Chapter 52

The Woman with Orbital Pain and Tearing

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Case History

A 66-year-old woman presented with a 1-year history of headache. The headaches were short-lasting (5 to 120 seconds) episodes of moderate or severe throbbing or stabbing pain in the left retro-orbital region. They were always accompanied by intense ipsilateral tearing, conjunctival injection, and nasal obstruction. No photophobia, phonophobia, or nausea was present. In the first 6 months after onset, the attacks were sporadic, occurring no more than 4 to 5 times a month. Subsequently, they became much more frequent. When she first came to our observation, she had been experiencing 10 to 30 attacks a day for 40 days. Sometimes, 5 to 10 episodes occurred in series, with minimal pauses between them. Most occurred in the morning and afternoon. However, rare attacks would wake the patient during the night. In her most recent visits, the patient reported that many attacks seemed to be provoked by stretching the neck or chewing vigorously.

She reported no benefit from aspirin, indomethacin, or other nonsteroidal anti-inflammatory drugs (NSAIDs). The family history was negative for headache disorders. Her personal history was unremarkable, except for hysterectomy at the age of 52 years. Physical and neurologic examinations revealed no abnormalities. Routine laboratory data were normal, except for mild hypercholesterolemia. A previous computed tomography scan of the brain and orbit did not reveal any abnormality.

Questions on the Case

Please read the questions, try to answer them, and reflect on your answers before reading the authors' discussion.

- What is the most likely diagnosis of the headache disorder and facial pain syndrome?
- Are further investigations or clinical tests necessary to confirm the diagnosis or rule out secondary headache?
- What are your suggestions for treatment?

Case Discussion

Diagnosis

The association of side-locked pain attacks in the area of the first branch of the trigeminal nerve with stereotyped ocular and nasal autonomic signs suggests the diagnosis of a trigeminal autonomic cephalalgia (TAC). This is a group of primary headaches that share the following three clinical traits: strictly unilateral, mainly orbital pain; accompanying ipsilateral autonomic symptoms; and short duration of attacks (less than 4 hours). According to Goadsby and Lipton, TACs include cluster headache (CHA), paroxysmal hemicrania, hemicrania continua (HC), short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT), and cluster-tic syndrome. Only two of these forms (CHA and the chronic form of paroxysmal hemicrania) were included in the first International Headache Society's (IHS's) 1988 classification of headache disorders and facial pain. Diagnostic criteria for paroxysmal hemicrania (including its episodic form), HC, and SUNCT have been proposed in recent years.

We considered several clinical features to arrive at the diagnosis in this case, bearing in mind all of the above headache syndromes, and also other short-lasting pain syndromes (trigeminal neuralgia, and idiopathic stabbing headache).

CHA was excluded because it is characterized by longer attack duration (15 to 180 minutes) than our patient was experiencing, and by her large number of daily attacks (not more than eight CHA attacks usually occur in a day). In addition, CHA attacks often tend to have distinct patterns

of occurrence: at the same time of the day, often waking the patient during the night, or late in the afternoon after work, or after meals; they are not triggered by mechanical factors.

HC is also unlikely. It is basically a condition of moderate intensity, continuous unilateral pain, although most patients report episodes of pain exacerbation that may be associated with oculonasal autonomic manifestations. However, the autonomic component is usually less prominent than in other TACs, and the exacerbations are generally of long duration (some hours to a few days).

The diagnosis of paroxysmal hemicrania is suggested by the high attack frequency (above five per day). However the duration of the attacks (5 to 120 seconds) in our patient is against this diagnosis. Although the shortest paroxysmal hemicrania attacks may last 2 minutes, in most cases they last 10 to 15 minutes, with a maximum of 30 minutes, according to the first revised criteria in the *International Classification of Headache Disorders–II* (ICHD-II) published in 2004.

