Chapter 4

The Teenager with Recurrent Headache

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Case History

This is the case of a 14-year-old girl with headaches since 6 years of age. When she was younger, she would stop playing, cry, occasionally vomit, and then lie down and go to sleep for 1 to 2 hours. Within the last year, the headaches had increased in frequency, occurring 4 to 6 times per month. She noticed that since she started menstruating, she would usually have one or two headaches prior to onset of menses.

The patient describes her headache as throbbing pain across her forehead and behind her eyes. Sometimes it may be more severe behind one eye. She has sensitivity to light and does not tolerate kitchen odors during her headache. The headache is often associated with nausea and occasionally with vomiting. Untreated, a headache lasts 6 to 24 hours and was usually relieved with sleep. She has no aura except for some very brief, bright "sparkles or stars" associated with her headache.

She has tried acetaminophen and ibuprofen with limited success. The medications do not completely relieve her pain unless she goes to sleep. Her primary-care physician has given her acetaminophen with codeine. This helps her sleep. She has been to the emergency room three times in the last year for headaches, where she received intravenous pain medication. Upon two occasions, she received neuroimaging studies (computed tomography scan).

She has noticed that certain odors, such as the cleaning solutions at school, may trigger headache. She has not noticed any dietary triggers or significant stress at home or school. She avoids slumber parties because she usually gets a headache when she attends one. She is an honor student, plays soccer and softball, takes violin lessons, and is active in the Girl Scouts. Often, she is up late studying, playing in a soccer match, or practicing her violin, and still gets up early for school. On the weekend, she may sleep in very late if no activities are planned for the day.

She suffers from fairly significant motion sickness. As her mother recalls, when the patient was a toddler, there were episodes when she would suddenly grab onto her mother's leg, cry, and refuse to walk for about 20 minutes, and then she would be fine. Her mother suffers from "sinus headaches" once a month, which are often accompanied by vomiting, and she frequently goes to bed when she has these headaches. In addition to her mother's suffering from headaches, the patient's paternal aunt has migraine. The patient's general and neurologic examinations are normal, and she has no other significant medical history.

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 appropriate diagnosis for the patient's headache?
- What diagnostic testing, if any, would you like to see done on this patient?
- What treatment would one initiate for this headache type and pattern?

Case Management

The patient was given the diagnosis of migraine without aura. She and her mother were educated on trigger avoidance as well as the benefits of regular sleep, regular meals, and regular exercise. She was given a headache diary and instructed on how to complete it, the importance of keeping a diary, and the importance of bringing it with her

when she returned for follow-up. She was prescribed zolmitriptan (orally disintegrating 2.5 mg tablets) as her acute therapy. She was instructed to take one tablet at the onset of headache, preferably while the pain was still mild. She could repeat a dose after 2 hours if she did not have complete relief of her migraine. She was also given a prescription for promethazine 12.5 mg tablets and was instructed to take this in conjunction with ibuprofen 400 mg if she did not get relief from zolmitriptan. She was told to return in 2 months for follow-up and reminded to bring her diary when she returned for the visit. She and her mother were urged to call the physician's office if she had problems with medications or exacerbation of headache prior to that visit.

When she returned for follow-up at 2 months, her diary revealed three headaches. Two responded very well to zolmitriptan 2.5 mg. One headache occurred at a sleepover and there was a delay in taking her acute medication. She subsequently responded to her rescue medication and sleep. In addition, she discovered that lack of sleep was a potent trigger for her and had taken steps to regulate her sleep habits better. This led to a dramatic reduction in the number of headaches.

Headache in Children

Treating migraine in children and adolescents should follow the same general principals as treating adults; however, some adjustments are made when treating a pediatric patient, and these will be discussed in more detail. General principals of management, as identified by the *US Headache Consortium Guidelines*, include the following:

1. Establish a diagnosis.
2. Educate patients about their condition and its treatment.
3. Establish realistic patient and treatment expectations.
4. Encourage patients to participate in their own management.
5. Develop an individualized management plan.

It is very important to establish the diagnosis of migraine and convey this clearly to the patient and parents. Many parents are concerned that there is an underlying organic cause for their child's headache, such as a brain tumor or aneurysm, and unless these fears are dispelled, treatment plans usually fail. Patients and parents are more likely to accept a treatment plan if they accept the diagnosis of migraine.

