Original Article

A Polysomnography Study of Kleine–Levin Syndrome in a Single Center

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Abstract

Background: Kleine–Levin syndrome (KLS) is a rare sleep disorder characterized by recurrent episodes of hypersomnia. Polysomnographic (PSG) researches of KLS have been reported only in few publications in the past decades. This study aimed to investigate the characteristics of PSG of KLS.

Methods: This study, which was conducted from March 2010 to July 2014, included seven patients diagnosed with KLS in the Sleep and Wake Disorder Center of Huashan Hospital, Fudan University (Shanghai, China). PSG and multiple sleep latency tests (MSLT) were performed during their episodes and the results were evaluated.

Results: Five of the seven patients were males. The mean age at KLS onset was 15.6 ± 3.6 years. The number of episodes ranged from 2 to 7. The duration of episodes lasted from 4 to 11 days. The sleep architecture and proportion were normal in most of the patients. The average value of mean sleep latency was 6.9 ± 4.1 min. No sleep-onset rapid eye movement (SOREM) was detected in three of the patients, whereas one patient experienced one period of SOREM, and such episodes occurred twice in other two patients.

Conclusions: We found that sleep architecture and proportion were normal in most KLS patients. However, the results of PSG and MSLT had no specificity for KLS patients.

Key words: Kleine–Levin Syndrome; Multiple Sleep Latency Test; Polysomnography

Introduction

Kleine–Levin syndrome (KLS) is a rare sleep disorder, mainly affecting adolescent males. This condition is characterized by recurrent episodes of hypersomnia associated with cognitive and behavioral abnormalities, including confusion, apathy, irritability, megaphagia (eating increased amounts of food), and hypersexuality. Between the episodes, the sleep patterns, cognition, and behavior of patients are normal.[1] Although no population-based studies reporting on KLS prevalence are available, it is generally estimated that there are only 1.5–2.0 cases per million people.[2-4]

At present, the pathogenesis of KLS is still unclear. Former studies show that the hypocretin level in KLS patients is normal.[5] Nevertheless, there are a limited number of investigations on the application of polysomnography (PSG) in KLS. Some evidence exists that the duration slow-wave sleep periods decreases during the first half of the episodes, and the length of rapid eye movement (REM) sleep periods is diminished in the second half.[2,6,7] The sleep efficiency is usually lower in patients with KLS than in healthy people. The multiple sleep latency test (MSLT) revealed no difference in mean sleep latency (MSL) and the number of sleep-onset REM sleep (SOREM) between the episodes and interictal periods.[8]

This study aimed to summarize the demographic parameters of KLS patients and determine the characteristics and applicability of PSG and MSLT in KLS patients.

Methods

Subjects

We performed a retrospective study including seven patients with KLS, who were diagnosed between March 2010 and

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July 2014 in the Sleep and Wake Disorder Center of Huashan Hospital, Fudan University, Shanghai, China. Institutional Review Board approval was not required for this clinical retrospective study. MSLT was conducted in all patients, following PSG. The diagnostic criteria for KLS were defined according to the International Classification of Sleep Disorders, 2nd edition. Patient exclusion criteria were the presence of narcolepsy or psychiatric disorder (especially bipolar disorder), or use of drugs or medications. All patients had been drug-free for at least 2 weeks at the time of the PSG recording. PSG and MSLT were performed during their episodes.

Polysomnography

Nocturnal PSG results were recorded using Compumedics System (Series E EEG/PSG, Compumedics Limited Global Corporate HQ, Victoria, Australia). PSG parameters were observed for at least 6 h. During PSG recording, data were collected by six electroencephalographic (EEG) channels, including those from two grounds and two reference electrodes (F3-A2, F4-A1, C3-A2, C4-A1, O1-A2, and O2-A1). EEG monitoring was applied following the instructions of the 10–20 international placement system. Electromyography activity was recorded from the submentalis muscle and right and left tibialis anterior muscles. Electrooculographic response was recorded bilaterally. Other channels of data collection included an electrocardiogram, determination of airflow, nasal pressure, abdominal, and thoracic breathing movement, and oxyhemoglobin saturation. MSLT was tested the day following PSG examination. The monitoring was repeated at least four times: at 9 a.m., 11 a.m., 1 p.m., and 3 p.m. The test was terminated if no sleep occurred within 20 min after turning off the lights. MSLT was performed for 15 min after sleep onset. The results obtained were analyzed according to the directions of the American Academy of Sleep Medicine Manual for Scoring of Sleep and Associated Events.[9]

Statistical analysis

All analyses were carried out using SPSS 20.0 (IBM Corporation, Armonk, New York, USA). Continuous data were summarized using mean and standard deviation (SD) or median and upper and lower quartile (Q1, Q3) depending on the distribution. Categorical data were described using count and percentages. Since the number of patients was lower than 20, we did not conduct any comparison tests.

