MAR Pediatrics (2023) 4:10

Case Report

Complex Presentation of Suspected Kleine-Levin Syndrome in a 14-Year-Old Male

Chadi AL ALAM, MD *, Lynn Srour[1], Rima Hazzouri[2], Marie Bou Nassif [3]

1. Lynn Srour, Medical student, year 6, University of Balamand.

2. Rima Hazzouri, Pediatrics and Neonatology, Aman Hospital, Doha, Qatar.

3. Marie Bou Nassif, Pediatrics and Neonatology, Aman Hospital, Doha, Qatar.

***Correspondence to:** Chadi AL ALAM, MD, Pediatrics and pediatric Neurology, American center for Psychiatry and Neurology, Abu Dhabi, United Arab Emirates- UAE. dr.alalam.chadi@gmail.com

Copyright

Received: 21 November 2023

Published: 01 December 2023

Abstract

This case report presents the perplexing medical odyssey of a 14-year-old male who, following a viral infection in November 2022, 1 year prior to presentation, and subsequent antiviral treatment, developed recurrent episodes characterized by hypersomnia, altered consciousness, and hallucinations. Despite an exhaustive series of negative test results, the elusive nature of the underlying cause persisted, prompting consideration of Kleine-Levin Syndrome (KLS). This rare sleep disorder, marked by episodic hypersomnia and cognitive disturbances, poses diagnostic challenges, often masquerading as psychiatric conditions. The patient's atypical presentation, including a unique variation in appetite and the correlation with antiviral treatment, adds complexity to the understanding of KLS. The interdisciplinary approach to management, involving professionals from diverse specialties, is crucial for navigating this intricate clinical landscape. This report contributes to the growing body of knowledge on KLS, emphasizing the need for continued vigilance in recognizing the syndrome's diverse manifestations and the importance of comprehensive and individualized diagnostic strategies.

Case Presentation:

This case involves a 14-year-old male with a perplexing medical history, initially triggered by a viral infection 1 year prior to presentation Following Oseltamivir phosphate treatment, the patient experienced recurring episodes lasting 7-10 days each, marked by excessive drowsiness, altered consciousness, confusion, hallucinations, and perceptual abnormalities. Despite extensive investigations, including negative electroencephalogram (EEG), Electromyography (EMG), and Magnetic resonance imaging (MRI) results, the underlying cause remains elusive.

The patient's symptoms emerged post-antiviral treatment, leading to severe fatigue, altered sleep patterns, and behavioral changes such as talking to himself and staring at family members. Visual and auditory hallucinations, coupled with a confusional state, occurred exclusively during the 7–10-day episodes. The frequency of these episodes has been approximately every 3 to 4 weeks, with a gradual reduction in visual hallucinations 3 months after the onset.

Premorbid Personality: Before the onset of symptoms, the patient was described as an average intelligence, articulate young man with no reported concerns.

Family History: The patient's family has actively sought alternative treatments, including herbal remedies, hyperbaric oxygen therapy, and stem cell treatment in India. Despite various interventions, there has been limited success, and the family has been informed that improvement may take up to three more months. No significant past medical history or developmental delays were reported. During non-episode periods, the patient was presented as stable, euthymic, with no thought disorders or psychiatric phenomena. Organic immune-mediated reactions to viral infections were suggested during the episodes.

Impression and Current Assessment:

The differential diagnosis includes PANADS, chronic fatigue syndrome, and immune-mediated syndromes following viral infections. A comprehensive Systemic lupus erythematosus (SLE) workup, including dsDNA, ANA, ANCA, CANCA, and PANCA, is negative. Whole exome sequencing is also planned to explore metabolic and periodic syndromes. Notably, a recent stem cell transplant in India aimed at addressing possible autoimmune factors yielded limited improvement.

