Chapter 31

The Man with Chronic Headaches and Few Other Symptoms

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Case History

A 38-year-old man has had occasional headaches for 10 years. He usually experiences up to six headaches per month, but the frequency of his headaches varies considerably. He describes the headaches as throbbing pain of moderate to severe intensity, which are variously localized at the back of the head and, at other times, bifrontally. Movement and exercise worsen the headaches. The headaches last up to 8 hours if untreated, although simple analgesics often lessen the pain within 2 hours. Sometimes, the headaches recur later on the same day, or upon awakening the following morning. The headaches do not awaken him from sleep. He denies associated visual, motor, or sensory disturbances, as well as nausea and vomiting. When the headaches are severe, he reports increased sensitivity to light, but denies sound sensitivity. The headaches are triggered by red wine, but are not triggered by food. They are more frequent and severe during periods of work or personal stress.

Over the last 3 months, the headaches have become more frequent. For the last month, he has had an average of two headaches per week, and the attacks have lasted up to 18 hours. The pain and associated features are unchanged; only the frequency and severity have increased. He requires 4 to 8 over-the-counter ibuprofen tablets (200 mg) 2 days per week.

The patient reports increased work-related stress over the last 4 months. He has been married for 10 years and has felt "down in the dumps" recently.

He decided to consult a neurologist because he was concerned about the increasing frequency of his pain as well as the pattern of analgesic use. He had gone to a primary-care physician before and received a diagnosis of tension-type headache.

The patient is otherwise in excellent health and takes only ibuprofen and daily multivitamins. He does not smoke or drink. He does not exercise regularly. His mother has a history of migraine. His general physical and neurologic examinations are unremarkable. He had a migraine disability assessment (MIDAS) score of 19, indicating moderate disability. His Beck Depression Inventory indicated mild depression.

Questions on the Case

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

- Does this patient fulfill criteria for episodic tension-type headache?
- What is the most likely diagnosis?
- What investigations should be done?
- What is the treatment strategy for this patient?

Case Discussion

The patient has some of the typical features of migraine: chronic recurrent headache, moderate to severe pain inten-

sity, of throbbing quality, and aggravated by physical activity and photophobia. He also presents some typical features of tension-type headache: bilateral headache, absence of nausea, vomiting, phonophobia, and aura. Although the headache fulfills some International Headache Society (IHS) criteria for migraine without aura (A, B, and C, Table 31-1), he does not have the associated symptoms required for diagnosis. Although he has photophobia, the IHS criteria require at least one of either nausea or vomiting or both photophobia and phonophobia. He fulfills some of the criteria for tension-type headache (A, B, and D, Table 31-2). Because his headaches were usually severe, were aggravated by exercise, and were throbbing (all migraine features), episodic tension-type headache was not his diagnosis (see Table 31-2).

In clinic and some population-based studies, large numbers of patients such as this one do not fully meet the IHS criteria for migraine with or without aura or the criteria for tension-type headache. Many of these patients meet criteria for probable migraine (IHS category 1.6), a migraine subtype where just one of the criteria for other types of migraine is missing (Table 31-3). The previously used term for probable migraine (PM) was migrainous headache. There are two subtypes of PM: PM without aura (just one criterion for migraine without aura is missing) and PM with aura (one criterion for migraine with aura is missing).

The manifestations of migraine are highly variable, and result in a broad spectrum of clinical presentations. Although many patients have all of the defining features of migraine, some patients have migraine features that fall below the strict diagnostic threshold. Thus, PM may be diagnosed if any of the following features of migraine is missing.

