Recurrent hypersomnia: a case report with polysomnographic findings

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Recurrent hypersomnia is an uncommon clinical problem that can be misdiagnosed and mistreated. I report a case of idiopathic recurrent hypersomnia. The clinical features, differential diagnoses, polysomnographic findings, possible aetiologies, and treatment are discussed.

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Introduction

Recurrent hypersomnia (RH) is characterised by episodes of excessive sleep lasting from a few days to several weeks. Patients may sleep for 18 to 20 hours a day and wake only to eat and void. The episodes are typically weeks or months apart with intervening periods of normal sleep. Recurrent hypersomnia can be monosymptomatic or may be associated with overeating and abnormal behaviours including sexual disinhibition and mental disturbances. The polysymptomatic form is known as Kleine-Levin syndrome.[1] Recurrent hypersomnia can be idiopathic, menstruation-related,[2] or secondary to neurological or psychiatric conditions. I describe the features and successful treatment of a patient with RH given lithium carbonate.

Case report

A 52-year-old Chinese woman was referred to our clinic in March 1993 with a complaint of periodic hypersomnia of two years' duration. No precipitating factor was identified. She had consulted various doctors, had received numerous investigations, and been treated with several different medications without success. Initially, the sleep episodes lasted for two to four days and were separated by one month. The problem deteriorated after one year, when each episode lasted for seven days and was separated by only two weeks. Each sleep episode started abruptly and was unrelated to her menstrual cycle. She slept all day, was tired, moved slowly, and ate very little. She was not depressed or irritable, and had no change in sexual interest during the attacks. Between the episodes she had good nocturnal sleep, did not complain of excessive daytime sleepiness, and could do housework. Her personality, marital relationship, and family atmosphere were good. She was a non-smoker, social drinker, and did not use caffeine or abuse other substances. She had no complaint of loud snoring, cataplexy, hypnagogic hallucination, or sleep paralysis. Her past health and family history were unremarkable.

Between hypersomniac episodes, physical and psychiatric examinations and basic blood tests were normal. An electroencephalogram (EEG) showed a normal amplitude and diffuse 7 to 9 Hz background with bilateral intermittent short runs of sharp slow waves of 2 to 4 Hz and 100 to 190 μV in amplitude over the frontal and central regions. Magnetic resonance imaging (MRI) showed a small infarct sized 1 x 0.5 cm in the left frontal white matter. No thalamic or hypothalamic lesion was detected. An all-night polysomnogram and multiple sleep latency test (MSLT) were also performed. The MSLT consisted of four naps recorded at 9.30 am, 11.30 am, 1.30 pm, and 3.30 pm. At the appropriate times, the patient retired to a sound-attenuated room and was instructed to try to fall asleep. The recording was terminated after 20 minutes whether or not the patient fell asleep. Between naps, the patient stayed in the ward sitting room and was kept awake by a nurse. She did not take any medications or caffeine before the sleep study. The results are shown in the Table. No apnoea, hypopnoea, or periodic limb movements were recorded.

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During a hypersomniac episode in August 1993, the polysomnogram and MSLT were repeated (Table). During the hospitalisation period, physical and psychiatric examinations and routine blood tests were unremarkable.

Methylphenidate, 5 mg, twice daily was prescribed to be taken at the onset of the next attack. The patient took it during one episode and did not find it useful. Because of her frequent attacks, lithium carbonate, 750 mg daily was prescribed as a prophylactic medication in October 1993. The patient took the drug irregularly, but the attacks had already become less frequent. From July 1994, she took the drug regularly and the sleep episodes totally subsided. The dosage of lithium carbonate was reduced from 750 to 500 mg in May 1995 because of hand tremor, but the therapeutic effect was maintained. The lithium level in September 1995 was 0.5 mmol/L. In May 1996, when she was taking the same dosage of lithium carbonate and her sleep pattern remained normal, the polysomnogram and MSLT was repeated (Table). As the patient has been taking lithium for more than one year and there is complete control of the hypersomnia, gradual withdrawal of lithium will be considered.

Discussion

Recurrent hypersomnia should first be distinguished from other causes of excessive sleepiness such as obstructive sleep apnoea syndrome, narcolepsy, or periodic limb movement disorder. Patients with RH present with recurrent rather than persistent sleepiness and features such as loud snoring, cataplexy, hypnagogic hallucination, or sleep paralysis are absent. Neurological conditions that can present as RH include tumours in the third ventricle, complications of encephalitis, head trauma, or cerebrovascular disease involving brain stem structures, petit mal absence status, or slit ventricle syndrome. Psychiatric disorders including recurrent depression, bipolar affective, dissociative and factitious disorder, and substance abuse can also be considered as differential diagnoses. Because of the rarity of RH and the occurrence of mental disturbances in Kleine-Levin syndrome, it is sometimes misdiagnosed as epilepsy or psychiatric illness. In this case, the patient presented with an atypical deteriorating course of RH. Except for the incidential finding of a small infarct in the frontal lobe, the neurological workup and psychiatric assessment did not identify secondary causes.

