Chapter 18

# The Woman with Several Headaches Each Hour!

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## Case History

A 51-year-old woman was referred in late 2002 with a 10-year history of head pain. She complained of 10 or more attacks per hour of pain that lasted from a few up to 60 seconds. The pain started in the right occipital region and radiated to the right frontal region as an electric shock or stabbing sensation. It was quite severe. There was no nausea, photophobia, or phonophobia, and no aggravation with movement. She did not feel restless or agitated. There were no premonitory and no aura symptoms. During the attacks, she had right-sided eye watering and right-sided ptosis, but no conjunctival injection, periorbital swelling, or rhinorrhea. Neck movement could trigger these attacks repeatedly and without a refractory period, but light touch did not. The longest break she had had was some hours over the previous 10 years.

Indomethacin 150 mg daily was not helpful, and carbamazepine 600 mg twice daily did not affect the headache, but it did reduce and almost eliminate the cranial autonomic symptoms. She was taking a diuretic for hypertension, and a tricyclic, dothiepin, for a diagnosis of depression. There was no family history of headache. In her personal history, she was a nonsmoker and never drank alcohol, for religious reasons. She worked on an assembly line.

On examination, she was well and weighed 76 kg. In the cranial nerves, the fields were full and the fundi were normal. The eye movements were full, with normal pursuit and saccadic movements, as well as normal vestibule-ocular responses. There was no facial asymmetry. There was no trigeminal sensory loss. In the limbs, there was no wasting or abnormal movements. Tone and power were equal and normal, and the reflexes symmetrical with downgoing toes. Gait and coordination were normal. There was a marked right greater occipital nerve tenderness, and pain with eye watering could be triggered from that point.

## Questions on the Case

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

- What is the most likely diagnosis, and what is the differential diagnosis?
- What, if any, investigations are required?
- Could this be trigeminal or occipital neuralgia?
- Is this patient's problem due to depression?
- What is the treatment of her problem?

## Case Discussion

This patient probably has a trigeminal autonomic cephalalgia (TAC). The diagnostic issue surrounds whether first, it is primary or secondary, and if primary, which of the TACs she has. This author takes the view that most patients with headache and cranial autonomic symptoms, often called secondary cluster headache, might be best described as secondary TACs, rather than imply necessarily one of the TAC phenotypes. Some patients will have striking phenotypes almost similar to a primary TAC, such as cluster headache, paroxysmal hemicrania, or short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT), and may teach some interesting lesson about the disorders. It is noteworthy that she came with a diagnosis of depression, although it was not clear how seriously that was considered as an explanation of her symptoms. She was greatly disabled by the symptoms, and sought both explanation and adequate management.

It is first necessary to develop a phenotypic diagnosis for the problem in order to consider the issue of secondary headache properly. Given that the patient has episodes of

pain with marked lacrimation, she probably has a TAC. The concept of a TAC has been incorporated into the second edition of the International Headache Society's (IHS) *Classification and Diagnostic Criteria for Headache Disorders, Cranial Neuralgias and Facial Pain* (ICHD-II 2004, Table 18-1). The attacks are short-lasting, unilateral, and have a neuralgic or neuralgiform character, so this raises the issue of SUNCT. SUNCT was not present in the first edition of the IHS classification. However, the patient does not have conjunctival injection, and even after sending one of her relatives to observe her, it was clear she did not, so the phenotype is "SUN*c*T." How should she be investigated, and is the absence of "C" a worry?

In general terms, it is hard to avoid investigating a case of SUNCT, even if the presentation is straightforward. The syndrome is rare and secondary cases are well recognized. These take the form of either posterior fossa or pituitary lesions. The physical examination is helpful: raised intracranial pressure or ataxia, in the posterior fossa lesion, visual field defects or even signs of hypothalamic-pituitary axis dysfunction in pituitary fossa problems will alert the physician. It is my practice to image SUNCT-like presentations, particularly alerting our radiologic colleagues to an interest in the posterior fossa and the pituitary region. This patient's magnetic resonance imaging (MRI) scans were normal. An added consideration is trigeminal neuralgia with cranial autonomic features, and many patients we have seen have had dedicated trigeminal nerve imaging, as well as magnetic resonance angiography. These do no harm unless they lead to trigeminal ganglion or posterior fossa surgery, which in my experience, is generally unhelpful in SUNCT.

If this is not a secondary headache, then which of the primary headaches could this be? The differential diagnosis is in essence the other TACs—cluster headache and paroxysmal hemicrania (covered elsewhere in this volume), a neuralgia, or idiopathic (primary) stabbing headache. To establish a diagnosis of the other TACs, we have to consider that the attacks on this patient are too short for cluster headache, and she has no restlessness, which is a feature in 90% of patients with cluster headache. For paroxysmal hemicrania, her attacks are rather short, albeit they can be very short in episodic paroxysmal hemicrania. The patient had no response to indomethacin. Was 150 mg daily enough, and is it possible to have paroxysmal hemicrania without an indomethacin response? These issues are best left to the appropriate chapter in this book. Sufficed to say, by ICHD-II 2004 criteria there should be an indomethacin response, so it is at least worth continuing to think about the case.

