during the pain attacks. There are several effective abortive and preventive treatment options.

The pain attacks of the other TACs are of higher frequency and shorter duration than cluster headaches and most show dramatic response to indomethacin treatment.

Pathophysiology

The pathophysiology of cluster headaches is not fully understood. Functional imaging studies during cluster attacks have demonstrated activation of an area in the posterior-medial inferior diencephalon. Dysfunction of orexin producing neurons may play a role [2].

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Epidemiology

The prevalence of cluster headaches is <1%. The male: female ratio is 4.3:1. The mean age of onset is 28 years. Genetic factors play an important role. Having a first degree relative with cluster headaches increases the risk nearly 40 fold. Smoking is considered a risk factor for the development of cluster headache, although does not seem to trigger cluster attacks. Alcohol use can trigger attacks during a cluster period but not during periods of remission. Some patients may have characteristic facial features with leonine facies and peau d'orange [2].

The epidemiology of the other TACs is described in Table 122.1.

Clinical Features

Cluster headaches can be episodic or chronic [1]. Episodic cluster headache is more common. Episodes may last weeks to month (typically 2 weeks to 3 months) alternating with periods of remissions of at least 1 month (typically 1 year). The chronic form occurs in 10–15% of cluster headache patients and is characterized by remissions lasting less than 1 month or no remission.

During the cluster episode attacks occur between once every other day to eight times per day, most commonly once or twice a day. Attacks last 15–180 min. They often have a circadian rhythm occurring at the same time each day,

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Table 122.1 TACs: Epidemiology, clinical features and treatment

	Cluster headache	Paroxysmal hemicrania	SUNCT[a]/SUNA[b]	Hemicrania continua
Female: Male	1–4.3	1:1–2.7:1	1:1.5	2:1
Attack frequency	Once every other day to 8/d	1–40/d	1–200/d	Chronic pain with acute exacerbations
Attack duration	15–180 min	2–30 min	1–600 s	Chronic pain
Abortive treatment	Sumatriptan Oxygen	N/A	Lidocaine infusion	N/A
Preventive treatment	(Prednisone) Verapamil Lithium	Indomethacin	Lamotrigine Topiramate Gabapentin	Indomethacin

[a]SUNCT: short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing
[b]SUNA: short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms

frequently at night. Episodes often occur in the spring or fall [1, 2].

The pain during cluster attacks is described as excruciating, like a "hot poker." The pain can be so severe that patients contemplate or commit suicide. Individual cluster attacks are unilateral, predominantly periorbital. A side shift during a subsequent attack may occur in up to 15% of patients. A sense of restlessness or agitation accompanies the pain [1, 2].

Ipsilateral autonomic signs and symptoms occur during the attack. They include conjunctival injection, lacrimation, nasal congestion, rhinorrhea, forehead and facial sweating, ptosis, miosis and eye lid edema. At least one of these symptoms must be present during a cluster attack [1].

The diagnosis is based on the clinical features [1]. Although cluster headache is considered a primary headache disorder, secondary causes need to be considered even in patients with the typical clinical presentation. Therefore, neuroimaging at the time of diagnosis is recommended. MR-imaging is the preferred imaging modality. Possible imaging findings include cerebral aneurysms of the carotid or anterior communicating artery, arteriovenous malformations, pituitary adenomas and sphenoid sinus disease [3].

The other TACs are described in Table 122.1. They are also characterized by unilateral severe pain attacks, accompanied by autonomic signs and symptoms, but they are of shorter duration and higher frequency [1]. Episodic and chronic paroxysmal hemicrania and hemicrania continua respond to indomethacin, while SUNCT (short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing) and SUNA (short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms) do not.

Differential Diagnosis

The differential diagnosis includes:
- Trigeminal Neuralgia.
- Primary stabbing headache.
- Cluster headache mimics.

Treatment

Treatment recommendations for TACs are based on expert consensus. The following are treatment recommendations for cluster headache [4, 5]. Treatment of other TACs is summarized in Table 122.1.

A. Acute treatment
   1. 100% nasal oxygen with non-rebreather mask at a flow rate of 12 L/min for 15 min. The flow rate can be increased if needed. This is typically well tolerated but contraindicated in patients with severe COPD. Treatment can be repeated with each cluster attack.
   2. Sumatriptan 6 mg s.c. Unless contraindicated this can be used twice in 24 h.

3. Alternatives include zolmitriptan nasal spray, sumatriptan nasal spray or oral zolmitriptan.
4. Other acute treatment includes intranasal lidocaine, oral ergotamine, or injectable dihydroergotamine (DHE).

B. Preventive Treatment
1. Steroids are indicated to induce remissions quickly. Prednisone at a dose 1 mg/kg per day for 5 days followed by a slow taper may induce remissions. Long-term steroid use should be avoided.
2. Verapamil is indicated for the prevention of chronic cluster headache and cluster episodes of >2 month duration. A typical starting dose is 240 mg/day. Doses as high as 960 mg/day may be necessary. The most common side-effects include constipation and dizziness. Cardiac conduction blocks and bradycardia are a concern. An ECG is recommended at doses above 240 mg/day and with each dose increase above 480 mg.
3. Although lithium has a good response rate (up to 78% in chronic cluster headache) it is not as well tolerated as verapamil. A typical dose is 900–1200 mg/day. Side effects include thyroid and renal dysfunction, tremor and cardiac arrhythmias. Lithium levels, renal, hepatic and thyroid function tests need to be monitored during treatment.
4. Other preventive treatment options include topiramate, valproic acid and melatonin.
5. Greater occipital nerve blocks can be effective in inducing short term remission or in patients with refractory chronic cluster headache.
6. Surgical and interventional treatment is considered investigational. This includes sphenopalatine ganglion stimulation, occipital nerve stimulation, vagus nerve stimulation and deep brain stimulation of the posterior inferior hypothalamus.

High Yield Points

- Cluster headache is the most common TAC.
- TACs are a group of primary headache disorders that are characterized by the severe, short-lasting and unilateral nature of the pain, accompanied by ipsilateral autonomic signs and symptoms.
- The diagnosis is based on the clinical presentation, although secondary TACs have been described. Neuroimaging is typically recommended at the time of diagnosis.
- Treatment response is usually good but varies between individual TACs.

Questions

1. Headaches during a cluster episode:
   A. last several seconds
   B. are triggered by cold air
   C. are accompanied by a sense of restlessness and agitation
   D. are accompanied by facial numbness
   Answer: C
2. The most appropriate abortive treatment for cluster attacks is:
   A. Sumatriptan s.c.
   B. Indomethacin
   C. Nasal oxygen
   D. A and C
   Answer: D
3. Indomethacin responsive headaches include:
   A. Cluster headache
   B. Migraine
   C. SUNCT
   D. Hemicrania continua
   Answer: D

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