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CASE REPORT Open Access

Periodic hypersomnolence in a young female patient: a case report and literature review

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Abstract

Background: Kleine–Levin syndrome (KLS) is a disease with periodic hypersomnolence accompanied by abnormal behavior with a rare prevalence in female.

Case presentation: Here, we report a young lady with chief complaint of hypersomnolence for 6 years of visits and any history of sleep attack, sleep paralysis, and cataplexy. Polysomnography was performed for the patient. The respiratory disturbance index was normal. In MSLT the patient had two SOREMs with mean sleep latency of 7 min. She was diagnosed as Kleine–Levin syndrome as the sleepiness symptoms had a periodic pattern without other characteristics of central hypersomnolence disorders. The patient did not report behavioral characteristics of KLS reported in previous literature. She improved spontaneously after a while in follow-ups without any further treatment.

Conclusions: Although KLS is reported rarely in female gender and there are previous defined behavioral symptoms for this syndrome, periodic pattern of sleepiness should raise this diagnosis after exclusion of other hypersomnolence causes.

Keywords: Sleepiness, Sleep, Polysomnography, Case report

Background

Kleine–Levin syndrome (KLS) is a rare reported disease that was first defined by Kleine as recurrent hypersomnia and Levin who reported periodic hypersomnolence accompanied by abnormal behavior [1]. American academy of sleep medicine characterizes the syndrome by recurrent episodes of hypersomnia associated with behavior disturbances, abnormal eating behaviors, and hypersexuality [2]. The disease is reported to be rare and most prevalent and reported among male adolescents [3]. Several reports indicate spontaneous disappearance of the disease. The cause is speculated to be unknown [4]. According to post mortem studies, viral and post-infectious encephalitis involving hypothalamus is hypothesized as a possible etiology [4]. Accordingly, HLA DQB1*02 has been associated with the disease [4, 5]. Most of the cases have an onset during second decade of life with male predominance [3].

5% of cases have been reported within family members, suggesting some degree of increased genetic susceptibility [3, 6]. Several factors and symptoms are reported before episodes of hypersomnia including fever, infection, upper airway infection, gastroenteritis, flu, alcohol or marijuana, head trauma, stress, mental effort, menses, lactation, sleep deprivation, local/general anesthesia, etc. [1].

The reported duration of the disease is very wide ranging 0.5–41 years [1]. Several patients report disappearance of the disease or its frequency and intensity by time. Hypersomnia episodes also have wide range 0.5–72 months with median of 3.5 months [1].

Major reported symptom among the patients and required for diagnosis is recurrent hypersomnolence [7,

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8]. The marked symptoms of narcolepsy including cataplexy and sleep paralysis are not observed [1]. The further associated symptoms in these patients are defects in memory concentration attention and other cognitive disturbances [6]. Eating behavior problems (megaphagia, craving of sweets, increased drinking), depression, irritability, abnormal speech, compulsion to sing, and write. Academic decline is reported among college and high school students [1, 6, 9].

Primary subjects of KLS have unremarkable physical examination. No neurologic focal lesion is found but, some have signs of autonomic dysfunction such as excessive sweating, salivation, tachycardia and hypertension [1, 6, 9]. Most cases of KLS are sporadic, however, 5% of cases have been reported within family members, suggesting some degree of increased genetic susceptibility; however, no genetic abnormality has been yet identified. Two cases of monozygotic twins with Kleine–Levin syndrome have been described [6]. No definite treatment is introduced for the disease and several medications such as lithium and stimulants have been applied [8].

As mentioned above reported cases of KLS in female is not as much as male gender and limited to case reports. Here, we describe a female case of KLS with its clinical presentation and medical examinations to explore more the presentation of the disease.

