Bedtime stories

Case 1: a sleepy student

Case history

A 17-year-old male was referred by his general practitioner. He was studying for "A"-level exams in fine art and media studies. The patient had a history of disturbed sleep and daytime somnolence since childhood. He was a snorer but there was no history of witnessed apnoeas. He reported waking every morning feeling unrefreshed. His Epworth Sleepiness Score (ESS) was 17 out of a possible 24. He regularly fell asleep on buses and while travelling in cars. His medical history included mild asthma, for which he took a salbutamol inhaler *p.r.n.* only. He also suffered from nasal congestion. He had mild dyslexia and was overweight, with a body mass index (BMI) of 27 kg per m^2. Routine blood tests, including thyroid function tests, were normal. Otherwise his history was unremarkable.

Task 1
Which of the following options best describes your next step?
a) Advise the patient to lose weight only.
b) Review the patient's sleep hygiene and advise him to get more sleep.
c) Arrange for the case to be reviewed by ear, nose and throat (ENT) surgeons only.
d) Recommend a mandibular advancement device to treat the patient's snoring.
e) Arrange for the patient to undergo an overnight sleep study.

N. Walters[1]
J. Jaye[2]

[1]St George's Hospital, and [2]Academic Dept Sleep & Breathing, National Heart & Lung Institute, Imperial College, London, UK.

Correspondence:
N. Walters
St George's Hospital
London
SW17 0QT
UK
E-mail: N.Walters@rbht.nhs.uk

J. Jaye
Academic Dept Sleep & Breathing
National Heart & Lung Institute
Imperial College
London
SW3 6NP
UK
E-mail: J.Jaye@rbht.nhs.uk

Answer 1

a) This answer is incorrect. While it may be one part of the advice you give, a BMI of 27 kg per m^2 will not account for these symptoms.
b) This answer is incorrect. The patient has a long history of daytime somnolence and his ESS is 17. Further investigation is indicated.
c) This answer is incorrect. Given the patient's history, this may form part of your management plan, but further investigation of his somnolence is also required.
d) This answer is incorrect. A mandibular advancement device may help the patient's snoring, but he has symptoms suggestive of obstructive sleep apnoea/hypopnoea syndrome and further investigation is warranted.
e) This answer is correct. The patient is a snorer, slightly overweight and has an abnormal ESS. He should undergo a sleep study.

This patient went on to undergo a respiratory sleep study (polygraphy). He was diagnosed with obstructive sleep apnoea (OSA) with an apnoea/hypopnoea index (AHI) of 30 events per h. He was subsequently started on nasal continuous positive airway pressure (CPAP) therapy and reported full compliance with the treatment.

He was also reviewed by ENT surgeons, who diagnosed mild nasal airway impairment on the right, rhinitis and turbinate hypertrophy. It was not felt that these findings required surgical intervention or that they were contributing significantly to the OSA.

The patient was referred to a tertiary centre, as the nasal CPAP therapy had not improved his daytime somnolence. His ESS was still 17 out of 24. The history was reviewed and on closer questioning, he gave a history of hearing people talking or having other sensory hallucinations as he was waking up. He also described a sensation of his neck feeling "floppy" and weakness in his fingers when he laughed.

Task 2

Which of the following options best describes your next step?

a) Repeat the respiratory sleep study to confirm the diagnosis of OSA.

b) Repeat the respiratory sleep study while on nasal CPAP therapy, to ensure the apnoeas have been treated adequately.

c) Refer to a psychiatrist.

d) Arrange for polysomnography (monitoring of respiratory variables plus additional electroencephalogram (EEG), electro-oculogram and electromyogram (EMG) assessment in order to stage sleep) and objective sleep latency test.

Answer 2

a) This answer is incorrect. The patient has had one sleep study apparently demonstrating OSA. He has not responded to treatment. Further questioning has elucidated more symptoms that require further investigation. The symptoms of his neck feeling floppy and his fingers becoming weak associated with emotion are suggestive of cataplexy. The auditory hallucinations he experiences when waking up are hypnagogic hallucinations.
b) This answer is incorrect. The patient is compliant with treatment and the "new" symptoms require further investigation.
c) This answer is incorrect. The patient has no psychiatric history and did not appear psychotic when assessed.
d) This answer is correct. The patient has features consistent with a diagnosis of narcolepsy: excessive daytime somnolence; cataplexy; and hypnagogic hallucinations.

