Rapoport Ch 15.qxd 10/15/08 1:09 PM Page 89

CHAPTER 15

THE MAN WITH NEVER-ENDING HEADACHES

LAWRENCE C. NEWMAN, MD

Case History

The patient is a 36-year-old man who reports an 8-year history of daily, constant headaches. The pain is described as a steady ache or squeezing sensation involving the forehead bilaterally, with radiation into the vertex and the occiput. When severe, the pain has a throbbing quality. The severity of the pain ranges from moderate to severe and tends to worsen as the day progresses. There is no worsening with activity. The patient reports pain upon awakening each morning, but denies that he suffers from sleep disruption secondary to the headaches.

The headaches are associated with difficulty concentrating and irritability, but photophobia, phonophobia, nausea, and vomiting are not experienced. No identifiable triggers are noted. There is no family history of headache.

Over the years the patient has consulted with his internist, two neurologists, a dentist, and an allergist. He has been treated with a variety of medications including propranolol, amitriptyline, antihistamines, and decongestants, all without benefit. Trials of over-the-counter analgesics and prescription pain-relievers were unhelpful. The patient takes no medications at this time as, “They don’t help, so why should I take anything?” Magnetic resonance imaging (MRI) of the brain, performed 1 year ago, was normal.

The patient’s general medical and neurologic examinations are normal.

Questions about This Case

- What are your diagnostic considerations?
- What is your differential diagnosis?
- How would you manage this patient’s headaches and what specific therapies would you recommend?
- What long-term management strategies would you suggest for this patient?

Case Discussion

Approximately 35 to 40% of patients seeking treatment at a headache subspecialty center suffer from daily or near daily headaches. The classification of frequent severe headaches is controversial, and has not yet been adequately addressed by the International Headache Society (IHS). Using the current IHS guidelines, our patient would receive the diagnosis of chronic tension-type headache (CTTH). These headaches, as reported by our patient, are typically described as a bilateral throbbing or pressure sensation of mild to moderate severity. The complete IHS criteria for CTTH may be found in Appendix 15–1.

Comparing our patient’s symptoms with the IHS criteria, however, it becomes obvious that the diagnosis of CTTH is not adequate. The patient reported in this case describes daily bilateral headaches, but complains at times of severe pain that has a throbbing quality. The presence of a throbbing component excludes CTTH using current IHS guidelines. Yet, throbbing pain, while characteristic of migraine, may occasionally be seen in tension-type headaches (TTHs). In clinical practice, the distinction between migraine and tension-type headaches may be difficult. Some investigators have suggested that TTHs may in fact represent two distinct headache syndromes; one would be a form of mild migraine and the other a headache disorder in which all features of migraine headache are absent.

Rapoport Ch 15.qxd 10/15/08 1:09 PM Page 90

Employing that scenario, this patient would be diagnosed with the first form of TTH.

Although not recognized by the IHS, many clinicians prefer the term chronic daily headache (CDH) when referring to headaches disorders that occur on a daily or near daily basis. Chronic daily headache represents a heterogeneous group of disorders. Epidemiologic studies suggest that these disorders are rare, affecting only 0.5% of the population, yet they account for the majority of patients consulting headache centers. [*Editors' note: Some studies indicate prevalence of these disorders in 4% of the population.*] Silberstein et al. recently proposed revisions to the IHS criteria for these frequent headache disorders. In their system, CDH is divided into primary and secondary disorders. The primary subtypes are further classified by duration; those occurring for fewer than or more than 4 hours per day. Those headaches occurring on a daily basis with an average duration of more than 4 hours include transformed migraine (TM), CTTH, new daily persistent headache (NDPH), and hemicrania continua (HC). Each disorder may be subclassified depending on the presence or absence of medication overuse. Appendix 15–2 lists the IHS criteria revisions proposed by Silberstein et al.

As our patient has denied overusing symptomatic medications, the management of his headaches should be less complicated than it otherwise might have been. The majority of patients with CDH overuse symptomatic medications. This pattern of overuse by headache patients often induces "rebound headaches," whereby medication overuse leads to the development of CDH in patients prone to episodic migraine or tension-type headaches. Interestingly, our patient had never experienced prior episodic headaches, instead he reports an eight-year history of daily, unrelenting headaches from the onset. Therefore the diagnoses of transformed migraine and new daily persistent headaches have been excluded.

The management of CTTH without analgesic overuse is multifactorial. Factors that are imperative in the treatment of this disorder include a long-term commitment on the part of the patient and physician, an understanding that control of headache not a "cure" is the goal of treatment, and possibly a team approach.