The attacks would be of an appropriate length for primary stabbing headache, but cranial autonomic symptoms are exceptional in that condition, and not prominent as this patient's tearing was. Could this be occipital neuralgia, as it was triggered with neck movement? SUNCT can be triggered with neck movement, and occipital neuralgia also does not have prominent autonomic features. Could this be trigeminal neuralgia? There are no trigeminal trigger areas; the attacks are rather long, the cranial autonomic features are too prominent, and of equal differential diagnostic importance, there was no refractory period to triggering in this patient. The latter two features are very helpful in differentiating ophthalmic division trigeminal neuralgia from SUNCT.

Lastly, and perhaps of most interest, is that this patient cannot have SUNCT, since she has no "C"! Does she defy the current or even the new classification? We have seen a number of patients with parts of what seems to be the SUNCT syndrome in which the "C" or "T" is missing. The new IHS classification invited proposed research criteria—criteria designed to be tested to evaluate new or emerging entities. Table 18-2 has the IHS appendix research (IHS-R) criteria for Section 3 of the classification. The Classification Committee recognized that there are as many questions as answers in primary headache, and sought to itemize issues by creating criteria for testing. Short-lasting unilateral neuralgiform headache attacks with cranial autonomic features (SUNA) recognizes that some patients present with an illness that behaves like SUNCT, but does not have both features, or indeed has another feature of cranial parasympathetic autonomic activation. This patient illustrates that principle, and would be best classified as having SUNA (IHS-R). The author's experience is that SUNA can be managed identically to SUNCT. The patient illustrates how a clear clinical history and appropriate physical examination can reveal new questions in clinical neuroscience, while allowing pragmatic management of the clinical problem.

**Table 18-1. Diagnostic Features of SUNCT**

| 3.3 Short-lasting Unilateral Neuralgiform Headache Attacks with Conjunctival Injection and Tearing (SUNCT) |
|---|
| Description: |
| This syndrome is characterized by short-lasting attacks of unilateral pain that are much briefer than those seen in any other trigeminal autonomic cephalalgias, and is very often accompanied by prominent lacrimation and redness of the ipsilateral eye. |
| Diagnostic criteria: |
| A. At least 20 attacks fulfilling criteria B to D |
| B. Attacks of unilateral orbital, supraorbital, or temporal stabbing or throbbing pain lasting 5 to 240 seconds |
| C. Pain accompanied by ipsilateral conjunctival injection and lacrimation |
| D. Attacks occur with frequency from 3 to 200 per day |
| E. Not attributed to another disorder |

Adapted from Headache Classification Committee of the International Headache Society, 2004.

**Table 18-2. International Headache Society Classification: Appendix**

Short-lasting Unilateral Neuralgiform Headache Attacks with Cranial Autonomic Features (SUNA)

The following proposed criteria for A3.3 SUNA (as an alternative to SUNCT) are for research purposes. Cranial autonomic features should be prominent to distinguish this disorder from ophthalmic division trigeminal neuralgia.

Diagnostic criteria:

A. At least 20 attacks fulfilling criteria B to E
B. Attacks of unilateral orbital, supraorbital, or temporal stabbing or throbbing pain lasting from 2 seconds to 10 minutes
C. Pain is accompanied by one of
   1. Conjunctival injection and/or lacrimation
   2. Nasal congestion and/or rhinorrhea
   3. Eyelid edema
D. No refractory period between triggered attacks
D. Attacks occur with frequency of ≥ 1 per day for more than half of the time
E. Not attributed to another disorder

A3.3.1 Episodic SUNA

Description:
SUNA attacks occurring in periods lasting 7 days to 1 year separated by pain-free intervals of ≥ 1 month

Diagnostic criteria:

A. Attacks fulfilling criteria for A3.3 SUNA
B. At least two attack periods lasting (if untreated) from 7 days to 1 year and separated by pain-free remission periods of ≥ 1 month

A3.3.2 Chronic SUNA

Description:
SUNA attacks occurring for > 1 year without remission or with remissions lasting < 1 month

Diagnostic criteria:

A. Attacks fulfilling criteria for A3.3 SUNA
B. Attacks recur over > 1 year without remission periods or with remission periods lasting < 1 month

Adapted from Headache Classification Committee of the International Headache Society, 2004.

## Management Strategies

Patients with headache require a clear diagnosis to develop a useful management strategy. Indeed, explaining the diagnosis and giving the patient some insight into their problem is as much part of the management process as any medicine. Primary headache patients from the disabled, but slightly unusual, migraineur through to the most unusual case of a trigeminal autonomic cephalalgia are well served by an explanation of their problem. The medical management of SUNCT/SUNA falls into two broad categories: acute exacerbation management and long-term preventive management.