He went on to undergo polysomnography. This revealed a sleep efficiency of 84.3% (normal). His rapid eye movement (REM) latency was 5 min (normal = 90 min) and AHI was 2 events per h. The polysomnography also showed that he went into REM sleep before stage 4 sleep, which is abnormal (REM-onset sleep). Overall, his sleep was fragmented and there were frequent arousals. There was mild sleep-disordered breathing (figure 1).

The morning following his polysomnography, he had an objective sleep latency test (the Oxford Sleep Resistance (OSLER) Test). This test examines the patient's ability to maintain wakefulness. The patient is left in a dark, quiet, warm room. The occurrence of sleep is assessed behaviourally rather than by EEG monitoring (as in the Multiple Sleep Latency Test (MSLT)). The patient is asked to respond by hitting a button each time a dim light flashes. The light flashes regularly for 1 s every 3 s and the test lasts a maximum of 40 min. If the subject fails to respond for 21 s (*i.e.* seven consecutive illuminations), the test is ended and it is assumed that the patient has fallen asleep. The test was carried out at 09:00 h, 11:00 h, 13:00 h and 15:00 h (table 1).

It is notable that, despite having had >8 h sleep the previous night, the patient fell asleep within 7 min at 09:00 h.

Based on the International Classification of Sleep Disorders (ICSD) [1], the patient was diagnosed with narcolepsy (see box on next page).

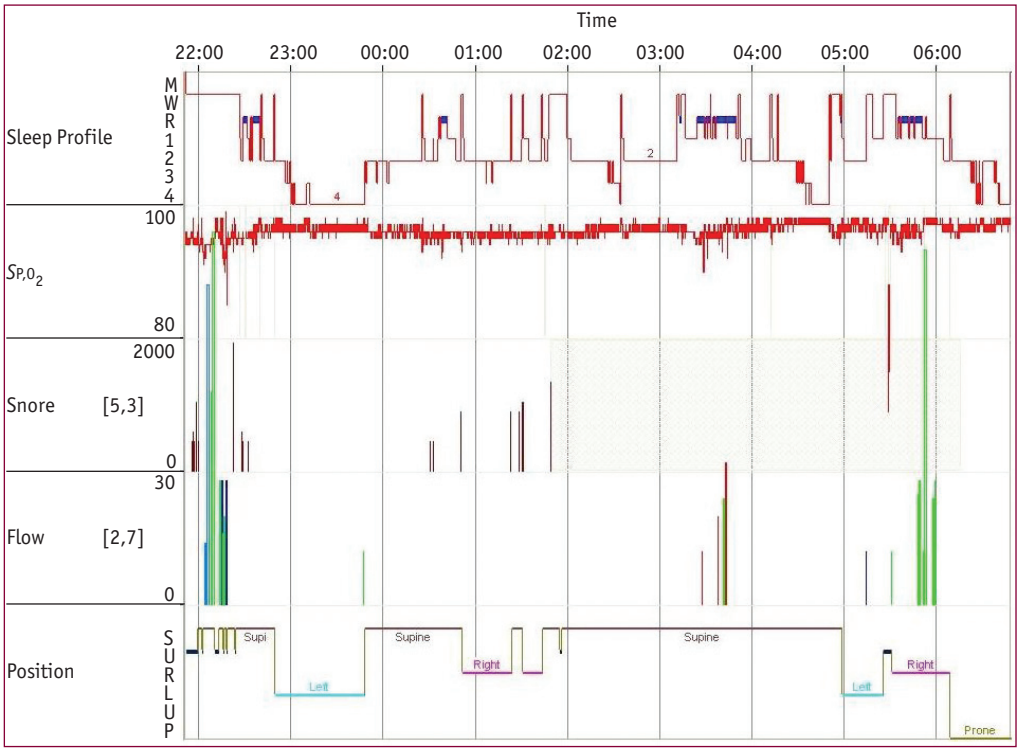

Figure 1
Polysomnography. Sp,O_2: arterial oxygen saturation, measured by pulse oximetry.

Table 1 The results of the patient's OSLER test

Trial number	*Time h*	*Presumed sleep latency min#*
1	*09:00*	*7*
2	*11:00*	*40*
3	*13:00*	*28*
4	*15:00*	*9*

#: maximum 40 min.