Case presentation

The patient was a 20-year-old woman with height 165, weight 50 kg. The patient's chief complaint was severe sleepiness for a week during each month without association with her menstruation period. The age of her menarche was 13 with no abnormality. The patient developed the symptoms for 6 years of visits. She had cognitive dysfunction during hypersomnolence periods including disorientation, abnormal behaviors, and impaired attention and memory. Patient's sleep hours are depicted in Table 1. Patient's Epworth Sleepiness Scale (ESS) was 20, Beck Depression Inventory was (BDI) 18, and Insomnia Severity Index (ISI) 14. She was a student and had history of taking fluoxetine, ritalin and lithium with no improvement. Clinical and neurological examination and MRI were normal. Wake EEG was normal. CSF analysis for hypocretin was not available in the region. The patient did not have medication use, or substance abuse.

The patient underwent full night polysomnography with multiple sleep latency test (MSLT). Fasting blood sugar, cholesterol, and lipid profile and serum iron TIBC were in normal range. Thyroid function test was in normal range. Ferritin was 23. In performed polysomnography, sleep-onset latency was 12 min. Time in bed was 10:32:07 and total sleep time was 9:33:30, accordingly sleep efficiency was 90%. Mean SpO_2 was 95% and min. SpO_2 was 90% during sleep. The patients had 35 awakenings after sleep onset and 8 REM periods with REM latency of 1:11 min. In MSLT, she reported sleep in three of four naps. Patient had two sleep-onset rapid eye movements (SOREMs) in four naps and her mean sleep-onset latency was 7 min. KLS diagnosis was made for the patient. She improved spontaneously after a while in follow-ups without any further treatment.

Table 1 Total sleep time recorded in different periods in sleep log by the patient

Number of days	Minimum (h)	Maximum (h)	Mean (SD)
13	4.00	9.00	7.15 (1.28)
13	6.00	8.00	7.46 (0.66)
11	4.00	9.00	5.90 (1.57)
14	4.00	7.00	5.92 (0.82)
14	5.00	8.00	6.57 (0.85)
7	6.00	7.00	6.42 (0.53)

Conclusions

KLS is a rare disorder characterized by recurrent episodic hypersomnia. Other associated symptoms include various behavioral and cognitive disturbances [2]. Male-to-female ratio is about 3:1 [1]. Females are often older at presentation than males [9]. This a noteworthy case because of not only the rarity of KLS especially in young females, but also having an infrequent narcolepsy-like pattern, two SOREMs and decreased sleep-onset latency in MSLT. The large number of cases is reported to be sporadic, as our patient [3, 10].

In 75% of cases, KLS onset occurred during the second decade or earlier [11]. The age at KLS onset is reported to be 16.9 ± 8.5 years (median: 15 years, range: 4–82 years) [1, 10, 12–14].

This syndrome is often missed, and there could be delays in diagnosis up to 2.5 years [5, 8], like diagnostic delay of our case. The patient was 20 years old when she was referred to us, but the onset of her KLS was at 14 years of age. She had frequent episodes of hypersomnolence and cognitive dysfunction for 6 years, and had history of taking fluoxetine, ritalin and lithium with no improvement. Our patient presented with hypersomnia and cognitive dysfunction but did not report eating disorder (anorexia or hyperphagia) or disinhibited behavior (such as hypersexuality). Almost all patients have symptoms of hypersomnia and cognitive disturbances such as confusion, concentration, attention and memory defects, while 66–75% had hyperphagia and 50–53% had sexual disinhibition [1, 9, 11].

Episodes of KLS present with an average of 19 episodes (median: 7 episodes, range: 2–130 episodes, mean ± SD: 12 ± 15 episodes). The episodes last between 2 and 80 days (sleep duration ranges: 15–24 h per day, median: 10 days, mean: 12 ± 9 days). Inter episode duration ranges from 0.5 to 72 months (median: 3.5 months, mean: 6 ± 10 months). The median duration of primary KLS is 8 years. The mean age at the end of KLS is reported to be 23 ± 12 years [2, 11, 15–20]. Our patient had almost 65 episodes, which lasted for 7 days. The range of inter-episode duration was 20–25 days. Between episodes she was totally normal, such as 96.4% patients. In a few cases, patients reported academic decline and a mild, long-lasting memory dysfunction between episodes [1, 15, 21, 22]. Her hypersomnolence episodes decreased gradually in frequency, duration, and intensity prior to termination and terminated with total and spontaneous recovery [1, 23].

