Case Report

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Missing the Diagnosis in a Young Woman with Repeated Hospital Admissions: A Case Report

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ABSTRACT:

Missing the diagnosis in a young woman with repeated hospital admissions: a case report

Kleine-Levin syndrome (KLS) is a rare sleep disorder characterized by various symptoms, such as recurrent episodes of hypersomnia, cognitive abnormalities, psychiatric symptoms, hyperphagia, and behavioral disturbances, and is often confused with other diseases. To date, a number of classic cases of KLS have been identified worldwide; however, incomplete forms of KLS without hyperphagia have rarely been reported. Here, we report a case of a repeatedly hospitalized 24-year-old woman who suffered from psychiatric symptoms, abnormal behaviors, cognitive abnormalities, and recurrent episodes of hypersomnia for eight years. During this period, she was admitted three times, and different diagnoses were considered because the symptoms differed each time. In view of the recurrent episodes of hypersomnia, we monitored the patient using polysomnography (PSG). Carbamazepine and methylphenidate extended-release tablets were used to treat the patient, and beneficial effects were observed. Therefore, when a patient presents with recurrent episodes of hypersomnia, particularly those lasting approximately 20 hours per day, we suggest that psychiatrists should the possibility of KLS.

Keywords: recurrent hypersomnia, Kleine-Levin syndrome, polysomnography

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INTRODUCTION

Kleine-Levin syndrome (KLS) is a rare sleep disorder characterized by recurrent episodes of hypersomnia associated with various symptoms, such as cognitive abnormalities, psychiatric symptoms, hyperphagia, and behavioral disturbances[1,2]. The etiology of KLS still remains unclear[3]. Upper respiratory tract infections[4-6], head injure[7-9], seizures[10], and autoimmune process[11,12] may be the underlying pathophysiology. Due to the different kinds of symptoms and no objective laboratory tests, neuropathological or imaging alterations can be identified, KLS, especially the atypical and incomplete form is often misdiagnosed as psychiatric or neurological disorders, such as depression, bipolar disorder, schizophrenia, and seizure disorders[11,13]. The demographic features indicated that KLS most commonly occurs in adolescent, especially

male[6,13,14]. Whereas, the cases of KLS in females have rarely been reported[15,16]. In this report, we present a KLS in a young woman with repeated admissions due to psychiatric and recurrent sleep problems.

CASE REPORT

In July 2012, a 24-year-old woman was admitted to our center for the third time. She was first admitted eight years ago with personality changes and decreased activity. In her recent visit, she behaved more oddly and was more sluggish than she was at previous visits; additionally, she was lethargic, and generally apathetic. She reported that she stayed at home and did not attend school. She felt confusion at times and was unable to relate to her surroundings. Furthermore, she was not concerned with personal hygiene. She reported increased sleepiness that lasted for one to two days (average sleeping time,18-20 hours/day). Her appetite was unchanged. These symptoms lasted for two months. Her vital signs were stable and her weight and BMI were 51 kg and 18.51 kg/m^2, respectively. Organic etiology was excluded. She was diagnosed with schizophrenia and prescribed risperidone with a maximum dosage of 6 mg per day for one and a half months. However, the patient did not respond. After being discharged from the hospital, she did not take any medicine. She presented with the same symptoms, but was able to function normally at times.

Six years ago, she was admitted for the second time. She presented with behaviors of loss of interest, apathy, hopelessness, and suicidal ideation. She also exhibited irritability and aggression towards her parents for a specific period of time. She preferred to sleep all day (average sleep time, 20-22 hours/day) for periods of two to three days. Neither hyperphagia nor hypophagia were present and her sexual interest level was unchanged. These symptoms persisted for six months. Her vital signs were stable and her weight and BMI were 52 kg and 18.87 kg/m^2, respectively. Organic etiologies were also excluded. We used the Mood Disorder Scale to exclude bipolar disorder, so she was diagnosed with major depressive disorder, and was prescribed sertraline with a maximum dosage of 150 mg per day for two months; however, she did not respond to the drug treatment. After being discharged from the hospital, the symptoms continued to recur in episodes.