Results

Demographics, triggers, and symptoms

Five patients were male and two female, giving a male/female ratio of 5/2. The mean age of the patient at KLS onset was 15.6 ± 3.6 years (range: 11–20 years), and the mean age of diagnosis was 17.0 ± 3.8 years (range: 13–22 years). The number of episodes ranged from two to seven, and their duration lasted from 4 to 11 days [Table 1]. The data of body mass index are shown in Table 1.

Several potential triggers of the disorder were identified during the first episode. In two patients KLS might have been caused by excessive alcohol consumption. One patient suffered from influenza, another had diarrhea, and third one was overtired. No obvious predisposing factors were identified in other two patients [Table 2].

Table 1: Clinical and demographic characteristics of patients with KLS

Patients No.	Sex	Age (years)	Age at onset (years)	BMI (kg/m^2)	Attack times	Duration of episodes (days)
1	Male	22	20	23.4	6	6–7
2	Male	13	13	16.3	2	11
3	Male	14	13	19.5	6	8
4	Male	13	11	19.5	7	7
5	Male	17	15	27.7	2	5
6	Female	19	17	22.0	2	4–10
7	Female	21	20	19.8	4	5

BMI: Body mass index; KLS: Kleine–Levin syndrome.

Hypersomnia occurred in all seven patients. During the episodes, the patients had cognitive and behavioral disorders, for example, depression, apathy, irritability, and derealization; five patients had eating disturbances. One of them was with hyperphagia and four with anorexia. Two of the seven patients experienced hypersexuality [Table 2]. In addition, there were two patients having autonomic nerve dysfunction, including facial flushing and profuse sweating. During the interictal phase, patients returned to normal.

Polysomnography

The results of PSG of each patient are presented in Table 3. Total sleep time ranged from 366.0 to 530.5 min, with a mean value of 453.6 ± 57.6 min. The mean value of sleep efficiency was 89.7% ± 8.9%, ranging from 76.8% to 97.3%. The mean values of sleep-onset latency and REM sleep latency were 6.6 ± 7.7 min (range: 0–23.0 min) and 76.4 ± 45.5 min (range: 8.0–146.0 min), respectively. The proportions of each sleep stage were shown as follow: the proportion of sleep Stage 1 was 9.3% ± 5.1% (range: 3.8%–17.0%); the proportion of sleep Stage 2 was 50.5% ± 8.2% (range: 37.1%–58.8%); the proportion of sleep Stage 3 was 18.4% ± 9.1% (range: 7.6%–33.7%); and the proportion of REM sleep was 21.8% ± 3.9% (range: 15.6%–26.2%).

Periodic limb movements

The results of periodic limb movements (PLM) parameters are shown in Table 4. The median (Q1, Q3) of PLM during wake index was 3.5 (2.1, 5.7), whereas the mean value of PLM during sleep (PLMs) index was 0.9 ± 0.8. The median (Q1, Q3) of PLM during non-REM sleep index and that of PLM during REM sleep index were 0.8 (0, 0.8) and 0 (0, 1.1), respectively. The median (Q1, Q3) of PLM arousal index was 0.1 (0, 0.2).

Multiple sleep latency tests

The data of MSLT of each patient are listed in Table 5. The average value of MSL was 6.9 ± 4.1 min. Three patients had no SOREM occurrence, whereas one patient had one SOREM episode, and other two patients had two who also met the MSLT criteria for narcolepsy (MSL <8 min, and two or more SOREMs).

Table 2: Triggers and symptoms of KLS

Patients No.	Triggers	Eating disturbances	Hypersexuality	Cognitive changes	Behavioral disorder
1	Alcohol intake	+ (anorexia)	+	+	+
2	Influenza	+ (anorexia)	+	+	+
3	Diarrhea	+ (anorexia)	−	+	+
4	Fatigue	+ (anorexia)	−	+	+
5	Alcohol intake	+ (hyperphagia)	−	+	+
6	Unknown	−	−	+	+
7	Unknown	−	−	+	+

The symbol of "+" means that the patient suffered from the symptom, and the symbol of "–" means the patient did not suffer from the symptom. KLS: Kleine–Levin syndrome.

