

# Case Report

## Sleeping Beauty Syndrome: A Case Report and Review of Female Cases Reported from India

Naresh Nebhinani, Navratan Suthar

### ABSTRACT

Kleine–Levin syndrome (KLS), also called “Sleeping beauty syndrome” is a rare, disorder predominantly reported in adolescent males, characterized by recurrent episodes of hypersomnia and to various degrees, hyperphagia, cognitive disturbances, and hypersexuality. Here, we are reporting a case of a middle-aged female, with 16 years delay in diagnosing KLS, poor response to most of the psychotropics, except good response to a combination of lithium, sertraline, and modafinil for last 12 months and also reviewing other female cases with KLS reported from India.

**Key words:** India, Kleine–Levin syndrome, Kleine–Levin syndrome in female, lithium, sleeping beauty syndrome

### INTRODUCTION

Kleine–Levin syndrome (KLS), also called “Sleeping beauty syndrome” is a rare disorder characterized by recurrent episodes of hypersomnia and to various degrees, hyperphagia, cognitive disturbances, and hypersexuality. The disease predominantly affects adolescent males although females have a longer disease course than males.<sup>[1]</sup> Over the years with raising awareness, KLS is reported more frequently in scientific literature.

Here, we are reporting a case of a middle-aged female, with 16 years delay in diagnosing KLS, with poor response to most of the psychotropics, except good response to a combination of lithium, sertraline, and modafinil for last 12 months. For clinicians’ awareness and better therapeutic decisions, we want to highlight

issues related to delay in diagnosing KLS, diagnostic workup, and management difficulties. We are also reviewing other female cases reported from India.

### CASE REPORT

Mrs. X, a 43-year-old married female, homemaker, educated up to 8<sup>th</sup> standard, presented in our outpatient psychiatric clinic in November 2014 with hypersomnolence, body aches, fatigue and off and on low mood. According to her husband, “she was feeling drawn toward her bed,” or “reluctant to get up in the morning.” Although patient remained arousable, patient was irritable and aggressive whenever prevented from sleep. The need for sleep was so intense that once she was found sleeping on the floor near the bathroom.

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She used to sleep 20–22 h with an irresistible urge for sleep. During awake state, she would appear apathetic, sad and having minimal interaction with others. Her speech would remain slurred with low in tone and volume or sometimes even not understandable. During the episode, her daily activities, household chores, food habits, personal care, and interpersonal relationship would disturb significantly, and she used to demand spicy food such as kachori, namkeen, and specific vegetables, unlike her premorbid self.

On detailed evaluation of illness characteristics and course, they reported that at the age of 27 years, after the birth of her daughter (2<sup>nd</sup> child) in 1998, for the first time, she started sleeping for 20–22 h with significant disturbance in her overall functioning, activities of daily living, and interpersonal relationship. The total duration of her illness was 16 years, with episodic course of similar presentation as mentioned above. Duration of each episode was from 2 to 15 days, with complete remission for 15 days to 4 months in between the episodes. Her general, systemic and neurological examinations were unremarkable. Her routine biochemical and endocrine parameters were within normal range. Electrocardiogram, electroencephalography (EEG), magnetic resonance imaging (MRI) brain and magnetic resonance angiography were found to be normal. The patient did not cooperate for polysomnography.

In November 2014, during her first consultation at outpatient psychiatric clinic, diagnosis of KLS was made as per diagnostic criteria of International Classification of Sleep Disorders<sup>[2]</sup> after ruling out other possible causes of hypersomnias such as idiopathic hypersomnia (IH), menstrual-related hypersomnia, narcolepsy, Kluver–Bucey syndrome, hypersomnia due to medical condition, hypersomnia due to drug or substance.

As in differential diagnoses- IH is another condition characterized by onset during adolescence, with increased daytime sleepiness, sleep drunkenness.<sup>[2]</sup> Episodic course and presence of other features along with hypersomnia ruled out IH in the index case. Menstrual-related hypersomnia was excluded as our patient did not have the episodes in relation to menstrual cycle and the episodes lasted longer than a week. Narcolepsy was excluded because other obligatory criteria-cataplexy, hypnagogic or hypnopompic hallucinations, and sleep paralysis were absent in index case.<sup>[2]</sup> Kluver–Bucey syndrome was ruled out because of the absence of hyperorality and visual agnosia.<sup>[2]</sup> Brain and hypothalamic structural abnormality was ruled out by normal MRI brain.