The diagnoses of paroxysmal hemicrania and HC were completely excluded when our patient did not respond to indomethacin (see Treatment, below). These forms are highly responsive to indomethacin, and this response is part of the diagnostic criteria for both.

SUNCT syndrome is characterized by pain paroxysms lasting 5 to 240 seconds according to the recently revised ICHD-II. Thus, they are shorter than those of other TACs and longer than those of most trigeminal neuralgia paroxysms. Accompanying autonomic manifestations are marked in all patients and invariably include conjunctival injection and lacrimation. Rhinorrhea or nasal obstruction may also be present. All these features fit very well with our patient's signs and symptoms, strongly suggesting SUNCT, which was in fact our final diagnosis. The fact that attacks were sporadic in the early months and became much more frequent (up to 30 per day) is also in accordance with this diagnosis, which requires between 3 and 200 attacks per day. The attack frequency may be irregular in SUNCT, with symptomatic periods interspersed with pain-free intervals. The short series of attacks sometimes reported by our patient (5 to 10 episodes with only indistinct breaks between) has been noted in published cases. Some patients may suffer almost continuous attacks for up to 3 hours. Triggering by mechanical stimuli is also peculiar to SUNCT.

Cluster-tic syndrome should be considered in the differential diagnosis. Patients with cluster-tic syndrome report two separate features: typical neuralgic bouts, similar to trigeminal neuralgia (hence "tic douloureux"), and CHA attacks. By contrast, the pain attacks in our patient were stereotyped, and were always accompanied by prominent autonomic symptoms.

Trigeminal neuralgia, itself involving the first branch of the Vth nerve, should also be considered in our case, in view of the localization of the pain and duration of the shortest paroxysms. According to IHS diagnostic criteria, trigeminal neuralgia paroxysms last from a few seconds to less than 2 minutes. However, it is important to note that mechanical triggering of paroxysms is not pathognomonic of neuralgia, but is also common in SUNCT. Furthermore, the fact that prominent oculonasal symptoms constantly accompanied the attacks in our patient definitively rules out trigeminal neuralgia. Autonomic disturbances are only observed in a minority of trigeminal neuralgia patients with V1 neuralgia, and when present, are usually mild. Lacrimation is the most common feature, whereas conjunctival injection, rhinorrhea, or a combination of these are extremely rare. Another typical feature of trigeminal neuralgia is the occurrence of refractory periods after the pain paroxysms; this is not present in SUNCT. In our patient, several consecutive paroxysms were provoked when she was asked to vigorously and repeatedly stretch her neck.

Onset of trigeminal neuralgia is usually after 40 years of age (typically between the fifth and seventh decades), whereas SUNCT may develop at any age including childhood.

Certain apparent cases of SUNCT resemble idiopathic stabbing headache ("ice-pick" pains, also termed "jabs and jolts syndrome"). Distinguishing between the two disorders can be difficult when the attacks are particularly short (1 second up to few seconds), which in fact is the attack duration for idiopathic stabbing headache, according to the new proposed IHS criteria. Other characteristics of idiopathic stabbing headache that help to differentiate it from SUNCT, and which were not present in our case, are absence of autonomic features, erratic pain localization, partial response to indomethacin, and frequent coexistence with other primary headaches (mainly migraine).

Tests and Investigations

We gave our patient indomethacin (50 mg, orally, tid). No change in frequency or pain severity was observed. This test was performed because a beneficial response to indomethacin has never been reported in SUNCT, but is typical and essential for the diagnosis of paroxysmal hemicrania and HC.

We also performed magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) of the posterior fossa, to exclude SUNCT secondary to organic disease. Table 52-1 lists the symptomatic SUNCT cases reported in the literature.