Accepting a diagnosis of migraine is as important as understanding the disease. Educating the parents and patient about the severity of the condition, the disability that is associated with attacks, and the underlying cause of the headache are all important in taking control of the illness. Patient education materials (eg, brochures, booklets, diaries, handouts, and lists of Web sites) can reinforce the teaching that the physician and nursing support provide in the clinic. Ongoing educational updates should occur at each office visit, which will reinforce the concepts of lifestyle modification, medication compliance, and trigger avoidance.

Managing patient expectations is important in achieving successful treatment goals over the long term. No single pain medication will be successful every time, and migraine is not just going to go away after one visit to the physician, although this may be what patients and parents expect from their health-care visit. Therefore, if these expectations are not discussed openly, patients and parents may be disappointed and may discontinue the treatment plan and not attend their follow-up office visits. Involving the patient, even if he/she is a child, will help improve the likelihood of treatment plan success. Teenagers often do not comply with a treatment plan if they were not included in its inception or if they do not feel it is a medication or treatment approach that is agreeable to them. It is particularly important to involve the adolescent patient in the decision-making process when caring for their migraine. Often, this can include dosage formulations, routes of administration, types of medication, and even environmental control or trigger avoidance.

Nonpharmacologic therapies can be employed easily with all patients, especially adolescents. There are basic lifestyle modifications to reinforce with adolescents, some with more success than others. Sleep patterns are often variable in an adolescent lifestyle, with sleep pattern changes often triggering or exacerbating migraine. Sleep deprivation, as in the present case presentation, is a frequent trigger in children and adolescents. Regular sleep routines can often improve headache frequency. Similarly, this group of patients is particularly known to have other lifestyle changes including irregular meals and irregular exercise patterns, among others, all of which may trigger or increase the frequency or intensity of attacks.

Stress is often a factor in children and adolescents with migraine. However, children are stressed in different ways than adults. School stress can include anxiety about workload, grades, relationships with peers, and difficulty in comprehending material in class. Extracurricular activities can also be quite stressful. Many children are overextended with school and extracurricular activities to the point of not having time to relax, play, and enjoy leisure reading or television. One of the responsibilities of the parent is to help monitor extracurricular activities for the children and limit the number of programs they are involved in; this may help decrease stress over being able to perform well, complete homework, and participate in other activities.

Other nonpharmacologic therapies, such as biofeedback, physical therapy, massage, and cognitive imagery, can also be helpful as acute interventions, as well as playing a role in prevention of migraine attacks. These treatments are particularly difficult in adolescents and children, mostly because they are time consuming, involve ongoing maintenance regimens, and can be expensive. Patients and families must agree that this treatment regimen is one that they are willing to participate in; otherwise, compliance can be a significant issue.

Medications used in the acute treatment of migraine attacks are divided into two major categories: medications specifically targeted toward the mechanisms involved in the pathophysiology of migraine (migraine-specific medications) and medications targeted more toward symptom control (nonspecific medications). Common nonspecific acute medications are listed in Table 4-1. Table 4-2 lists the available migraine-specific therapies with their formulations and available doses.

There is limited clinical evidence regarding nonspecific therapies for acute migraine therapy in children and adolescents. One study, carried out by Hamalainen and colleagues, compared acetaminophen, ibuprofen, and placebo in a double-blind crossover study in 88 children, 4 to 15 years of age. Each child treated headaches with acetaminophen (15 mg/kg/dose) or ibuprofen (10 mg/kg/dose) or placebo. They found that both acetaminophen and ibuprofen were statistically significant when compared to placebo; ibuprofen was more efficacious than acetaminophen.

In another single center, double-blind, parallel group trial, Lewis and colleagues compared ibuprofen suspension (7.5 mg/kg/dose) to placebo in a group of children 6 to 12 years of age. There were 45 children in the ibuprofen arm and 39 children in the placebo arm of the study. The authors found that headache response at 2 hours was significantly better in the ibuprofen group (76% of attacks) compared to the placebo group (53% of attacks, $p = .006$). Pain-free response was 44% compared to 25% for placebo ($p < .07$). Only 1 child in the ibuprofen arm needed rescue medication compared to 15 children in the placebo arm ($p < .001$).

This study suggests that ibuprofen is effective as an acute therapy for children with headache. However, when the data were analyzed more closely, there appeared to be a difference in headache response and recurrence rates between male and female subgroups. The question remains, however, as to whether this difference is due to some biological difference in migraine between boys and girls. Differences in response to treatment are not normally reported for migraine medications tested by gender in adults; however, there are no prospective studies that have specifically tested this clinical question with regard to efficacy of migraine medications. Additional studies are needed to further investigate whether there might be confounding factors influencing these results. As this was a small study, selection bias also may be considered.

