

MASQUERADES OF CLUSTER HEADACHE

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ABSTRACT

Many cluster headache (CH) patients waited several years to be accurately diagnosed because their symptoms are often mistaken for sinusitis or a dental disorder.¹ Patients have also been mistakenly diagnosed as analgesic drug abusers or suffering from a psychiatric illness. This case report illustrates how a young lady was diagnosed to have cluster headache after several years of consultations with ophthalmologists for eye swelling and redness. It also highlights the importance of pain assessment and a general and holistic approach to medical care which is the main distinguishing feature of Family Medicine.

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CASE REPORT

A 40 year old lady, Michelle, presented with recurrent episodes of swelling and drooping of eyelids associated with redness of conjunctiva, increased lacrimation and periorbital pain. Attacks were sudden, episodic, usually unilateral (bilateral on one occasion), either eye could be affected. Each attack often lasted for one to two weeks with the eye redness and swelling gradually increasing in intensity to a maximum and subsided with or without medication. At times when it was severe, it would be associated with an intense throbbing headache around the eye on the same side. Michelle's eye problem has gone on for 5 to 6 years, about one attack every 2 to 3 months. She described the occurrence of these attacks as conforming to a consistent definite pattern; attacks that she would anticipate coming before they were due. Recovery in between attacks was complete; the eyes would be back to normal without any visible signs or discomfort.

Michelle has been healthy all along and did not have any other illnesses in the past. She works as a finance manager in a private bank. She is married to an architect. They have three teenage sons who are studying at a private secondary school. She does not smoke, takes alcohol only on social occasions. Michelle denies having any joint pain, backache, chronic diarrhoea, skin rash, difficulty in breathing, weakness of upper or lower limbs, seizures, loss of weight or fever. However she agreed that her job is quite stressful and lately she has some difficult times coping with behavioural changes of her three sons going through adolescent phase.

She has consulted several ophthalmologists in the various private hospitals for past 5 to 6 years. Frequent consultations and visual tests did not indicate any infective

or allergic conjunctivitis, uveitis, keratitis, glaucoma or any systemic illness. There was no retinopathy, no impaired vision other than refractory error. She was told she could have dry eyes and was prescribed Tears Naturale by one ophthalmologist. Another told her it could be due to problems associated with use of contact lenses. Another suggested it could be due to allergy or some form of inflammation of the eyes but did not know what the underlying cause was. On various different occasions, she was prescribed steroid, NSAID and antibiotic eye drops and at times oral NSAIDs and antibiotics. Michelle was doubtful if these medications actually reduced her eye swelling and redness other than reducing her pain temporarily.

Blood tests done were all normal. Imaging studies were not done before. No definite diagnosis was made. On two occasions there was redness and swelling of the external pinna on the same side as the affected eye. She was diagnosed to have perichondritis and was prescribed oral antibiotics by an ENT specialist.

In recent months, her attacks were becoming more frequent, each episode lasted longer, eye swelling and redness were more severe, and there was increasing intensity of periorbital pain and headache.

At the first consultation with a Family Physician, detailed pain assessment of her headache and eye complaints were conducted. Clinical assessment showed that:

Michelle's headache was described as severe, throbbing, drilling pain around the right eye and over the right fronto-temporal area. That was the first time she experienced such severe, excruciating pain. Usually pain was not so bad and was tolerable for a few hours after taking paracetamol or diclofenac. Numerical rating score of pain was estimated

to be 9-10 out of 10. Each episode of pain lasted about 2 to 3 hours. It recurred about 2 to 4 times a day, more so in the evening and middle of the night when it would wake her up from sleep. Paracetamol and diclofenac did not seem to help this time. Rest of pain characteristics was as described in the first paragraph.

Examination of Michelle's right eye showed ptosis and swelling of upper eyelid. Conjunctiva was injected with the presence of reddish pinkish blotches; the appearance similar to those of subconjunctival haemorrhage but the blotches were not as bright red and not as well defined as in the latter condition. Palpebral conjunctiva did not appear to be injected. The cornea appeared clear. The pupil of right eye appeared slightly smaller than that of left eye. There was increased lacrimation in the same eye. Visual acuity was not affected. Her left eye appeared normal.

The upper part of pinna of right ear appeared swollen and inflamed, with increase in skin temperature and tenderness on palpation. The external auditory canal and tympanic membrane of the same ear appeared normal. The left ear appeared normal.

