Chapter 2
Diagnosis of Trigeminal Autonomic Cephalalgias

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Introduction

The trigeminal autonomic cephalalgias (TACs) refer to a specific group of primary headaches characterized by unilaterality, associated cranial autonomic features, and specific duration of pain. The major TACs as listed by the International Classification of Headache Disorders, third edition, beta version (ICHD-3) are listed in Table 2.1 and, to differentiate them, the Other Primary Headache disorders (covered in Chap. 3) are listed in Table 2.2.

The term "probable" is used in the ICHD-3 to mean a headache is missing one ICHD-3 criterion to make the diagnosis. Probable TACs are under ICHD number 3.5. The probable headaches are excluded from our tables for simplicity, utility, and clarity.

Remember that if the patient is missing a single criterion, the headache diagnosis becomes "probable." As discussed in Chap. 1, when a patient is missing a criterion, the possibility of a secondary cause increases, and serious consideration should be given to doing a careful workup for secondary causes. Essentially, a probable diagnosis should raise your suspicions for sinister etiology.

Diagnostic Features of the TACs: How to Make the Diagnosis

As with any other painful condition, making a correct diagnosis is 90 % of the battle and helps direct proper therapy. This is particularly important with the TACs, as some of these headaches can be differentiated by a response to certain medications, such as indomethacin.

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S. J. Tepper, D. E. Tepper (eds.), *The Cleveland Clinic Manual of Headache Therapy, Second Edition,* DOI 10.1007/978-3-319-04072-1_2,

Table 2.1 The major trigeminal autonomic cephalalgias (TACs), ICHD-3

ICHD-3 number, name (abbreviation)
3.1 Cluster headache (CH)
3.1.1 Episodic cluster headache (ECH)
3.2.1 Chronic cluster headache (CCH)
3.2 Paroxysmal hemicrania (PH)
3.2.1 Episodic paroxysmal hemicrania (EPH)
3.2.2 Chronic paroxysmal hemicrania (CPH)
3.3 Short-lasting unilateral neuralgiform headache attacks (SUNHA)
3.3.1 Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT)
3.3.1.1 Episodic SUNCT
3.3.1.2 Chronic SUNCT
3.3.2 Short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms (SUNA)
3.3.2.1 Episodic SUNA
3.3.2.2 Chronic SUNA
3.4 Hemicrania continua (HC)

Table 2.2 The major Other Primary Headaches, ICHD-3 (covered in Chap. 3)

ICHD-3 number, name (abbreviation)
4.1 Primary cough headache
4.2 Primary exercise headache
4.3 Primary headache associated with sexual activity
4.4 Primary thunderclap headache (PTH)
4.5 Cold-stimulus headache
4.5.1 Headache attributed to external application of a cold stimulus
4.5.2 Headache attributed to ingestion or inhalation of a cold stimulus
4.6 External-pressure headache
4.6.1 External-compression headache
4.6.2 External-traction headache
4.7 Primary stabbing headache
4.8 Nummular headache
4.9 Hypnic headache
4.10 New daily persistent headache (NDPH)[a]

[a] Also covered in Chap. 4

Table 2.3 Clinical pearls on probable headaches

- If a patient is missing a single criterion for an ICHD-3 diagnosis, the headache diagnosis becomes "probable"
- When a patient is missing a criterion, the possibility of a secondary cause increases, and serious consideration should be given to doing a careful workup for secondary causes
- A probable diagnosis should raise your suspicions for sinister etiology

Table 2.4 Duration of the TACs

- Hemicrania continua (HC): Continuous pain with exacerbations daily or several times a week lasting hours to days each
- Cluster headache (CH) attacks: 15–180 min
- Paroxysmal hemicrania (PH) attacks: 2–30 min
- Short-lasting unilateral headache attacks (SUNHA); short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT)/Short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms (SUNA) attacks): 1–600 s