One year prior, before her third admission, she began to work, but performed poorly in social activities, was constantly late for work, and slept during work. Her average sleep time was 19-21 hours per day for periods of three to four days. She did not want to perform tasks or talk to colleagues. Furthermore, she felt hopeless and did not want to participate in activities, but functioned normally when she was completely awake. She did not exhibit hyperphagia or hypophagia, and showed no signs of hypersexuality. She was administered various antipsychotics including paliperidone, ziprasidone, and olanzapine in other hospital outpatient clinics. On her third admission, her vital signs were stable and focal neurological signs were excluded. Routine blood and urine tests, blood glucose, and liver and renal functions were within normal limits. Her endocrine tests, electrocardiogram, electroencephalogram, cerebrospinal fluid (pressure, appearance, cells, proteins, glucose, chloride, and immunoglobulin), and brain MRI were also normal. Her weight and BMI were 51 kg and 18.51 kg/m^2, respectively. She and her parents denied any abuse of alcohol or illicit substances. However, her mother recalled that the patient had suffered a moderate cough, sneezing, and nasal discharge one week before her first illness. Her family history was negative for psychosis. In view of the recurrent episodes of hypersomnia over a period of eight years, we monitored her polysomnography (PSG) (Figure 1) for one night after five days of withdrawal from medications. Sleep data were collected and scored using the Alice 5 Diagnostic Sleep System (Philips Respironics, Bend, OR, USA). A clinical diagnosis of an incomplete form of Kleine-Levin syndrome (KLS) was considered because of the symptoms of recurrent episodes of hypersomnia lasting eight years, which were associated with features of

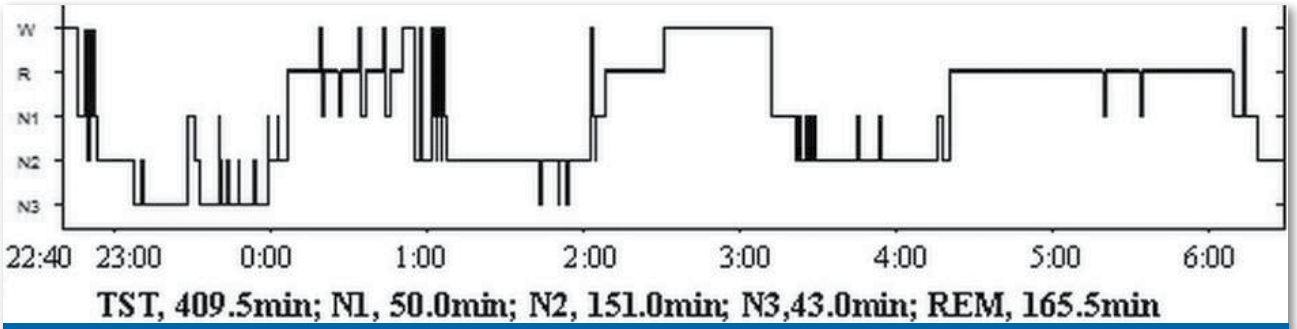

Figure 1: Sleep study or polysomnogram (PSG). The polysomnography for one night obtained five days after withdrawal of medication, shows the consistency was poor, the efficiency reduced and the structure fragemented, including an increase in non-rapid eye movement stage one (N1, 12.2%; normalpercentage, 5%) a decrease in non-rapid eye movement stages two (N2, 36.9%; normal percentage, 50%) and three (N3, 10.5%; normal percentage, 20%), and an increase in rapid eye movement (40.42%; normal percentage, 25%).
TST, total sleep time; W, wake; REM, rapid eye movement; N1, Non-rapid eye movement stage one; N2, Non-rapid eye movement stage two; N3, Non-rapid eye movement stage three.

psychiatric symptoms, cognitive abnormalities, and abnormal behaviors including manner of apathy, nonsense talking, sluggish, and not cared about personal hygiene without hyperphagia and hypersexuality, and interspersed with periods of normal sleep, cognition, behavior, combined with the characteristics of the PSG (see Figure 1). After the PSG and clinical diagnosis of KLS, carbamazepine (100 mg three times daily) and methylphenidate extended-release tablets (18 mg per day) had been used for the treatment. This single case report study was conducted in accordance with the declaration of Helsinki and was conducted with approval from the Ethics Committee of West China Hospital, Sichuan University. Written informed consent was obtained from the patient.