Current Diagnosis Suspicions:

Given the negative findings in extensive workups, a diagnosis of Kleine-Levin Syndrome is highly suspected. The recurrent nature, episodic symptoms, and lack of significant abnormalities during non-episode periods align with KLS characteristics. Further evaluation and follow-up are crucial to confirm this diagnosis.

This challenging case highlights the intricate interplay between viral infections, immune responses, and psychiatric manifestations. The pursuit of a conclusive diagnosis remains ongoing, emphasizing the importance of continued monitoring, interdisciplinary collaboration, and further investigations into potential autoimmune factors.

Discussion:

Kleine–Levin Syndrome (KLS) is a rare sleep disorder characterized by recurrent episodes of hypersomnia and various degrees of behavioral or cognitive disturbances, hypersexuality, and hyperphagia. KLS is the

most common recurrent sleep disorder, with a prevalence of 1–2 per million populations (7). This disease typically affects adolescent males, and each episode can last from a week to 1–2 months, with asymptomatic periods between episodes. The majority of patients had cognitive disturbances such as confusion, concentration, attention, and memory defects (4). While the exact cause remains unknown, possible etiologies include trauma, psychological disturbance, toxins, infections, serotonergic, or dopaminergic neurotransmitter abnormalities, and autoimmunity (1). It is very challenging to make the diagnosis of KLS, as it mainly relies on the exclusion of other potential causes and on the careful examination of clinical symptoms during episodes. Kleine-Levin syndrome, while rare, is often misdiagnosed or unrecognized and should be considered in any teenager presenting with recurrent episodes of hypersomnia concurrent with cognitive changes, depersonalization, or disinhibition (5).

Functional neuroimaging during the symptomatic period of Kleine–Levin syndrome revealed frequent transient hypoactivity in the thalamic region, with lesser degrees of hypoactivity noted in the hypothalamus, frontal and temporal regions (8). These anomalies suggest a potential autoimmune-induced inflammation, with infectious agents like Epstein-Barr virus (EBV) and Streptococcus possibly playing a role. The thalamic involvement aligns with similarities to clinical presentations seen in patients with hypothalamic or third ventricle tumors. Neuroimaging also detects abnormalities in the hypothalamus, amygdala, and temporal lobe gray matter. Abnormalities in serotonin and dopamine neurotransmitter metabolism have also been reported (9), while cerebrospinal fluid hypocretin levels may be normal or slightly decreased.

Although no definitive treatment has been found, psychotropic agents such as lithium and antidepressants have been explored, with varying degrees of success. Lithium was found to significantly improve abnormal behavior, reduce the duration of episodes, and decrease relapses, improving the recovery of symptoms (2). Despite the challenges, the prognosis of KLS is generally fair, marked by spontaneous symptom resolution and a decrease in the intensity and frequency of episodes over time.

The interdisciplinary management of KLS involves healthcare professionals from diverse specialties, including primary care pediatricians, neurologists, psychologists, and others. The awareness of this condition across medical disciplines is pivotal for improved patient care and outcomes.

In the presented case, the clinical presentation of the patient aligns with the classic features of KLS, offering the opportunity to explore the nuances and variations within this syndrome. The patient's history reflects the typical age of onset during adolescence, with recurrent episodes of hypersomnia lasting for several days to weeks. Hypersomnia, a major clinical symptom of KLS, is mandatory for diagnosis and was present in all

cases (4). The literature focuses on the prevalence of the disease among males, in line with the observation that our patient is a teenage boy. Moreover, the episodic nature of KLS, where individuals are entirely asymptomatic between episodes, is also evident in our patient's history.

One distinctive aspect noticed in our case is the reported decrease in appetite, which deviates from the characteristic hyperphagia associated with KLS. Seventy-five percent of patients had an alteration in their eating behaviors during episodes of KLS, with the majority experiencing megaphagia, preferring sweets (2). However, our patient's experience of decreased appetite introduces a unique aspect to the manifestation of the symptoms of KLS. This variation raises intriguing questions about the spectrum of symptoms, the diversity and variability within KLS, and the potential for atypical presentations of the disease.