Table 2.5 Initial clinical pearls on diagnosis of TACs

- Agitation is a common feature for both CH and HC, and is not listed as a criterion for PH or SUNHA in ICHD-3
- When no autonomic features are present and cluster is suspected, ask about agitation
- Unilateral photophonophobia is often present in TACs, especially HC
- Make sure the patient has had a very good MRI. Diagnosis of a TAC should provoke a workup for a hypothalamic or pituitary lesion; as many as 10% of patients with TACs will have an abnormality of this region or the posterior fossa
- Within SUNHA, SUNA is just SUNCT without a red eye or tearing
- SUNHA is in a different location (V1) compared to trigeminal neuralgia (TN; V2–3). SUNHA, unlike TN, is associated with autonomic features
- A woman with frequent CH-like attacks should make the clinician think of paroxysmal hemicrania (PH)

Duration of TACs

Wags have stated that the longer the name of the paroxysmal TAC, the shorter the duration. Hemicrania Continua (HC) is continuous. Eighty-five percent of Cluster Headache (CH) attacks last between 15 and 180 min. Paroxysmal Hemicrania (PH) attacks are between 2 and 30 min. And the duration of Short-lasting Unilateral Headache Attacks (SUNHA), including Short-lasting Unilateral Neuralgiform headache attacks with Conjunctival injection and Tearing (SUNCT) and Short-lasting Unilateral Neuralgiform headache attacks with cranial Autonomic symptoms (SUNA), is measured in seconds (1-600 s).

The current ICHD-3 criteria for the diagnosis of the TACs are listed in the subsequent tables. As noted above, the TACs are grouped into Section 3 of the ICHD-3, and while these headaches are similar in many ways, the response to medications can vary markedly. Each will be discussed separately, but not before some points are made. These clinical pearls on TACs are listed in Table 2.5.

In both HC and CH, if the autonomic features are not manifested, an equally important criterion listed is the sense of restlessness and inability to sit still during an attack. There is a minority of patients who, during an HC exacerbation or a cluster attack, will not manifest obvious ipsilateral sympathetic paresis (miosis, ptosis, Horner's) or parasympathetic discharge (conjunctival tearing, rhinorrhea, etc.). In such cases, the patient must report (or a companion must report) that the patient

will rock, pace, or otherwise appear agitated. One of my cluster patient's wife told me that the patient was groaning and holding his involved eye; next to him on the pillow was a handgun! This degree of agitation is not required or listed for PH or SUNHA.

Never underestimate the severity of the pain of CH! CH is called the "suicide headache" for good reason.

As many as 50% of patients with TACs will refer their symptoms of photophonophobia to the ipsilateral, painful side, in contrast to migraineurs, who usually complain of bilateral light and sound sensitivity. HC, in particular, manifests unilateral photophonophobia in at least half of patients, and ipsilateral photophonophobia should make the clinician think seriously about a TAC diagnosis.

The diagnosis of a TAC should provoke a workup for a hypothalamic or pituitary lesion; as many as 10% of patients with TACs, in particular SUNHA, will have an abnormality of this region or the posterior fossa on a good imaging study, in particular SUNHA. If the clinician has not visualized a magnetic resonance imaging (MRI) with and without contrast as part of the workup, repeating one should be considered.

SUNA is simply a SUNHA without the red eye or tearing, so SUNA and SUNCT are very similar. Neither is indomethacin responsive; both tend to respond to antiepilepsy drugs such as lamotrigine or gabapentin.

Trigeminal neuralgia (TN) does not manifest autonomic features and is only rarely in V1, so location and associated autonomic features distinguish SUNHA from TN, even when the duration of attacks is similar. In addition, SUNHA is usually heralded by stabs of pain, sometimes in a sawtooth pattern, not seen in TN.

A woman with frequent cluster-like attacks, especially if not terribly agitated, should make the clinician think of PH rather than CH, due to gender alone. After ruling out secondary causes, an indomethacin trial may be indicated.

Diagnosis of Cluster Headache

CH, the most common of the TACs, are generally more common in males, starting as early as the second decade. CH can persist well into life, as far as into the seventh decade. They are called clusters because they tend to cluster at the same time(s) of the year, with cycles or periods of daily attacks lasting for weeks to months in the episodic variety, and remissions lasting for months to years. This is considered to be a reflection of the relationship of these headaches with circadian and circannual periods and the effect of light–dark cycles on the suprachiasmatic nucleus of the hypothalamus, by way of the retinal–hypothalamic–pineal pathways.

