

CHAPTER 3

THE PATIENT WITH RECURRENT HEADACHES SINCE CHILDHOOD

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Case History

This 31-year-old woman has had recurring headaches since childhood. During her teens and twenties, the headaches occurred around the time of her menstrual period. In the year or so prior to her presentation, her headaches had increased in frequency and were occurring four to six times a month, although the character and symptoms of the headaches had not changed. When she was younger, she believed that the headache and nausea that she frequently experienced at the time of her menstrual period were episodes of the flu.

In addition to the headache, she has had years of gastrointestinal (GI) symptoms. These GI symptoms consisted mainly of indigestion and heartburn, along with bloating and excessive gas. She could not correlate these GI symptoms with her headache. These symptoms had been extensively evaluated by radiography, as well as upper GI endoscopy, and an ultrasound examination of the gallbladder. The results of these studies were normal, and she was diagnosed as having irritable bowel syndrome and was told that her headache and GI symptoms were due to her being nervous.

Her headache was described as being a throbbing pain in the temples. The pain could be on either the right or left side, or at times occur bilaterally. There was also discomfort across the bridge of the nose and behind her eyes. The headache could occur upon awakening but did not wake her during the night. She always had her worst headache associated with her menses. She also noted that if she slept late in the morning she would probably get a headache.

The day before her headache, she would feel tired and weak and stated that her head “felt heavy.” She had no visual symptoms prior to or during her headache,

and she had no neurologic symptoms prior to or during her headache.

The headache was accompanied by sensitivity to light and noise, dizziness, weakness, and nausea with frequent vomiting. Interestingly enough, she found that the pain in her head seemed to ease with vomiting as well as with sleep. She also would become constipated when she had a headache. Her headaches would generally last 1 to 2 days.

A review of her history revealed that there was no family history of migraine. She rarely drank alcohol and had stopped smoking 7 years prior to her visit. She drank four cans of cola per day. She admitted to being tense and anxious; however, she denied having any significant psychological problems. She had had two pregnancies and she noted that her headache was less frequent during the pregnancies.

She was taking ibuprofen and aspirin as medication for her headaches. Other medications included metoclopramide, lorazepam, and sucralfate. She was using suppositories of trimethobenzamide for nausea. Past medications had included cimetidine, ranitidine, cisapride, and thiethylperazine, all of which were given for her stomach symptoms, but none of which gave her any relief from them.

On physical examination she weighed 127 lb. and her blood pressure was 98/70. The results of the physical examination itself lay entirely within normal limits, except for some mild tenderness in the midabdomen.

She underwent a psychophysiologic evaluation in the biofeedback department. She was found to have a high autonomic nervous system arousal which is manifested by low skin temperatures in her hands. It was felt that she had stress at work but had no major psychopathology. It was felt that she would be a good candidate to benefit from further behavioral therapy.

Questions about This Case

- What is the most likely diagnosis for this 31-year-old woman?
- Are any further diagnostic studies necessary? Would they help in the diagnosis?
- In regard to treatment, does she need daily medication as prophylaxis, as well as an abortive agent which would be taken at the onset of an attack? What specific agents would you suggest?
- She has suffered from chronic upper GI symptoms. These do not necessarily occur at the same time as her headache attacks. She has had extensive evaluation and has been unresponsive to many medications. Is there a correlation with her headache?

Case Discussion

This patient has had recurrent headaches since childhood. She has never been diagnosed as suffering from migraine and has been told that her symptoms are due to nerves. She has had a lot of GI symptoms in recent years, and has had extensive GI studies. Since all of the GI studies have been negative, she was diagnosed as having functional GI stress or irritable bowel syndrome, and her headache was felt to be due to tension. She admits to being a tense person, a worrier, and somewhat compulsive. A psychologic assessment did not demonstrate any major psychopathology.

Unfortunately, many patients who suffer from migraine without aura, i.e., without a well-defined focal deficit which precedes the headache, are not diagnosed as such. Many physicians still think of migraine as that sick headache which is associated with an aura. About 80% of patients with migraine have migraine without aura. The diagnosis of migraine has become easier with the introduction of the International Headache Society classification in 1988. Diagnostic criteria are given for the primary headache syndromes. This patient has had recurring headaches with nausea and dizziness associated with her menstrual cycle since childhood, and yet no physician has ever diagnosed her as having migraine. She was labeled as having premenstrual syndrome (PMS) and being tense and nervous.

