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Kleine Levine syndrome (Sleeping beauty): A case report from Saudi Arabia

Case Report

Wadha Alotaibi, MD[1] and Gawahir Mukhtar, MD[2*]

[1]*Head section of Pediatric Pulmonary unit, Department of Pediatrics, King Fahad. Medical City, Riyadh, Kingdom of Saudi Arabia*

[2]*Pediatric Pulmonary unit, Department of Pediatrics, King Fahad. Medical City, Riyadh, Kingdom of Saudi Arabia*

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***Corresponding author:** Dr. Gawahir Mukhtar, Pediatric Pulmonary unit, Department of Pediatrics, King Fahad. Medical City, Riyadh, Kingdom of Saudi Arabia

Abstract

Background: Kleine – Levin syndrome (KLS), also called "Sleeping beauty syndrome" is a rare sleep disorder characterized by recurrent episodes of hypersomnia, hyperphagia, cognitive disturbances, and hypersexuality.The underlying pathophysiology remains unknown.Kleine-Levin syndrome is often misdiagnosed as depression, bipolar disorder, psychosis, seizures, or intoxication. The disorder is at the interface of neurology and psychiatry. Attacks decrease in frequency and eventually cease in most cases of adolescent onset.

Case presentation: we are reporting the first case of KLS from Saudi Arabia, a 14-year-old boy, with delay in diagnosing KLS. His history started 2 years prior to presentation with fever which was treated imperially, after that started to have excessive sleepiness up to 20 hours per day, with difficulty to awake him from sleeping.The patient was admitted 2 times to other hospital and was diagnosed and treated as epilepsy.His sleep study and multiple sleep latencies test (MSLT) reported severely reduced sleep latency confirming pathogenic sleepiness. The diagnosis of KLS was made as per diagnostic criteria of International Classification of Sleep Disorders after ruling out other possible causes of hypersomnia. The patient responded well to treatment with modafinil and other anti-psychosis medications.

Conclusion: KLS is a rare sleep disorder with a lot of psychiatric symptoms that can be wrongly diagnosed as neurological or psychiatric illness, hence, it is important for clinicians to have high index of suspicion on such atypical presentations.

There is no definitive treatment for KLS, however some cases showed clinical improvement with some medications. The prognosis of KLS is considered to be good with spontaneous remission in most of the cases in later years.

Potential research directions are to explore infectious, autoimmune, metabolic and genetic causes.

Key words

Kleine – Levin,children, Saudi Arabia, case report

Introduction

Kleine – Levin syndrome (KLS), also called "Sleeping beauty syndrome" is a rare sleep disorder which characterized by periods of excessive sleep, mental disturbances, voraciouseating, and hypersexual desire [1]. The underlying pathophysiology remains unknown. Symptoms and disease course follow typical patterns, but Kleine-Levin syndrome is often misdiagnosed as depression, bipolar disorder, psychosis, seizures, or intoxication [2]. Disorder is at the interface of neurology and psychiatry. No objective biochemical, neuropathological or structural imaging alterations have been identified.Typical episodes last from a few days to several weeks (median 10 days) or rarely months and end suddenly. The prevalence is unknown but it is rare and estimated to be 1.5 case per millionpopulations. Young males are usually affected, but it reported also in females. Although onset occurs during adolescent in 81% of cases, first episode has been reported in children younger than 12 yearswith youngest being aged 4 years.More than 50% of cases that start before the age of 12 years or after age of 20 years remain unresolved after 25 years.Attacks decrease in frequency and eventually cease in most cases of adolescent onset [3].

Case report

14 – year – old boy was referred from other hospital as a case of recurrent hypersomnia with abnormal behavior of 2-year duration, for further management.

His history started 2 years prior to presentation with fever which was treated empirically, after that started to have excessive sleepiness up to 20 hours per day, with difficulty to awake him from sleeping, initially there was no medical intervention until he became unable to communicate or concentrate. He lost his interest and started to have inappropriate words, hypersexual desire, in addition to throbbing headache over the left temporal area. During awake state, he would appear apatheticwith minimal interaction with others. His speechwould remain slurred with low tone and volume or sometimes even not understandable. The patient was irritable and aggressive whenever prevented from sleep. No other neurological symptoms. In between the attacks, he was completely normal.

The patient was admitted 2 times to other hospital and was diagnosed as epilepsy. He received carbamazepine and valproate for 2 years without significant improvement.

The patient was born through normal vaginal delivery without any complications. He had normal neuropsychomotor development but poor school performance. He was fully vaccinated and no history of previous diseases.

At physical examination, the patient was looking well, normal growth parameters and no dysmorphic features or anyother systemic abnormality.

Hospital course: The patient was admitted initially to epilepsy and monitoring unit. EEG monitoring showed no epileptiform discharge. Neuroimaging done for him including brain magnetic resonance imaging(MRI), magnetic resonance spectroscopy (MRS) andmagnetic resonanceangiography (MRA) which showed left thalamic lesion with involvement of the thalamic tract (sensory and motor), the under cause of the above mentioned lesion is undetermined. His routine biochemical and endocrine parameters were within normal range. The pediatric pulmonary team were consulted and sleep study with sleep multiple latencies (MSLT) were requested. The result of the sleep study showed total recording time of 522.2 minute, total sleep time 513.5 minute, sleep efficiency 98.3%. No evidence of epileptiform activity was noted, no periodic limb movement noted during sleeping. No significant sleep pathology noted.