Her face generally appeared flushed but there was no definite area of swelling or skin tenderness on the right side of her face; rhinorrhoea was not observed.

General examination did not show the presence of fever or any skin rash. Blood pressure and pulse rate were within normal limits. Systemic examination of ear, nose and throat, respiratory, cardiovascular, gastro-intestinal, musculoskeletal, central nervous system and cranial nerves were unremarkable except for those ophthalmological findings of the right eye.

Characteristic features of Michelle's headache, its episodic occurrence with normal intervals in between attacks and associated features of periodicity and rhythmicity points towards the diagnosis of a vascular headache. Transient presence of eyelid swelling with ptosis, miosis, conjunctival injection and increased lacrimation during attacks supports the diagnosis of a cluster headache rather than a migraine. Normal examination findings of the eyes by the many ophthalmologists together with its long duration without any negative sequelae rules out serious inflammatory eye disorders such as acute glaucoma, allergic conjunctivitis, uveitis, iritis, keratitis, scleritis and episcleritis. Absence of other systemic signs and symptoms and normal blood test results suggested that connective tissue disease or relapsing polychondritis (a rare inflammatory disorder of the cartilage with multiple systemic manifestations) was not a likely diagnosis. The Family Physician made a clinical diagnosis of cluster headache.

Michelle was prescribed empirical treatment of a short course of prednisolone and prophylactic treatment with amitriptyline. Though not the first line of recommended treatment, amitriptyline was chosen in view of her psychosocial stress at home and at workplace with concurrent associated signs and symptoms of anxiety. Explanation and information articles on cluster headache were given to Michelle to empower her to help herself. She was given reassurance that she was not going to lose her eyesight as this was her greatest fear. She was advised that exercise, relaxation therapy and stress coping strategy could help to reduce the frequency of her cluster headache attacks.

Michelle's eye problem and headache responded dramatically to a course of prednisolone. Headache, swellings of eyelids and ear subsided after two doses of prednisolone on the first day; eye redness gradually diminished on the second day. By the third day the affected eye was back to normal. For past 5 months there was one more mild attack that lasted 3 to 5 days with minimal eye swelling and redness and insignificant discomfort around the eyes not amounting to description of an excruciating headache like before.

CASE DISCUSSION

INTRODUCTION

A new primary headache group named the trigeminal-autonomic cephalalgias (TACs) involves activation of trigeminovascular nociceptive pathways with reflex cranial autonomic activation.² All these headache syndromes have two features in common: short-lasting, unilateral, severe headache attacks and accompanying typical cranial autonomic symptoms. To date, the following syndromes belong to the TACs:

- Episodic and chronic cluster headache
- Episodic and chronic paroxysmal hemicrania
- SUNCT syndrome (short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing)

These syndromes differ in duration, frequency and rhythmicity of the attacks and in the intensity of pain and autonomic symptoms, as well as treatment options (Table 1).

Table 1. Clinical comparison of cluster headache with related headache syndromes²

	Cluster headache	Paroxysmal hemicrania	SUNCT syndrome
Epidemiology			
Gender (M:F)	3:1	1:3	8:1
Prevalence	0.9%	0.02%	Very rare
Age of onset	28–30 years	20–40 years	20–50 years
Pain			
Quality	Boring, throbbing	Boring	Stabbing
Intensity	Extremely high	High	Moderate to high
Localization	Periorbital	Orbital, temporal	Orbital, temporal
Duration of attack	15–120 min	2–45 min	5–250 sec
Frequency of attack	1–8/day	1–40/day	1/day to 30/hour
Autonomic symptoms	strong (++)	strong (++)	modest (+)
Circadian rhythmicity	modest (+)	rare	none
Alcohol trigger	strong (++)	infrequent	rare

WHAT IS CLUSTER HEADACHE?