1. Number of attacks and duration: To meet IHS criteria for migraine, patients must have five attacks that last 4 to 72 hours each. These criteria can be met even if attacks last less than 4 hours or more than 72 hours on average, if five attacks of appropriate duration have occurred. If the attacks last more than 72 hours and there is disability, status migrainosus is the diagnosis. If the attack lasts more than 72 hours, without disability, then PM is the diagnosis. If the attacks last less than 4 hours, or there were less than five attacks, then PM is the diagnosis. If 15 or more attacks occur each month, then chronic migraine (1.5.1) may be the diagnosis.
2. Pain features: Two of four pain features are required for the diagnosis of migraine without aura (see Table 31-1). If one or no pain features are present and all other criteria are met, then PM is the diagnosis.
3. Associated symptoms: Migraine attacks must have either nausea or vomiting, or both photophobia and phonophobia. If there are no associated symptoms or if just one of photophobia or phonophobia is present and all other migraine criteria are met, then the patient has PM.
4. Aura: One of the aura criteria (IHS categories 1.2.1 to 1.2.6) is missing.

Table 31-1. International Headache Society Criteria for Migraine without Aura

A. At least five attacks fulfilling criteria B to D
B. Headache attacks lasting 4 to 72 hours and occur < 15 days per month (untreated or unsuccessfully treated)
C. Headache has at least two of the following characteristics:
   1. Unilateral location
   2. Pulsating quality
   3. Moderate or severe pain intensity
   4. Aggravation by or causing avoidance of routine physical activity (ie, walking or climbing stairs)
D. During headache at least one of the following:
   1. Nausea and/or vomiting
   2. Photophobia and phonophobia
E. Not attributed to another disorder

Table 31-2 International Headache Society Criteria for Episodic Tension-Type Headache

A. At least 10 episodes fulfilling criteria B to E. Number of days with such headache ≥ 1 day per month and < 15 days per month for at least 3 months (more than or equal to 12 days and less than 180 days per year)
B. Headache lasting from 30 minutes to 7 days
C. At least two of the following pain characteristics:
   1. Pressing/tightening (nonpulsating) quality
   2. Mild or moderate intensity (may inhibit, but does not prohibit activities)
   3. Bilateral location
   4. No aggravation by walking stairs or similar routine physical activity
D. Both of the following:
   1. No nausea or vomiting (anorexia may occur)
   2. Photophobia and phonophobia absent, or one but not the other may be present
E. Not attributed to another disorder

The prevalence of PM in the general population is not fully established. A population-based study assessing 4,000 40-year-old males and females using the IHS criteria found that the lifetime prevalence of PM was 2.5%, with a male:female ratio of 1:1.2. A similar prevalence was found in the American Migraine Study II (2.6%, 63% female). However, Henry and colleagues screened 10,585 subjects aged 15 years and older, selected to be representative of the French general population, and found a standardized prevalence for migraine (IHS categories 1.1 and 1.2) of 7.9% (11.2% for women and 4.0% for men) and 9.1% for PM (IHS category 1.6). In this study, PM was more prevalent than migraine. In a recent US health-plan study, the prevalence of PM was 14.5% (19.6% in women, 13.1% in men) in those who had received medical care for any reason in the last year.

As discussed above, the IHS considers PM as a subtype of migraine. Several lines of evidence support this hypothesis:

1. A genetic study showed a link between some PM sufferers and migraine without aura.
2. A randomized clinical trial showed that PM sufferers respond well to sumatriptan, whereas patients with pure tension-type headache do not.
3. PM shows an epidemiologic profile that resembles migraine, although the female preponderance is less strong. In the US study, prevalence was highest in the 36- to 45-year-olds (16.7%) and Caucasians (15.2%). Prevalence was lowest in the 46- to 55-year-olds (12.4%) and "other" racial categories (9.8%). Like PM, migraine also shows a female preponderance, peak prevalence in middle life, and a lower prevalence in African and Asian Americans.
4. PM shows decrement in headache-related quality of life (HRQoL) and substantial disability relative to the control population, similar to, but less severe than, the profile seen in usual studies of migraine. Unadjusted means for the SF-12 mental health summary component (MCS-12) were significantly lower in PM than controls (50.2 vs 53.1). Similarly, scores for the SF-12 physical health summary component (PCS-12) were also significantly lower in PM patients (mean = 48.8) than in controls (mean = 51.2). The prevalence of moderate or severe disability (MIDAS Grades III and IV) for PM was 12.8%, compared to 3.2% in the control group. When adjusting for covariates (gender, age, race, education, occupation, and income), a similar pattern was seen to migraine (adjusted probability ratio [PR] = 3.81).
5. Similar to migraine, PM is comorbid with depression. The overall prevalence of major depression among PM patients was reported to be 19.5%, compared to 10.3% in the control group (unadjusted PR = 1.89). When adjusting for covariates (gender, age, race, education, occupation, and income), the adjusted PR was 2.22.

