Diagnostic dilemma of Kleine–Levin Syndrome Mimicking Bipolar Depression: Case Report and Five-Year Follow-up

To the Editor,

Kleine–Levin syndrome (KLS) is a rare disorder characterized by recurrent hypersomnia, hyperphagia, cognitive disturbances, and hypersexuality that predominantly affects adolescent males.[1] The role of the hypothalamus in regulating sleep, appetite, and sexual behaviors suggests an underlying hypothalamic pathology.[2] The periods of somnolence and hyperphagia can mimic severe depression. A brief period of high energy following these episodes may be mistaken for mania.[3]

Lithium has been proposed as a treatment for KLS, with 36.6% of patients becoming episode-free.[4] However, the time frame in which individual symptoms respond is unknown. This case report tries to fill this gap. The patient's informed consent was taken for publication.

Case Report

A 24-year-old male was referred to our outpatient department with the diagnosis of resistant bipolar depression with mixed features. He had episodes (each lasting 2–3 weeks, 3–4 episodes per year) of mood swings, excessive sleep (18–20 hours a day), voracious appetite, and hypersexuality for two years. Each episode started abruptly; he would sleep for 18–20 hours, wake up to void and overeat, and get physically aggressive if his sleep was interrupted. He got sexually promiscuous and masturbated 4–5 times per day while watching porn. His mood fluctuated, and he could be depressed, irritable, or angry. During the episode, he had trouble reading, writing, doing simple calculations, and remembering. After the end of the episodes, his mood was elated for 1–2 days, with decreased sleep, before becoming normal. In between the episodes, he had normal functioning.

He had shown no response to the olanzapine–fluoxetine combination, risperidone, valproate, lamotrigine, or lurasidone. Modafinil and methylphenidate decreased sleep duration during the episode but made him angry and violent towards others and were discontinued.

TABLE 1.

Response of Lithium on Different Symptoms of KLS.

Year of Lithium Treatment	Frequency/Duration of Sleep Episode	Hyperphagia	Hypersexuality/Mood Swings/Angry Outburst/ Depression
1st year	No change	No change during the episode	Improved
2nd year	Two episodes in a year, no change in duration of each episode	No change during the episode	Improved
3rd year	One episode of ten days duration	Improved compared to the past	Improved
4th year	No more episodes	No more episodes	No more episodes
5th year	No more episodes	No more episodes	No more episodes

The differential diagnoses included metabolic and endocrine abnormality, encephalopathy, narcolepsy, temporal lobe epilepsy, and KLS. Systemic and neurological examinations and routine biochemical and endocrine parameters were within normal range. Electrocardiogram, electroencephalography, and magnetic resonance imaging of brain revealed no abnormalities. Sleep study and multiple sleep latency test were done in the interepisodic period; however, they did not reveal any gross abnormality of sleep architecture, obstructive sleep apnea, or narcolepsy. There was no past or family history of psychiatric illness or drug abuse.

Based on the clinical presentation, normal systemic and neurological examinations, and absence of investigation findings, the patient was diagnosed with KLS based on the International Classification of Sleep Disorder criteria.[5] He was started on lithium, with serum level maintained at 0.6–0.8 mEq/L, and followed up for the next five years. There was a dramatic improvement in the behavioral symptoms. In the next episode, he did not report any mood swings or hypersexuality. However, the decrease in the frequency and duration of the episodes of hypersomnia was slow. The patient became asymptomatic in the fourth year of starting lithium (**Table 1**). No adverse effect was noted.

Discussion

Recurrent hypersomnia is also seen in endocrine and metabolic disorders, depressive disorders, and nonconvulsive status epilepticus.[6] Although hyperphagia and hypersomnia can occur in a depressive state, the clinical triad of hypersomnia, hyperphagia, and behavioral disturbances (including sexual disinhibition) is characteristic of KLS. Also, hypersomnia of ≥18 hours is rarely seen even in the most severe depression. KLS has a benign clinical course, with spontaneous resolution of symptoms. Its diagnosis is based on clinical features, and no specific diagnostic laboratory tests are available.[2]

KLS and bipolar disorder (BD) both have episodic nature, chronic recurrent course, shared symptomatology, and are idiopathic. In addition, immune-mediated inflammation, circadian disruptions, and genetic vulnerability in the form of *TRANK1* region polymorphism are also shared between the two disorders.[3,7] Similar cases to ours have been reported in literature where KLS was misdiagnosed as BD.[3] Our case re-emphasizes the need for KLS to be included in the differential diagnosis of BD. Interestingly, in our patient, lithium was not prescribed for BD.

Evidence of the efficacy of a specific pharmacotherapy is still scarce in KLS. However, several possible treatments have been proposed (e.g., amphetamines for treating the episodes and lithium for prophylaxis of recurrences).[8]

In our case, lithium dramatically improved mood swings and hypersexuality, but the effect on the duration and frequency of sleep and hyperphagia was late in onset. Hypersomnia and hyperphagia may be slow to resolve, underscoring the need to continue lithium for at least two years to see any response. Early response of the behavioral component of KLS with lithium may predict future response to the hypersomnia–hyperphagia domain. However,

the possibility of spontaneous resolution of KLS could not be ruled out. Further study is needed to clarify this.

Conclusion

KLS is often misdiagnosed as BD, so it should be considered in its differential diagnosis. Lithium has been shown to improve the outcome. However, different symptom domains of KLS may respond differently, with an early response seen in the behavioral domain.

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Allergic Cutaneous Drug Eruptions with Quetiapine: A Case Study

To the Editor,

Multiple psychotropic medications (mood stabilizers, antipsychotic drugs, benzodiazepines) are often prescribed to patients with bipolar affective disorder with severe and difficult-to-treat mood episodes. The use of medications in higher doses and in combination is associated with adverse drug reactions. Cutaneous eruptions are not uncommon with certain psychotropic medications. Here, we report a rare cutaneous adverse drug reaction associated with quetiapine dose increment in a young male with bipolar affective disorder.

A 22-year-old man with heavy built (weight 92 kg and height 185 cm; body mass index: 26.88) with bipolar affective disorder developed fever followed by generalized bullous eruptions after two days of increment of quetiapine dose (from 600mg/day to 800 mg/day), which were not there at the time of quetiapine initiation. The patient had developed similar (in their morphology and distribution) drug eruptions with chlorpromazine (1000 mg/day) and clozapine (150 mg/day), given previously to treat the same episode, both of which were discontinued due to the development of the eruptions (before initiation of quetiapine, two weeks back). The patient was initiated on quetiapine since skin eruption is a very rare side effect of this medication.[1] He was also taking sodium valproate as a mood stabilizer at a dose of 2000 mg/day and lorazepam 4 mg/day. Opinion was taken from dermatology and medicine departments to evaluate the causes of fever and cutaneous eruptions. The patient was investigated with liver function and kidney function tests and complete blood counts. All the investigations were within normal limits except for a marginal increase in eosinophil percentage (7%).

The lesions were characterized by circular, discrete, bullous eruptions surrounded by erythema (**Figure 1**). The erosive lesions had a well-defined border surrounded by ill-defined hyperpigmentation after rupturing of the bulla. The lesions were mostly distributed over the trunk and the extremities (both flexure and extensor surfaces) and were itchy; however, they were not photosensitive.