

# TWO PATIENTS WITH SEVERE UNILATERAL HEADACHES

ANDREW J. DOWSON, MBBS, MRCP

## Case History I

A 52-year-old lady presented with a history of daily short, severe headaches. She experienced about 1 to 3 attacks per day, and this condition had been ongoing for many years. The individual headaches were stereotypical: she had pain in the right eye, which would then go red and watery, and the nose would block ipsilaterally. The symptoms lasted between 30 and 180 minutes and were very debilitating. She had no other associated symptoms, although she had noted that any alcohol was likely to trigger further individual headaches. The majority of attacks occurred in the evening and at night, so although her work life was minimally affected, her social and domestic lives were severely disrupted.

Over the years, she had tried various acute treatments, including oxygen, injectable sumatriptan, and a variety of formulations of ergotamine, all without much success. In addition, she had tried a range of prophylactic treatments, including verapamil, sodium valproate, lithium, tricyclic antidepressants, indomethacin, pizotifen, and methysergide. The only prophylactic agent to have been helpful was methysergide, which reduced the frequency and severity of breakthrough attacks. Although long-term treatment with methysergide is not recommended, as its use has been associated with retroperitoneal fibrosis and pleural and heart-valve fibrosis, this patient found that if she stopped the drug for even a few weeks, there was a marked increase in both the frequency of her headaches and the associated debilitation.

Over the previous 5 years, short courses of steroids had been found to be quite helpful in controlling her attacks. In June 1997, it was decided that she should stop methysergide treatment for 2 months of the year, in line with prescribing recommendations, during which time she should

take steroids at the lowest possible dose. There was discussion at this stage about the possibility of introducing continuous low-dose steroids.

In September 1998, while taking methysergide, she was admitted with renal failure. She had an ultrasound examination, followed by a computed tomography scan, which confirmed the diagnosis of retroperitoneal fibrosis. Her erythrocyte sedimentation rate was raised, and her plasma creatinine levels peaked at 430  $\mu\text{mol/L}$ . She started treatment with high-dose steroids, and after 1 week, her renal function had considerably improved (plasma creatinine: 150  $\mu\text{mol/L}$ ).

In December 1998, she was reviewed in the headache clinic, and it was clear at this time that she should not recommence treatment with methysergide. It was decided to try gabapentin 100 mg three times a day, increasing over a few days to a maintenance dose of 900 mg per day in three equal doses. Acute treatment with oxygen via a mask was the option chosen in an attempt to reduce the severity of breakthrough attacks.

After 3 to 4 months treatment with gabapentin, she returned to the clinic and reported that treatment had been highly successful. During this period, she had only had mild attacks, occurring approximately twice a week, and these had been triggered by alcohol. Prior to taking gabapentin, any alcohol would have triggered a full-blown attack, and therefore, she had been unable to drink alcoholic beverages for many years. Thus, gabapentin reduced both the frequency of her attacks, and more importantly for this patient, allowed her to lead a normal social life with her partner, enjoying alcohol in moderation. Her only side effect from the medication was some minor dizziness and sleepiness, but she felt this was a small price to pay for what she regarded as an 80% improvement in her overall control of headaches compared with when she had been treated with methysergide.

## Case History II

A 44-year-old male patient presented with a 9-year history of chronic head pain due to short, severe headaches. He could have up to 10 attacks per day, with individual attacks being stereotyped. They affected his left eye, which then became red and watery, and the nose would block ipsilaterally. Attacks lasted up to 2 hours at their worst. He had previously tried prophylactic treatment with indomethacin, amitriptyline, and propranolol, both individually and in combination, but none of these approaches had proved effective. Acute treatment with subcutaneous sumatriptan 6 mg was successful in relieving his pain within 10 minutes. However, because of the high frequency of his attacks, this resulted in the need for 8 to 10 injections per day. Although this number of injections was unpleasant, and is outside the recommended limits for sumatriptan usage, they were accepted by the patient as the only effective treatment option available. In addition, as a self-employed manual worker, the large number of injections was the only way in which he could achieve a reasonable quality of life and minimize the disruption to his work, social, and domestic activities.

There was no other medical history of note, and general and neurologic examinations were normal.

The patient was keen to reduce the number of daily injections required, and over the next few months, tried prophylactic treatment with verapamil and sodium valproate, without much success. Acute treatment with oral zolmitriptan 5 mg, in combination with oxygen, relieved his attacks within a few minutes. As zolmitriptan had to be used in combination with oxygen to be effective, this was only practical when the patient was at home. Therefore, if he was away from home, it was still necessary to use sumatriptan injections to relieve his attacks. Nevertheless, he was able to halve his daily requirement for sumatriptan from 8 to 10 injections per day (to treat 8 to 10 attacks) to approximately 4 injections per day, with the remaining attacks treated with 4 to 6 doses of zolmitriptan at 5 mg each dose.

For this patient, it was not possible to reduce the frequency of his attacks. However, the patient felt that zolmitriptan was a useful addition to his treatment package. The reduction in number of injections needed had two major effects. First, he felt that his treatment had improved, and second, his relationship with his doctor improved. In addition, the change in treatment was associated with a significant cost saving: attacks treated with injectable sumatriptan cost less than the oral formulation of other triptans. Also, reducing the number of injections needed from 8 per day down to 4 per day would result in saving several hundred dollars each week.