Cluster headache, also known as histamine headache, is a form of neurovascular headache. Cluster refers to a grouping of headaches, usually over a period of several weeks. This condition is rare; affecting less than 1% of population.³ It is more common in males than in females. The male-to-female ratio was 6:1 in the 1960s but now is 2:1. Cluster headaches usually begin in middle adult life. The mean age of onset is 30 years for men and later for women.⁴

The pathophysiology of cluster headaches is not well understood. The trigeminal nerve (maxillary and ophthalmic divisions of the nerve) may be responsible for neuronal discharge causing vascular dilatation that brings on the cluster headaches. Discharge from autonomic nervous system induces sympathetic impairment (e.g. Horner syndrome) and parasympathetic activation (e.g. lacrimation, rhinorrhoea, nasal congestion) effects. The circadian rhythm of cluster headaches suggests that the hypothalamus may be the site of activation.⁴

In a case report, a patient developed cluster headache after exenteration of the ipsilateral orbit. This case illustrates that the prominent eye findings in cluster headache are epiphenomena and not critical to the development of the pain itself.⁵

Many triggers can bring on headaches during a cluster period, such as alcohol, nicotine, high altitudes (trekking,

air travel), fumes from volatile chemicals and nitrates (bacon and preserved meat) in food. Maintaining a regular sleeping schedule can help prevent the onset of cluster periods.⁶ A number of other precipitating factors have been noted in a smaller number of patients and these include stress, exertion, exposure to heat or cold, glare (including sunlight), hay fever attacks, and, occasionally, the ingestion of specific foods (chocolate, eggs, dairy products) and drugs (those that cause blood vessel dilation, such as nitroglycerin, and various blood pressure medication).⁷ Triggers usually have an effect only during active cluster cycles. When the disorder is in remission, such triggers rarely set off the headaches.³

WHAT ARE THE DIAGNOSTIC FEATURES THAT POINT TOWARDS SUSPICION OF CLUSTER HEADACHE IN THIS CASE?

Cluster headache is usually described as excruciating pain (hot-poker or stabbing sensation), typically located in the ocular, frontal, temporal and periorbital region. Pain often radiates to the upper teeth, jaw and neck. Each episode of headache is brief in duration, often lasting a few minutes to a few hours.⁴ The pain usually is unilateral, with 60% of patients reporting headaches on the right side, but 14% of patients report a side shift during an attack and 18% report involvement of different sides in subsequent attacks⁶ (Table 2).

Table 2. Characteristic features of cluster headache⁴

Pain is described as:

Character - Lancing and severe
 Sudden onset - Peaks in 10-15 minutes
 Unilateral facial - Remains on the same side during the cluster period
 Duration - 10 minutes to 3 hours per episode
 Character - Boring and lancing, as if eye is being pushed out
 Distribution - First and second divisions of the trigeminal nerve (Approximately 18% - 20% of patients complain of pain in the extratrigeminal areas [e.g., back of the neck, along carotid artery])
 Frequency - May occur several times a day for 1 - 4 months (often nocturnal)
 Periodicity - Circadian regularity in 47%

Remission - Long symptom-free intervals occur in some patients. The average remission is 2 years but ranges from 2 months to 20 years

Associated autonomic signs of parasympathetic hyperactivity and sympathetic impairment include ipsilateral ptosis, miosis, lacrimation, conjunctival injection and rhinorrhoea.⁴ Other clinical presentations include facial flushing or pallor, tenderness on palpation of the ipsilateral carotid artery, bradycardia and abnormal feeling of scalp hairs.⁶ The absence of aura, nausea or vomiting has helped distinguish cluster from migraine headaches, but recent studies indicated that 14% of patients with cluster headache experienced aura, 51% had a personal or family history of migraine, 56% reported photophobia, 43% reported phonophobia and 23% reported osmophobia⁶ (Table 3).

Table 3. Autonomic involvement in cluster headache^{3,4}

Parasympathetic overactivity

Ipsilateral lacrimation and conjunctival injection (84% - 91%)
 Nasal congestion and rhinorrhea(48% - 75%)
 Ipsilateral eyelid edema and droopy eye
 Ipsilateral miosis or ptosis
 Ipsilateral forehead and facial perspiration (26%)
 Restlessness/agitation (90%)
 Intolerance to light and noise

Ocular sympathetics paralysis

Mild Horner syndrome (e.g., ptosis, miosis, anhidrosis)

Other autonomic presentation

Bradycardia
 Facial flushing or pallor
 Scalp and facial tenderness

Ipsilateral carotid tenderness (in some patients)

Cluster headache is sometimes described as "suicide headache" because of its severity and "alarm clock" headache because of its periodicity.^{3,6} The 2 existing forms of cluster headache are:

1. Episodic clusters with at least 2 cluster phases lasting 7 days to 1 year separated by a cluster free interval of 1 month or longer.
2. Chronic form, in which the clusters occur more than once a year without remission or the cluster-free interval is less than 1 month.^{3,4}

Criteria for diagnosis of cluster headache are listed in Table 4.

