CASE REPORT

Preventive Effect of Lithium on "Kleine–Levin Syndrome"

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Abstract

Kleine–Levin syndrome (KLS) is a rare sleep disorder characterized by periodic excessive sleepiness, hyperphagia, hypersexuality, and varying degrees of cognitive and behavioral disturbances. Here, we report a typical case of Kleine–Levin syndrome associated with deterioration of academic performance because of excessive sleepiness. He was started on modafinil and lithium, to which he showed good response.

Keywords: Hyperphagia, Hypersexuality, Hypersomnia, Kleine–Levin syndrome, Lithium, Sleeping beauty.

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Background

Kleine–Levin syndrome is called sleeping beauty syndrome. Symptoms of KLS are periodic hypersomnia, hyperphagia, and hypersexuality, and it is associated with cognitive and behavioral disturbances. Willi kleine, a German psychiatrist, reported series of cases of periodic somnolence in 1925[1]; and Max Levin[2] described morbid hunger associated with periodic somnolence; then, this sleep disorder was named KLS by critchley in 1962.[3] Researchers said that during an attack, many patients reported amnesia of the episode, and in a few cases, they found that academic performance is being deteriorated with a mild and long-lasting memory dysfunction, which occurs between episodes. KLS is a rare and complex neurological sleep disorder associated with psychiatric symptoms, so it is also called a neuropsychiatric disorder. The episodes of KLS are cyclical, and symptoms last for days, weeks, or even months; during that time, all normal daily activities are stopped so that the affected persons are not able to attend work, school, or not able to care for themselves. Most of the patients are bedridden, not communicative, even when awake they look tired. The disorder is rarely noticed in females.[4] It affects adolescent males, usually around the age of 16 years to the late teens. Although there have been cases in females and older men, males to be affected three times as often as females, but on average, women had a longer disease course than men.

Case Description

A 20 -year-old single male, student of 11th standard, belonging to a low socioeconomic group, presented to our psychiatric outpatient clinic with a history of excessive sleep episodes, loss of interest in studies, irritability, low mood, voracious hunger, and sexual disinhibitions such as pubic masturbation, singing obscene songs loudly at home, and touching without their consent. The onset was acute, without any precipitating factors, and the course was episodic with an average of 7–10 days of an episode every month that lasts for 5 months.

He was found to be sleeping more than usual with an average of 14–16 hours a day. It was difficult to wake him up while he was sleeping; he woke up from his bed with disturbed behavior such as irritability, anger outburst, and confused. It was associated with hyperphagia, and he would eat unusually more quantities of food. Initially, his weight was 68 kg; later, it increased up to 71 kg due to excessive eating. There was no positive past or family history of meningitis, head injury, and epilepsy. There was no history of drug abuse. His routine laboratory investigations were normal, which showed complete blood cell count: white blood cells (WBCs) 5380/µL, red blood cells (RBCs) 4520/µL, platelets 180000 µ/L, lymphocytes 2800/µL; serum electrolytes: sodium 144 mmol/L, potassium 3.78 mmol/L, chloride 104 mmol/L; liver function test: alanine transaminase 48 µ/L, aspartate transaminase 46.30 µ/L, bilirubin total 8.50 µmol/L, bilirubin direct 3.50 µmol/L; renal function test: creatinine level 83 µmol/L and blood urea nitrogen 4.40 mmol/L; and endocrine evaluation: serum prolactin level 350 µ/L, free thyroxine (FT4) 13 pmol/L, free triiodothyronine (FT3) 6.02 pmol/L, thyroid-stimulating hormone (TSH) 2.748 µ/L; and radiological parameters unremarkable. The electroencephalogram was done, which is normal. A complete neurological and medical examination was done, which showed no significant findings. The patient was diagnosed clinically with a case of Kleine–Levin syndrome. The genetic screening was not done because this facility is not available at our hospital. He was put on modafinil 100 mg oral daily dose for 30 days but no satisfactory result was seen so he has switched to lithium 400 mg twice a day. The patient was reviewed on follow-up after 1 month, and his symptoms decreased but were not up to the mark. On the second follow-up after 2 months, the patient started to show good response with lithium, and we found that he was maintaining well with no episodes of excessive somnolence. Also, he showed improvement in academic performance as well as decreased his hypersexuality.