It is noteworthy to mention the diagnostic delay of 16 years, as earlier she was labeled as depression

or conversion disorder at other centers, as patient presented with low mood, body aches, fatigue, hypersomnia. Atypical depression may also present with hypersomnia, hyperphagia. As disease mimics and shares psychiatric conditions in many ways, so there was a delay in the diagnosing KLS. Periodicity and poor response to medications (antidepressants, antipsychotics, and anxiolytics) raised suspicion on the previous diagnoses at our first consultation.

Initially, she had good response with tablet lithium carbonate 400 mg twice a day during her follow-up at our center, but due to recurrent hypersomnia, dose of lithium carbonate was gradually hiked to 900 mg and later 1200 mg (serum lithium level were 0.61 and 0.73 mmol/L, respectively). She had significant improvement but developed fine tremors and weakness hence lithium was reduced to 900 mg/day. However, due to reemergence of hypersomnia, we added tablet modafinil 100 mg. The patient reported improvement in duration and frequency of hypersomnolence episodes. For fatigue, reduced interaction, and off and on low mood, tablet sertraline 100 mg was added later. At present, she has been maintaining well for last 12 months, except 5–6 shorter periods of hypersomnia for 12–24 h.

## DISCUSSION

Index case is of worth reporting due to rarity of KLS especially in females, hence misdiagnosis is common, like diagnostic delay of 16 years in the index case. The original triad of hypersomnia plus hyperphagia plus hypersexuality is not mandatory for the diagnosis of KLS as it is present in only 45% patients, hence only hypersomnia is kept as an obligatory criterion. Index patient presented with hypersomnia with other atypical features but did not report hyperphagia and hypersexuality. Several psychotropics have been reported beneficial, but lithium is reported most effective as a widely used prophylactic agent.<sup>[3]</sup> Similarly, index patient reported significant improvement with lithium therapy.

In our electronic search, by PubMed and Google Scholar, we found 36 cases with KLS reported from India, of them 8 were females.<sup>[4-11]</sup> In 75% of cases, KLS onset occurred during the second decade or earlier. The first episode was preceded with fever in 50% of cases, while in others with postpartum psychosis, familial conflict and stress. Somnolence episodes lasted from 3 days to 25 days. Hyperphagia was present in 75%, and sexual disinhibition was reported in 50% of patients. Other symptoms were cognitive disturbances (confusion), behavioral abnormalities, irrelevant talk, apathy, derealization, and perceptual disturbances. All eight

cases were sporadic with no family history of similar illness. One patient had an abnormal EEG finding, and one patient had abnormal computed tomography finding, rest had no abnormality in routine tests and radiological investigations. Two patient out of 8 improved spontaneously without any medication, while rest were given lithium, modafinil, armodafinil, oxcarbazepine, methylamphetamine [Table 1]. Similar to earlier reported cases, index case had hypersomnolence episodes from 2 days to 15 days duration. Similar to the case reported by Mudgal *et al.*, index patient had KLS during postpartum period and had onset at a similar age (27 years).<sup>[8]</sup> Compared to reported female cases from India, index patient had somewhat difficult presentation in terms of onset of KLS at 27 years of age, frequent episodes of hypersomnolence of last 16 years, and so far have received several psychotropics, but still not achieved complete remission. She did not have hypersexuality but reported an increased craving for spicy food during episodes [Table 1].

Arnulf *et al.* in systematic review of 186 cases with KLS reported longer disease course in females, with comparable age of onset, episode frequency and duration, and lower frequency of hypersexuality than males.<sup>[1]</sup> Similarly, on comparing index case with reported male cases from India, we found significantly longer duration of illness in index case (16 years) compared to 1–4 years in male cases.<sup>[12]</sup> Index case had onset of KLS at 26 years of age whereas reported male cases had onset from 7 to 24 years of age.<sup>[12]</sup>

To conclude, KLS is a neurological disorder with a lot of psychiatric coloring, therefore, a case may present to a neurologist, physician, or psychiatrist depending on patients' awareness, feasibility, and predominant symptoms. Hence, it is important for clinicians to have high index of suspicion on such atypical presentations. Any case presenting with episodic hypersomnolence should be evaluated thoroughly with multidisciplinary approach for timely diagnosis and rational treatment.