Diagnosis is based on historical and physical findings. The pattern of recurrence, periodicity and rhythmicity of near-daily attacks lasting for days, weeks or months are the keys to diagnosis. There are no abnormalities to be found upon a physical or laboratory investigation other than Horner's syndrome occasionally. In approximately 70% of patients with cluster headaches, the carotid artery is palpably tender at several points in the neck.⁷ The cluster headache syndrome, with all autonomic symptoms, on-off alcohol sensitivity, ipsilateral tender carotid artery and clocklike periodicity of attacks, has not been associated with any underlying intracranial structural abnormalities.¹ Imaging studies are not diagnostic but are useful to exclude other causes in selected patients at the early stage.⁶

A transitory, partial Horner's syndrome (pupillary miosis and lid ptosis) occurs in two-thirds of patients when they are examined during attacks and is a useful sign in the differential diagnosis of facial pain. It is highly characteristic of the cluster headache syndrome and, after repeated occurrences; it may become a permanent feature.⁷

Table 4: Diagnostic criteria of cluster headache²

The International Classification of Headache Disorders

- A: At least five headache attacks fulfilling criteria B - D
- B: Severe or very severe unilateral orbital, supraorbital and/or temporal headache attacks, which last untreated for 15-18 minutes. During part (but less than half) of the time course of the cluster headache, attacks may be less severe, less frequent or of shorter or longer duration
- C: The headache is accompanied by at least one of the following symptoms ipsilateral to the pain:
1. Conjunctival injection or lacrimation
 2. Nasal congestion and/or rhinorrhoea
 3. Eyelid oedema
 4. Forehead and facial sweating
 5. Miosis and/or ptosis
 6. A sense of restlessness and agitation
- D: The attacks have a frequency from one every other day to 8 per day
- E: History or physical and neurological examination do not suggest any other disorder and/or they are ruled out by appropriate investigations

Episodic cluster headache:

At least two cluster periods lasting 7 days to 1 year separated by pain-free periods lasting >1 month

Chronic cluster headache:

Attacks occur for more than 1 year without remission or with remission <1 month

Probable cluster headache:

Attacks fulfilling all but one criteria for cluster headache

In Michelle's case, periodicity and rhythmicity of headaches with its characteristic features that conforms to that of an excruciating neuropathic pain, points towards the diagnosis of episodic cluster headache. Ipsilateral presentation of eye and ear swelling with redness, presence of transient Horner's syndrome and dramatic response to empirical treatment with prednisolone further supports the diagnosis. Confirmation by the ophthalmologists that there was no primary eye disorder ruled out important differential diagnoses of acute glaucoma, uveitis, scleritis, allergic or infective conjunctivitis.

WHAT ARE THE FACTORS CONTRIBUTING TO THE DELAY IN DIAGNOSIS OF CLUSTER HEADACHE IN THIS CASE?

Despite a cluster headache's distinguishing characteristics, its relative infrequency and similarity to such disorders as sinusitis, acute eye problems and dental disorders can lead to misdiagnosis. Some cluster patients have had tooth extractions, sinus surgery or psychiatric treatment in futile efforts to cure their pain.⁸

In this case report patient's cluster headache was wrongly perceived to be due to acute primary eye disorders for several years. Factors contributing to delay in the diagnosis include:

- Direct access and self referral of patient to specialist care in our private healthcare system.
- Lack of continuity of care by the same physician.
- Specialised compartmental medical care, whereby ophthalmologists are focused mainly on eye disorders to the exclusion of other general medical conditions.
- Patient's focus of concern on the eye swelling and redness was partly due to her past experience with problems associated with use of contact lenses and her fear of loss of vision.
- Eye signs were physically visible to both doctor and patient, while headache was not. Hence the importance of red eye overrode that of headache until the excruciating pain became intolerable and not responding to simple analgesia.
- Detailed pain assessment was not done. Pain was assumed to be secondary to the red swollen eye. Red eye was not perceived as epiphenomena of a neurovascular headache.
- Cluster headache is relatively uncommon.
- Because of the periodicity and rhythmicity of the condition, it was not very certain whether the prescribed eye drops and oral medication actually improved the condition or whether the eye redness and pain went off on its own.

HOW CAN GENERAL PRACTITIONERS MANAGE CLUSTER HEADACHE?

