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A case of Kleine-Levin syndrome successfully treated with Escitalopram

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Abstract

Kleine-Levin syndrome (KLS) is an extremely rare relapsing-remitting neuropsychiatric condition characterized by recurrent incidents of major hypersomnolence along with hyperphagia, hypersexual behavior, and mood or cognitive disturbances alternating with asymptomatic periods. Here, we present a case of a young male chiefly presenting with recurring episodes of acute onset behavioral changes. The patient's episodes were characterized by repetitive incidents of prolonged sleep for more than 20 h, followed by social withdrawal and apathy. He was diagnosed with KLS because of the periodic patterns of hypersomnolence accompanied by other cognitive and mood disturbances and lacked characteristics of central hypersomnolence disorders or atypical depression. There are varying success rates among medications such as lithium, stimulants such as modafinil, antiepileptics such as carbamazepine and valproate. Similarly, the use of antidepressants such as tricyclic agents and selective serotonin reuptake inhibitors has largely been negative. Our case report addresses a patient with KLS who was successfully treated with 20 mg of Escitalopram.

Keywords

Escitalopram, episodic hypersomnolence, hyperphagia, Kleine–Levin syndrome, adolescent sleep disorder

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Introduction

Kleine-Levin syndrome (KLS) was first reported as an unsolicited finding by Brierre de Boismont in 1862.[1] It was since then followed by independent reports from Kleine[2] and Levin[3] in 1925 and 1936, respectively, and cited as a disorder by Critchley and Hoffman[4] in 1942. KLS is characterized by episodes of severe hypersomnolence, morbid hunger, hypersexuality, behavioral, and cognitive symptoms alternating with asymptomatic periods.[1,12] While the behavioral symptoms may include irritability, anxiety, depression, aggressiveness, exhaustion, and apathy, cognitive manifestations involve derealization, confusion, disorientation without urinary incontinence, impaired communication (speaking and reading), concentration, decision-making, memory, multitasking, and hallucinations.[1,5]

Most patients return to a normal state of the sleep-wake cycle and cognitive performance in-between episodes; however, 20%–25% of the patients continue to exhibit cognitive (memory and attention deficits) and behavioral (mood and anxiety disorders) changes in-between episodes.[6,12] Although the clinical guidelines for diagnosis are well-established today, the syndrome and its etiology, pathogenesis, and treatment are still under-investigated.[6,7,12] In a systematic study by Arnulf et al.,[8] obstetric complications (for instance, prolonged labor, hypoxia, or premature or post-term birth) were reported in 25% of the 108 cases studied, with them also having an increased probability of genetic disorders (including autism spectrum disorder, developmental delay of unknown cause, Klinefelter's syndrome, mental retardation, von Willebrand syndrome, and polycystic kidney disease) in comparison to controls. As the symptomatology of this disorder mimics psychiatric illness, the patient may present to a psychiatrist or a neurologist and may get misdiagnosed as bipolar disorder, psychosis, or intoxication due to the highly infrequent nature of the disease (fewer than 1.5 cases per million population).[1,8] Henceforth, it is essential for neuropsychiatrists to be aware of KLS.

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Case report

A 23-year-old male was brought into a psychiatric ward by his parents. He was a farmer by occupation in a sub-rural setting in India. The patient had well-adjusted premorbid history, insignificant family history, as well as an inconsequential personal and absent substance abuse history.

His parents reported recurrent episodes of abnormal sleeping patterns in the patient for the past 6 months. Furthermore, there was no history of any stressor, infection, psychiatric illnesses, or seizures. There was an acute onset of behavioral change characterized by 2–3 episodes per 2 weeks (ranging from 15 to 17 days) of prolonged sleeping for more than 20 h, during which he did not get up even for food or self-care purposes. Each event was succeeded by approximately a week (4–7 days) of the patient remaining apathetic, irritable, disruptive, and having reduced awareness of his surroundings. The patient reported feeling detached from his surroundings (derealization), suffering frequent headaches, and heightened sensitivity to light and noise. All the more, the subsequent episodes had a history of short-lasting (i.e. 2–3 days) depressive symptoms either preceding the episode or often following it. Furthermore, during the following incidents of hypersomnolence, he used to get up once (after 14 h of continuous sleep) for a brief duration of 15–20 min for food and urination with similar symptoms of cognitive and behavioral changes following the event each time. His behavior used to return to normal eventually, and he lacked a history of any sexually disinhibited behaviors or hyperphagia. The duration of hypersomnolence and the following symptoms of cognition and behavior became briefer with each passing episode.