Approximately 85% of all CHs are *episodic*; the cluster period or cycle, as it is called, spontaneously remits, and there will be freedom from CH attacks for a month or longer each year in episodic cluster headache (ECH).

The remaining cluster sufferers have *chronic* clusters in which they will have headaches daily or near daily and will not be free from a CH attack for any period of a month or more in a given year. Chronic cluster headache (CCH) may start de novo, but generally evolves from the episodic variety.

Table 2.6 Diagnostic criteria for cluster headache, ICHD-3

A. ≥5 attacks fulfilling B–D
B. Severe or very severe unilateral orbital, supraorbital, or temporal headache attacks, untreated lasting for 15–180 min
C. Either or both of the following
   1. At least one of the following symptoms or signs, ipsilateral to the headache
      A) Parasympathetic activation
         a. Conjunctival injection or lacrimation
         b. Nasal congestion and/or rhinorrhea
         c. Eyelid edema
         d. Forehead and facial sweating
         e. Forehead and facial flushing
      B) Sympathetic paresis
         f. Horner's or partial Horner's (miosis, ptosis)
      C) Miscellaneous
         g. Sensation of fullness in the ear
   2. A sense of restlessness and agitation
D. The attacks have a frequency QOD to 8/day during an active period
E. Secondary causes excluded

Episodic cluster headache (ECH)
- At least two cluster periods lasting 7 days to 1 year, separated by pain-free periods lasting ≥1 month

Chronic cluster headache (CCH)
- Attacks occur for >1 year without remission or with remission for <1 month

Probable cluster headache: attacks missing one criterion

Table 2.7 Clinical pearls on diagnosing cluster

- Attacks are short, sharp, and severe (triple S; SSS) and occur with an average frequency of 1–3/day
- Attacks manifest parasympathetic activation and sympathetic paresis with agitation
- Attacks occur with alarm clock periodicity
- Circadian and circannual periodicity are seen frequently in CH, but usually not the other TACs
- Cluster patients in cycle rarely, if ever, drink alcohol, due to the severity of the trigger
- Smoking and obstructive sleep apnea are common in cluster patients
- In about one-third of the cluster patients, there can be low-level ipsilateral interictal pain, making it sometimes difficult to differentiate from HC, but the intensity of the continuous pain is generally worse in HC

Most cluster attacks are severe and retro-orbital. They are not throbbing; rather, they are described as burning, boring, stabbing, or tearing. Attacks are short, sharp, and severe (triple S; SSS).

Cluster attacks are manifested by parasympathetic activation (scleral injection, lacrimation, diaphoresis, nasal stuffiness, and/or rhinorrhea). Less common is a Horner's or partial sympathetic paresis with ptosis and/or miosis. As noted above, agitation is the rule, and cluster attacks are generally shorter than 3 h in duration. Major diagnostic criteria for CH are listed in Table 2.6.

There is a circadian alarm clock periodicity to the attacks, attacks occurring at the same time of day or night, and a circannual periodicity with the cluster periods

occurring at the same time of year, often with the changing of the clocks for daylight savings time. The periodicity feature of CH, extremely useful in diagnosis and not usually seen in the other TACs, is not included in the ICHD-3 criteria.

Attacks can be precipitated by alcohol, fumes such as gasoline fumes, excessive exercise, and napping. Cluster patients in cycle rarely, if ever, drink alcohol. Cluster patients are commonly smokers, however.

In about 30% of cluster and PH patients, a low-level pain can persist ipsilaterally interictally. The patients describe this as a "ghost pain" between attacks. The continuous pain of HC is generally more severe, averaging 6–7/10 in intensity.

Diagnosis of the Paroxysmal Hemicranias

The Paroxysmal Hemicranias (PH) are defined by an absolute response to indomethacin. The headaches are similar in quality to cluster pain, but the pain is shorter lasting and more frequent during any given day.

As with CH and HC, there are both *episodic* and *chronic* PH subforms. Episodic Paroxysmal Hemicrania (EPH) occurs in periods lasting 1 week to a year, and its occurrence is separated by pain-free periods lasting 1 month or longer (remissions). When cycles of attacks of PH last more than 1 year without remissions lasting 1 month or longer, the headache qualifies as Chronic Paroxysmal Hemicrania (CPH). This distinction is identical to that in CH.