Treatment

Our patient had tried several prophylactic treatments before she came to us. Antimigraine drugs (flunarizine [not available in the United States] and propranolol) had proven completely ineffective. Carbamazepine was also ineffective. On the basis of recent literature reports, we decided to try lamotrigine,

Table 52-1. Case Reports of Symptomatic SUNCT Syndrome

Vascular malformation, cerebellopontine angle Bussone et al. *Cephalalgia* 1991;11:123–7
Vascular malformation, cerebellopontine angle Morales et al. *Cephalalgia* 1994;14:301–2
Cavernous angioma, brainstem DeBenedittis. *Cephalalgia* 1996;16:503–6
Infarction, dorsolateral brainstem Penart et al. *Cephalalgia* 2001;21:236–9
Prolactinoma (2 cases) Massiou et al. *Neurology* 2002;58:1698–9
Prolactinoma (2 cases) Levy et al. *Euro J Neurol* 2003;10:169–73
Leiomyosarcoma, sinus cavernosus Kaphan et al. *Cephalalgia* 2003;23:395–7
Craniosynostosis Moris et al. *Cephalalgia* 2001;21:157–9
Basilar impression (SUNCT-like) Ter Berg and Goadsby. *J Neurol Neurosurg Psychiatry* 2001;70:244–6
Astrocytoma, pontocerebellar angle Blattler et al. *Neurology* 2003;60:2012–3 (abstract)

starting at 25 mg per day and increasing to 50 mg per day over a week. With this regimen, the frequency of attacks did not change, but the intensity declined substantially. After 2 weeks, however, she experienced an abrupt increase in attack frequency (up to 40 attacks per day, mainly at night), with a parallel increase in pain intensity and autonomic manifestations. We increased the lamotrigine gradually (25 mg every 7 days). At 100 mg per day, an 80% reduction in frequency was obtained, and at 150 mg per day the attacks ceased completely. Three months later, the lamotrigine was stopped without any recurrence of attacks. The patient has been pain free over the ensuing 15-month follow-up. She did not complain of any side effects while on lamotrigine.

Management Strategies for Short-lasting Unilateral Neuralgiform Headache Attacks with Conjunctival Injection and Tearing

SUNCT is considered refractory to medication. In contrast to other short-lasting headaches with autonomic disturbances, it is unresponsive to indomethacin; several drugs employed in other primary headaches, particularly in other TACs (verapamil, lithium salts, and corticosteroids), have often been reported to be ineffective.

The most-used drug for trigeminal neuralgia—carbamazepine—has also been tried in SUNCT. In about half of the cases, a partial or transitory effect was seen (including in two cases with symptomatic SUNCT).

Recently, other antiepileptic drugs have been tried, with more promising results. Gabapentin, at doses in the range 900 to 3,600 mg per day, has been used in six patients, and was clearly effective in three of them.

Five patients have been treated with topiramate (150 to 200 mg per day), but only one experienced a significant improvement.

Encouraging results have been obtained with lamotrigine. Five open-label studies have been published in which 11 patients were successfully treated: 8 with complete remission and 3 with significant improvement (to their complete satisfaction). The doses used ranged from 125 to 200 mg per day. Side effects, the most common of which is skin rash, are generally avoided by starting at 25 mg a day, increasing in weekly 25 mg steps.

Surgical procedures have been tried to relieve pain in SUNCT patients. Six patients who underwent the Jannetta procedure, retrogasserian glycerol rhizolysis, or balloon compression of the trigeminal ganglion, had good outcomes. No beneficial effects were found in a study of two patients treated for severe SUNCT: one of them received glycerol rhizotomy, gamma-knife radiosurgery, and microvascular decompression of the trigeminal nerve; the other received gamma-knife radiosurgery and two microvascular decompressions of the trigeminal nerve.

To conclude, SUNCT is recognized as a rare, difficult-to-treat headache syndrome in the category of the TACs. However, recent data suggest that lamotrigine is often effective, and in the absence of more effective treatments, may be considered the current first-choice drug. Gabapentin and topiramate may be second-choice options. Confirmation of the efficacy of these drugs should proceed by randomized, double-blind, placebo-controlled trials. However, the rarity of SUNCT, and the dramatic clinical manifestations in most patients, make it difficult to perform such studies. Surgical procedures must be considered in drug-resistant cases, and are the most appropriate treatment in most symptomatic cases.