International Classification of Sleep Disorders criteria for diagnosing narcolepsy [1]

a) Excessive daytime somnolence or sudden muscle weakness.
b) Recurrent daytime naps for >3 months.
c) Sudden bilateral loss of muscle tone in association with intense emotion (cataplexy).
d) Associated features: sleep paralysis, hypnagogic hallucinations and automatic behaviours.
e) Polysomnography demonstrates one or more of: sleep latency <10 min, REM latency <20 min, MSLT mean <5 min, two or more episodes of REM-onset sleep.
f) Human leukocyte antigen typing shows DR2 positivity.
g) Absence of other medical or psychiatric disorders which could explain symptoms.
h) Other sleep disorders may be present but are not primary cause of symptoms.

The minimal criteria for diagnosis are b+c, or a+d+e+g.

For all patients with narcolepsy, it is vital to have an unequivocal diagnosis. The management of narcolepsy is multidimensional. With this patient, it was important to plan strategic naps during the day to enable him to continue his studies effectively. Patients with narcolepsy typically need 2–3 naps of 10–15 min duration throughout the day. This is in addition to ensuring that they have adequate amounts of nocturnal sleep. Employers, education authorities, family and friends need to be educated and understanding.

The somnolence can be treated with stimulants such as modafinil, methylphenidate and dexamphetamine, with modafinil usually used as first-line therapy.

Cataplexy can be managed effectively with venlafaxine or clomipramine and these have the benefit of suppressing REM sleep. Sodium oxybate is a second-line treatment for cataplexy, but also reduces somnolence.

Very often, these patients have fragmented sleep patterns and medication, such as zopiclone or zolpidem, can help to consolidate their night's sleep.

This patient was treated with modafinil, and the CPAP therapy was stopped as his AHI returned to within the normal range. At his first review, his ESS had fallen to 10 and he was functioning much better in school.

Case 2: an episodically irritable aerobics teacher

Case history

A 22-year-old dance/aerobics instructor and gymnasium manager presented with episodes of hypersomnolence since the age of 16 years. She had had nine episodes over a 5-year period, which usually lasted for ~7 days, and eight shorter episodes over the previous year. The episodes were initially related to menstruation but that was no longer the case, and she was now taking the oral contraceptive pill.

Between episodes she was asymptomatic, completely fit and well, with an ESS of 1. She reported always having had difficulty initiating sleep, and that her sleep was interrupted and lasted no longer than 5–6 h per night.

Her mother explained that there was no obvious precipitating factor. She stated that the episodes began with a glazed expression and irritability, and that the patient would cease to communicate and would then take to her bed to sleep and eat sweets. She was unable to concentrate and seemed confused. Her memory was also affected.

She was unable to work during the episodes and her irritability and violent resistance (including scratching and biting) made it difficult for her mother to get her to hospital. She attended the emergency department on three occasions, when her haematology and biochemistry screen, including thyroid function tests were normal.

During somnolent episodes, the patient reported pinching herself in order to determine whether she was dreaming or awake and had also pinched and bitten other family members to check that they were really there. She described the episodes as a frightening experience, often feeling as if she was watching herself from outside her body. As a consequence, she preferred to be asleep.

She was on no other medication and was not known to snore. Her weight was 64 kg and she had no other known sleep disorders. Her medical history included meningitis at the age of 10 years, and a head injury at 15 years. Both parents were alive and well and there was no history of psychiatric or mental illness or sleep disorder in the family, and no history of epilepsy. She was a nonsmoker, drank <10 UK units of alcohol per week (<100 mL of 100% ethanol equivalent) and denied drug use of any kind. Physical examination was entirely normal.

Task 1
What diagnoses could be responsible for daytime somnolence in this patient?

a) Narcolepsy
b) OSA
c) Idiopathic hypersomnia
d) Insomnia
e) Circadian disorder
f) Menstruation-related sleep disorder
g) Other

Answer 1

a) This is unlikely: the bouts of somnolence with entirely normal daytime alertness between episodes would be unusual and there are no other features, such as cataplexy, sleep paralysis or hypnagogic hallucinations.

b) This too is unlikely: the patient is not a snorer, OSA is relatively rare in premenopausal females with normal BMI and there no other features of this condition.

c) Idiopathic hypersomnia is characterised by excessive daytime somnolence which is not explained by other conditions such as narcolepsy, sleep apnoea, *etc*. However, symptoms are relatively stable are not usually cyclical, and there are no personality changes.

d) Although the patient describes poor sleep initiation and fragmented sleep between episodes, she is excessively somnolent during episodes, not consistent with insomnia.

e) A circadian rhythm sleep disorder should be considered. The patient has a cyclical disorder. The key feature of circadian sleep disorders is a misalignment between the individual's sleep pattern and that which is desired or a societal norm. Circadian disorders include: delayed sleep phase syndrome, when the desire to sleep comes progressively later at night; advanced sleep phase disorder, when individuals become sleepier earlier in the evening; and jet lag (time-zone disorder). For these patients, whose time clock runs on a >24 h or <24 h cycle, a pattern becomes evident. However, such conditions are not characterised by periods of protracted somnolence.

f) Menstruation-linked hypersomnia is unlikely: the episodes appeared to be associated with menstruation initially, but this is no longer the case.