Is PM a condition worthy of treatment? As discussed, PM is associated with a significant risk of disability as defined by MIDAS grade. PM is also associated with decrements in HRQoL in comparison with controls. Although migraine appears to be more severe on most measures than PM, PM is a worthy target of treatment.

Table 31-3. International Headache Society Criteria for Probable Migraine

1.6.1 Probable migraine without aura
Diagnostic criteria: A. Fulfills all but one of criteria A to D for 1.1 migraine without aura B. Not attributed to another disorder
1.6.2 Probable migraine with aura
Diagnostic criteria: A. Fulfills all criteria but one for one of the types of migraine aura (1.2.1 to 1.2.6). B. Headache that meets criteria B to D for migraine without aura (1.1) begins during the aura or follows aura within 60 minutes C. Not attributed to another disorder

Management Strategies

Once a clinical diagnosis of PM is made, the next step is to assess disability as well as comorbidities, in order to develop an individualized treatment plan. The *US Headache Consortium Guidelines* recommends a stratified care approach to migraine patients based on their level of disability, to help physicians target patients who require careful assessment and treatment. This is probably also a valid approach to the treatment of PM.

Figure 31-1 provides a schematic view of how MIDAS (Figure 31-2) might be used to provide appropriate treatment, based on the patient's level of headache-related disability. All patients require a specific diagnosis, and education about their disorder and self-management strategies. At the time of consultation and diagnosis, the PM patient completes a MIDAS questionnaire (or has their disability assessed by another disability instrument) and is categorized into a MIDAS grade (I to IV). A MIDAS score of 0 to 5 (MIDAS Grade I) or 6 to 10 (MIDAS Grade II) indicates relatively low medical need. Simple analgesics are appropriate for first-line acute treatments for these patients. If simple analgesics are unsuccessful, then triptans may be needed. A MIDAS score of 11 or over (MIDAS Grade III or IV) indicates a relatively high treatment need. Specific acute therapies, such as the triptans, are likely to be needed by these patients, together with daily preventive medications when necessary. In patients with contraindications to triptans, we prefer nonsteroidal anti-inflammatory agents alone or in combinations with a prokinetic such as metoclopramide.

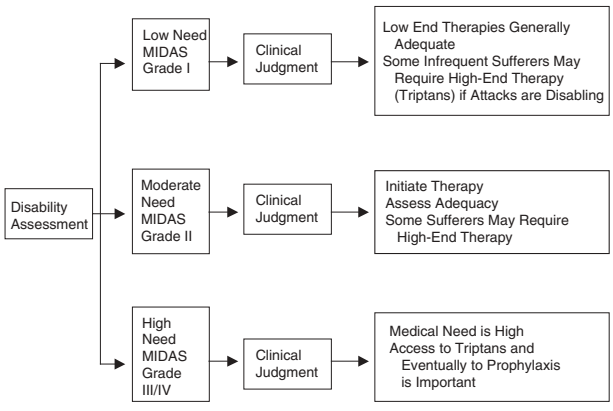

Figure 31-1. Potential utility of the MIDAS questionnaire in relating migraine severity to treatment choice.

MIDAS Questionnaire	Days
1. How many days in the last 3 months did you miss work or school because of your headaches?	_____
2. How many days in the last 3 months was your productivity at work or school reduced by half or more because of headaches (do not include days you counted in question 1 where you missed work or school)?	_____
3. How many days in the last 3 months did you NOT do housework because of your headaches?	_____
4. How many days in the last 3 months was your productivity in household work reduced by half or more because of your headaches (do not include days you counted in question 3 where you did not do household work)?	_____
5. How many days in the last 3 months did you miss family, social, or leisure activities because of your headaches?	_____

Figure 31-2. Migraine Disability Assessment (MIDAS) questionnaire.