EPH is more rare than CPH, the opposite of CH, where the episodic subform is more common. In EPH, the disorder occurs equally in males and females, while in CPH there is a female predominance. CH always has a male predominance, regardless of subform.

Attacks of PH can be less severe than CH, but in the same location. The attacks are quite short, up to 30 min only, allowing for 15 min of overlap with CH attacks. The usual duration of a PH attack is 14 min, so it is usually easy to tell from SUNHA or TN. SUNHA attacks are from 1 s to 10 min, but average duration is 50 s. However, there is an overlap of a 2–10-minute duration between SUNHA and PH, so indomethacin can be the important distinguishing feature, as SUNHA does not respond to indomethacin. TN attacks are much shorter, there are no autonomic features, and are usually in V2–3, while PH is in V1.

More than half of the time, PH attacks occur more than five times per day by ICHD-3 criteria, so attacks usually occur more frequently in PH than CH. The frequency of CH attacks can be up to eight times per day, so the frequency of the two disorders can overlap, but this is rare. In general, CH attacks occur one to three times daily, and PH attacks occur with a mean frequency of eight times per day. SUNHA attacks can occur hundreds of times per day.

Patients are less frequently agitated in PH than with CH. Agitation is not a diagnostic criterion for PH, but is for CH.

There is no circadian or circannual periodicity. PH attacks occur at random.

Table 2.8 Diagnostic criteria for paroxysmal hemicrania, ICHD-3

A. ≥ 20 attacks fulfilling B–E
B. Attacks of severe unilateral orbital, supraorbital, or temporal pain lasting 2–30 min
C. Headache is accompanied by ≥ one of the following:
   1. Ipsilateral conjunctival injection or lacrimation
   2. Ipsilateral nasal congestion or rhinorrhea
   3. Ipsilateral eyelid edema
   4. Ipsilateral forehead and facial sweating
   5. Ipsilateral forehead and facial flushing
   6. Sensation of fullness in the ipsilateral ear
   7. Ipsilateral miosis and/or ptosis
D. Attacks have a frequency of > 5/day for > 50 % of the time, although periods with lower frequency can occur
E. Absolute responsiveness to therapeutic doses of indomethacin
F. Secondary causes excluded

Episodic Paroxysmal Hemicrania (EPH)
- At least two PH periods lasting 7 days to 1 year, separated by pain-free periods lasting ≥ 1 month

Chronic Paroxysmal Hemicrania (CPH)
- Attacks occur for > 1 year without remission or with remission for < 1 month

Table 2.9 Clinical pearls on diagnosing paroxysmal hemicrania

- Since cluster is a disease of men, think PH when you see a woman who reportedly has CH
- EPH occurs equally in men and women. CPH is more common in women
- If the cluster is refractory, especially if there is no response to subcutaneous sumatriptan or O2, think PH
- If there is no alarm clock periodicity or agitation, think PH
- If attack frequency is high (> 5/day) or attack duration is short (30 min), think PH over CH
- If you think PH, try an indomethacin trial before proceeding with CH treatment
- There is an overlap in duration of attacks between CH, PH, and SUNHA, so once again, indomethacin may be the way to the diagnosis of PH

Finally, and most importantly, the diagnosis of PH is made by absolute responsiveness to indomethacin. If you have ruled out secondary causes and think the patient could have PH, try an indomethacin course first before treating as if it is cluster.

Diagnosis of SUNHA (SUNCT and SUNA)

In the third edition of the ICHD, the category SUNHA includes the two recognizable forms of SUNCT and SUNA. SUNCT and SUNA are very brief headaches with prominent cranial autonomic features that can deceive the clinician because they can be triggered by cutaneous stimuli, similar to TN. These headaches are characterized by paroxysms of short-lasting (1–600 s) stabbing tic-like pain. Average duration of each attack is around 50 s. The duration of these severe attacks was expanded from 5–240 s in ICHD-2 to 1–600 s in ICHD-3.