Task 2

What investigations would you request?

Answer 2

Polysomnography to exclude narcolepsy or other sleep disorder, plus MSLT or OSLER test to exclude narcolepsy, although this patient has an ESS of 1 in asymptomatic periods, which is not consistent with narcolepsy.
EEG to exclude epilepsy, magnetic resonance imaging (MRI) and computed tomography (CT) of the brain to exclude focal brain lesion, as well as a lumbar puncture to exclude meningitis, encephalitis and other remittent neurological diseases.
Actigraphy could be considered if a circadian disorder is a high probability.

Investigations

The patient had previously been referred to a neurologist, who carried out brain MRI and CT with no abnormalities detected. EEG was reported as normal. Lumbar puncture for cerebrospinal fluid (CSF) was not performed as the patient had been completely well and active between episodes. Presentation with the first episode could warrant this test, as it could exclude meningitis and encephalitis.

Polysomnography during an episode

Unattended full polysomnography was performed at home 4 days post-onset of an episode. The patient appeared to be asleep when the technician arrived, was minimally responsive when her mother attempted to wake her and remained lying in bed and gave little assistance during equipment set-up. She appeared to be asleep for the majority of the set-up. She had to be cajoled into sitting up and was supported by both her mother and the technician while the equipment was attached, to prevent her from lying down and going back to sleep. When aroused from sleep, she was clearly irritated. It was noted that the bed was strewn with sweets.

The following morning the patient was still in bed. Her mother reported that after difficulty initiating sleep with the equipment attached, the patient managed to sleep for a few hours but awoke and removed all of the apparatus.

The total recording time was 5 h 18 min. Sleep efficiency was 42%, sleep latency was 2 h 31 min, REM latency was 56 min. REM sleep was 4.9%, stage 2 sleep was 27.5% and slow-wave sleep (SWS) was 60.4% of total sleep time. There were no significant respiratory disturbances; AHI was 2 events per hour, oxygen desaturation index (ODI) was 0 and there was no evidence of periodic limb movement disorder. Notably, the technician finished the set-up at approximately 23:30 h. Although the patient appeared to have been asleep for most of the set-up time, the EMG and EEG had the appearance of wakefulness (figure 2).

