

## CLINICAL CORRESPONDENCE

## Episodic hypnic headache?

C Lisotto, F Mainardi<sup>1</sup>, F Maggioni<sup>1</sup> & G Zanchin<sup>1</sup>*Headache Unit, Hospital of San Vito al Tagliamento and <sup>1</sup>Headache Centre, Department of Neurosciences, University of Padua, Padua, Italy**Prof. Giorgio Zanchin, Headache Centre, Department of Neurosciences, University of Padua, via Giustiniani 5, 35128 Padua, Italy. Tel. +39 49 8213600, fax +39 49 8751770, e-mail giorgio.zanchin@unipd.it Received 1 October 2003, accepted 27 November 2003*

Hypnic headache is a primary headache disorder, which occurs exclusively during sleep and usually begins after the age of 60 years. It was first described by Raskin in 1988 (1), as a sleep-related headache, that regularly awakened patients at a consistent time of night; the pain was diffuse, persisting for 30–60 min, without autonomic symptoms. Hypnic headache was not included in the first edition of the International Headache Society (IHS) classification. In the second edition this headache was classified in section 4.5, included in the group of 'Other primary headaches' (2). At the time of this writing 82 patients with this disorder have been described (3–29). The possible pathophysiology and the pharmacological treatment of this headache have been recently discussed and analysed (30, 31), as well as its relationship with REM sleep (14, 27, 28). A symptomatic case that developed after an ischaemic stroke in the pontine reticular formation was also reported (29). The natural history of hypnic headache is not well known. The review of the published cases suggests that hypnic headache tends to be a chronic unremitting disorder. To better understand the natural history of hypnic headache, we have prospectively followed 4 patients with this disorder since 1998. The first two cases, diagnosed in 1998 and 1999, respectively, were published previously (13, 17); the other two cases, of new description, were first seen in 2000. Hypnic headache was the main diagnosis in 0.09% of all headache patients and notably in 1.4% of geriatric patients (above the age of 65 years) seen in our Headache Centre from 1998 to 2002.

**Case report***Case 1*

Case 1 is a female, aged 76 years. The headache started in 1998 and we first saw her 7 months later. She was awakened from sleep on a nightly basis,

often when she was sleeping, with moderate to severe, dull, bilateral headaches with maximal pain felt in the frontal region. Each headache usually lasted 45 min; she had to rise from bed and felt relief when walking. The patient complained of occasionally having a slight bilateral lacrimation and a mild nausea. She was able to return to sleep when the headache was resolved, more promptly after taking a cup of coffee. Only sporadically, approximately 10% of the time, after falling back to sleep she was awakened with another similar headache, usually occurring 2 h after the first attack. Results of neurological examination were normal. Gadolinium enhanced MRI of the brain revealed nonspecific white matter changes. The laboratory tests were normal, except for a moderately increased sedimentation rate. Because of this abnormality a biopsy of the temporal arteries was performed and was found to be negative. The patient was taking verapamil at a daily dose of 120 mg for arterial hypertension. She was initially treated for 6 months with lithium, 450 mg at bedtime. This treatment resulted in an improvement of her headache frequency with only 1 attack per week. After we recommended that the patient regularly take a cup of coffee in the late evening in association with lithium, the headaches abated. Both drugs were administered for 6 months, then we established the intake before bedtime of caffeine alone and the headaches did not recur for the following 10 months. The nocturnal headaches then recurred, despite the regular intake of caffeine, but with a lower, moderate intensity. We restarted lithium 300 mg at bedtime, in association with a cup of coffee and the headaches almost completely disappeared. The patient is still taking this combined treatment, but any attempt to discontinue the drugs resulted in a prompt recurrence of headache. In this case hypnic headache can be defined chronic, with good response to the prophylactic treatment.

### Case 2

Case 2 is a male, aged 71 years. The headache began in 1996, with a frequency of at least 5 attacks per week. At that time he was diagnosed with a non-classifiable headache and was empirically given a combined treatment with dihydroergotamine and caffeine. The headaches gradually ceased and the treatment was tapered after 8 months, with no recurrence of the pain. When the nocturnal attacks relapsed in 1999, we were able to diagnose hypnic headache. The pain was bilateral, described as steady, affecting the anterior aspect of the head; it was moderate in severity and lasted usually 30 min. No relationship with dreams was reported. The patient had to get out of bed, but then was able to resume sleep, more easily after taking a cup of coffee. No autonomic features were reported. Neurological examination, blood chemistries and brain MRI were normal. We recommended the regular intake of two cups of coffee before bedtime and the patient became almost completely headache free for 3 months, thereafter the attacks completely ceased. Caffeine treatment was prolonged for 3 more months and then was stopped, with no subsequent recurrence of the attacks in the 3 years since. In this case the temporal pattern of hypnic headache seems to be episodic. Up to now two different active periods, without a specific seasonal pattern, have occurred and they both responded to the treatment with caffeine.