## Questions on the Cases

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

- What are the diagnoses of the headaches?
- What are the clinical features leading to the diagnoses?
- What are the acute and preventive treatment strategies for treating these severe, short headaches?

## Case Discussion

Both of these patients had cluster headache, a rare but excruciating syndrome that, unlike migraine, is more prevalent in men than in women. The exact prevalence of cluster headache in the general population is unknown, but has been estimated to be around 0.25% (0.4% in men and 0.08% in women). Epidemiologic studies consistently demonstrate a prevalence ratio of between 3.5:1 and 7:1 between genders. Cluster headache is characterized by intermittent attacks of excruciatingly painful unilateral headache, accompanied by symptoms such as conjunctival injection, lacrimation, nasal congestion, rhinorrhea, forehead and facial sweating, miosis, ptosis, and eyelid edema. Headache is sudden in onset, frequently occurs around the eyes, and is often described as a boring sensation. They last 15 to 180 minutes (average 45 minutes) and the headaches occur with a frequency ranging between once every other day to 8 times daily. There are two forms of cluster headache: episodic and chronic. Episodic cluster headache is most common (80 to 90% of patients) and is characterized by periods of headache lasting from weeks to months, and interspersed by months to years of remission from symptoms. In contrast, the 10 to 20% of patients who experience chronic cluster headache have symptoms for more than 1 year, with pain-free periods of less than 14 days.

Cluster headache is perceived, particularly in primary care, to be a difficult condition to treat. Common names for cluster headache include "alarm clock headache" because of the typical disturbance of sleep pattern, and also "suicide headache" because of the severity of the pain and its extremely high impact.

In a recent audit of the King's College (London, UK) Headache Service, some 3% of patients seen within the service had a diagnosis of cluster headache. This was a surprisingly low figure, as the King's College Headache Service is one of only four such clinics in the capital, with an approximate catchment of 15 million, and indicates that the prevalence of cluster headache may be lower than thought.

## Management Strategies

Since cluster headaches are of short duration, abortive treatment must be rapid in onset. Oxygen is effective in around

70% of patients, usually providing relief within 5 to 10 minutes. However, the necessary equipment means that this may be an impractical approach to treatment. Codeine-containing drugs and ergotamine have also been used successfully. Intravenous dihydroergotamine is effective, but intranasal administration, which would be more convenient for patients, has been shown in one study to decrease pain intensity but not attack duration. In recent years, subcutaneous sumatriptan has been shown to be effective. However, multiple doses may be required to treat repeat headaches, and the maximum recommended dose of two injections per day may either restrict the potential benefit of this treatment or patients may choose to exceed this limit. This method of treatment may therefore be unacceptable. Currently, only one published trial has demonstrated the efficacy of an oral triptan in the treatment of cluster headache, with zolmitriptan 10 mg showing significant activity versus placebo in the treatment of episodic cluster headache.

These cases demonstrate two particular problems. The first is that of side effects developing from regular prophylactic treatment with methysergide. This agent is not commonly used in headache practice in the United Kingdom, although it is recognized as being one of the most powerful prophylactic agents for use both in cluster headache and in migraine. Gabapentin has been used successfully in many chronic pain conditions and it is interesting to note its success in this particular scenario.

The second case history involved a patient with chronic cluster headache, who had used subcutaneous sumatriptan extensively over a 7- to 8-year period. This had a very serious implication on the drug budget for the general practitioner, but it was the only effective treatment for this particular patient. A recent study has shown zolmitriptan to be beneficial in the acute phase of episodic cluster headache, but in a population of patients with chronic cluster headache, no significant effect relative to placebo could be demonstrated. However, in this instance, a patient with chronic cluster headache found zolmitriptan to be helpful when used in combination with oxygen. This mode of treatment was not only more acceptable to the patient than frequent injections, but was associated with a favourable outcome in terms of the general practitioner's budget.

### Case Summary

- Acute treatment of cluster headache involves use of triptans (sumatriptan or zolmitriptan), oxygen, or ergots.
- Transitional treatment may require steroids.
- Preventive treatment involves the use of verapamil, valproate, gabapentin, lithium, or methysergide. The latter should be limited to 6 months of use, if possible, to prevent idiosyncratic fibrotic complications.

- Given the severity of the disorder, flexibility is necessary for clinical treatment.

### Selected Readings

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### Editorial Comments

Dr. Dowson points out several key features of treatment of cluster headache. First, every patient with cluster headache needs acute treatment for attacks, preferably fast treatment such as injectable sumatriptan or oxygen. Second, the use of steroids as a transitional therapy can be a compassionate bridge while establishing prophylaxis. Third, prevention may require multiple medications and multiple tries to get it right; and even then, adverse effects of medicines, such as the described fibrosis with methysergide, sometimes overwhelm even the best intentions. Fourth, cluster headache patients are often desperate for relief, and flexibility by the treating physician can lead to better results and better relations

with these unfortunate individuals with suicidal headaches. Episodic cluster headache can be considerably easier to manage than its chronic variant; however, these two cases give some valuable therapeutic approaches and options. Compare this case with that of

Dr. Dahlöf's in Chapter 16, "The Young Man with Recurrent Severe Headache."

FINAL DIAGNOSIS:

Chronic cluster headache