Successful treatment depends in large part on establishing the correct diagnosis; secondary causes of CDH must always be excluded. Comorbid medical and psychiatric conditions, if present, must be identified and addressed. After a thorough history and examination, a simple explanation of the diagnosis and underlying pathogenesis of the patients' headache disorder should be presented. Terms attributing the disorder solely to stress or tension should be avoided. Most patients can be appropriately treated on an outpatient basis, although sometimes hospitalization is required.

The most efficacious treatment plans incorporate both pharmacologic and nonpharmacologic therapeutic modalities. Mood disturbances are common in patients suffering from daily headaches and need to be appropriately managed. When appropriate, stress management, relaxation techniques, biofeedback, and individual and family psychotherapy all have a role in treating CTTH. Occasionally, physical therapy (including hot and cold compresses, massage therapy, stretching, and nerve blocks) is employed.

Treatment strategies employing simple analgesics, either alone or combined with caffeine, i.e., butalbital, isometheptene, or codeine, and nonsteroidal anti-inflammatory agents (NSAIDs), are the mainstay of acute therapies. Limits must be set, and patients educated, regarding the potential for medication overuse leading to the development of "rebound" headaches. The choice of acute treatment depends upon the frequency and severity of the patient's headaches and the associated symptoms.

For patients complaining of mild to moderate pain, the use of simple analgesics including oral acetaminophen, or acetylsalicylic acid, nonsteroidal anti-inflammatory agents, or caffeine-containing medications often suffice. For more severe headaches or when the above agents are ineffective, it may be appropriate to use prescription medications such as the more potent NSAIDs (ketoprofen, naproxen, indomethacin, ketorolac, butalbital-containing medications, or the combination of acetaminophen, isometheptene, and dichloralphenazone. Once again, strict limits must be set as these agents are capable of producing "rebound headaches," and butalbital has a high addiction potential. If nausea is present, the concurrent use of an antiemetic (metoclopramide, chlorpromazine, or prochlorperazine) or suppository analgesic formulations (indomethacin) is useful.

Prophylactic therapy is warranted in patients in whom headache frequency is greater than twice weekly or when the duration of the headache exceeds 4 hours daily. Preventive therapy is also indicated to prevent overuse of symptomatic medications with subsequent "rebound" in patients with frequent headaches. The choice of preventive agent should take into account other comorbid conditions. Medications frequently prescribed for this condition include the tricyclic antidepressants, selective serotonin reuptake inhibitors (SSRIs), beta-blockers and calcium channel blockers, and anticonvulsants.

The tricyclic antidepressants amitriptyline, nortriptyline, desipramine, and doxepin are the most often prescribed. Dosages required are usually much lower than for depression. We generally begin with 10 to 25 mg at bedtime, gradually increasing the dose by 10 to 25 mg every week. Side effects include sedation, dry mouth, and weight gain.

Rapoport Ch 15.qxd 10/15/08 1:09 PM Page 91

The SSRIs are more easily tolerated than the tricyclic antidepressants and they too can be prescribed in lower doses than are required for depression. Commonly prescribed SSRIs include fluoxetine, paroxetine, and sertraline.

The typical "antimigraine" medications may also be used as preventive therapy for CTTH. The use of the beta-blockers propranolol and nadolol and the calcium channel blockers verapamil and diltiazem has been successful according to anecdotal evidence. The dosages employed are similar to those used for migraine. The antiseizure medication divalproex sodium also appears to be useful in the treatment of this disorder. The dosages used are similar to those for migraine. We generally begin with 125 mg, twice daily, and gradually increase to a maximum of 1250 mg per day in divided doses. Table 15–1 lists the commonly prescribed preventive medications.

The patient presented in the case report would not appear to have a secondary cause of CDH as his headaches are long-standing and without progression, his medical and neurologic examinations are normal, and a prior MRI of his brain was normal. He has not been overusing symptomatic medications that could induce headaches, in fact he takes no medications as they do not help. Therefore the issue of "rebound" does not come into play.

Although the patient reports having being treated with propranolol and amitriptyline, we are not told of the doses used or the length of time they were prescribed. All too commonly patients have been prescribed the correct medications but in inadequate doses. Additionally, many patients (or their physicians) prematurely discontinue treatment because of a perceived lack of efficacy. The full therapeutic effect of the preventive medications may take 2 to 6 months to be felt. Therefore we need to inquire as to past doses and length of treatment. If the prior agents were discontinued prematurely or if subtherapeutic doses were employed, a second trial at an appropriate dosage may be useful.