### Case 3

Case 3 is a female, aged 65 years. The nocturnal headaches started in 1999 and we first evaluated her in 2000. The pain was diffuse, all over the head, constant and of moderate to severe intensity. It lasted usually 60 min and occurred every night, exclusively during sleep; there were no associated autonomic symptoms. Occasionally the patient awakened from vivid dreams with a hypnic headache. The severity increased if she remained supine and she felt slightly relieved if she was upright. Medical history was unremarkable; neurological examination, routine laboratory studies and brain MRI were within normal limits. Since the onset the attacks had occurred in bouts of 2–3 months with intervening spontaneous breaks of 4–5 months. When she was first seen she was 2 weeks into a bout. She commenced lithium 150 mg at bedtime, taken together with a cup of coffee and her headaches almost completely ceased after 10 days. This regimen was maintained for 2 months and when the treatment was tapered, no

relapse was noted. When the nocturnal headaches recurred within 4 months, they again settled rapidly when lithium 150 mg before bedtime and caffeine were restarted and resumed for 45 days. The 3-year follow up observation confirmed a remitting relapsing temporal pattern, similar in many aspects to episodic cluster headache; no predictable periodicity was observed. Each bout responded to treatment, given for a period ranging from 45 to 60 days, with ensuing spontaneous remissions on average of 4–5 months. In this case hypnic headache can be considered episodic, with spontaneous remissions and active periods, which responded to preventive medical treatment.

### Case 4

Case 4 is a female, 73 years old. In 2000 she started complaining of nocturnal headaches that awakened her from sleep approximately 5 nights per week. We evaluated the patient 3 months after the onset of the symptoms. The headaches were located in the frontal area bilaterally, described as dull, moderate in intensity. The pain lasted usually 90 min and could be improved by walking and drinking coffee; it was not observed during dreaming periods. Examination and MRI of the brain were normal. Lithium was initiated at a dose of 300 mg taken together with a cup of coffee at bedtime and there was a rapid reduction in headache frequency and severity of approximately 80%, which was sustained over the following months. When we tried to discontinue the treatment, the headaches returned every night within 10 days and were promptly relieved when the drugs were restarted. During a 3-year follow up period the patient continued to require lithium nightly. In this case the course of hypnic headache appears to be chronic, with good response to treatment.

## Discussion

In the second edition of the IHS classification the comments on hypnic headache do not specify whether spontaneous or drug-induced remissions can occur (2). It has not been determined yet whether this headache type can be subdivided according to its length of history and persistence. The outcome of hypnic headache after diagnosis is not yet well known. It can be assumed that this disorder is chronic, since most patients are reported to have daily headaches even for many years before diagnosis. The review of the published cases shows that on average the diagnosis of hypnic headache was made  $4.7 \pm 5.9$  years after the first attacks started, ranging

from 1 week (19) to 30 years (8). In most studies the analysis of the patients is retrospective and the follow up beyond the initial therapeutic response is relatively short. Retrospective studies of long-history headaches have several drawbacks, since the frequency and the characteristics of the attacks at onset cannot be exactly recalled. In the literature we found 25 patients with hypnic headache who have been followed up for at least 2 years (1, 8, 9, 16, 21, 26). In two different studies published by the same authors 2 years apart there is an overlap of patients, that can vitiate the follow up analysis (8, 16). Moreover in the first of the two studies it is reported that the mean duration of time from diagnosis to follow up evaluation of the 17 observed patients is  $3.6 \pm 1.5$  years (range 0.5–7 years). This means that some of them were followed for less than 2 years, since the specific data for the single patients are lacking (8). In another study one patient presented a complete remission, that was persistent over the 2-year follow up with flunarizine 5 mg at bedtime, but the length of this treatment is not specified (9). Two other patients responded completely to 600 mg lithium before bedtime and were subsequently tapered off this treatment without recurrence of the headache. These patients were followed, respectively, for 5 and 10 years (1). A similar outcome was reported by the same author for another male patient treated with 450 mg lithium nightly, but he was followed for less than 2 years. The drug had been stopped after 2 months because of extrapyramidal side-effects (1). In a further study a female patient had a remission with 400 mg lithium before bedtime taken for 3 months and after the withdrawal she was pain free for the next 10 months. The patient afterwards had 2 relapses, the first lasting 10 days after travelling across time zones, the second associated with a depressive reaction. The first recurrence resolved spontaneously by travelling back home, while the second relapse was treated successfully with lithium (400 mg), dothiepin (75 mg) and alprazolam (0.25 mg twice a day). Given this temporal pattern,

