Successful Long-term Management of a Child with Kleine-Levin Syndrome with Low-dose Lithium

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ABSTRACT
Kleine-Levin syndrome (KLS) is a rare disorder characterized by episodic hypersomnia along with cognitive and behavioral disturbances (i.e., hyperphagia and hypersexuality). It is commonly seen in a young male. Not much is known about its long-term management; however, many reports suggest the usefulness of anticonvulsants and lithium for the same. We hereby report a case of childhood KLS from India who was successfully treated with low-dose lithium and discuss the relevant literature.

Key words: Hypersomnia, Kleine-Levin syndrome, lithium

INTRODUCTION
Kleine-Levin syndrome (KLS) is a rare disorder characterized by recurrent hypersomnia associated with hypersexuality, compulsive eating, and cognitive disturbances. It is generally considered a rare disease, and data on its prevalence are almost nonexistent. Due to the scarcity of available literature, the management of this patient is often based on case reports and case series. There are only few cases reported from India. We report a classic case of KLS in a child with a good response to low-dose lithium.

CASE REPORT
Master T, a 10-year-old child, studying in 6th class and belonging to Hindu nuclear family, was brought to our outpatient department (OPD) with the illness of 5-month duration with as episodic course. His illness started after he developed a high-grade fever along with cough with expectoration and chest pain. It lasted for 3–4 days and responded to oral antibiotics. However, after 5–6 days of starting these symptoms, family members noticed a change in his behavior. He would seem to be restless and would keep pacing inside the home. He was found to be sleeping more than his usual self (12–15 h in total). He would fall asleep while talking to family members during daytime, unlike his previous self. On occasions, he would deny identifying his mother. He was also seen crying incessantly during daytimes. His food intake doubled, and he started demanding foods such as ice-cream and chocolates more frequently. He would seem to be in a hurry while eating food (subjective excessive hunger reported...
to mother frequently). He even tried to bite mobile phone (no reason stated). He stopped going to school stating his inability to concentrate within 2 days of onset of symptoms. He remained unusually quiet for 1–2 h 2–3 times a day and would not respond even when directly spoken to. He repeated the same sentence multiple times on being asked something. He remained completely normal in between for some hours; however, he would not be able to recollect any behavioral problem during this time. Such symptoms lasted for 10–12 days. Thereafter he became his premorbid self except amnesia for the entire illness period, irritability, and stubborn behavior along with anger outbursts in more than usual frequency.

After 3 months, the patient developed cellulitis around his shoulder because of injuries he sustained during a brawl with his classmate. He again had a high-grade fever. He was admitted to a private hospital. On the 5th day of admission, he suddenly became fearful stating that someone is trying to kidnap him. It lasted for 10–15 min, during which he was pointing to the wall as if someone was standing there. Although he was discharged after 2 days of this episode, his previous symptoms of hypersomnia, hyperphagia, excessive crying, irritability, impaired speech, running around, and inability to concentrate reemerged. Furthermore, a new set of symptoms emerged. He would be found rubbing his genital in front of his mother and sister. This would occur 10–15 times a day, unlike his previous self. He would continue to do so despite repeated warnings given by his parents. He also kept going to the bathroom repeatedly with an excuse to urinate but would be found rubbing his genitals instead. His self-care was impaired. There was neither history of disorientation to time/place/person nor history of depressive or anxiety symptoms during this time. There was no history or family history of any major medical or psychiatric illness. He was subsequently brought to our OPD for further management and was admitted in child psychiatry ward.

On examination, the patient’s general physical and systemic examinations were normal. Mental status examination revealed decreased attention concentration and decreased speech output. A provisional diagnosis of KLS was kept. Routine investigations (complete blood counts, liver and renal function tests, urine routine and microscopy, and chest X-ray), electroencephalography (EEG), thyroid profile, and magnetic resonance imaging (MRI) brain were performed to rule out the possible organic cause, all of which were found to be normal. The patient was started on low-dose lithium, and sulfur–lithium range was decided to be kept at 0.40–0.50 mEq/L. He responded to treatment and was discharged after 2 weeks with complete remission of his symptoms. The patient was stabilized on 450 mg of lithium/day in divided doses. The patient continued to follow-up monthly. Regular serum lithium monitoring was done on OPD basis which ranged between 0.35 and 0.50 mEq/L. The patient is under follow-up till date (i.e., 2 years after discharge) and has been maintaining well. He has no further episodes despite suffering from viral/bacterial infections on 2–3 occasions during this period.