Case Summary

- This woman had a 1-year history of headache.
- Short-lasting (5 to 120 seconds) painful paroxysms in the left orbital region, always accompanied by intense tearing, conjunctival injection, and nasal obstruction (all ipsilateral to the pain), were the presentation.
- She had 10 to 30 attacks a day, some of these at night.
- Attacks were often triggered by elongating the neck or chewing vigorously.
- NSAIDS, antimigraine prophylactics, and carbamazepine were ineffective.
- Cerebral MRI and MRA were normal.
- She had good response to lamotrigine at 150 mg per day.

Table 52-2. Diagnostic Criteria for SUNCT

A. At least 30 attacks fulfilling criteria B to E
B. Attacks of unilateral moderately severe orbital or temporal stabbing or throbbing pain lasting 15 to 120 seconds
C. Attack frequency 3 to 100 per day
D. Pain is associated with at least one of the following signs or symptoms on the affected side, with 1 being most often present and highly prominent:
   1. Conjunctival injection
   2. Lacrimation
   3. Nasal congestion
   4. Rhinorrhea
   5. Ptosis
   6. Eyelid edema
E. At least one of the following:
   1. There is no suggestion of one of the disorders listed in groups 5 to 11
   2. Such a disorder is suggested, but excluded by appropriate investigations
   3. Such a disorder is present, but the first headache attacks do not occur in close temporal relation to the disorder

Adapted from Goadsby PJ and Lipton R, 1997.

Overview of Short-lasting Unilateral Neuralgiform Headache Attacks with Conjunctival Injection and Tearing

When dealing with a patient presenting with unilateral, short-lasting pain in the orbital region, and ipsilateral autonomic symptoms, the differential diagnosis has to take into account several headache forms. Depending on the case characteristics, paroxysmal hemicrania, other TACs, V1 trigeminal neuralgia, and idiopathic stabbing headache should be considered.

When the paroxysms are short-lived, accompanied by impressive conjunctival injection and tearing on the pain side, and are unresponsive to indomethacin, the most likely diagnosis is SUNCT.

However, patients with a clinical diagnosis of SUNCT must be investigated by MRI with contrast and also MRA to exclude symptomatic forms arising from infiltrating or vascular conditions.

We also suggest that the patient should be encouraged to keep a diary of attacks, noting duration, severity, and accompanying symptoms. Some attacks should be observed at first hand.

TABLE 52-3 Diagnostic Criteria of SUNCT Proposed for the Revised Version of the International Headache Society Classification (2004)

A. At least 20 attacks fulfilling criteria B to D
B. Attacks of unilateral orbital, supraorbital, or temporal stabbing, or pulsating pain lasting from 5 to 240 seconds
C. Pain accompanied by ipsilateral conjunctival injection and lacrimation
D. Attacks occur with a frequency of 3 to 200 per day
E. Not attributable to another disorder

SUNCT was first described by Sjaastad and colleagues in 1989, but specific diagnostic criteria enjoying a wide consensus have now been drawn up (Table 52-2). SUNCT is included in the revised version of the IHS classification of headache disorders (2004) (Table 52-3).

Selected Readings

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Editorial Comments

There are few headache disorders that are as intriguing as those with associated autonomic symptoms and signs. Cluster headache is the prototypical disorder, but now we can add the TACs, and these are fascinating disorders clinically, because of their relative rarity, marked symptoms and severity, as well as their unique and sometimes refractory nature. Their neurobiologic basis is now better defined and studied, but until complete, the most important aspects of these disorders are accurate diagnosis, thorough investigation, and treatment. Lamotrigine is worth trying in SUNCT. This is a very comprehensive and excellent review of SUNCT and other TACs.

Final diagnosis:

Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT)