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Case Report Open Access

Kleine-Levin Syndrome in a Young Woman Triggered in Travel: A Case Report From Iran in COVID-19 Arena

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Abstract

Introduction: Kleine-Levin syndrome (KLS) is a rare disorder often associated with recurrent hypersomnia, first described by Klein in 1925 but named in 1942 by Critchley and Hoffman. KLS is more common in adolescence and is also more common in men than women. It must be distinguished from repetitive depressive disorder, or psychotic disorder.

Case Presentation: In this report, we present a 27-year-old woman with KLS who showed symptoms such as overeating and mood changes, unwillingness to talk to anyone, and a sedentary lifestyle. Meanwhile, during these periods, other symptoms such as lack of speech, decreased energy, lethargy, and slowness of mental and mood movements were observed in the patient. Eventually, with lithium consumption, her symptoms improve significantly. However, the exact cause of this syndrome and its definitive treatment is still unknown and will require further reports and studies.

Conclusion: According to the reported case, KLS may be triggered by travel and migration, and in such a situation, may respond well to lithium.

Keywords: Insomnia, Travel, Lithium, Sleep

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Introduction

Kleine-Levin syndrome (KLS) is a rare, recurrent sleep disorder that Kleine first described in 1925. In 1990,[1] the syndrome was classified by the International Classification under Sleep Disorders (ICSD).[2]

The diagnosis of this syndrome is based on clinical manifestations, and no valid biomarkers have been realized,[3,4] but in most cases, it appears in adolescence. The exact prevalence of this syndrome is unknown and is considered a rare disorder.[3]

Most cases were presented in western countries. Notably, Israel was a country with a significant incidence; hence, the Jewish heritage may be susceptible to the disorder.[5]

According to studies conducted hitherto, most patients with this syndrome shared acute upper respiratory infections and acute bronchitis. Some of the pathogens in this syndrome include Epstein-Barr virus, varicella-zoster virus, herpes zoster virus, influenza A, and adenovirus. Other irritants include alcohol consumption, head trauma, insomnia, psychological stress, menstruation, breastfeeding, anesthesia, cognitive disorders, behavioral disorders, hyperphagia, and hyperactivity. However, some patients do not certainly show any specific stimuli.[5,6]

Electroencephalography (EEG), brain imaging and cerebrospinal fluid (CSF) evaluation, and neurological examination can usually be employed for diagnosis. Meanwhile, the suggested treatments include lithium, carbamazepine, fluoxetine, valproate, and moclobemide, which have been of great benefits. Among stimulants, only amphetamines significantly alter drowsiness.[7]

In this report, we present a young woman in COVID-19 pandemic whose travel became a predisposing factor to her illness causing exacerbation of sleep attacks with mood changes.

Case Presentation

The patient is a 27-year-old woman, right-handed, married, without pregnancy, childless with a sleep disorder while traveling, has symptoms such as overeating and mood instability, unwillingness to talk to anyone, and a sedentary lifestyle. The patient's symptoms began at the age of 9. There was no history to suggest early-onset depression, multiple rhinitis, tonsillitis, attention deficit hyperactivity disorder, restless leg syndrome, psychotic disorder, night terror, or cataplexy. There was no evidence of any neurological disorder, head trauma, epilepsy, smoking cessation, or substance misuse. Her craniofacial examination was remarkable and intact.

Also, in these periods, other symptoms such as lack of speech, decreased energy, boredom, psychomotor retardation, and dysphoric mood were observed. (Beck Scoring Patient: 6). The patient also complained of excessive daytime sleepiness between attacks (Her Epworth Sleepiness Scale (ESS) score was 12).