His physical examination was normal, and blood investigations such as complete blood picture, folate, vitamin B12 levels, serum electrolytes, lactate, ammonia, urine for abnormal metabolites, copper studies were within normal limits, and neuropsychological assessments and EEG studies were unremarkable. Initially, a provisional diagnosis of KLS *versus* a differential diagnosis of atypical depression was made and was started on Escitalopram 10 mg/day. On subsequent follow-ups based on his mood diary, the diagnosis of atypical depression was considered less likely. By the end of follow-up at 6 months, the frequency and severity of episodes reduced, and the period of remission increased from a fortnight to more than 3 months after starting the Escitalopram. His final dose was 20 mg/day, and he was remarkably doing well on that dose.

Discussion

KLS is a rare relapsing-remitting neuropsychiatric condition, and its prevalence is undetermined.[1,8] A founder effect is implicated among Israel and American Jews for having the highest incidence of KLS.[1,9] The acute, irregular, severe (>18 h/day of sleep) onset of hypersomnolence episodes and rapid resolution of mood symptoms distinguish atypical depression and menstruation-related hypersomnia from KLS. Other organic conditions such as narcolepsy can cause episodes of hypersomnia, but the presence of cataplexy, hypnagogic/hypnopompic hallucinations, and excessive daytime somnolence distinguishes this entity from KLS.[7,10,11] Regarding the etiology, limited literature exists on the possible association of preceding history of an upper respiratory tract infection, head injury, fever, inflammatory encephalitis, or an autoimmune phenomenon, rarely a channelopathy involving the pathways of circadian rhythms.[1,12] Literature on treatment and management of preventing recurrences is limited and non-satisfactory. Among the studies that exist, treatment during KLS episodes is focused on modafinil, methylphenidate, amphetamine, and neuroleptics. In the same study by Arnulf et al.,[1,8] while methylphenidate and amphetamine gained the support of physicians in terms of reducing the severity of KLS episodes, modafinil was reported to have the highest patient satisfaction. With regards to preventing recurrence, antidepressants (including sertraline, fluoxetine, amitriptyline, clomipramine, fluvoxamine, mirtazapine, and citalopram), lithium, carbamazepine, and other anti-convulsants have been frequently mentioned with lithium, valproic acid, and other anti-epileptics gaining approval from both patients and physician.[1,8]

Selective serotonin reuptake inhibitors (SSRIs) can potentially help alleviate the recurrences by fending off the mood changes that precede and/or follow the hypersomnia. Varying degrees of mood changes have been implicated in approximately 50% of the patients with KLS.[12] Albeit, more extensive longitudinal studies are warranted among the KLS patients with mood changes to study the possible efficacy in preventing recurrences with antidepressants.

The limited available literature, mainly from the case series or reports on the use of SSRIs, has largely been negative unless in improving comorbid depressive symptoms.[1] It was also challenging for us in this particular case to rule out natural remission as spontaneous remission takes place in approximately 72% of cases with reduced severity of symptoms and hypersomnolence as the patients advance in aging. However, this process may take months to years.[12] In our patient, the remission was directly correlated with the timings of medication. Hence our case may add valuable information to the literature on the role of SSRI in KLS.

Conclusion

KLS is an extremely rare psychiatric condition characterized by recurrent episodes of hypersomnolence associated with various other manifestations such as hyperphagia, hypersexual behavior, and mood or cognitive disturbances alternating with asymptomatic periods. Evidence on treatment and management for averting relapses is limited and non-satisfactory, especially in regards to the use of SSRIs as

the mainstay to fend off relapse. Our case report attempts to add valuable information to the literature on the role of SSRI in KLS.

Declaration of conflicting interests

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Ethical approval

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Informed consent

Written informed consent was obtained from the patient(s) for their anonymized information to be published in this article. The subject had decision capacity to provide written informed consent.

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