**DISCUSSION**

KLS is a rare neuropsychiatric disease with the first description almost 80 years ago.[2,3] However, the recent data suggest that it is more prevalent than generally thought. A study recruited more than 100 new cases sequentially in a single year which was comparable with the bulk of previously reported cases.[4]

The previous reports suggest that apart from hypersomnia, these patients exhibit many other symptoms including cognitive dysfunction, eating disorders, disinhibition, and altered perception/derealization. According to the International Classification of Sleep Disorders-3 criteria, there must be at least two episodes of hypersomnia with an episodic course to make a diagnosis of KLS.[1] Our patient exhibited two episodes of such hypersomnia along with hyperphagia, hypersexuality, irritability, decreased attention and concentration, mutism, and altered perception. A study done in a sample of 108 patients with KLS suggests that apart from hypersomnia, cognitive impairment and altered perception are seen in 100% of patients with KLS.[4] However, the specific symptoms (frequency) are hyperphagia (66%), hypersexuality (53%), irritability (65%), and memory impairment (66%). KLS patients show preference to sweet foods as also seen in this case.[4] One interesting finding was of hypersexuality despite the fact that the patient had not reached puberty yet. However, the hormonal analysis was not performed in our case to look for the potential hormonal cause of hypersexuality, unlike the previously published cases. There are cases in literature that suggest that patients masturbate even “to the point of bleeding.” Another important difference between previous reports and our case is the presence of a continued behavioral change in the form of irritability and anger outbursts between the episodes.

Although etiology of KLS is largely unknown, underlying hypothalamic pathology is suggested. The hypothalamus has a role in sleep, appetite, and sexual behaviors. Some reports suggest generalized EEG slowing and hypoperfusion in areas such as the hypothalamus and frontal lobe.[5] However, all investigations including EEG and MRI brain were
found to be normal in our case. Viral and autoimmune etiology has also been suggested, which is evident in our case too by the presence of infection before the illness onset in both episodes.

The most important issue is the treatment of such cases. There is little literature on the acute treatment as well as long-term maintenance of these patients. The most effective treatment suggested in various case reports is lithium. Lithium is the only drug with a higher response rate as compared to medical abstention. However, a recent report of 108 patients suggested its effectiveness in only 24% of cases.\(^4\) Although our patient did not experience any major side effect despite using lithium for long term with good response, the evidence for this practice is small. One systematic review of 186 cases of KLS reported the use of lithium in only 29 cases, out of which 12 had no more relapses.\(^6\) Although few cases suggest benefit of stimulants in KLS patients, this benefit is limited to sleep symptoms with not much effectiveness for other cognitive and behavioral symptoms. Other mood stabilizers and antidepressants are less effective.

There are very few published reports of KLS from India. One such case of an adolescent male with KLS did not respond to lithium despite the blood levels to be as high as 0.8 mEq/L, unlike our case.\(^7\) The patient responded well to the treatment with valproate which was then continued for 5 years. Few other Indian cases also responded well to the treatment.\(^8\)

Not much is known about the long-term course of the illness. One study reported a median duration of illness of 4–8 years while median duration of the episode is 10 days. Male sex, early childhood onset, and symptoms such as hypersexuality have been suggested to be associated with longer duration of illness and poor prognosis.\(^4\) However, in our case, the patient did not have any further episode for 2 years despite having these poor predictors present.

In conclusion, lithium monotherapy in a low dose could be an effective treatment in patients with KLS (especially children). However, there is a need for long-term follow-up studies in patients with KLS to provide more data on maintenance treatment of these patients.

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**Conflicts of interest**
There are no conflicts of interest.

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