For the first time, these symptoms were identified by her teacher at school age. Her teacher noticed that she was asleep most of the time. For a while, these symptoms disappeared in the case study but reappeared after marriage and during travel. The patient did not report fear, stress, or hatred during the trip, and the trip had not evoked any bad memories or experiences for her, and she did not have any secondary gain. In terms of personality, the case is an introverted and shy person who does not express herself. Body mass index (BMI) was higher than 35. Meanwhile, the hypnogram (Figure 1) and multiple sleep latency test (MSLT) report (Table 1) of the case under study were given, which can indicate her frequent periods of oversleeping (Figure 1). In the sleep log two weeks after the first visit, she slept continuously for an average of 10 hours a day. The recurrence of attacks was irregular but about one to four epileptic events happened a year, lasting between 2 and 7 days. Attacks improved without much intervention. There was no history of unavoidable sleep attacks, cataplexy, sleep paralysis, or hypnogogic and hypnotic hallucinations. Most of the attacks were relevant to land travel. She had no air travel, geographical latitude, shift work, or restless leg.

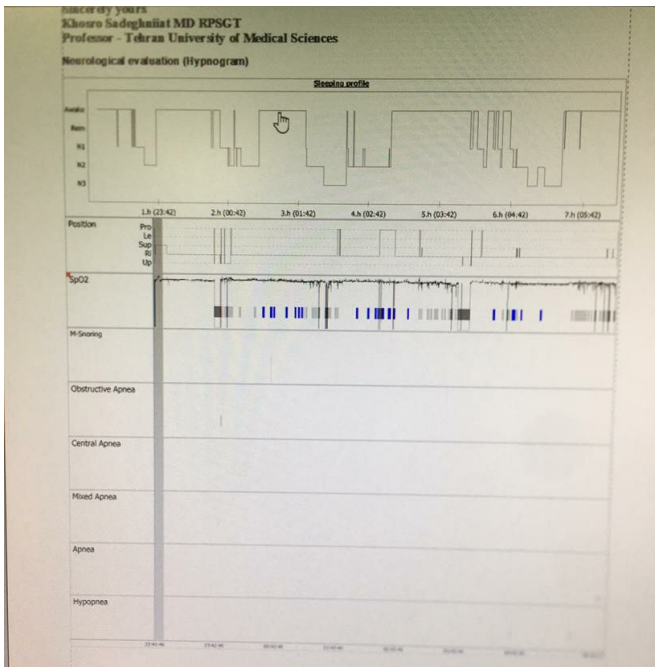

Figure 1. Hypnogram Diagram .

In addition, she had a history of rheumatoid arthritis, lumbar disc herniation, and depressive disorder. Notably, she had not used oral contraceptive.

The patient's lab data included thyroid tests in the normal range. A neurological examination was performed according to the drowsiness periods. Neurological tests at standard intervals were standard. To investigate the causes leading to drowsiness, brain imaging, metabolic and toxic examination of blood and urine were conducted. Due to high BMI and drowsiness, polysomnography was performed to evaluate the pattern and possible respiratory arrest during sleep. In nocturnal polysomnography, the patient's brain waves showed a stable and age-appropriate system. The first and second stages of NREM (Non-rapid eye movement) sleep increased, and REM sleep decreased, which was probably due to low sleep efficiency. There was also no evidence of sleep apnea.

The following information is related to the patient's polysomnography and MSLT (Table 2): (It should be noted that the tests were performed in the intervals between drowsiness attacks).

Sleep characteristic (Table 3): MSLT was conducted in four

Table 1. Multiple Sleep Latency Test (MSLT)

	Nap 1	Nap 2	Nap 3	Nap 4	Mean
Start time	07 :08	08:57	10: 56	12: 56	
End time	07: 28	09: 32	11: 24	13: 30	
Recording length	20	35	28	34	29.5
Total Sleep time	3.8	23.4	3.5	18	12.175
Onset to sleep	14.5	10.6	17.6	13.6	14.075
Onset to REM sleep	No REM	No REM	No REM	No REM	

Table 2. Seep laboratory findings

Total sleep time	184.6 min
Wake after sleep onset	205 min
Sleep onset latency	17.4 min
Sleep efficiency	42%
Stage N1	23.3%
Stage N2	54.46%
Stage N3	22.49%
Stage R	0
Apnea-Hypopnea Index	0
Mean SpO2	95%
Lowest saturation	92%
Stage 1	Increased
REM stage	Decreased
sleep efficiency	Decreased

Table 3. Sleep Characteristics

Mean sleep-onset latency	14.075 min
Sleep onset REM period (SOREMP)	No

naps every 2 hours and the patient slept during all naps.