The migraine-specific medications have been extensively studied in adults, and there are growing data regarding children and adolescents. There are several studies that have examined the efficacy and tolerability of sumatriptan in children under 12 years of age. In an open-label study, MacDonald treated 17 children, aged 6 to 16 years, with subcutaneous sumatriptan. Linder treated 50 patients, aged 6 to 18 years, with subcutaneous sumatriptan at a dose of 0.06 mg/kg. He found a headache response rate of 78% at 2 hours with 26% responding in 30 minutes and

Table 4-1. Nonspecific Medications Often Used as Acute Migraine Therapy

Acetaminophen
Herbal Supplements
Feverfew
Goodies powder
BC powder
NSAIDs
Ibuprofen
Naproxen sodium
Combination Agents
Aspirin/acetaminophen/caffeine
Butalbital/acetaminophen/caffeine
Isometheptene/dichloralphenazone/acetaminophen (systemic)
Narcotics
Codeine

NSAIDs = nonsteroidal anti-inflammatory drugs.

Table 4-2. Migraine-Specific Acute Therapies

Almotriptan	
Tablets	6.25 mg, 12.5 mg
Ergots	
Dihydroergotamine mesylate	
Injection	1 mg subcutaneous, intramuscular, or intravenous
Nasal spray	4 mg
Frovatriptan	
Tablets	2.5 mg
Naratriptan	
Tablets	2.5 mg
Rizatriptan	
Tablets	5 mg, 10 mg
Sumatriptan	
Injection	6 mg
Nasal spray	5 mg, 20 mg
Tablets	25 mg, 50 mg, 100 mg
Zolmitriptan	
Nasal spray	5 mg
Tablets*	2.5 mg, 5 mg
Eletriptan	
Tablets	20 mg, 40 mg

*Orally disintegrating tablets.

46% responding within 1 hour. The recurrence rate was only 6%. In both studies, sumatriptan injection was fairly well tolerated, with 84% in Linder's study rating the treatment good to excellent.

In an open-label, retrospective study, Hershey and colleagues assessed the efficacy and tolerability of sumatriptan nasal spray in children aged 5 to 12 years. Of 10 patients assessed, 1 had no response, 2 had a 50% response, and 6 patients had a 100% response, with 47 of 52 attacks (83%) responding to medication. In a randomized, double-blind, placebo-controlled crossover trial of 14 children aged 6.4 to 9.8 years, Ueberall and Wenzel evaluated the efficacy and tolerability of sumatriptan nasal spray. They found that 12 of 14 children reported a decrease in pain intensity after sumatriptan compared to 6 of 14 after placebo ($p = .031$). Complete headache relief was reported by 9 of 14 children after sumatriptan versus 2 of 14 after placebo ($p = .016$). These small studies suggest that sumatriptan given subcutaneously or intranasally is effective in treating migraine in children of ages 6 to 12 years. However, Hamalainen and colleagues treated 23 children, aged 8.3 to 16.4 years, with oral sumatriptan in a double-blind, placebo-controlled crossover trial. They found no statistically significant difference between sumatriptan and placebo for the primary endpoint, > 50% reduction in pain intensity (7 of 23 for sumatriptan and 5 of 23 for placebo), and pain-free response (5 of 23 for sumatriptan and 2 of 23 for placebo). However, when asked which treatment they preferred, 13 of the 23 children preferred sumatriptan whereas only 2 chose placebo.

The migraine-specific therapies have been more extensively studied in adolescents over 12 years of age in large multicenter, randomized, double-blind, placebo-controlled, parallel-group trials. In a study of 302 patients comparing sumatriptan 25 mg, 50 mg, and 100 mg tablets to placebo, the primary endpoint of 2-hour headache response was not significantly different from placebo (49% for 25 mg, 50% for 50 mg, 51% for 100 mg compared to 42% for placebo) although all three doses of sumatriptan were significant compared to placebo at 3 hours (65%, 64%, 69% compared to 45%) and 4 hours (73%, 73%, 74% compared to 53%). The 50 mg dose was significant compared to placebo at 90 minutes (47% compared to 30%) whereas the 25 mg (38%) and 100 mg (38%) doses were not. Two things to note about this trial are that the placebo rate was quite high compared to the approximately 30% seen in most adult triptan trials. There was also no dose-response curve seen with response rates very similar for all 3 doses of sumatriptan except for 25 mg at 90 minutes.