The MSLT reported severely reduced sleep latency confirming pathogenic sleepiness. This MSLT result contributed to polysmnography diagnosis of narcolepsy, yet the patient clinical presentation of Kleine Levine syndrome maybe responsible for the diagnosis.

The diagnosis of KLS was made as per diagnostic criteria of International Classification of Sleep Disorders [(1)] after ruling out other possible causes of hypersomnia. His HLA typing of DQB1*1 came positive for DQB1*02, DQB1*03 which has mentioned in the literature as possible association with the disease.

Patient was started on modafinil 100 mg daily and he showed significant improvement as the duration of hypersomnia became shorter. He was transferred to adult sleep clinic after he became beyond pediatric age group. He receivedrisperidone, fluoxetine in addition to modafinil. Patient was seen by psychiatrist because ofdepression symptom which was controlled.

Currently the patient is stable, euthymic mood, no suicidal thought or psychosis symptoms, but still having hypersexual desire.

Discussion

Brierre de Bosmont in 1862 was perhaps the firstreported case of KLS. The condition took the name from Willi Kleine who, in 1925, explained a series of cases of periodic hypersomnia and also from Max Levin who in 1930, described a case of periodic hypersomnia and hyperphagia [4]. Kleine -Levin syndrome has mild, moderate and severe form. In mild forms, adolescents experience symptomatic periods of about 2 to 3 times per year of average duration 1 week. In moderate forms patients experience monthly episodes of 7-10 days each or have fewer 1 to 2 times per year) but long episode up to 6 months and mostly affected children and adolescents, and it associated with alteration in the cognition, apathy and extended period of sleeping (12 to14 hour) with loss of the normal circadian rhythm. In severe cases patients can experience 40 -80 episodes in rapid succession with possible long-term alteration of attention or mood. Hyperphagia and hypersexuality are often cited as characteristic symptoms of Kleine -levin syndrome and were viewed as mandatory diagnostic criteria before the 2005 international guideline were published. Isabelle et al reported hyperphagia in only 71 (66%) of 108 patients and hypersexuality in 57 (53%). This symptom of hyper sexuality affects boys more than girls and frequently manifests as substantially increased masturbation or demands on sexual partners. In our case, he presented with hypersexuality and no hyperphagia, actually he was having poor appetite. Apathy affects all patients including our case. Adolescent often stop normal activities such as washing and styling their hair [5].

Naresh et al, in a recent comprehensive review mentioned 36 cases with KLS reported from India, 8 of them were females. The first episode was preceded with fever in 50% of cases, as in our index case, while in others with postpartum psychosis, familial conflict and stress.

The triad of hypersomnia, hyperphagia and hypersexuality is not mandatory for the diagnosis of KLS as it is present in only 45% patients. Hypersomnia is kept as an obligatory criterion. Our patient presented with hypersomnia which was improved after starting the medication.

The disease starts in the majority of patients (81%) in the teens, with a median of 15 years as in our patient [(4)].

Many studies of physiopathology for KLS showed hypothalamic dysfunction, which would justify the alterations of the sleep regulatory system, sexual behavior and increased appetite. However, some studies were not capable of identifying consistent abnormalities [5,6]. In our case his brain MRA showed left thalamic lesion with involvement of the thalamic tract (sensory and motor).

In favor of post- infectious autoimmunity, a European group recently identified the human leucocyte antigen (HLA) subtype DQB1*02 as possibly being associated with the disease [7,8]. In our case we were able to detect this (HLA) subtype DQB1*02.

However, there is no definitive proof for it, since there are no studies that found that correlation [9,10]. Even though 98% of the cases are sporadic, there are also reports of familiar cases with multiple cases of KLS. Homozygous twins do show the syndrome after a case of flu and HLA research found the presence of the alleles DQB1*0302/0601 and DRB1*0407/1502, strengthening the hypothesis of an immunologic etiology and genetically associated [11].

Although Kleine -Levin syndrome is classified as a sleep disorder, the findings in polysomnography sleep studies are often difficult to interpret and are affected by whether sleep is monitored for 1 night or during24-hourperiod, at the beginning or at the end of an episode, and during the first or a later episode. In 18 patients monitored for 24 hours during episodes, the total sleep duration recorded was around 11-12 hour. Multiple sleep latency tests are difficult to be done in patients with Kleine-Levin syndrome during the episode, but it might show a narcolepsy like pattern. In our case his MSLTresult showed some features of narcolepsy.

Most patients with KLS used to demonstrate high level of body mass index (BMI) due to elevated blood levels of leptin which was not applicable to our case.

There is no definitive treatment for KLS, although some aspects of the disease can be managed with medication, such as stimulants (modafinil and methylphenidate). lithium and carbamazepine have been used for some cases successfully, however using these drugs might unmask episode -related psychiatric and behavioral symptoms by waking up the patient and do not improve cognitive abnormalities. Most patients benefit from reassurance, maintenance of simple hygiene routine and management at home [(5)]. Our patient showed significant improvement after starting modafinil for him.

Conclusion

KLS is a rare sleep disorder with a lot of psychiatric symptoms that can be wrongly diagnosed as neurological or psychiatric illness. The framework of core symptoms of hypersomnia, slowed cognitive functions, apathy and derealization should supersede the previously recognized hypersomnia-hyperphagia- hypersexuality triad. Hence, it is important for clinicians to have high index of suspicion on such atypical presentations.

There is no definitive treatment for KLS, however some cases showed clinical improvement with some medications.

The prognosis of KLS is considered to be good with spontaneous remission in most of the cases in later years.

Potential research directions are to explore infectious, autoimmune, metabolic and genetic causes**.**

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