KLS has been categorized into mild, moderate, and severe forms [10]. Accordingly, our patient can be categorized as moderate form. In the moderate form of KLS, patients have more frequent episodes, about 1 per month lasting 7 to 10 days; alternatively, patients experience fewer episodes (2 or 3) per year but the episodes are prolonged (lasting 3–6 months) [10, 24].

While several triggers have been reported to be associated with the initial episodes of hypersomnolence in KLS (61% of patients), there are no known causal links [1].

The most frequent factor was an infection at the disease onset (a flu-like illness or a non-specific fever) in more than two-thirds of the patients, other triggers have been reported, such as alcohol consumption, head trauma or sleep deprivation, already stressed by some authors, seems associated with onset of KLS [1, 3, 15, 17, 25–28]. The initial episode of our patient hypersomnolence was associated with a severe emotional stress.

Her EEG had suspicious spike and wave in PSG at one of episodes, however, further evaluation by neurologic revealed normal pattern of EEG. Her EEG was done in wakefulness and was normal. Completely normal EEG findings are seen in only about 30% of patients with KLS. In 70% of the patients, a non-specific diffuse slowing of background EEG activity, such as the alpha frequency band being slowed toward 7–8 Hz, was observed. Low-frequency, high-amplitude waves also occur [1, 10, 29]. Rarely, isolated spike discharges, self-limited photo-paroxysmal response or sharp waves are observed, but are considered of no clinical significance [1, 15, 30, 31].

In her PSG, sleep-onset latency was 12 min; total sleep time was 573 min (Stage 1, 10%; Stage 2, 61%; Stage 3–4, 19.8%; REM sleep, 9.2%), accordingly sleep efficiency was 90%. The patients had 8 REM periods. REM latency was 1:11 min. In other reports, mean total sleep time was 445 ± 122 min during the night (Stage 1, 6 ± 4%; Stage 2, 56 ± 9%; Stage 3–4, 19 ± 11%; REM sleep, 19 ± 6%) during an episode [1, 32, 33]. Rapid eye movement (REM) sleep as a percentage of total sleep time is greater during attacks compared to asymptomatic periods. There was increased total sleep time, but decreased sleep efficiency and frequent awakenings from sleep stage N2 [10, 32]. REM sleep is commonly reported during daytime sleep recordings or multiple sleep latency tests (mean sleep latency: 3 ± 1.1 min). Consistent with our patient, in one report, 21% had a narcolepsy-like pattern (≥ 2 sleep onset in REM periods) [1, 32, 33].

In MSLT, She reported sleep in three of four naps. Patient had two sleep-onset rapid eye movements (SOREMs) in four naps and her mean sleep-onset latency was 7 min. In two other reports, adolescents with KLS demonstrated the MSLT criteria for narcolepsy (MSL < 8 min, and 2 ≤ SOREM episodes) during the symptomatic period [34, 35] compared to when they were asymptomatic [10]. The overall mean sleep latency at MSLT was 9.51 ± 4.82 min in other researches [36–39].

Here, we reported a rare case of KLS in a young patient who had a periodic hypersomnolence pattern with a narcolepsy-like pattern in her MSLT without commonly reported behavioral characteristics of KLS in previous reports. The paper highlights attention of sleep medicine specialists towards patients' reported symptoms and sleep pattern throughout the time instead of sticking to objective criteria such as MSLT that could be misleading as in this patient.

Abbreviations

KLS: Kleine–Levin syndrome; ESS: Epworth Sleepiness Scale; BDI: Beck depression inventory; ISI: Insomnia Severity Index; MSLT: Multiple sleep latency test; SOREMs: Sleep-onset rapid eye movements.

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ZBA contributed in patient visits', follow-ups, designing the manuscript and writing it. SJ contributed in writing the manuscript. AN contributed in patient follow-ups, designing the manuscript and writing it. All authors have read and approved the manuscript.

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Availability of data and materials

Supporting data of this case report are available in the case of request by the journal.

Declarations

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