This patient has had recurrent retro-orbital and temporal throbbing headache. It can be unilateral but also is bilateral at times and may shift from side to side. She is aware of tightness in her neck which accompanies the throbbing pain in her temples. Many of the headaches are present upon awakening but do not awaken her earlier than usual. She has many associated symptoms with her headache. Quite typical are GI symptoms including nausea, vomiting, and anorexia. Gastrointestinal symptoms

are second only to the head pain as the most frequent symptoms of migraine. This woman not only had nausea and vomiting, but also had severe constipation for the duration of her headaches. Other typical migraine symptoms that she suffered were sonophobia, photophobia, dizziness, and generalized weakness.

She was able to identify very few trigger factors. She was unable to determine which foods would set off a headache. She always had 2 to 3 days of headaches with her menstrual periods, and, like many women with menstruation-related migraine, she had very few headaches during her two pregnancies. Sleeping late would often be associated with a headache attack. Most people with migraine will have fewer headaches if they keep to a regular schedule of eating and avoid skipping meals. The headaches that occur when patients sleep late are probably due to prolonged hours of fasting and delay in eating breakfast at their normal time.

Stress may well be an important factor in increasing the frequency of migraine attacks. This patient has had trouble at work, feeling that she was not appreciated. She did miss a fair amount of work due to her headaches, and this caused conflict with her supervisor. She has since quit this job and has found other employment.

A biofeedback assessment showed that she would probably benefit from learning some relaxation techniques and behavioral therapy. Unfortunately, as often happens, her insurance did not cover biofeedback therapy and she never returned for further sessions.

Her GI symptoms consisted of nausea, heartburn, and epigastric pains, as well as frequent constipation. She had a lot of nausea with her headache but she could not correlate the epigastric pains with her headache. These non-headache symptoms are felt to be secondary to the same underlying pathophysiology that causes migraine headaches. It is of interest that in the past 4 years, since undergoing treatment for her headache, this patient has seen marked improvement in her GI symptoms while on prophylactic medication for migraine. Several medications used for upper GI symptoms had been ineffective in controlling her discomfort.

As far as treatment is concerned, in this case, one needs to consider daily preventive medication because of the frequency of her attacks. Because this patient has no contraindications to the use of beta-blockers, and because beta-blockers are effective prophylactic drugs for migraine, she was started on nadolol. Her low blood pressure (98/70) was of some concern, but usually the use of either beta-blockers or calcium channel blockers has little effect on normal or low blood pressure. She has done quite well on nadolol. She was initially started on 20 mg, and this has been increased over 4 years so that she has now been on 200 mg per day for the past 2 years.

When she felt that nadolol was losing its effect, she was prescribed verapamil but she had increased headache, nausea, and vomiting. Diltiazem was also tried, but this had no effect on the frequency and the severity of her headaches. Nadolol was reinstated, and the dose increased to the current level of 200 mg daily.

Other preventive medications in controlling migraine without aura include the tricyclic antidepressants. This might be a good choice for her because of her anxiety but these tend to be very sedating and she had no difficulty sleeping. The tricyclic antidepressants are an excellent choice for preventive therapy for those patients who are having trouble sleeping. Nonsteroidal drugs are often beneficial in the preventive treatment of migraine but they were avoided in this case because of the patient's significant GI symptoms. Recently valproic acid has been approved for migraine prophylaxis. Nausea, however, is a side effect of this drug, and it is not as effective as the beta-blockers or calcium channel blockers.

Regarding abortive therapy, I usually start with isometheptene mucate. This is usually combined with a sedative and acetaminophen. This agent is well tolerated and is often effective. Patients must use it early in the attack and they must use a sufficient amount. Usually two capsules are used at once followed by one or two capsules in an hour. More effective abortive agents such as ergotamine tartrate and sumatriptan have more side effects. This patient has done very well on isometheptene mucate and only needs to take one capsule followed by another capsule in an hour. Her headache is usually well controlled in about 4 hours. She did try oral sumatriptan tablets but had a recurrence of her headache in 12 hours. Isometheptene mucate, sumatriptan, and ergotamine tartrate are all vasoconstrictive agents.

Another group of medications that is often helpful for the acute treatment of migraine is the rapid-acting anti-inflammatory drugs. Meclofenamate, ibuprofen, and naproxen sodium are the ones used most often. They need to be taken in a fairly large dose at the onset of migraine.

