Case Report

Armodafanil for the treatment of Kleine-Levin syndrome

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Abstract

Kleine–Levin syndrome (KLS) is a rare disorder characterized by recurrent episodes of hypersomnia and to various degrees, behavioral or cognitive disturbances, compulsive eating behavior, and hypersexuality. There is no definite treatment for KLS and several pharmacological agents have been tried with variable success. We report the case of a young male with KLS who showed a favorable response to armodafinil.

Key Words : Kleine–Levin syndrome, Armodafanil

Introduction

Kleine–Levin syndrome (KLS) is a rare disorder characterized by recurrent episodes of hypersomnia and to various degrees, behavioral or cognitive disturbances, compulsive eating behavior, and hypersexuality.\(^1\) As per the International Classification of Sleep Disorders (ICSD) diagnostic criteria modified in 1990\(^2\), KLS has been defined as a syndrome with recurring episodes of undue sleepiness lasting some days, which may or may not be associated with hyperphagia and abnormal behavior.\(^2\)

The diagnosis of KLS is entirely clinical and there are no specific laboratory tests to establish the diagnosis. It is mostly a diagnosis of exclusion, where a physician must eliminate a long list of other conditions which could mimic the symptoms of KLS. Treatment options for management of KLS have not been very successful. Various pharmacological agents like antidepressants, antipsychotics, mood stabilisers, amphetamines, and even ECT have been tried but with limited success. However, use of lithium has been reported to prevent relapses.\(^3\)

We report the case of a young male with KLS who showed a favorable response to armodafinil.

Case Report

A 24-year old unmarried male, shopkeeper by occupation, presented with an episodic illness of one year duration. Patient had a total of four episodes over past year and presented for psychiatric treatment during the 4th episode with chief complaints of excessive sleep. He was accompanied by his father and information appeared to be reliable and adequate.

Nearly one year back, the first episode started soon after the patient had a train journey lasting for 30 hours. Soon after reaching home, he complained of decreased energy, dream-like state and sleepiness. He felt lethargic and did not feel like interacting with anybody or carrying out daily activities. He also reported that objects seemed heavier than usual and complained of decreased energy. He slept for 18–20 hours in a day for next one week and would wake up only for the purpose of taking his meals and daily ablutions. Sometimes, he had to be awakened.
forcibly by the family members to carry out daily activities. His appetite was, however, normal and there was no increase in food intake. During the same period, he also reported excessive sexual fantasies and more involvement in the masturbatory practices (about five to six times in a day) compared to his usual self (about once in one or two days). These complaints of excessive sleep and increased sexuality lasted for a period of about a week, after which the episode remitted by itself and patient resumed baseline functioning. He maintained well for next nine months during which he never experienced any complaints.

After nine months of asymptomatic period, he reported having two more episodes over a span of three months, each episode lasting for nearly 7-8 days. Both of these episodes started abruptly without any precipitating factor or stressor. During these episodes, help was sought from a local practitioner, who prescribed analgesics and multi-vitamin injections, with little benefit. Patient presented to psychiatric out-patient clinic on the second day of 4th episode. This episode, similar to prior episodes, was characterized by excessive sleepiness, lethargy, decreased energy and excessive sexual fantasies.

Patient had an uneventful birth and developmental history. There was no family history of psychiatric or neurological illness. After a thorough assessment, a diagnosis of Kleine-Levin syndrome (KLS) was made as per diagnostic criteria of International Classification of Sleep Disorders (ICSD,1990). The routine blood tests, including complete haemogram, kidney function tests, liver function tests and urine R/M, all of which were within normal limits. CT scan head and EEG were normal.

The treatment was initiated with armodafinil, 50 mg on day 1 and increased it to 150 mg/day from next day onwards. He showed improvement in sleepiness within 1-2 days of starting treatment. There was a visible improvement on the second day of armodafinil, with total sleep duration decreasing from 20 hours to only 10 hours per day. The patient felt more energetic and was able to perform the routine chores which were expected of him. He reported a subjective improvement in symptoms, with no feeling of being in a ‘dream like state.’

While there was improvement in sleep and energy levels, there was no immediate decrease in the sexual fantasies experienced by patient. Patient resumed functioning and was sleeping ≤ 10 hours within 2-3 days of treatment. He did experience a gradual decline in the sexual fantasies and reached baseline level over a period of three months.

In view of multiple episodes over past one year and favorable short-term response with armodafinil, it was planned that patient will continue with armodafinil for relapse prevention. Patient has remained symptom-free, taking 150 mg/day of armodafinil for 8 months of regular follow up till date.

Discussion

As such, there is no definitive treatment for KLS during episode as well as the inter-episodic period. There are no randomized, placebo-controlled trials for pharmacological treatments of KLS. During the interepisodic period, various mood stabilisers, such as lithium, carbamazepine, valproate, phenytoin, and phenobarbital have been tried, keeping in view some similarities between bipolar disorder and KLS. Of these, only lithium has been found to have a response rate which is significantly higher than medical abstention. Lithium has been found to reduce the chances of relapse, though little/no literature is available regarding the appropriate serum levels for the treatment of KLS. Various stimulants, including
methylphenidate, modafinil, D-amphetamine, ephedrine, methamphetamine, amphetamine can be used to treat sleepiness, but unfortunately do not improve sluggish cognition or other elements of the altered mental state. Modafinil has been reported to successfully treat a patient of KLS in a previous case report from India. Existing literature suggests inconsistent results with use of modafinil, though it has been found to be ‘partially successful’ in reducing sleepiness in 21% of patients in a series of 43 KLS patients.

To our knowledge, there is no previous case report on the use of Armodafanil in the treatment of KLS. Armodafanil is the R-enantiomer of modafinil, a wake-promoting agent, that primarily affects areas of the brain involved in controlling wakefulness. The efficacy of once-daily armodafanil in improving wakefulness in adult patients with excessive sleepiness associated with obstructive sleep apnoea/hypopnoea syndrome (OSA), narcolepsy or shift work sleep disorder (SWSD) in four large (n > 195), double-blind, multinational trials of 12 weeks’ duration has been well documented. As compared to Lithium which has a narrow therapeutic index and requires a regular monitoring of serum levels, armodafanil is relatively safer and does not require close monitoring. As compared to other stimulants, Armodafanil was preferred in view of its low addiction potential. Though use of armodafanil in KLS has not been documented, we tried it in view of its mechanism of action, usage in other conditions with excessive day time sleepiness and the advantages over other pharmacological agents.

The case report suggests that armodafanil could be used in treating KLS during the episode and possibly, for relapse prevention. It is worthwhile to mention that patient is under follow up for only eight months, which is a relatively short duration. The effect of armodafanil on course and relapse prevention needs to be studied carefully in longer follow up periods. More systemic research is warranted to study the long-term effects of this drug on the course of Kleine-Levin syndrome.

References


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