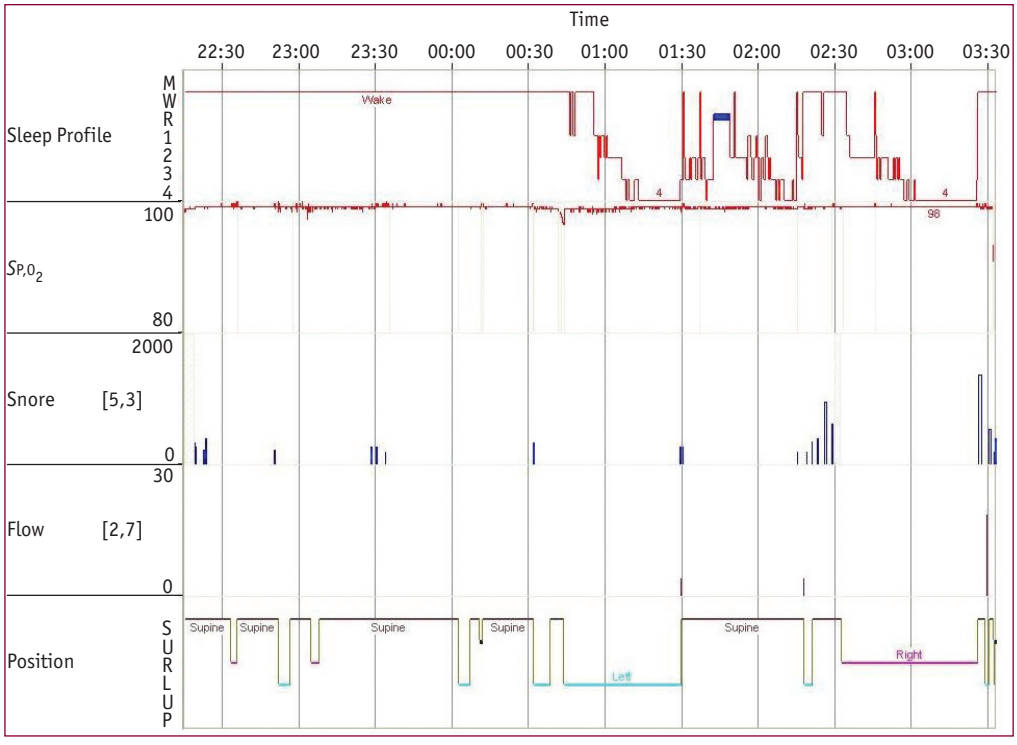

Figure 2
Polysomnography during an episode. $Sp,0_2$: arterial oxygen saturation, measured by pulse oximetry.

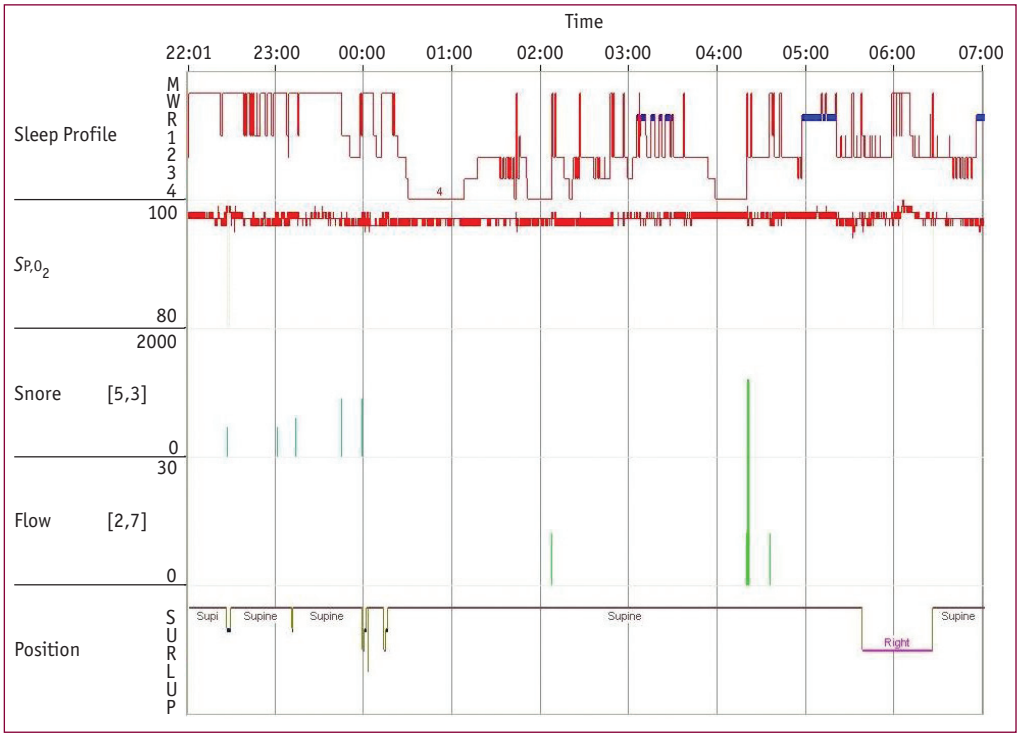

Figure 3
Polysomnography during an asymptomatic period. Sp,O_2: arterial oxygen saturation, measured by pulse oximetry.

Polysomnography during an asymptomatic period

The patient attended the sleep laboratory for a second sleep study during an asymptomatic period. She appeared bright, cheerful and alert and exhibited no unusual behaviour. She reported remembering the technician had visited during the episode, but she was not able to recall what had occurred.

The sleep study report showed total sleep time of 6 h 45 min, sleep efficiency of 75%, sleep latency of 44 min, REM latency of 4 h 19 min. REM sleep was 10%, stage 2 sleep was 52% and SWS was 30.9% of total sleep time. The sleep report is shown in figure 3. Again, there were no significant respiratory disturbances (AHI 0.6, ODI 0) or periodic limb movements. Some abrupt awakenings from SWS were noted.

It is difficult to compare the two sets of polysomnographic results, because only the first 2.5 h of sleep were captured in the study performed during the episode, and a higher percentage of SWS would be expected during this period. Sleep latency was increased markedly during the episode compared with the asymptomatic study. However, the studies did exclude OSA and periodic limb movement disorder, and neither study was consistent with narcolepsy (see case 1).