This patient has found the use of metoclopramide to be very helpful. She doses herself with this agent prior to taking her isometheptene mucate. Metoclopramide is often helpful in controlling nausea and also enhances the absorption of any of the abortive agents. Migraineurs, in general, have decreased intestinal absorption predominantly due to gastric stasis.

This patient is very pleased with the control of her headaches on the regimen of nadolol 200 mg per day and the use of metoclopramide and isometheptene mucate for the acute attacks. She still has about three attacks per month, the worst of which occurs with her menstrual period.

Management Strategies

- Make the diagnosis of migraine without aura. Any recurrent headache accompanied by a wide variety of other symptoms is likely to be migraine. The more severe attacks usually occur with the menstrual period.
- One needs to decide whether to use daily prophylactic medications as well as abortive agents, or only abortive agents. Consider prophylactic medication when the patient has three or more attacks per month or when the attacks last for a very long time.
- Help the patient to identify various trigger factors such as foods, stress, erratic eating, and sleeping habits. Other factors that seem to play a role in migraine are the menstrual cycle and weather changes. One cannot do much about the weather changes, and hormone therapy has not been very satisfactory for migraine sufferers.
- Consider nonpharmacologic therapies such as biofeedback, relaxation techniques, and physical therapy. Physical therapy is helpful when there is much neck and shoulder tightness accompanying the headache.
- Patients such as this one need to be followed, and the medications need to be adjusted or even changed depending on their effectiveness and their side effects. Prophylactic medication should be increased to the point where headaches are well controlled or until there are uncomfortable side effects. Migraineurs often require higher doses of calcium channel blockers and beta-blockers than are used to treat hypertension, and they often require lower doses of tricyclic antidepressants than are needed to treat depression.
- The long duration of symptoms and a normal computed tomography scan done 2 months before the patient's visit make further lab and imaging studies unnecessary. Her headaches had not changed over the years other than in their increased frequency. A common cause of increased frequency and severity of migraine is mild hypertension, but her blood pressure was normal.

Case Summary

- This patient has migraine without aura and probably migrainous GI symptoms.
- Even though this patient has a typical history of migraine without aura, she was not previously diagnosed as such and suffered from years of headache and GI symptoms, which had been diagnosed as being due to stress and tension. Migraine without aura remains underdiagnosed by the medical profession.
- This patient has done very well on nadolol, although the dosage has needed to be increased. Beta-blockers remain the drugs of choice for migraine prophylaxis if there is no contraindication. Other medications that

are useful for the prevention of migraine include the calcium channel blockers (usually verapamil), tricyclic antidepressants, valproic acid, and the nonsteroidal anti-inflammatory drugs.

- Abortive agents useful in the treatment of migraine include isometheptene mucate (combined with dichloralphenazone and acetaminophen), ergotamine tartrate, sumatriptan, and the short-acting nonsteroidal anti-inflammatory drugs. The use of metoclopramide prior to any of these abortive agents is often very useful in controlling nausea and potentiating the effects of the abortive agents.

Overview of Migraine without Aura

It is felt that about 80% of all migraine sufferers have migraine without aura. Epidemiologic studies are difficult, however, because many patients with migraine will have both migraine without aura and migraine with aura. Most patients who do not have an aura will never have an aura; whereas, people who have migraine with aura will often have some typical migraine headaches that are not preceded by an aura. Therefore, at any one time one might make a different diagnosis.

In spite of all that has been written about headaches and migraine, it is remarkable how many physicians still do not diagnose migraine unless the patient describes a typical aura. The fact that migraine with or without aura very frequently starts in childhood is also not well recognized. It has been demonstrated that about 50% of patients with migraine have had their first headache by the age of 15. The International Headache Society (IHS) classification of headache, which was published in 1988, provides diagnostic criteria for the various types of primary headache syndromes. Many headache physicians do not use this classification in their daily clinical practice and rely only on the history that the patient presents, and on their own diagnostic expertise as to whether the headache is of a migrainous type. The IHS classification has been very useful in research studies where all headache patients can be classified according to the IHS criteria.

There is much debate as to whether migraine with aura and migraine without aura have the same basic pathophysiology. Some studies have demonstrated differences in the circulation and metabolism of the brain prior to the two types of migraine whereas other studies have not demonstrated any significant differences. The fact that many patients who suffer primarily from migraine with aura will also have some migraine attacks without aura leads me to believe that they are manifestations of the same basic pathophysiology. There are also patients who have migraine without aura and have never had migraine

with aura who develop aura symptoms without headache in their later years.