the authors defined the patient's hypnic headache as a remitting-relapsing form (21). The nocturnal headaches persisted chronic at follow up in 7 cases, with no response to any drug (8, 16, 26). For 10 patients hypnic headache resolved with treatment, but continued to require sustained therapy. The attacks relapsed whenever medication was discontinued (1, 8, 16). In two of these 10 cases, acute medications could abort successfully the single headache episodes and no preventive treatments were given (8). Hypnic headache ceased spontaneously after a prolonged active period in 4 patients, with no treatment (8, 16). According to the outcome data obtained from the literature, it is possible to subdivide the observed cases into two different patterns, chronic and episodic. The chronic pattern was noted in patients who continued to have frequent attacks (>15 times per month) with no response to treatment and in subjects whose headaches disappeared with treatment but relapsed as soon as the therapy was discontinued. The episodic pattern was observed in patients who had prolonged active periods and subsequent sustained remissions. This pattern includes patients who had a complete drug-induced remission from an active period persisting after drug withdrawal, subjects whose headaches abated spontaneously without any treatment and patients with a remitting-relapsing course (Table 1).

As far as our patients are concerned, two can be included in the chronic pattern group, whilst the other two are affected by an episodic form of hypnic headache. Their clinical characteristics and in particular the temporal pattern of their headaches are summarized in Table 2.

The two patients with chronic hypnic headache responded successfully to a treatment with 300 mg lithium associated with a cup of coffee before bedtime, having a reduction in headache frequency and severity by approximately 80%. Any attempt to taper the therapy resulted in an almost immediate recurrence of the nocturnal headaches, thus the patients continued to require the treatment nightly during

**Table 1** Hypnic headache: outcome after diagnosis (follow up of at least 2 years)

Outcome	No. of patients	References
Chronic pattern		
1. Chronic, no response to treatment	7	[8, 16, 26]
2. Chronic, remitting with treatment, relapsing after withdrawal	10	[1, 8, 16]
Episodic pattern		
1. Episodic active period, remission with sustained treatment, no recurrence	3	[1, 9]
2. Episodic active period, spontaneous remission with no treatment	4	[8, 16]
3. Episodic, remitting-relapsing	1	[21]

**Table 2** Clinical characteristics of study group

Case no.	Gender	Current age (years)	Onset of headache (date)	Temporal pattern
1	Female	76	1998	Chronic from onset
2	Male	71	1996	Episodic, with remissions of at least 2 years
3	Female	65	1999	Episodic, with remissions of at least 4 months
4	Female	73	2000	Chronic from onset

**Table 3** Proposed new subdivision for hypnic headache

## 4.5 Hypnic headache

## 4.5.1 Episodic hypnic headache

- A. Attacks fulfilling criteria A-E for 4.5 hypnic headache
- B. At least two attack periods lasting 7–365 days and separated by pain free remission periods of  $\geq 1$  month

## 4.5.2 Chronic hypnic headache

- A. Attacks fulfilling criteria A-E for 4.5 hypnic headache
- B. Attacks recur over  $>1$  years without remission periods or with remission periods lasting  $<1$  month

follow up period, respectively, of 5 and 3 years. The other two patients have an episodic, remitting-relapsing hypnic headache. Case 2 had only two active periods up to now, with remissions lasting, respectively, 2 and 3 years. Case 3 experienced episodes of attacks and periods of remission, with a pattern similar for many aspects to episodic cluster headache. Each active period responded to 150 mg lithium plus caffeine at bedtime, administered usually for 2 months and the following remissions lasted on average 4–5 months. The headache remained remitting-relapsing with consistent duration of pain free periods over the following 3 years of observation. In view of our findings we propose that hypnic headache be divided in two subtypes, chronic and episodic. We suggest that cyclic periods of this disorder should be denoted by the term 'episodic hypnic headache' and for those who have not experienced a remission of at least 1 year, the disorder may be called 'chronic hypnic headache'. We present a new subdivision for hypnic headache, analogous to the structure of cluster headache and paroxysmal hemicrania criteria, as has been established in the second edition of the IHS classification (Table 3).

More prospective studies of hypnic headache patients are required to evaluate the long-term out-

come of this disorder. Publication of further cases and follow up observations will assist in better understanding the clinical characteristics and possibly the pathophysiology of this condition.

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