Cluster headache in primary care:
unmissable, underdiagnosed and undertreated

Despite the substantial disability caused by headache disorders, they remain underdiagnosed and undertreated and in many cases the needs of the sufferer remain unmet. Cluster headache is one of the most painful conditions a GP will ever see and cluster sufferers may find themselves passing through ENT, ophthalmic or maxillo-facial departments with many years of intense suffering before a diagnosis is finally made.

Cluster headache is a syndrome with a prevalence of approximately 0.1% characterised by a trigeminal distribution of pain, ipsilateral cranial autonomic features and a striking tendency to circadian and circannual periodicity. Unlike migraine where females predominate there is a male:female ratio 5:1.[1] The most common age of onset is the third or fourth decade of life and available evidence suggests that it is a lifelong disorder in the majority of sufferers, but with longer remission periods over time.[2] Although the exact pathogenesis remains unclear, the underlying abnormality is in the posterior hypothalamus with subsequent trigeminovascular and cranial autonomic activation.[3] Alcohol, nitroglycerine, exercise, and elevated environmental temperature are recognised precipitants but allergies, food sensitivities, reproductive hormonal changes and stress do not appear to have any significant role.

There are three significant features of cluster headache. First, the severity of the pain which is always unilateral. Whereas migraine suffers will want to avoid movement, cluster headache sufferers prefer to move about. The pain of cluster is often described as 'a red hot poker in the eye' and of such severity that the typical reaction is to bang the head against the wall, often pacing the room or rocking back and forth. Secondly, the duration of the pain is shorter than migraine ranging typically from 15 minutes to 3 hours. It has an abrupt onset and cessation. Thirdly, cluster attacks are accompanied by at least one cranial autonomic feature which is present on the side of the pain. For example, conjunctival injection, lacrimation, miosis, ptosis, eyelid oedema, rhinorrhoea, nasal blockage and forehead or facial sweating.[4] These features are transient, lasting only for the duration of the attack, with the exception of partial Horner's syndrome; where ptosis or miosis may persist.

A cluster headache is a single attack whereas a cluster period is an episode during which there are frequent cluster headaches. The average cluster period lasts between 6 and 12 weeks and often a striking circannual periodicity is seen, the cluster periods occurring in the same month of the year. Cluster headache is classified according to the duration of the cluster period. Eighty to ninety per cent of patients have episodic cluster headache where bouts last more than a week but are separated by remissions lasting more than 4 weeks. The remaining patients have chronic cluster headache in which either no remission occurs within 1 year or the remissions last less than 1 month.

Due to the rapid onset of pain, the most effective abortive agents are those that involve parenteral or nasal administration. Subcutaneous sumatriptan 6 mg (the only triptan available for parenteral use) is the drug of choice with a rapid effect and high response rate.[5] Unlike migraine, it can be prescribed at a frequency of twice daily, on a long-term basis if necessary without risk of tachyphylaxis or rebound.[6] There is placebo-controlled evidence for the use of both sumatriptan (20 mg)[7] and zolmitriptan (5 mg)[8] by nasal spray, and it is effective for many patients. Inhalation of 100% oxygen, at 7–12 L/min, is rapidly effective in relieving pain in the majority of sufferers.[9] It should be inhaled continuously for 15–20 minutes via a non-rebreathing facial mask. Recent regulatory changes have made it possible for the practitioner to order suitable equipment which was previously unavailable on prescription. (see www.bash.org.uk for oxygen guidelines.) Intranasal lignocaine serves as a useful adjunct to other abortive treatments but is rarely adequate alone. Opiates, non-steroidal anti-inflammatory drugs and combination analgesics have no role in the acute management.

The aim of preventive therapy is to produce a suppression of attacks and to maintain remission with minimal side effects until the cluster bout is over, or for a longer period in patients with chronic cluster headache. Patients who have short, infrequent cluster periods can benefit from short-term prevention with corticosteroids[10] or methysergide.[11] Treatment with steroids should be limited to a short intensive course of 2–3 weeks in tapering doses. For example, prednisolone 1 mg/kg to a maximum of 60 mg once daily for 5 days, thereafter decreasing the dose by 10 mg every 3 days. This is a useful option for GPs in patients with infrequent cluster bouts. Methysergide is a potent prophylactic for short cluster bouts but its significant side effects, that include pleural fibrosis or retroperitoneal fibrosis, dictate use under specialist advice.