An extensive review of the available pharmacologic options is beyond the scope of this chapter. Some of the available acute options are listed in Table 31-4, and the evidence regarding their use has been extensively reviewed. Preventive options are listed in Table 31-5. Once deciding to initiate preventive pharmacotherapy, several general principles of management may prove helpful:

- Begin the preventive medications at a low dose and gradually increase the dose over weeks or months if necessary. For example, if no side effects emerge, the desired clinical response has not yet been achieved, and the ceiling dose for the drug had not been reached, then the dose can be escalated.
- Manage the patient's expectations regarding the time and extent of clinical benefit. Many preventive medications take 3 or 4 weeks or longer for a therapeutic response at a particular dose; patients need to be

Table 31-4. Selected Acute-Care Therapies for Migraine

Generic Treatment	Doses
Analgesics (monotherapy)	
Aspirin tablets	325–650 mg
Acetaminophen tablets	325–1,000 mg
Combination Analgesics	
Aspirin plus acetaminophen plus caffeine tablets	250 mg plus 250 mg plus 65 mg
Isometheptene mucate plus acetaminophen plus dichloralphenazone tablets	65 mg plus 325 mg plus 100 mg
Butalbital plus aspirin plus caffeine tablets	50 mg plus 325 mg plus 40 mg
Butalbital plus acetaminophen plus caffeine tablets	50 mg plus 325 mg plus 40 mg
Ergotamine Alkaloids	
Erogotamine tartrate plus caffeine tablet	1 mg plus 100 mg
Ergotamine tartrate plus caffeine suppository	2 mg plus 100 mg
DHE nasal spray	0.5 mg per nostril (repeat in 15 min once for 2 mg total dose)
DHE intramuscular or subcutaneous	1 mg
NSAIDs	
Diclofenac K tablets	50–100 mg
Flurbiprofen tablets	100–300 mg
Ibuprofen tablets	200–1,200 mg
Naproxen tablets	250–500 mg
Naproxen sodium tablets	550–1,100 mg
Piroxicam tablets	40 mg
Tolfenamic acid tablets	200–400 mg
Diclofenac sodium intramuscular	50 mg
Opiate Analgesics	
Butorphanol nasal spray	1–2 mg
Triptans	
Almotriptan tablets	12.5 mg tablets
Eletriptan tablets	20 mg or 40 mg
Frovatriptan tablets	2.5 mg
Naratriptan tablets	1 mg or 2.5 mg
Rizatriptan tablets	5 mg or 10 mg
Rizatriptan orally disintegrating tablets	5 mg or 10 mg
Sumatriptan tablets	25 mg, 50 mg, or 100 mg
Sumatriptan nasal spray	5 mg or 20 mg
Sumatriptan subcutaneous self-injection	6 mg
Zolmitriptan tablets	2.5 mg or 5 mg
Zolmitriptan orally disintegrating tablets	2.5 mg or 5 mg
Zolmitriptan nasal spray	5 mg

DHE = dihydroergotamine; NSAIDs = nonsteroidal anti-inflammatory drugs.

patient and compliant with the agreed-upon treatment plan. Up to two-thirds of the patients given any of the drugs listed in Table 31-5 will have a 50% reduction in the frequency of headaches. Breakthrough headaches are inevitable and must be managed with acute treatment. It is important to explain the side effects of these drugs and engage the patient in the decision-making process.

- Establish a comprehensive migraine management plan that includes long-term goals, tips on when the medication needs to be changed, and a regular office visit schedule. Also included is specific information on adverse reactions that may warrant discontinuing the medication, returning to the clinic, calling the office, or even going to the hospital on an emergency basis.