Headache diary, lifestyle changes and behavioral therapy³

Patients should be advised to keep a headache diary and record a description of the attacks and possible trigger factors. The patients are advised to avoid alcohol and smoking and other factors that may potentially trigger cluster headache attacks. Behavioral approaches such as relaxation therapy combined with biofeedback can be a helpful accompaniment to drug treatment. These approaches can help with pain management and enable patients to feel more in control of their condition.

Pharmacological treatment

Pharmacological treatment of cluster headache is based on empirical data rather than on a pathophysiological concept of the disease.⁹ Level A recommendation includes the following¹⁰:

Abortive treatment for acute attack

The first option for the treatment of acute attacks of cluster headache should be the inhalation of 100% oxygen with at least 7 l/min over 15 min or with the subcutaneous injection of 6mg sumatriptan. An alternative would be sumatriptan 20mg nasal spray or zolmitriptan 5mg nasal spray, with the disadvantage of a slower onset but the advantage of being able to treat more attacks in 24 hours than with injected sumatriptan.

Prophylaxis treatment

Steroids are very effective initial prophylactic option, rapidly suppressing attacks during the time required for the longer-acting preventive agents to take effect. The use of at least 60 to 100mg prednisone (or equivalent corticosteroid) given orally per day over 5 days (then tapering down) is recommended.

Preventive treatment

As many patients have between one and eight short-lived attacks a day, repeated attempts at abortive therapy may result in overmedication or toxicity. The primary goal of preventive therapy is to produce a suppression of attacks and to maintain remission over the expected duration of the cluster period. Prophylaxis of cluster headache should be tried first with verapamil at a daily dose of at least 240mg. Maximum dose depends on efficacy or tolerability, ECG controls are obligatory with increasing doses. Other prophylactic drugs are lithium (particularly effective for chronic cluster headache), methylsergide, pizotifen, nifedipine, verapamil, phenelzine, amitriptyline, ergonovine, indomethacin and cyproheptadine.

Surgical intervention for difficult cases^{3,10}

For patients who are completely refractory to all known medical therapy and continue to experience repeated attacks of pain chronically, a number of aggressive procedures can be attempted. These include percutaneous glycerol injections into the trigeminal cistern, trigeminal sensory rhizotomy, percutaneous radiofrequency trigeminal rhizotomy, superficial petrosal neurectomy, trigeminal branch avulsion and decompression of the nervus intermedius.

CONCLUSION

Pain is a subjective and multidimensional experience consisting of physiological, physical, sensory, affective, cognitive, behavioural and socio-cultural components. For any form of headache or facial pain, pain assessment is important in formulating a correct diagnosis. Good pain assessment itself will give a clue to diagnosis of cluster headache since laboratory and imaging studies are of not much help other than to rule out other differential diagnoses. A greater understanding of cluster headache among primary care physicians, ear/nose/throat specialists, ophthalmologists, psychiatrists and dentists could improve better recognition and treatment of this debilitating disorder.

REFERENCES

1. Vast majority of cluster headache patients are initially misdiagnosed. Dutch Researchers Report. World Headache Alliance. Article 2003-08-21. Available from: <http://www.w-h-a.org/>
2. Headache Classification Committee of the International Headache Society. The International Classification of Headache Disorders, 2nd ed. Cephalalgia. 2004;24(Suppl 1):1-160
3. Headache, Cluster-In-Depth Report-New York Times Health. Available from: www.nytimes.com
4. Lori K Sargeant, Michelle Blanda. eMedicine Emergency Medicine. Headache, cluster. Available from: <http://emedicine.medscape.com/article/792150-overview>
5. McKinney AS. Cluster headache developing following ipsilateral orbital exenteration. *Headache*. 1983;23(6):305-6
6. Beck E, Sieber WJ, Trejo R. Management of cluster headache. *Am Fam Physician*. 2005;71(4):717-24
7. World wide cluster headache support group. Medical information about cluster headaches. Available from: www.clusterheadache.com/about.html
8. Headache - Hope through research; NINDS - WrongDiagnosis.com. Available from: http://www.wrongdiagnosis.com/article/headache_hope_through_research_ninds.htm
9. May A. Cluster headache: pathogenesis, diagnosis, and management. *Lancet*. 2005;366(9488):843-55
10. A Maya, M Leoneb, J Afra, et al. EFNS guidelines on the treatment of cluster headache and other trigeminalautonomic cephalalgias. *Eur J Neurol*. 2006;13(10):1066-77