Table 2.10 Diagnostic criteria for SUNHA (SUNCT/SUNA), ICHD-3

A. ≥ 20 attacks fulfilling B–D
B. Attacks of unilateral orbital, supraorbital, or temporal moderate to severe stabbing or pulsating pain, lasting 1–600 s and occurring as single stabs, series of stabs, or in a sawtooth pattern
C. Pain is accompanied ipsilaterally by ≥ one of the following
   1. Ipisilateral conjunctival injection or lacrimation[a]
   2. Ipsilateral nasal congestion or rhinorrhea
   3. Ipsilateral eyelid edema
   4. Ipsilateral forehead and facial sweating
   5. Ipsilateral forehead and facial flushing
   6. Sensation of fullness in the ipsilateral ear
   7. Partial Horner's: ipsilateral miosis and/or ptosis
D. Attack frequency of ≥ one/day for ≥ 50 % of the time when the disorder is active
E. Secondary causes excluded

- SUNCT: Short-lasting Unilateral Neuralgiform headache attacks with Conjunctival injection and Tearing
- SUNA: Short-lasting Unilateral Neuralgiform headache attacks with cranial Autonomic symptoms

[a] The absence of conjunctival injection and tearing but the presence of other cranial autonomic features suggests SUNA

Table 2.11 Clinical pearls on SUNHA

- Pain is maximal in V1 distribution, unlike trigeminal neuralgia (TN)
- There are autonomic features invariably, unlike TN
- As in TN, cutaneous triggers are common in SUNHA, but unlike TN, movement of the neck can also be a trigger in SUNHA
- Moderate to severe intensity
- Pain is stabbing, burning, electric-like
- Brief paroxysms of pain lasting 1–600 s each (mean 50 s)
- Attacks peak within 2–3 s
- Attack frequency varies from 1/day to 30/hour
- No latency or refractory period
- Stabs are the rule, either alone, as a herald for an attack, or in a sawtooth pattern
- SUNHA is not indomethacin responsive and usually responds to lamotrigine or gabapentin
- Remember: SUNHA is rare, which is why the workup is crucial! The most common secondary cause is a pituitary lesion

The attacks can present with isolated stabs of pain in the orbit or the temporal region or anywhere in the head, and can occur hundreds of times a day. SUNCT/SUNA can alternately present with groups of stabs (sawtooth pattern) separated by complete or incomplete resolution of the pain. A single stab can herald an attack. There may be periods of remission, or there may be no days of remission.

Unlike TN, which as noted above, SUNHA attacks might resemble because of cutaneous triggers and duration, SUNHA attacks generally do not exhibit a refractory period. Also, TN occurs < 5 % of the time in V1; SUNCT/SUNA pain is usually in V1. Time to peak for SUNHA is about 2–3 s. SUNHA attacks are longer in duration (typically 30–120 s) than TN (typically 1–3 s). SUNCT, as the names infers, is

associated with both conjunctival injection (redness) and tearing, and there may be other ipsilateral autonomic signs. SUNA may have conjunctival injection or tearing but not both together, and other autonomic features occur.

Secondary headaches may masquerade as SUNHA, including brainstem strokes, arteriovenous malformations, pituitary tumors, arterial dissections of the vertebral artery, or demyelination. It is therefore mandatory to investigate all suspected cases of SUNCT/SUNA or to personally review high-quality imaging if it has been performed.

There have been several small case series of SUNCT being cured by resection of pituitary tumors. The pathophysiology and explanation for these cures is mysterious.

Remember, SUNHA is rare. Be vigilant in a search for secondary causes.

Unfortunately, SUNHA does not respond to indomethacin as do PH and HC. Treatment for SUNCT/SUNA will be discussed in Chap. 11, but is usually lamotrigine or gabapentin.

Pathophysiology of the TACs: What you Need to Know

There is now a substantial body of evidence that the spectrum of TACs and the Other Primary Headaches are related in their pathophysiological origin, as one would suspect, since they generally share many clinical features. Recent advances with positron emission tomography (PET) scanning and functional MRI have demonstrated areas of activation in the posterior hypothalamus for all of the TACs during the headache phase. In addition, the expected areas of the cortical and subcortical pain matrix show activity in response to the pain. Table 2.12 displays the areas of hypothalamic activation.