Task 3
Based on the results of the investigations and the clinical information, suggest a diagnosis.

Answer 3

Clinically, there is only one highly likely diagnosis. Kleine–Levin syndrome (KLS) is a form of recurrent hypersomnia characterised by episodes of hypersomnia that resolve spontaneously. It differs from other forms of recurrent hypersomnia in that the episodes must be associated with at least one of a range of cognitive and behavioural disorders, the most prevalent of which are irritability, megaphagia, and hypersexuality [1].

A systematic literature review by ARNULF *et al*. [2] identified 186 cases of KLS. Table 2 describes the frequency of symptoms during episodes.

Onset of disease

KLS typically has its onset during adolescence. It is more prevalent in males and is rarely familial. There is often no obvious precipitating factor, although trivial infections such as flu-like illness have been reported prior to the onset of KLS symptoms. There is no evidence of a single, consistent cause of infection found where the precipitating infectious agent was identified [2].

The onset of KLS symptoms has also been associated with stroke, encephalitis and brain injury and in these circumstances it is considered secondary KLS.

Table 2 Frequency of symptoms during episodes of KLS

Symptom	*Patients with symptom %*
Hypersomnia	*100*
Cognitive disorders	*96*
Abnormal speech	*60*
Confusion	*51*
Amnesia	*48*
Derealisation	*24*
Hallucinations	*14*
Delusions	*16*
Eating behaviour disorders	*80*
Megaphagia	*78*
Craving for sweets	*12*
Increased drinking	*8*
Binge eating	*6*
Decreased appetite	*5*
Food utilisation behaviour	*4*
Depression	*48*
Irritability	*92*
Other behavioural disorders	
Hypersexuality	*43*
Compulsion to sing, write, pace	*29*

Adapted from [2], with permission from the publisher.

Description of episodes

Patients sleep 12–24 h per day, in severe cases waking spontaneously only to eat and/or void. The duration and frequency of episodes varies widely between patients (figure 4), mean±SD duration 12±9 (range 2.5–80) days, mean±SD interepisode duration 6±10 (range 0.5–72) months [2]. Between episodes, patients are well and all symptoms usually resolve.

Typically, the disease goes into remission in the third decade of life. The frequency and duration of episodes, and the intensity of symptoms, tend to diminish as the disease progresses. Median disease duration is 8 years.

Secondary KLS patients tend to be older at onset and have more frequent episodes with longer duration. See table 3 for a comparison of primary and secondary disease courses.

Patients are often obese due to voracious, compulsive eating during episodes. This patient was atypical as her physically active employment as a dance and aerobics teacher helped to control her weight.

Investigations

There is no definitive test to identify KLS. Investigations are performed to exclude other

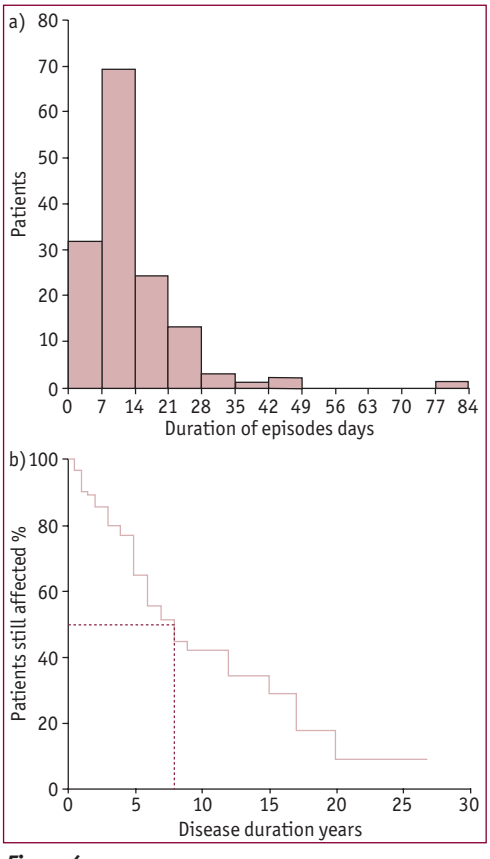

Figure 4

a) Length of KLS episodes. b) Duration of disease.