DISCUSSION

KLS is a sleep disorder characterized by recurrent episodes of hypersomnia, and the patient should have at least one of its associated features: (1) cognitive abnormalities, such as a feeling of unreality, confusion, or hallucinations; (2) abnormal behavior, such as irritability, aggression, or odd behaviors; (3) hyperphagia, and (4) hypersexuality[1].The diagnosis of KLS is very difficult because no specific examination method has been established, and it has always depended on clinical symptoms[12]. Thus, KLS, especially the atypical and incomplete form, is consistently confused with other diseases owing to its clinical complexity[3,17].

For eight years, KLS was not considered as a diagnosis for our patient, and this may be attributed to several factors. First, this case involved a young woman, and demographic analyses have suggested that the majority of KLS patients are adolescent males[6]. Second, although she had an increased sleep time, the predominant clinical symptoms and main complaints during her three admissions were psychiatric manifestations, such as feelings of confusion, personality changes, decreased activity, and depressive feelings. Third, she did not suffer from hyperphagia or hypersexuality. These findings led the psychiatrist to focus more on various psychiatric symptoms and neglect the sleeping problems or fail to consider them as psychiatric symptoms. Although no specific examination for KLS has been established, research on sleep study or polysomnogram (PSG) has indicated a low sleep efficiency during attacks, a decreased duration of slow-wave sleep, sleep onset REM periods, reduced REM sleep near the end of sleep, and sleep fragmentation[18]. The PSG features of this patient were mostly consistent with those of previous reports[6], except the REM stage was increased. Studies have indicated that antipsychotics may increase REM sleep[19,20]. In a previous PSG study of patients with KLS, all participants met the criteria for antipsychotic use absence before PSG recording[17]. Although there

was a five-day withdrawal period for the different kinds of antipsychotics administered in other hospitals including paliperidone, ziprasidone and olanzapine) in our patient, the long-term influence of these drugs on PSG cannot be excluded. Additionally, one study found that atypical KLS with reduced REM only represented 7.5% of cases[17]. Therefore, the KLS symptoms may also affect the PSG results. PSG in KLS needs to be studied further.

KLS may be triggered by several factors, such as infection, fever, head trauma, sleep deprivation, stress, menstruation, and hypothalamic dysfunction[6,18,21,22]. Studies have shown that infection or fever can disrupt blood-brain barrier function and that they are associated with increased catabolism. These non-specific factors might enhance the accumulation of toxic aminoacids or proteins in metabolic pathways with partially deficient enzyme activity[3,6]. Therefore, the pathophysiology of this patient may be due to upper respiratory tract infections.

To date, no definitive treatment for KLS is available. However, stimulants, anticonvulsants, and mood stabilizers can be beneficial[3,7,23,24]. For this patient, an anticonvulsant combined with a stimulant was effective. In the three-month follow-up period, no episodes of hypersomnia were observed, and the psychiatric symptoms disappeared.

Based on this case, we suggest that if a good response is not achieved with antipsychotics or antidepressants in patients with symptoms associated with increased sleep, especially sleep lasting for approximately[20] hours per day, psychiatrists must consider the possibility of KLS. Furthermore, changes in PSG records should be carefully reviewed to suggest KLS.

The results reported in this study should be considered in light of certain limitations. Firstly, the patient had been followed-up only for three months, therefore, further research is needed to elucidate the definite treatment, prevention, and management during each episode. Secondly, although five-day withdrawal period for the medications had been applied in the patient, the long-term effect of the antipsychotics on PSG cannot be excluded. So, PSG studies should be considered in time before the medications administered in the patient suffered from obvious sleep disturbance.

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