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Discussion

This article is associated with the neuropsychiatric disorder, because the patient had symptoms of excessive sleep, which is the most prominent symptom reported during each of the episodes, and behavioral disturbances are noted such as anger outbursts, irritability, and academic performance decline, along with sexual disinhibition and excessive eating. Based on this, we diagnosed a case of Kleine–Levin syndrome. KLS is easily misdiagnosed as a personality disorder or major mental illness; therefore, it is important to have a high suspicion, in any case, presenting with complaints of episodic hypersomnolence and after ruling out differential diagnosis like Kluver–Bucy syndrome, atypical depression, and substance abuse. Even though there are no definitive guidelines for treatment, lithium and modafinil have been tried in our patients for short period for symptomatic treatment and prevention of relapse, and we got dramatic and preventive effects with no recurrence of symptoms. Lithium is also useful in cluster headache and bipolar disorder. Maintenance of lithium shortens the mean duration of episodes, with no severe side effects being observed in our patient. In high-frequency episodes of KLS and severe behavioral changes, lithium may become a treatment option, so lithium should without a doubt be tried as a therapeutic and preventive option for KLS.

The etiology and pathophysiology of KLS are unknown, but certain factors can increase the risk for this condition such as genetic predisposition, hypothalamic dysfunction, an infection like flu, and autoimmune disease.[5] In some cases, it has been reported that abnormalities or imbalance is seen in serotonin and dopamine metabolism.[6] KLS may be associated with an injury in the hypothalamus; the symptoms may be related to malfunction of the hypothalamus that governs sleep, appetite, and sexual behaviors.

This disorder should be differentiated from narcolepsy and sleep apnea hypersomnia syndrome. In patients with KLS, hypersomnia occurs for 18 hours a day, and it ranges from 3 days to 3 weeks and manifests at least once a year.[7] The course of this disorder is variable with remissions and recurrences, which could last for years. The researchers said that KLS is more commonly caused by stress, physical exhaustion, travels, brain trauma, and surgeries with local or general anesthesia, lactation, alcohol abuse, sleep deprivation, menstruation, an infection, and the use of drugs.[7] Some patients present with headaches, orthostatic hypotension, fainting episodes, peripheral vascular complaints of Raynaud's phenomenon, and rarely, hypnagogic hallucinations, and sleep paralysis. The patient may also associate with intense dreams and nightmares; if he got up from the bed, he may become aggressive and irritated. Hypersexuality is more frequent among men.

There are no definitive management guidelines. Various medications have been used during episodes in many case reports, and it has been found that none of them have been subject to randomized controlled trials. Prevention of subsequent episodes is said to be achieved with lithium,[8] valproate,[9] carbamazepine, or antidepressants, as moclobemide and tricyclics. Lithium is the only drug that appears to have a preventive effect, and its response rate is 41%. In some case reports, it has been shown that a good response occurs with lithium. When the drug was withdrawn, recurrence of symptoms occurs, and when lithium was reintroduced, they recovered again. It is not known if other mood stabilizers have an effect on the condition and response to treatment has often been limited. Anti-depressants do not prevent a recurrence.

Conclusion

This case report throws light on Kleine–Levin syndrome, which is supposed to be a rare, but not uncommon disorder, and due to deficit research data available, it is more likely to cause unfit and misleading diagnosis. KLS is known for more than a century, with well-defined clinical features. Because of the rarity of the disorder, it is unclear and not able to identify underlying biological cause or treatment.

Clinical Significance

For physicians, they need to be vigilant and to have high index suspicion mainly for a typical presentation to avoid delay in diagnosis or making the improper diagnosis. In the future, we need to focus on further research on genetic etiology and management of this disorder.

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