The above findings ruled out narcolepsy and idiopathic hypersomnia. Brain MRI was normal and taking lithium 300 mg tablet was started at night.

This case responds positively to lithium intake, and the symptoms of the disease are reduced. However, the investigation of this disease and its cause will require more studies and discussion.

Due to the fact that polysomnography and MSLT were not performed during the patient's hypersomnia, in MSLT, the patient's MSL was 07.14 minutes and there was no sleep onset REM period (SOREMP), and the patient did not meet the diagnostic criteria for narcolepsy.

Discussion

KLS was characterized in 1898 by periodic oversleeping and was also described as morbid hunger.[8] As for our case, she had several seizures with morbid hunger following her travel.

Also, the diagnosis of this syndrome is clinical, and up to now, no specific laboratory test alone is currently available to diagnose this syndrome.[9] After a comprehensive and accurate account, we presented psychiatry and neurology history. In addition to hypersomnia and cognitive dysfunction in patients, other symptoms such as eating behavior disorders such as hyperphagia, craving for sweets, increased drinking, binge eating, decreased appetite and food utilization behavior, depression, irritability, hypersexuality have been observed.[3,10] Common causes associated with KLS include stroke, genetic or developmental diseases, hydrocephalus, cervical region cancer, autoimmune encephalitis, or severe infectious encephalitis.[3] We did not find these causes in our case.

The first case of the syndrome was reported in 1942, it was thought to be specific to men, but later women with KLS were reported.[8] In this female case, eventually her symptoms were reduced with lithium. We have limited resources on this syndrome, but there have been reports of lithium that have played a significant role in treating the symptoms. However, long-term use of lithium can have side effects.

Given that in some people the symptoms of this disease have started with a viral cold,[11] it seems that our case may also face this problem. In other words, the person may have an infection while traveling, which aggravates the symptoms.

Therefore, the patient was advised to follow several considerations and tips when traveling to prevent colds and avoid going to places where there is a possibility of transmission of the virus and infection. This may be effective in the prevention of the onset of the disease and reducing the symptoms of this person.

In some people, the symptoms of this syndrome decline with taking antihistamines,[7] suggesting that allergies may play a role in exacerbating the symptoms. It is therefore recommended to avoid allergens immediately if you encounter an allergen such as pollen while traveling because it taking antihistamines may be effective in aggravating the symptoms of this syndrome.

Given the role of autoimmunity in the pathology of KLS,[12] it is possible that rheumatoid arthritis in this case has exacerbated the symptoms of this syndrome. However, more studies are required to diagnose and treat this syndrome.

In a study, it was highlighted that viral infections in winter and Coronavirus disease were the possible etiology to trigger KLS.[13] We did not identify any signs or symptoms of coronavirus disease in this patient; however, it is suggested that COVID-19 morbidity can predispose to this condition.

Conclusion

According to the reported case, KLS may be triggered by travel and migration, and in such a situation, may respond well to lithium. But it is presumed that COVID-19 morbidity can predispose to this condition. We hope that the case study in this report can have a profound impact on future studies.

Authors' Contributions

RB, HA, PF, MA, and SB prepared substantial contributions to the conception or design of the work; MA, SB, and RB wrote the primary draft. HA, RB and PF supervised it. RB revised and finalized it and MA submitted it.

Conflict of Interest Disclosures

The authors have no conflict of interest.

Ethical Approval

Current study was approved by Shahid Sadoughi University of Medical Sciences ethics committee, Yazd, Iran with code of IR.SSU.REC.1400.244. Also the patient's consent was obtained.

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