Patients with long bouts of episodic cluster headache or chronic cluster headache will require longer-term preventive treatment. Verapamil is the preventive drug of choice given in higher doses than those used for cardiological indications.[12] Lithium is an alternative preventive agent; topiramate, sodium valproate, pizotifen, and gabapentin are also used, but they have not been proved to be effective. Surgery is a last-resort measure in treatment-resistant patients. Recently, neuromodulatory procedures, such as electrode implantation and stimulation, are replacing destructive procedures that interrupt nerve pathways and carry a higher morbidity.[13]

Although the time to diagnosis in

cluster headache is improving it remains underdiagnosed and poorly managed. An important first step for the GP is to be aware of the diagnosis and understand that it is very different from migraine from the perspective of pathophysiology and management. Other rare primary headaches such as paroxysmal hemicrania and SUNCT (Short-lasting Unilateral Neuralgiform headache attacks with Conjunctival injection and Tearing) syndrome can present with cluster like symptoms and symptomatic cluster has been described after infectious, vascular and neoplastic intracranial lesions. Any atypical features in the history or abnormalities on neurological examination warrant further investigations to search for secondary causes but stable, low frequency, intermittent cluster can be managed in primary care.

David Kernick
GP at St Thomas Health Centre, Exeter

Manjit S Matharu
Specialist Registrar, Department of Epilepsy, Institute of Neurology, London

Peter J Goadsby
Head of department, Headache Group, Institute of Neurology, London

REFERENCES

1. Sjaastad O, Bakketeig LS. Cluster headache prevalence. Vágá study of headache epidemiology. *Cephalalgia* 2003; **23:** 528–533.
2. Igarashi H, Sakai F. Natural history of cluster headache. *Cephalalgia* 1996; **16:** 390–391.
3. May A, Bahra A, Buchel C, *et al*. Hypothalamic activation in cluster headache attacks. *Lancet* 1998; **352:** 275–278.
4. Headache Classification Committee of The International Headache Society. The International Classification of Headache Disorders (2nd edn). *Cephalalgia* 2004; **24:** 1–195.
5. The Sumatriptan Cluster Headache Study Group. Treatment of acute cluster headache with sumatriptan. *N Engl J Med* 1991; **325:** 322–326.
6. Ekbom K, Waldenlind E, Cole J, *et al*. Sumatriptan in chronic cluster headache: results of continuous treatment for eleven months. *Cephalalgia* 1992; **12:** 254–256.
7. Van Vliet JA, Bahra A, Martin V, *et al*. Intranasal sumatriptan in cluster headache — randomized placebo-controlled double-blind study. *Neurology* 2003; **60:** 630–633.
8. Cittadini E, May A, Straube A, *et al*. Zolmitriptan nasal spray is effective in the acute treatment of cluster headache: a double-blind placebo-controlled crossover study [abstract]. *Cephalalgia* 2005; **25:** 921.
9. Fogan L. Treatment of cluster headache. A double-blind comparison of oxygen v air inhalation. *Arch Neurol* 1985; **42:** 362–363.
10. Couch JR, Jr, Ziegler DK. Prednisone therapy for cluster headache. *Headache* 1978; **18:** 219–221.
11. Curran DA, Hinterberger H, Lance JW. Methysergide. *Res Clin Stud Headache* 1967; **1:** 74–122.
12. Leone M, D'Amico D, Frediani F, *et al*. Verapamil in the prophylaxis of episodic cluster headache: a double-blind study versus placebo. *Neurology* 2000; **54:** 1382–1385.
13. Franzini A, Ferroli P, Leone M, Broggi G. Stimulation of the posterior hypothalamus for treatment of chronic intractable cluster headaches: first reported series. *Neurosurgery* 2003; **52:** 1095–1099.

ADDRESS FOR CORRESPONDENCE

David Kernick
The St Thomas Medical Group, The St Thomas Health Centre, Cowick Street Exeter EX4 1HJ.
E-mail: su1838@eclipse.co.uk