Table 3: Sleep architecture and proportion of patients with KLS

Items	Patients No.						
	1	2	3	4	5	6	7
Total sleep time (min)	495.5	447.0	530.5	484.5	366.0	394.0	458.0
Sleep efficiency (%)	93.5	97.3	95.2	96.6	76.8	77.3	90.9
Sleep-onset latency (min)	0	8.0	3.0	1.5	4.0	23.0	7.0
REM sleep latency (min)	56.5	44.0	146.0	8.0	74.0	105.5	100.5
Sleep stage 1 (%)	14.4	3.8	5.4	4.6	9.3	17.0	10.4
Sleep stage 2 (%)	58.8	37.1	53.1	52.7	55.1	55.8	40.7
Sleep stage 3 (%)	7.6	33.7	16.5	16.4	15.6	11.5	27.6
REM sleep (%)	19.2	25.4	25.1	26.2	20.1	15.6	21.3

REM: Rapid eye movement; KLS: Kleine–Levin syndrome.

Table 4: PLM parameters of KLS

Items	Patients No.						
	1	2	3	4	5	6	7
PLMw index	0	32.2	2.3	3.8	3.5	2.1	5.7
PLMs index	0	2.0	0.8	0.6	1.5	0	1.6
PLMs-NREM index	0	2.3	1.1	0.8	1.8	0	0.2
PLMs-REM index	0	1.1	0	0	0	0	6.8
PLMs arousal index	0	0.1	0.2	0	0.5	0	0.1

KLS: Kleine–Levin syndrome; PLMw: Periodic limb movement during wake; PLMs: Periodic limb movement during sleeps; REM: Rapid eye movement; NREM: Nonrapid eye movement.

Table 5: Multiple sleep latency tests of KLS

Items	Patients No.						
	1	2	3	4	5	6	7
MSL (min)	5.4	6.4	6.8	3.1	5.5	15.9	5.1
SOREM	2	2	1	0	1	0	0

MSL: Multiple sleep latency; SOREM: Sleep-onset rapid eye movement; KLS: Kleine–Levin syndrome.

Discussion

In this study, we found that most patients with KLS were male (the proportion was 5/7). KLS onset occurred during the second decades of life, which was in agreement with previous reports.[3,4,10] All patients had hypersomnia, accompanied by cognitive and behavioral disorders during the episodes. Depression, apathy, irritability, anxiety, and derealization were the most common manifestations of the cognitive disorders. Decreased appetite was more common than megaphagia, which was not consistent with the findings of previous studies.[11-13] Furthermore, some patients had aggressive behavior. In addition, two of them had automatic nerve disorders, such as facial flushing and profuse sweating. The triggering factors were similar to those identified in our earlier investigation.[3] Nevertheless, in this study, excessive alcohol consumption was determined as the main causative factor of KLS.

The findings of previous examinations revealed that during nocturnal PSG, slow-wave sleep percentage decreased during the first half of episodes, and REM sleep percentage declined during the second half.[6,7,14] Some limitations of the present investigation have to be outlined. In this study, the patients underwent PSG test only once. We could not compare the PSG data from the first half of episodes with those from the second half. Nonetheless, we found that most patients were with normal sleep architecture and proportion. However, interestingly, we discovered that the percentage of slow-wave sleep in two patients increased, and the proportion of sleep Stage 1 was also elevated in other two patients, which had rarely been reported in the scientific literature before. The results of MSLT evidenced that tendency for experiencing sleepiness was obvious in six patients. Two patients met the MSLT criteria for narcolepsy (MSL <8 min, and two or more SOREM episodes). Nevertheless, SOREM features differed from patient to patient. Therefore, no specificity of SOREM events was detected in KLS patients, and these episodes cannot be a diagnostic criterion for KLS.[2,8]

Furthermore, the PLM analysis results indicated that there was no abnormality found in the patients with KLS. To the best of our knowledge, the PLMs index is considered abnormal when it is above 5 per hour.[15] In our patients, all values of this index were in a very low level. The results indicate that the regulation of muscle activity is not damaged in KLS patients, not like that in patients with narcolepsy.[16,17]

In conclusion, there is no specificity of PSG in KLS patients. Some patients manifested normal sleep patterns, whereas other experienced extremities, such as abnormally light or increasing deep sleep. Furthermore, the results of MSLT are also highly dependent on the particular individual studied. We suggest that MSLT should not be a criterion for the

diagnosis of KLS, nor should it be considered a tool to differentiate KLS from narcolepsy.

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Conflicts of interest

There are no conflicts of interest.

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