HC offers a mirror image of CH and migraine functional imaging. Cluster manifests activation in the ipsilateral hypothalamus, HC the contralateral hypothalamus. Some scientists feel that migraine manifests activation in the contralateral upper brainstem, HC the ipsilateral upper brainstem.

Anatomically, there are reciprocal connections between the posterior hypothalamus and the trigeminal nucleus caudalis (TNC), the site of origin of the second order nociceptive neuron. In the last decade, there have been more than 50 patients who have had implantation of deep brain stimulators (DBS) in the ipsilateral hypothalamus for drug refractory CH and other TACs. There are no controlled studies of DBS for TACs, except to note that turning off working stimulators without patient knowledge has resulted in return of headaches.

For CH, in 60% of patients there has been a greater than 50% decrease in the frequency of headaches, and in 30% there has been a complete response with DBS. However, there has been one death and several transient ischemic attacks (TIAs) and strokes in the course of implanting DBS for CH.

It is now apparent that stimulation of this hypothalamic site promotes the relief of the headache and does not stimulate the pain, suggesting that the posterior hypothalamus is a key area of modulation for cluster and TAC pain. This is discussed further, along with other stimulation approaches, in Chap. 12 on treatment of the TACs and other primary headaches.

Table 2.12 Areas of hypothalamic stimulation seen with the TACs

Headache	Hypothalamic activation area (with respect to side of pain)
Cluster headache	Ipsilateral posterior hypothalamus
Paroxysmal hemicrania	Contralateral hypothalamus
Hemicrania continua	Contralateral hypothalamus and ipsilateral upper brainstem
SUNCT	Ipsilateral or bilateral hypothalamus
SUNA	Absent in patients with extraocular autonomic phenomena

Table 2.13 Differential points among the paroxysmal TACs. (Adapted from Goadsby et al. 2010)

Features	Cluster headache	Paroxysmal hemicrania	SUNCT/SUNA
Gender (M/F)	3–6/1	1/1	1.5/1
Pain quality	Stab/sharp/throb/poker	Stab/sharp/throb/poker	Stab/sharp/throb/poker
Severity	Very severe	Severe–very severe	Severe
Distribution	V1 > C2 > V2 > V3	V1 > C2 > V2 > V3	V1 > C2 > V2 > V3
Attack frequency	Every other day–8/day	Mean 11; up to 30/day	Mean 100; >100/day
Attack length	15–180 min	2–30 min	1–600s
Migraine features			
Nausea	50%	40%	25%
Photo-/phonophobia	65%	65%	25%
Triggers			
Alcohol	Yes	Yes	No
Nitroglycerin	Yes	Yes	No
Cutaneous	No	No	Yes
Agitation/restlessness	90%	80%	65%
Episodic/chronic	9/1	1/2	1/9
Circadian/circannual periodicity	Yes	No	No
Treatment efficacy			
Oxygen	70%	None	None
Sumatriptan subcutaneously	90%	20%	10% or less
Indomethacin	Almost none	100%	None

M male, *F* female, *C* cervical, *V* trigeminal

The Paroxysmal TACs: Telling Them Apart

CH, PH, and SUNHA constitute the paroxysmal TACs, in that the minority of patients have continuous pain, and the continuous pain is generally not severe. HC, on the other hand, is a continuous TAC. Table 2.13 outlines major points that help differentiate the paroxysmal TACs from one another.

Table 2.14 Hemicrania Continua (HC), ICHD-3 criteria

A. Unilateral continuous CDH for > 3 months with moderate to severe exacerbations
B. At least one of the following ipsilateral to the side of pain
   1. Conjunctival injection
   2. Lacrimation
   3. Nasal congestion
   4. Rhinorrhea
   5. Ptosis
   6. Miosis
   7. Eyelid edema
   8. Forehead or facial sweating or flushing
   9. Sense of fullness in the ear
   10. Restlessness or agitation or worsening of pain with movement
C. Complete response to therapeutic doses of indomethacin, with a trial up to at least 225 mg/day
D. Not secondary
E. Remitting subtype: Interruptions of pain for ≥ 1 day without treatment
F. Unremitting subtype: continuous pain with no remission periods of pain for ≥ 1 day for ≥ 1 year