Table 3 Frequency of symptoms during episodes of KLS

	Primary KLS	*Secondary KLS*	*p-value*
Patients n	*168*	*18*	
Males %	*69*	*67*	*0.83*
Age of onset years	*18.9±72.3*	*26.1±17.5*	*0.0002*
Disease course median±SEM yrs	*8±2*	*10±2*	*0.24*
Episode duration days	*11.7±8.9*	*31.4±56.5*	*0.0001*
Interval duration months	*5.9±9.6*	*6.8±9.3*	*0.73*
Episodes n	*11.9±14.5*	*38.3±72.6*	*0.0005*
Time incapacitated days	*135.5±168.5*	*673.5±1245*	*<0.0001*
Megaphagia %	*80*	*83*	*0.95*
Hallucinations or delusions %	*26*	*44*	*0.1*
Hypersexuality %	*43*	*28*	*0.2*

Data are presented as mean±SD, unless otherwise stated. Reproduced from [2], with permission from the publisher.

causes, and the diagnosis based on history and PSG exclusion of other sleep disorders. Serum biochemistry and haematology, sex hormone levels, plasma and CSF analysis, CT and MRI of the brain are all usually normal.

Task 4
What treatment would you propose?

Answer 4

There is no recommended treatment. KLS is a rare condition and there have been no randomised controlled trials of treatment, primarily due to a lack of patient numbers, variability of episodes between patients, and the difficulty in determining efficacy given the natural evolution of the disease and spontaneous remission. Many drugs have been used in open-label trials in an attempt to alleviate the symptoms and/or prevent reoccurrence of episodes, but few have had the desired outcome.

Lithium has been used with some success to prevent recurrences [3–5] and improve mood. Amphetamines are the only stimulant that has been shown to be effective in treating the hypersomnolence [2], though these do not resolve (and potentially exacerbate) the behavioural and cognitive disorders, particularly irritability. Other stimulants have been of little success and can worsen the symptoms of hypersexuality. Modafinil has been ineffective and neuroleptics, phototherapy, and electrotherapy, have not shown any advantage over absence of therapy [2] Antidepressants are equally ineffective, but a trial may exclude depression as a diagnosis. This patient had previously had a trial of olanzapine from the neurologist, which had no effect. She was offered a trial of other drug therapy to counter the hypersomnia, but declined as the episodes were so unpleasant that she felt she would prefer to sleep through them.

Discussion

Polysomnography studies are difficult to carry out due to the mood and behavioural changes during episodes, as was the case with this patient, who self-terminated the study. There is little consensus on the polysomnography findings, with studies variously reporting reduced sleep efficiency, reduced sleep and/or REM latency, increased wake time after sleep onset, decreased SWS, and frequent awakenings from stage 2 sleep.

Symptoms change over the course of the episode, hypersomnia often dominating early on and weakening toward the end of the episode. Therefore, the timing of the polysomnography is likely to affect the results and may be responsible for the variability of previous polysomnography findings. A recent study of 19 KLS patients by HUANG *et al*. [6] showed no significant difference in any sleep stage or sleep efficiency on polysomnographic data recorded during episodes compared to asymptomatic periods. There was a tendency for decreased SWS and REM, but this did not reach significance. However, the researchers found that over the course of the episode there was a tendency for the proportion of SWS to increase and the proportion of REM sleep to decrease compared with baseline asymptomatic levels.

The exact aetiology of KLS is unknown and there is little evidence to suggest the condition is linked to narcolepsy [5, 7].

There are five reported cases of familial KLS [5, 8–10] including a Saudi family with four out of six affected members showing HLA-DQB1*02 homozygosity. Coupled with an increased prevalence in the Jewish population [11], this suggests some genetic susceptibility [12].

Several theories have been suggested to be the cause of KLS, including neurotransmitter imbalance [13, 14] and an autoimmune abnormality [5, 7, 8]. More recently, single photon emission computed tomography (SPECT) studies in five subjects have shown hypoperfusion of the thalamus during episodes compared with asymptomatic periods in all cases [15]. Various SPECT studies in single patients showed hypoperfusion in other parts of the brain [16–19]. Studies of KLS patients at autopsy have shown signs of inflammatory encephalitis within the hypothalamus and thalamus [20–22].

In summary, KLS is a rare disorder with unknown aetiology, occurring more often in males (this patient was atypical in this respect) with onset in adolescence. There may be a history of trivial infection or head injury. Recurrent episodes of hypersomnia are coupled with at least one of a range of cognitive, mood and behavioural abnormalities, predominantly irritability, megaphagia and hypersexuality. Between episodes the patients are entirely well. The frequency and duration of episodes usually lessens over the course of the disease, with spontaneous remission in the third decade of life. There is no recommended medical treatment.