Table 31-5. Selected Preventive Therapies for Migraine

Generic Treatment	Doses
Anticonvulsants	
Divalproex sodium tablets*	500–1,500 mg per day
Gabapentin tablets*	300–3,000 mg
Levetiracetam tablets	1,500–4,500 mg
Topiramate tablets*	50–400 mg
Zonisamide capsules	100–400 mg
Antidepressants	
MAOIs	
Phenelzine tablets	30–90 mg per day
TCAs	
Amitriptyline tablets*	30–150 mg
Nortriptyline tablets	30–100 mg
SSRIs	
Fluoxetine tablets	10–40 mg
Sertraline tablets	25–100 mg
Mirtazapine tablets	15–45 mg
Paroxetine tablets	10–30 mg
SNRI	
Venlafaxine tablets	37.5–225 mg
Beta-Blockers	
Atenolol tablets*	25–100 mg
Metoprolol tablets	50–200 mg
Nadolol tablets	20–200 mg
Propranolol tablets*	30–240 mg
Timolol tablets*	10–30 mg
Calcium Channel Antagonists	
Verapamil tablets*	120–720 mg
Nimodipine tablets	40 mg three times daily
Diltiazem tablets	30–60 mg three times daily
Nisoldipine tablets	10–40 mg per day
Amlodipine tablets	2.5–10 mg per day
NSAIDs for Prevention	
Naproxen sodium tablets*	550–1,100 mg per day
Ketoprofen tablets	150 mg per day
Mefenamic acid tablets	1,500 mg per day
Flurbiprofen tablets	200 mg per day
Serotonergic Agents	
Methysergide tablets*	2–12 mg
Cyproheptadine tablets	2–16 mg
Pizotifen tablets*	1.5–3 mg
Miscellaneous	
Montelukast sodium tablets	5–20 mg
Lisinopril tablets	10–40 mg
Botulinum toxin A injection	25–100 units (intramuscular)
Feverfew tablets	50–82 mg per day
Magnesium gluconate tablets	400–600 mg per day
Riboflavin tablets	400 mg per day
Petasites 75 mg*	75 mg twice daily

*Evidence for moderate efficacy from at least two well-designed, placebo-controlled trials.

MAOIs = monoamine oxidase inhibitors; NSAIDs = nonsteroidal anti-inflammatory drugs; SNRI = serotonin and norepinephrine reuptake inhibitor; SSRIs = selective serotonin reuptake inhibitors; TCAs = tricyclic antidepressants.

Case Summary

- This patient has throbbing, severe headaches aggravated by exercise. These headaches do not fulfill criteria for tension-type headache (see Table 31-2). The presence of photophobia without phonophobia and the absence of nausea or vomiting do not allow the diagnosis of migraine (see Table 31-1).
- This headache fulfills criteria for PM, a subtype of migraine (IHS category 1.6). In addition to meeting diagnostic criteria, headache exacerbation by red wine and photophobia are typical of migraine.
- As with other forms of migraine, investigations are not needed unless atypical signs or red flags are present. In this patient, although there was headache exacerbation during stress, the other clinical features and the normal examination were judged sufficiently reassuring not to warrant imaging.
- This patient has moderate disability. Using the stratified approach, an oral triptan would be our choice for the acute treatment. Because the patient has two attacks per week, we discussed preventive treatment. The patient did not like the idea. As stress was a trigger, we gave him progressive relaxation exercises and stress management. His headaches responded well to triptans and decreased in frequency, perhaps due to stress management. Had the frequency not declined, we would have re-addressed preventive treatment.

Selected Readings

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Editorial Comments

All headache specialists have long acknowledged the existence of migraine in patients that do not meet all prior IHS criteria for migraine without aura (1988). Such patients were treated as having migraine and, as would be expected, most responded. This new category of "probable migraine" is most welcome and makes sense clinically. Importantly, the careful epidemiologic work done in this migraine subtype gives us more confidence in managing this disorder. One suspects many of these patients were diagnosed with tension-type headache in the past. One also must ask, why does migraine play its full symphony on occasion (ie, migraine with aura), and at other times just strike up part of the orchestra of neurobiologic events (ie, probable migraine)?

Final diagnosis:

Probable migraine (formerly migrainous headache)