Hemicrania Continua

HC is one of four primary daily headaches, covered in Chap. 4. However, it is a TAC as well, and since ICHD-3 classifies it in the TAC section, it is also covered here. HC is a continuous, side-locked, generally moderate (6/10 intensity) headache associated with cranial autonomic symptoms, with periodic severe intensity exacerbations. By definition, this headache is indomethacin responsive. Because HC has these qualifying autonomic characteristics, it is categorized as a trigeminal autonomic cephalalgia or TAC in ICHD-3, the only TAC that is continuous most of the time. However, as noted above, agitation can substitute as a diagnostic criterion for the autonomic features, or also can occur with them.

The ICHD-3 criteria for HC are quite specific, but there are detailed descriptions of patients with this syndrome suggesting that clinical presentations can be more variable. Still, most have a dramatic indomethacin response.

The official criteria are that the headache be strictly one-sided and continuous for at least 3 months. Periodic exacerbations occur in which the pain becomes moderate to severe (usually severe), and autonomic features such as ipsilateral lacrimation, conjunctival injection, ptosis, miosis, nasal stuffiness, or rhinorrhea occur. The response to indomethacin is incorporated in the diagnosis, and the criteria specify "complete response."

Cittadini and Goadsby described in detail 39 patients with HC, and added a number of common clinical features, in addition to the ICHD-3 criteria. The daily baseline side-locked headache of HC can be mild, although they described the continuous headache as averaging 6/10 intensity in their case series.

The exacerbation frequency was daily in about half and 5/7 days in another third, so the step-up to severe is frequent. Severe exacerbation length was from 30 min to 72 h for the most part.

Triggers for exacerbation turned out to be common and were similar to migraine, including stress or let down from stress, and alcohol, the latter also a trigger for CH. More than two-thirds of patients were agitated or restless with severe exacerbations, and more than one-fourth were described as aggressive (generally verbally, not physically). These symptoms are also similar to those found in CH.

Many patients with HC have other additional features or variable presentations. First, it is worth remembering that often patients with HC come in complaining about the exacerbations, not the daily headache. Asking about the presence or absence of headache-free time helps find patients with CDH, especially HC. This is a critical clinical point: Ask whether the patient has any truly headache-free days, that is, days without any residual or mild pain.

Additional features of HC include a foreign body sensation in the ipsilateral eye. This is variously described as like an eyelash or grit or sand. Sometimes, patients will complain that they can never get their contact lens comfortable on that side, and the sensation is also described as "itchy eye."

Ice-pick pains or primary stabbing headaches, also indomethacin responsive, frequently occur on the same side as the HC. Primary stabbing headaches are covered in Chap. 3, Other Primary Headaches. It is useful to ask a patient with HC-associated features about ice-pick pains, although they do occur in 40% of migraineurs as well.

The use of a daily nonsteroidal anti-inflammatory drug (NSAID) is frequently seen in patients with indomethacin-responsive syndromes. Thus, a patient coming in with side-locked daily headaches taking daily ibuprofen should raise suspicion for HC. Ibuprofen and other NSAIDs are close enough to indomethacin to provide some HC patients with partial relief, better than alternatives. The same behavior can be seen in patients with PH.

In ICHD-2, the severe exacerbations in HC were described as CH-like with autonomic features. However, HC exacerbations may mimic migraine, not cluster, in some patients, and the exacerbations may be triptan responsive, so in ICHD-3 the cranial autonomic symptoms are included in the criteria for HC diagnosis, but the exacerbations are described as "moderate or greater intensity" and not otherwise characterized.

Cittadini and Goadsby reported photophonophobia in around 75% of their HC patients, ipsilateral in about half. As previously noted, in case of unilateral photophonophobia a clinician should start thinking about a TAC, and if the pain is continuous and at least moderate, specifically about HC.

Many patients with HC reported by Cittadini and Goadsby had personal or family histories of migraine, often with histories of motion sickness.