To confirm hypersomnia and to exclude epileptic status and organic pathology, EEG, polysomnographic study, and brain imaging are essential. It is also important to rule out psychiatric disorders. Two kinds of polysomnographic study can be used to assess the degree of hypersomnia in patients with RH—continuous 24-hour sleep recording or MSLT. In our patient, MSLT during hypersomniac episodes documented the increased sleep propensity.

The aetiology of idiopathic RH remains elusive, but symptoms such as excessive sleep, overeating, and disinhibited behaviours can be interpreted as manifestations of hypothalamic dysfunction. Because of its recurrent nature, viral encephalitis involving the hypothalamus, with reactivation of infection during each hypersomniac attack is possible. This hypothesis is partially supported by findings that the onset of some cases of idiopathic RH are preceded by an influenza-like syndrome, abnormal hormonal secretion during sleep episodes,[3] and pathology in the hypothalamus on post-mortem examination.[4] In some cases, EEGs obtained during episodes of hypersomnia showed general slowing of the background and paroxysmal bursts of theta activity; the abnormal EEGs normalised after sleep episodes.[5] Nevertheless, CT scan and MRI studies were usually negative.

The polysomnographic findings of our patient require explanation. There was a shortened rapid eye movement (REM) latency between hypersomniac episodes. During a hypersomniac attack, REM latency was further reduced and wakefulness after sleep onset was increased. When the RH was controlled by lithium, polysomnography detected a reduction of REM, stages 3 and 4 sleep, and a lengthening of REM latency. The findings during hypersomniac episodes in this patient have been previously reported.[6] Although shortened REM latency is non-specific and has been found in normal ageing, psychiatric disorders, narcolepsy, following cessation of alcohol and drugs such as benzodiazepine and antidepressants, and following recovery of sleep deprivation, there is no evidence that the above conditions occurred in this patient.

Based on our polysomnographic findings, sleep phase advance may be postulated as an alternative aetiology of idiopathic RH. There may be an inherent phase advance drive in affected subjects as evidenced by a slightly shortened REM latency before a hypersomniac attack. With certain stresses to the circadian rhythm, the sleep-wake phase position moves forward during a hypersomniac episode and patients experience sleepiness during the daytime and at night, shortened REM latency, and disturbed sleep. The effectiveness of lithium may be due to its possible ac-

Table. Polysomnographic studies of a patient in a period of normality between hypersomniac episodes, during a hypersomniac episode, and after treatment with lithium

	Between episodes	During hypersomnia	During lithium treatment
All-night polysomnogram			
Sleep duration (min)	478	478	471
Sleep efficiency (%)	98	89	91
Stage 1* (%)	3	3	4
Stage 2* (%)	62	50	69
Stage 3 and 4*	13	17	6
Stage REM*† (%)	20	19	12
Sleep latency ‡ (min)	4.5	2.5	6.5
REM latency § (min)	63.5	55	182
Multiple sleep latency test			
No. of naps able to sleep ‖	1	3	1
Average stage 1 latency ¶ (min)	15	6	16
Occurrence of REM sleep during nap	No	No	No

* Proportion of total sleep duration in sleep stage 1, 2, 3, 4, or REM
† REM rapid eye movement
‡ Sleep latency is time between night-off to first epoch of stage 2
§ REM latency is time between first epoch of stage 2 to first epoch of stage REM, REM latency of a 50-year-old Caucasian normal subject is approximately 75 minutes[10]
‖ Number of naps out of four during which the patient was able to fall asleep within 20 minutes
¶ Average of four naps, stage 1 latency is time between night-off to first epoch of stage 1, stage 1 sleep latency of naps when the patient could not fall asleep is taken as 20 minutes, average stage 1 latency of normal subjects during multiple sleep latency test should be more than 10 minutes.[11]

tion of delaying the phase position of circadian rhythm, resulting in a reduction of REM sleep and a lengthening of REM latency.[7] The use of this hypothesis to explain daytime sleepiness in idiopathic RH should be considered as tentative. Shortened REM latency, a feature suggestive of sleep-wake phase advance is nonspecific and not always associated with daytime sleepiness. The manifestation of sleep-wake phase advance may depend on individual cases and how the cycle has been advanced.

Treatment of RH includes symptomatic and preventive measures. The former are oriented towards control of the hypersomniac episode. Stimulant drugs are, at most, effective for a few hours only. When sleep episodes are frequent enough to disturb personal and family life, preventive measures are needed. Some positive results have been reported with lithium carbonate[8] and moclobemide.[9] In our case, the negative effect of medications prescribed by previous doctors plus the methylphenidate argues against the placebo effect of lithium, although an ABA design could more accurately demonstrate the drug effect. In the case of menstruation-related periodic hypersomnia, use of an ovulatory inhibitor has been successful in a few reported cases.[2]

The prognosis of idiopathic RH is unknown. No long term follow up studies of idiopathic RH have been performed. In some reported cases of Kleine-Levin syndrome, the course is benign with a decrease in duration, severity, and frequency of hypersomniac attack over several years.

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