### Acute Exacerbations

In SUNCT/SUNA, exacerbations refer to periods where patients have such a load of repeated and unremitting attacks as to render their health and well-being threatened. This can happen to patients who, for example, have prominent triggering from talking, chewing, or swallowing, where they have trouble eating or drinking. We have found that intravenous lidocaine in this setting is remarkably effective, when given by infusion at rates of 1 to 4 mg/min. We have found that this can result in short- to medium-term remissions, although it may be that these were simply coexistent with a spontaneous recovery. The IHS-R criteria (see Table 18-2) recognizes that SUNA has an episodic and a chronic form, so that for some patients, the natural history is to remit. From a pragmatic viewpoint, it can be very helpful to patients to demonstrate that it is possible to stop their attacks. The other approach we have used is to inject the ipsilateral greater occipital nerve. This is likely to work through the trigeminocervical complex, and is generally recognized to be useful in primary headache. We use corticosteroid and lidocaine, and have seen, again perhaps as natural history, short- and medium-term improvement.

### Preventive Approaches

The literature suggests three first-line treatments of SUNCT/SUNA (ie, lamotrigine, topiramate, and gabapentin), and one adjunctive treatment, carbamazepine. Each of the three front-line medicines has had published reports, but there are no controlled clinical trials in SUNCT/SUNA. We have found that most patients who respond to lidocaine will respond to one of these medicines, and have found lamotrigine to be the most effective. The patient described responded to lamotrigine 50 mg twice daily. It is interesting that she had developed a response in terms of the cranial autonomic features. We have seen a number of patients who reported partial benefit with carbamazepine, but never with complete control of attacks.

## Case Summary

- A 51-year-old female presents with a 10-year history of short-lasting unilateral neuralgiform headache attacks with tearing. She best fits the IHS-R criteria for SUNA.
- She had attacks triggered by neck movement and local tenderness of the greater occipital nerve, palpation of which activated the cranial autonomic outflow. She had responded, in terms of the cranial autonomic symptoms, to carbamazepine.
- She responded, in terms of the pain, to lamotrigine, which is probably the treatment of choice in SUNCT/SUNA. She had a short-term response to ipsilateral greater occipital nerve injection, which is sometimes seen in this syndrome.

## Overview of Trigeminal Autonomic Cephalalgias

Trigeminal autonomic cephalalgias are a fascinating group of primary headache syndromes that entrain the reflex connection of the trigeminal nociceptive afferents with the cranial parasympathetic outflow. The clinical aspects of SUNCT/SUNA are described above. In this final section, I shall discuss some anatomic and physiologic aspects of the TACs, since ultimately it is this that determines many of the clinical features of the disorders.

The pain-producing innervation of the cranium projects through branches of the trigeminal and upper cervical nerves to the trigeminocervical complex from whence nociceptive pathways project to higher centers. This implies an integral role for the ipsilateral trigeminal nociceptive pathways in TACs. The ipsilateral autonomic features suggest cranial parasympathetic activation and sympathetic hypofunction. Goadsby and Lipton suggested that the pathophysiology of the TACs revolves around the trigeminal autonomic reflex. There is considerable experimental animal literature to document that stimulation of trigeminal afferents can result in cranial autonomic outflow, the trigeminal autonomic reflex. In fact, some degree of cranial autonomic symptomatology is a normal physiologic response to cranial nociceptive input, and patients with other headache syndromes may report these symptoms. The distinction between the TACs and other headache syndromes is the degree of cranial autonomic activation.

It follows that cranial autonomic symptoms are prominent in the TACs due to a central disinhibition of the trigeminal autonomic reflex. Supporting evidence is emerging from functional imaging studies: a functional MRI study in SUNCT syndrome and a positron emission tomography study in cluster headache have both demonstrated ipsilateral hypothalamic activation. Hypothalamic activation is specific to these syndromes and is not seen in migraine or in experimental ophthalmic trigeminal distribution head pain. There are direct hypothalamic–trigeminal connections, and the hypothalamus is known to have a modulatory role on the nociceptive and autonomic pathways. Hence, SUNCT/SUNA syndrome is probably due to an abnormality in the hypothalamus, with subsequent trigeminovascular and cranial autonomic activation. What marks TACs is central disinhibition; hence, similar pain in, for example, trigeminal neuralgia or experimentally induced head pain results in less-noticeable rather than prominent cranial autonomic activation. Similarly, for SUNCT/SUNA, because the index problem is disinhibition, there is no centrally induced refractory period that accounts for this notable difference when compared to trigeminal neuralgia.

In conclusion, the TACs offer an excellent opportunity to understanding the fundamental anatomy and physiology of trigeminal nociceptive processing, while providing a fascinating clinical problem at the same time. The clinical aspects can be dissected by the sharpest tool that the physician can possess, not equalled by any battery of tests—the careful history.

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## Selected Readings

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## Editorial Comments

The recent description of the TACs by the author and his colleagues moved the clinical understanding of this group of disorders further in terms of defining anatomic localization of symptoms and signs, but also in terms of treatment options for these generally rare disorders. Furthermore, there is a continuing emphasis on ensuring that there are no secondary causes, and if considered, to investigate such cases vigorously. What is interesting in this case is that Dr. Goadsby, once again, leads the way in defining subtypes of the TACs, and suggests a new entity—SUNA. Clinicians will welcome this case. It makes sense that the evolution of the understanding in this area should advance. Study this case carefully, as it is very instructive indeed!

Final diagnosis:

Trigeminal autonomic cephalalgia—SUNCT or SUNA?