The patient does not describe features of a mood disorder. If he did, using an SSRI or tricyclic would be helpful. I would probably begin therapy with nortriptyline or an SSRI such as paroxetine first. If there was no benefit after an appropriate trial, I would next consider divalproex sodium. Acute pain could be managed with a long-acting NSAID for milder attacks and isometheptene for more severe pain. Daily and weekly limits should be explained at the time of issuing the prescription. If psychologic issues are uncovered, psychotherapy, behavioral modification, and stress management should be employed.

If outpatient measures fail or are suboptimal, hospitalization for intravenous dihydroergotamine mesylate (DHE) may prove helpful. The DHE protocol has already been discussed in another chapter.

Management Strategies

- Exclude secondary causes of headache.
- Establish the correct diagnosis.
- Ensure analgesic overuse with subsequent "rebound" headache is not present.
- Identify comorbid medical and psychiatric conditions.
- Educate the patient regarding diagnosis and prognosis.
- Review prior medications; was dosing and duration of treatment adequate?
- Limit acute therapies, and match properties of agent to patient's symptoms.
- Begin trial of preventive agent, gradually increasing the dose to limit side effects.
- Continue therapy until therapeutic effects are obtained, side effects become intolerable, or the maximum dose has been attained.
- Employ nonpharmacologic therapies.
- Consider hospitalization for treatment-resistant patients.

TABLE 15-1. Selected Prophylactic Medications for CDH

Class	Tricyclic	SSRI	Beta-Blocker	Calcium Channel Blocker	Antiseizure
Medication	Nortriptyline	Paroxetine	Nadolol	Verapamil	Divalproex sodium
Starting dosage (mg)	10–25	10	40	40–80	125–250
Effective dosage (mg)	25–125	10–30	40–120	240–360	500–1250
Contraindications	Urinary retention, glaucoma, cardiac conduction disturbances	Mania	Asthma, CHF, depression, Raynaud's disorder	Heart block, hypotension	Liver disease, bleeding disorders
Potential side effects	Sedation, weight gain, dry mouth	Sedation, weight gain	Sedation, depression, bradycardia	Constipation, bradycardia	GI upset, sedation, alopecia, tremor, liver enzyme abnormalities, platelet dysfunction

Rapoport Ch 15.qxd 10/15/08 1:09 PM Page 92

Case Summary

- The patient is suffering from chronic tension-type headaches without analgesic overuse.
- The IHS criteria for daily severe headaches does not adequately address this issue.
- Clinically, tension-type headaches may have features of migraine.
- Alternative classifications of CDH have been proposed.
- There is no *best* treatment for this disorder; therapy should be guided by the individual patient profile.
- Management strategies are outlined, and serve only as a guide.

Overview of Chronic Daily Headache

The International Headache Society divides tension-type headaches into episodic and chronic varieties. Tension-type headaches can last minutes to days. The pain is usually described as a squeezing or tightening sensation and is of mild to moderate intensity. Patients typically describe the headache as a tight band encircling the head or as a vise squeezing the skull. The pain is invariably bilateral and is not worsened by routine activity. The TTH begins at some point during the day and then increases in intensity as the day progresses; nocturnal awakening secondary to headache is uncommon and should prompt a search for an underlying pathology. The IHS guidelines allow for photophobia and phonophobia individually. Nausea, but not vomiting, is occasionally reported by patients with the chronic form. When headaches meeting these criteria occur more often than 15 days per month for more than 6 months, the IHS terms them chronic tension-type headaches.

Unfortunately, patients presenting to the physician with frequent headaches without any underlying pathology pose a diagnostic dilemma. Typically patients with CDH are diagnosed as having CTTH using the current IHS guidelines. Newman et al., using data obtained from the American Migraine Study, reported that although 0.5% of the population suffer from severe daily head-aches, only 3% meet IHS criteria for CTTH. Further complicating the issue, these daily headache sufferers account for the majority of patients consulting headache subspecialty clinics.

Recently, Silberstein et al. proposed new revisions to the IHS classification. Using their system, CDH is divided into primary and secondary varieties. The primary forms are further subdivided on the basis of average daily duration. According to this classification scheme, CDH with a duration of 4 hours or more per day include transformed migraine, CTTH, new daily persistent headache, and hemicrania continua.