Additionally, the precipitating factors noted in our case, which was the antiviral treatment, align with the literature, which suggests a correlation between KLS episodes and various triggers. Prior to the onset of symptoms, patients are usually subjected to a triggering event. Of all the reported triggers, infection and fever are by far the most common (3). The seasonal pattern observed in the onset of the first episode, with a peak in December, corresponds with findings indicating a higher frequency of initial episodes during the autumn and winter seasons.

The negative findings in extensive workups, including negative EEG, EMG, and MRI results, further contribute to the diagnostic challenge, emphasizing the need for a comprehensive and individualized approach. The prevalence of KLS may be underestimated as it is often misdiagnosed with psychiatric conditions, especially early in the disease course (5). The partial improvement post-IV vitamin supplements and limited success with stem cell treatment add layers to the complexity, suggesting potential immune-mediated factors.

Clinicians should remain vigilant to the possibility of KLS in cases with overlapping symptoms, recognizing that the syndrome may manifest in different ways across individuals.

Conclusion:

In conclusion, the presented case highlights the diagnostic complexities of Kleine-Levin Syndrome (KLS), emphasizing the need for an interdisciplinary approach. The patient's unique manifestation with decreased appetite adds to the variability within the syndrome. The correlation between symptom onset and antiviral treatment, coupled with negative findings in extensive workups, underscores the diagnostic challenges and

the importance of individualized evaluations. Clinicians should remain vigilant for KLS in cases with overlapping symptoms, recognizing its diverse presentations. This case contributes valuable insights into the intricate interplay between viral infections, immune responses, and psychiatric manifestations in the context of KLS.

References

1. AlShareef SM, Smith RM, BaHammam AS. "Kleine-Levin syndrome: Clues to aetiology." Sleep Breath. 2018 Sep;22(3):613-623. DOI: 10.1007/s11325-017-1617-z

2.Shah, F. (2023, August 8). "Kleine-Levin Syndrome (KLS)." StatPearls - NCBI Bookshelf. Link

3.Huang YS, Guilleminault C, Lin KL, Hwang FM, Liu FY, Kung YP. "Relationship between Kleine-Levin syndrome and upper respiratory infection in Taiwan." Sleep. 2012;35(1):123–129. [PMC free article] [PubMed]

4.Ramdurg, S. (2010). "Kleine-Levin syndrome: Etiology, diagnosis, and treatment." Annals of Indian Academy of Neurology. 2010 Oct;13(4):241-6. DOI: 10.4103/0972-2327.74185

5.Miglis MG, Guilleminault C. "Kleine-Levin syndrome: A review." Nat Sci Sleep. 2014 Jan 20;6:19-26. DOI: 10.2147/NSS.S44750

6.Afolabi-Brown, O., & Mason, T. B. (2018). "Kleine-Levin Syndrome." Paediatric Respiratory Reviews. 2018;25:9–13. DOI: 10.1016/j.prrv.2016.12.004

7.AlShareef SM, Smith RM, BaHammam AS. "Kleine-Levin syndrome: Clues to aetiology." Sleep Breath. 2018 Sep;22(3):613-623. DOI: 10.1007/s11325-017-1617-z

8.Assi B, Yapo-Ehounoud C, Baby MB, Aka-Diarra E, Amon-Tanoh M, Tanoh C. "The Kleine-Levin Syndrome: A Rare Disease with Often Delayed Diagnosis-A Report of Two Cases in the Department of Neurology of the University Hospital of Cocody (Côte d'Ivoire)." Case Rep Neurol Med. 2016;2016:8929413. DOI: 10.1155/2016/8929413

9.Ramdurg S. "Kleine-Levin syndrome: Etiology, diagnosis, and treatment." Ann Indian Acad Neurol. 2010 Oct;13(4):241-6.