However, if a patient with a history of migraine presents with chronic daily headache (CDH) which is side locked and is taking large daily quantities of NSAIDs, especially when mixed with caffeine, the diagnosis of medication overuse headache (MOH), chronic migraine, or transformed migraine with rebound becomes possible.

An indomethacin trial is often the only way to distinguish between chronic migraine with medication overuse and HC with migrainous exacerbations. Indometha-

Table 2.15 Clinical pearls on diagnosing HC

- Foreign body sensation in the ipsilateral eye or itchy eye
- Overuse of other NSAIDs
- Daily baseline headache can be mild, instead of moderate; average baseline headache intensity is 6/10
- Exacerbations can mimic migraine or cluster, and the exacerbations can be triptan responsive. Exacerbations occur frequently, often daily or near daily and are of moderate or greater intensity
- An indomethacin trial may be the only way to distinguish HC with migrainous exacerbations from chronic migraine with medication overuse
- Agitation and aggression during the exacerbations is common
- Dislike of light and noise can be ipsilateral and entirely unilateral
- The indomethacin trial should be to at least 225 mg/day
- Indomethacin responsiveness does not prove that a patient has primary HC, and an imaging study is necessary

cin will work completely in HC patients before they are weaned from the overused NSAIDs or other medications.

The required indomethacin dose is frequently high. In about one-third of the Cittadini and Goadsby series, 300 mg/day was necessary; one patient required 500 mg daily dosing. As noted, the ICHD-3 recommends at least a trial up to 225 mg/day. It is worth trying to lower the daily dose months after stability and headache suppression is achieved.

Indomethacin responsiveness is not diagnostic. Diagnostically, secondary headaches mimicking HC can be indomethacin responsive. Because HC is somewhat uncommon, a baseline MRI is necessary to exclude secondary causes, as in all of the TACs.

In ICHD-3, HC is subdivided into remitting and nonremitting subtypes. These subtypes correspond to chronic and episodic cluster and other TACs, but the criteria are a bit different. For cluster and other TACS, 1 month of no headaches per year is required for ECH, otherwise it is chronic. For HC, the remitting subtype manifests a pattern of pain that is not continuous but is interrupted by remission periods of ≥1 day without treatment. The HC unremitting subtype manifests a pattern of continuous pain without remission periods of ≥1 day for ≥1 year. The ICHD-3 notes that the majority of HC is the unremitting subtype.

Clinical pearls on diagnosing HC are summarized in Table 2.15.

Conclusions

There are four primary types of TACs: CH, PH, SUNHA, and HC. The first three are paroxysmal; HC is continuous. However, the first three paroxysmal TACs can have continuous lower-level headaches as well.

Two of the TACs are indomethacin responsive, PH and HC.

Table 2.16 Final clinical pearls on the TACs

- All TACs require careful imaging, specifically an MRI without and with contrast and a special look at the sella and posterior fossa
- Cluster, paroxysmal hemicrania, and SUNHA are primarily paroxysmal, although may have continuous lower-level headaches
- The continuous headache of HC is generally at least 6/10 in intensity
- The two TACs that are indomethacin responsive are PH and HC
- The two TACs that are associated with severe agitation are CH and HC
- The two forms of SUNHA are SUNCT and SUNA
- CH and PH are subdivided into episodic forms with remissions of at least a month a year and chronic forms with no remissions
- HC is subdivided into a remitting form with remissions of at least a day a year and a chronic form with no remissions
- SUNHA is subdivided into a form with both conjunctival tearing and injection, SUNCT, and a form with other autonomic features, SUNA

All of the TACs generally manifest autonomic features, usually parasympathetic activation, occasionally sympathetic paresis with a partial Horner's. Two of the TACs are associated with significant agitation, CH and HC.

All TACs require careful imaging before deciding that they are primary. This involves an MRI without and with contrast and a special look at the sella and posterior fossa.

CH and PH are subdivided into episodic forms with remissions of at least a month a year and chronic forms with no remissions. HC is subdivided into a remitting form with remissions of at least a day a year and a chronic form with no remissions. SUNHA is subdivided into a form with both conjunctival tearing and injection, SUNCT, and a form with other autonomic features, SUNA.

Suggested Reading

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