Many patients suffering from migraine without aura will have prodromal symptoms. A migraine aura is a focal, visual, or neurologic symptom, which lasts less than 1 hour and is followed by a headache within 1 hour of the end of the symptoms. Prodromal symptoms are generalized and vague and last hours to days prior to the onset of the migraine attack. Such symptoms as depression, irritability, fatigue, and hunger are common prodromal symptoms. Patients or spouses and family can come to recognize that a headache will be coming on within a day or two because of some of these prodromal symptoms. Prodromal symptoms, which are manifestations of cerebral dysfunction, are further evidence that migraine starts in the brain, with the blood vessels reacting secondarily to neurologic dysfunction.

The migraine attack has been divided by Blau into five phases. Not all patients have these five phases, and they may overlap in some patients. The first phase is a prodromal phase, which is a change in mood or behavior, and, as mentioned, occurs for hours or days before the headache begins. The second phase, which is the aura when it does occur, is a well-defined focal deficit lasting less than an hour. The third phase is the headache phase, with the pain and other associated symptoms. The termination phase, which is the fourth phase, is the lessening of pain, and the fifth phase, which Blau calls the postdrome, consists of residual symptoms such as fatigue that occur after the pain has ceased.

The onset of most attacks of migraine is in the morning. It is unusual for the headache to actually awaken the patient but frequently the headache is present when the patient awakens. Headaches that are present upon awakening often are more difficult to control because patients do not take their abortive therapy as early in the attack as they would have had they recognized the onset of the headache. Although migraine without aura is usually a unilateral throbbing or pulsatile pain, many patients do have bilateral pain. Nausea and vomiting are the second most common symptoms. A symptom that I find very helpful in differentiating migraine without aura from other types of headache, such as tension-type headache, is that migraine is usually aggravated by any physical activity. Patients with migraine will want to go to a dark room and be very quiet. Photophobia and phonophobia as well as osmophobia are all commonly associated symptoms of the migraine attack. In addition to nausea, vomiting, and anorexia, other GI symptoms such as diarrhea or constipation are not uncommon.

Generalized fatigue may occur as a prodromal symptom but is very common in the postdrome phase after the headache pain has ceased. Chills and sweats also

may occur. Migraine without aura is truly a generalized condition with systemic manifestations. The typical attack of migraine without aura lasts between 4 and 72 hours. Any migraine lasting longer than 72 hours fits the criteria for status migrainosus and usually has to be dealt with differently.

The diagnosis of migraine without aura is solely based on the history of the patients. We have found it useful to send out a questionnaire to patients prior to their initial visit so that they can spend some time thinking about some of the aspects of their headache. It is very difficult for patients to remember details of the onset of their headache and various associated symptoms when presenting to the doctor's office for the first time. Often they will consult with parents and then present some history of having had migrainous symptoms at a much earlier age than they had suspected. The complete history of all other symptoms will often unfold as one sees a patient over several visits.

Patients often request that the physician do imaging studies to exclude disease in the head. Scans are not usually necessary for anyone who has had a recurring headache for many years. It is helpful to remember that patients who have headache due to an organic disease usually also have neurologic symptoms and abnormalities on physical examination. Indications for considering imaging patients include a recent onset of headache or a change in the pattern or frequency of their headache. Certainly the development of any neurologic symptoms warrants close scrutiny with examination and probably scanning. If the headache frequency or pattern changes, it is good practice to do some laboratory studies as well. Anemia, electrolyte disturbances, thyroid disorders, or other endocrine disorders may have developed and may be a factor in a changing migraine pattern.

Migraine without aura, like migraine with aura, is an inherited condition. It is, therefore, very important to tell the patient up front that at present there is no cure for their headaches, and that successful treatment will consist of trying to reduce the frequency and severity of their attacks and to abort the attacks quickly when they occur. Many patients have unreasonable expectations that the headache can be cured and completely eliminated with some of the new drugs that they have heard about. Successful treatment of migraine involves a close partnership of the patient with the treating physician.