In a study of sumatriptan nasal spray, the investigators tried to correct some of the issues with the oral sumatriptan study. This study evaluated sumatriptan nasal spray 5 mg, 10 mg, and 20 mg versus placebo. The investigators required that subjects had headaches lasting longer than 4 hours in addition to meeting International Headache Society criteria for migraine with or without aura. Subjects were required to self-administer study medication at home under the supervision of their parents. A total of 507 patients were enrolled. The primary endpoint was headache response at 2 hours. The results are shown in Figure 4-1. Only the 5 mg dose was statistically significant from placebo ($p < .05$). Ten and 20 mg doses were not statistically significant, although there was a clear trend toward significance. One can also note the lack of a dose-response curve.

A large study of rizatriptan used similar inclusion criteria as the sumatriptan nasal spray study. In addition, patients were instructed to take study medication within 30 minutes of onset of a moderate to severe attack. The primary endpoint of 2-hour pain relief was achieved in 66% of subjects treated with rizatriptan 5 mg compared to 56% for placebo, which was not statistically significant. Post hoc analysis found that for those attacks treated on weekdays, the response rate was 66% for rizatriptan and 61% for placebo. However, for those attacks treated on weekends, the response rates were 65% and 36%, respectively. The response rates were essentially the same for rizatriptan, but the placebo response rate for weekends was much lower than during the week. It was also more consistent with placebo response rates seen in the adult clinical trials.

Adverse events were essentially the same between active drug and placebo with the exception of taste disturbance with sumatriptan nasal spray. Overall, these medications are very well tolerated. There was one serious adverse event of facial nerve ischemia with an unclear relationship to study medication in the sumatriptan nasal spray open-label extension phase. In summary, there have been over 1,650 subjects of between 12 and 18 years of age involved in clinical trials published thus far, with an excellent tolerability and safety record.

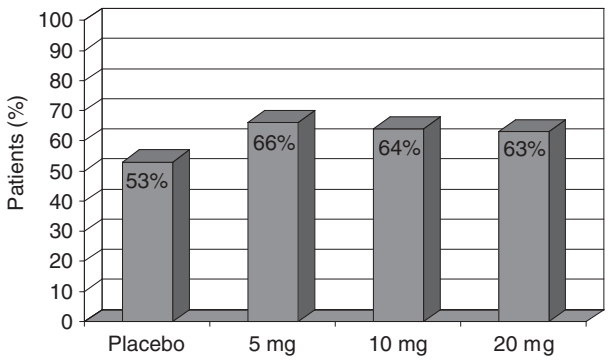

Figure 4-1. Two-hour headache response. Reproduced with permission from Winner et al, 2000.

Treatment of migraine in children and adolescents requires a similar comprehensive approach to management as it does in adults, with several additional factors. One is treating both the migraine sufferer and family, even more so than in adults. Parents are often relating history, have a much more controlling affect on their children's lives, and are often concerned about organic disease. If both the patient and parents are not accepting of the treatment plan, it will never be successful. The use of migraine-specific medications should be considered early in the course of treatment so as not to deny significant treatment benefit. The goal of therapy is to achieve effective headache relief without paying a significant penalty in terms of tolerability and safety. It is quite reasonable to use nonspecific medications, such as acetaminophen and ibuprofen, as first-line acute therapy, as long as they are used in appropriate doses (15 mg/kg/dose up to 1,000 mg maximum for acetaminophen; 10 mg/kg/dose up to 800 mg for ibuprofen). It is then important to have adequate follow-up arranged so that the treatment plan can be modified appropriately without a long delay.

Selected Readings

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Editorial Comments

Children with headache are a special group to diagnose and manage. Migraine is common in children of all ages, and it requires considerable expertise to care for the patient, and in most instances the parents, as there is a great need for adequate communication and explanation. Migraine-specific therapies that have been successful in adults, based on evidence to date, are not always useful in children and adolescents. Triptans have not yet been approved in the United States for use in children under the age of 18 years, although studies show them to be safe. Most pediatric neurologists such as Dr. Pearlman use triptans cautiously, even in much younger children. He also overviews the current evidence on such medications and their usage, and wisely prescribes on the basis of experience and individual consideration in this particular case. One suspects that further studies done in children and adolescents will yield more favorable results for all therapies, especially the triptans, but until then, the judicious use of migraine-specific medications along with traditional nonspecific medications and nonpharmacologic therapies remain the mainstay of management of migraine in these age groups. There is a lot of hope for future effective migraine management strategies here, and Dr. Pearlman outlines the essential components of adequate care.

Final diagnosis:

Adolescent migraine without aura