References

1. *International Classification of Sleep Disorders: Diagnostic and Coding Manual. 2nd Edn. Chicago, American Academy of Sleep Medicine, 2005.*
2. *Arnulf I, Zeitzer JM, File J, Farber N, Mignot E. Kleine–Levin syndrome: a systematic review of 186 cases in the literature. Brain 2005; 128: 2763–2776.*
3. *Hart EJ. Kleine-Levin syndrome: normal CSF monoamines and response to lithium therapy. Neurology 1985; 35: 1395–1396.*
4. *Goldberg MA. The treatment of Kleine-Levin syndrome with lithium. Can J Psychiatry 1983; 28: 491–493.*
5. *Dauvilliers Y, Mayer G, Lecendreux M, et al. Kleine–Levin syndrome: an autoimmune hypothesis based on clinical and genetic analyses. Neurology 2002; 59: 1739-1745.*
6. *Huang YS, Lin YH, Guilleminault C. Polysomnography in Kleine–Levin syndrome. Neurology 2008; 70: 795–801.*
7. *Visscher F, van der Horst AR, Smit LM. HLA-DR antigens in Kleine–Levin syndrome. Ann Neurol 1990; 28: 195.*
8. *Katz JD, Ropper AH. Familial Kleine–Levin syndrome: two siblings with unusually long hypersomnic spells. Arch Neurol 2002; 59: 1959–1961.*
9. *Janicki S, Franco K, Zarko R. A case report of Kleine–Levin syndrome in an adolescent girl. Psychosomatics 2001; 42: 350–352.*
10. *Thacore VR, Ahmed M, Oswald I. The EEG in a case of periodic hypersomnia. Electroencephalogr Clin Neurophysiol 1969; 27: 605–606.*
11. *Arnulf I, Lin L, Gadoth N, et al. Kleine–Levin syndrome: a systematic study of 108 patients. Ann Neurol 2008; 63: 482–493.*
12. *Bahammam AS, Gadelrab MO, Owais SM, Alswat K, Hamam KD. Clinical characteristics and HLA typing of a family with Kleine–Levin syndrome. Sleep Med 2008; 9: 575–578.*
13. *Chesson AL Jr, Levine SN, Kong LS, Lee SC. Neuroendocrine evaluation in Kleine-Levin syndrome: evidence of reduced dopaminergic tone during periods of hypersomnolence. Sleep 1991; 14: 226-232.*
14. *Koerber RK, Torkelson R, Haven G, Donaldson J, Cohen SM, Case M. Increased cerebrospinal fluid 5-hydroxytryptamine and 5-hydroxyindoleacetic acid in Kleine–Levin syndrome. Neurology 1984; 34: 1597–1600.*
15. *Huang YS, Guilleminault C, Kao PF, Liu FY. SPECT findings in the Kleine–Levin syndrome. Sleep 2005; 28: 955–960.*
16. *Arias M, Crespo Iglesias JM, Perez J, Requena-Caballero I, Sesar-Ignacio A, Peleteiro-Fernandez M. Kleine–Levin syndrome: contribution of brain SPECT in diagnosis. Rev Neurol 2002; 35: 531–533.*
17. *Portilla P, Durand E, Chalvon A, et al. SPECT-identified hypoperfusion of the left temporomesial structures in a Kleine–Levin syndrome. Rev Neurol 2002; 158: 593–595.*
18. *Landtblom AM, Dige N, Schwerdt K, Safstrom P, Granerus G. A case of Kleine–Levin syndrome examined with SPECT and neuropsychological testing. Acta Neurol Scand 2002; 105: 318–321.*
19. *Peraita-Adrados R. Síndrome de Kleine-Levin: aportación diagnóstica de la SPECT cerebral [Kleine-Levin syndrome: diagnostic contribution made by brain SPECT]. Rev Neurol 2003; 36: 599.*
20. *Fenzi F, Simonati A, Crosato F, Ghersini L, Rizzuto N. Clinical features of Kleine–Levin syndrome with localized encephalitis. Neuropediatrics 1993; 24: 292–295.*
21. *Takrani LB, Cronin D. Kleine–Levin syndrome in a female patient. Can Psychiatr Assoc J 1976; 21: 315–318.*
22. *Carpenter S, Yassa R, Ochs R. A pathologic basis for Kleine–Levin syndrome. Archives of neurology. 1982; 39: 25–28.*