Management of migraine without aura includes both pharmacologic and nonpharmacologic modalities. Patients should be advised to keep regular living patterns and to avoid erratic sleep patterns and eating patterns. Skipping meals is a common trigger of a migraine attack. Excessive tiredness or excessive sleeping, which result in patients not eating for long periods of time, can

aggravate migraine. Perhaps 10 to 15% of patients can identify certain foods which may trigger an attack. Patients who have migraine without aura may find substances triggering attacks at one time, but not always. This is very frustrating for patients, but it seems that above a certain threshold, and when there are multiple factors present, any one substance may act as a trigger. Women with migraine are much more prone to have a headache at the time of menses. If the weather is changeable and they ingest some chocolate or alcohol, they may find the alcohol provokes a headache. At other times of the month, alcohol may not induce a headache. Keeping a diet diary and writing down all of the foods they ingested within 24 hours prior to the onset of headache will often help patients identify a food or substance which may act as a trigger.

Stress, as well as depression, may play a role in the frequency and severity of migraine attacks. Biofeedback training along with other means of relaxation may help reduce the severity and frequency of attacks. In patients who have a significant amount of muscle tension in the neck and shoulders, physical therapy and exercise on a regular daily basis may help as well.

Although some of these nonpharmacologic techniques are helpful in reducing the frequency and severity of migraine, the mainstay of treatment is pharmacologic. The decision whether or not to use daily prophylactic medication is based on consultation and discussion with the patient. Some patients who have very frequent attacks just do not want to take daily medication. Other patients who may only have one attack a month are so fearful of the attack that they want to take something daily in the hope that the attack will not occur or will be less intense. In general, however, daily preventive treatment should be considered for patients having three or more attacks per month. [*Editors' note: Some headache specialists would consider that preventive treatment is needed for a patient who gets six attacks or more per month and who gets long-lasting relief without side effects from a triptan.*] In the United States, the only preventive agents approved by the Food and Drug Administration (FDA) for migraine are the beta-blockers propranolol and timolol, methysergide, and divalproex sodium. Other beta-blockers are useful as well, and the calcium channel blockers, particularly verapamil, have been found to be fairly effective. Numerous studies have demonstrated the effectiveness of tricyclic antidepressants in the management of migraine as well. The nonsteroidal anti-inflammatory drugs can be quite beneficial in migraine prophylaxis. Their long-term use, however, needs to be closely monitored, and GI symptoms are frequent side effects. The patient may have other medical problems, which would contraindicate the use of these medications.

The best approach to the use of these preventive medications is to start with a fairly low dose and gradually increase the amount used depending on the patient's response or side effects. In many instances these agents are not used long enough. Frustration on the part of both the physician and the patient leads to frequent changing to other medications. Some of these preventive agents, particularly verapamil and divalproex sodium, may take 6 to 8 weeks before one sees a significant reduction of headache frequency and severity. Often patients have their drugs changed every couple of weeks and never give the medication an adequate trial.

Whether the patient is put on preventive medication, all patients with migraine need abortive therapy, i.e., something to take at the time of the acute attack. Ergotamine tartrate, which is usually combined with caffeine, has been very effective for many years. Unfortunately this agent makes many people nauseated. Isometheptene, which is combined with dichloralphenazone and acetaminophen, is not as effective but certainly is better tolerated and often will be helpful. It is important to use enough of these abortive agents and to use them early in the attack. The rapid-acting anti-inflammatory drugs such as meclizolamine, ibuprofen, and naproxen sodium, when used in large amounts early in the headache attack, are often very effective.

A newer agent, sumatriptan, is effective in about 60 to 65% of patients and is available as an oral medication, as a nasal spray, or in self-injectable form. Our studies have shown that about 40% of responders do so to 25 mg in the oral form. Another 40% need 50 mg and about 20% need 100 mg or more. The dose seems to be quite variable, probably because of the variation in absorption during a GI attack. Zolmitriptan, naratriptan, and rizatriptan are new abortive agents available as oral tablets.

Summary

In summary, migraine without aura is the most common type of migraine, but is often not diagnosed. Helping the patient to recognize the factors that trigger their headache will help reduce the frequency of attacks. Good prophylactic and abortive medication is available, so that most patients with migraine without aura can control their attacks.

Selected Readings

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Editorial Comments

Migraine is more than headache, with many varied presentations, some stereotypical, and many systemic symptoms and manifestations. This case by Dr. Kunkel explores the nature of migraine symptoms and the importance of associated gastrointestinal symptomatology. The case is rich in description, and his management suggestions and strategies are sound and reflect the experience of a seasoned clinician. When neurologic aura does not accompany migraine, diagnosis can be more difficult. The fine line between repetitive usage of abortive agents, such as the triptans, and institution of preventive agents will become more defined in the future. In the meantime, approaches to therapy as outlined in this case are most welcome.