Transformed migraine (TM) occurs in patients with a prior history of episodic migraine. Although the majority of sufferers of TM overuse analgesics or ergotamine-containing medications, a subset of migraineurs spontaneously "transform" without overusing medications. Over time, headache frequency increases so as to occur on a daily or near-daily basis, but as the frequency increases, the typically associated migrainous features lessen, and the headache more closely resembles CTTH. Nonetheless, headaches meeting the IHS criteria for migraine still sporadically occur.

According to this new classification, CTTH adds to the IHS criteria the requirements of either a past history of episodic TTH or the history of an evolving headache which gradually increased in frequency over a 3-month or longer period.

New daily persistent headache (NDPH), unlike CTTH or TM, occur in patients without a prior history of headache. These patients usually report the abrupt onset of headache beginning over a period of fewer than 3 days and then continuing unabated. Many patients can recall the exact time and day the headache began; in some it may follow a viral illness. Although the characteristic features of NDPH are similar to CTTH, it is distinguished by the absence of a prior history of migraine or TTH.

Hemicrania continua is an uncommon headache disorder characterized by a continuous low-level baseline hemicranial headache with superimposed exacerbations of more severe pain. Exacerbations can last minutes to days and may be associated with the autonomic features of cluster headache. This disorder is uniquely responsive to treatment with indomethacin. A full description of the disorder may be found in Chapter 23.

To date, the pathophysiology of CDH is uncertain. Recent evidence points to several putative mechanisms including defective pain modulation, abnormalities within the central pain pathways within the brain stem, and abnormal excitation of peripheral nociceptive fibers.

As CDH represents a heterogeneous group of disorders, treatment must be aimed at the specific headache disorder. Both pharmacologic and nonpharmacologic therapies should be employed, and analgesic overuse must be identified and discontinued. Outpatient strategies employing symptomatic medications and preventive agents combined with behavioral modification (as outlined above) are very useful, although occasionally hospitalization is required. Treatment outcome is generally quite good, but requires commitment on the part of the patient and family. While no "cure" exists, it is possible to attain control of the headaches. Treatment failures or resistant cases should be referred to subspecialty centers for comprehensive treatment modalities.

Rapoport Ch 15.qxd 10/15/08 1:09 PM Page 93

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Editorial Comments

What exactly is chronic daily headache (CDH)? Does it exist as a separate entity? It is extremely difficult to answer the preceding questions based on our current knowledge. However, the debate continues to find the answers and the concept of CDH has great clinical utility. Dr. Newman's case and discussion allow us to consider CDH in a clinical context. All headache physicians see numerous cases of this nature, and one can only hope that this entity will be ultimately defined in neurobiologic terms, allowing precise and definitive therapy to be applied.

Appendix 15–1: Classification of Headache, after the International Headache Society Classification, 1988

Chronic Tension-Type Headache

A. Average headache frequency >15 days/month (180 days/year) for >6 months fulfilling criteria (B–D)
B. At least two of the following pain characteristics:
   1. Pressing/tightening quality
   2. Mild or moderate severity (may inhibit but does not prohibit activity)
   3. Bilateral location
   4. No aggravation caused by walking up or down stairs or by similar routine physical activity
C. Both of the following:
   1. No vomiting
   2. No more than one of the following: nausea, photophobia, and phonophobia
D. No evidence of underlying disease

Appendix 2: Criteria for CDH, Proposed by Silberstein et al., 1994

Primary Headache (duration >4 hours)*

- Transformed migraine (TM)
- Chronic tension-type headache (CTTH)
- New daily persistent headache (NDPH)
- Hemicrania continua (HC)

Proposed Criteria for Transformed Migraine

A. Daily or almost daily (>15 days/month) head pain for >1 month
B. Average headache duration of >4 hours/day (if untreated)
C. At least one of the following:
   1. History of episodic migraine meeting any IHS criteria 1.1–1.6
   2. History of increasing headache frequency with decreasing severity of migrainous features over at least 3 months
   3. Headache at some time meets IHS criteria for migraine 1.1–1.6 other than for duration
D. Does not meet criteria for daily persistent headache or hemicrania continua
E. No evidence of underlying disease

Proposed Criteria for New Daily Persistent Headache

A. Average headache frequency >15 days/month for >1 month
B. Average headache duration >4 hours/day (if untreated); frequently constant without medication but may fluctuate
C. No history of tension-type headache or migraine which increases in frequency and decreases in severity in association with the onset of NDPH (over 3 months)
D. Acute onset (developing over >3 days) of constant unremitting headache
E. Headache is constant in location? (Needs to be tested)
F. Does not meet criteria for hemicrania continua
G. No evidence of underlying disease.

* May occur with or without medication overuse.