**Table 1: Female cases with Kleine-Levin syndrome reported from India (including index case details)**

Author	Patient demography	Clinical characteristics (All had hypersomnolence)	Specific tests	Treatment	Outcome
Malhotra <i>et al.</i> , 1997	14 years female	Onset at 12 years Symptoms -hyperphagia, social and sexual disinhibition Duration of episode: 3-4 days	EEG: Right temporoparieto-occipital sharp wave	No treatment given	Remitted spontaneously after five episodes
Aggarwal <i>et al.</i> , 2011	22 years female	Onset at 16 years; precipitated by fever Symptoms-hyperphagia, confusion, irrelevant talk, sexualdisinhibition Duration of episode: 15-20 days	USG abdomen, MRI brain, EEG - normal. Serum prolactin, LH, FSH, and TFT-normal	Methylamphetamine 25 mg Modafinil 100 mg	Asymptomatic during 2 years follow-up
Singh <i>et al.</i> , 1990	35 years female	Onset at 23 years, precipitated after altercation at home Symptoms-increased appetite Duration of episode: 10-25 days	EEG - normal CT head-parenchymal atrophic changes	No treatment given	Corrected itself spontaneously
Khanna <i>et al.</i> , 2015	18-years female	Onset at 18 years, precipitated after tuberculosis meningitis Symptoms-lethargy, apathy, hypersexuality Duration of episode: 1-3 weeks	MRI brain, CSF, EEG, polysomnography were normal	Anti-tuberculosis therapy Lithium carbonate	Complete remission with lithium
Dasgupta <i>et al.</i> , 2014	17-years female	Onset at 15 years, precipitated by febrile illness Symptoms-irritability, hyperphagia, desire for specific food, derealization Duration of episode: 8-10 days	EEG, MRI brain, polysomnography were normal	Armodafinil 150 mg Lithium carbonate 600 mg	Armodafinil was stopped. No further episodes in next 2 years on lithium
Mudgal <i>et al.</i> , 2014	30 years female	Onset at 26 years, after postpartum psychosis Symptoms -anger outburst Irritability, hyperphagia, hypersexuality	EEG, CT, MRI brain-normal. SPECT-hypoperfusion of bilateral frontal lobes	Armodafinil 300 mg oxcarbamazepine 1200 mg	Maintaining well at 6 months follow-up
Sharma and Sharma 2009	13 years female	Onset at 11 years Symptoms - hyperphagia Duration of episode: 6-7 days	LH, FSH, GH, GnRH, EEG, CSF, MRI brain- normal	Lithium 900 mg	No follow-up details
Vinay <i>et al.</i> , 2010	11 years female	Onset at 9 years, precipitated with viral fever Symptoms -decreased energy Apathy, fearfulness Duration of episode: 6 days	TFT-normal	Modafinil during episodes (no prophylaxis)	Reduced frequency, duration and severity of episodes
Index case Nebhinani and Suthar	43 years female	Onset at 27 years, precipitated after the birth of 2 <sup>nd</sup> child Symptoms- hypersomnia, body aches, fatigue, and off and on low mood	Routine biochemical, endocrine parameters, EEG, MRI brain and MRI angiography -normal	Lithium 900 mg, Modafinil 100 mg, Sertraline 100 mg	Maintaining well at 12 months follow-up

MRI – Magnetic resonance imaging; EEG – Electroencephalography; USG – Ultrasonography; FSH – Follicle stimulating hormone; LH – Luteinizing hormone; SPECT – Single-photon emission computerized tomography, CT – Computed tomography; GH – Growth hormone; GnRH – Gonadotropin-releasing hormone; CSF – Cerebrospinal fluid; TFT – Thyroid function test

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### Conflicts of interest

There are no conflicts of interest.

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