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A Review of Kleine-Levin Syndrome

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ABSTRACT:

Kleine-Levin syndrome, also known as recurrent hypersomnia or periodic hypersomnolence, is a rare sleep disorder marked by recurrent episodes of severe hypersomnia coupled with behavioural and cognitive disturbances like compulsive eating, hypersexuality, derealization, apathy, and confusion. There are weeks or months of regular sleep and behaviour in between episodes, which can last anywhere from a few days to many weeks. This article will examine the epidemiology, pathophysiology, clinical characteristics, diagnosis, and management of Kleine-Levin syndrome.

Keywords: Kleine-Levin syndrome, Hypersomnia

INTRODUCTION:

Recurrent episodes of hypersomnia accompanied by behavioural, cognitive, and psychological alterations and a sense of derealization are the hallmarks of Kleine-Levin syndrome, an episodic condition. Adolescent boys are primarily affected by the illness. Kleine-Levin syndrome is typically regarded as an incredibly rare disease, despite the fact that there are no population-based studies reporting on its prevalence. [1]

SIGNS AND SYMPTOMS:

Kleine-Levin syndrome symptoms typically appear after a specific trigger, such as an infection, lack of sleep, drinking alcohol, exposure to anaesthesia, or head trauma. Initial signs of sleepiness include a few hours of exhaustion and headache, and then evolve to bouts of excessive sleep lasting between 14 and 21 hours. These extended naps might last for several hours and have no discernible circadian regularity. Patients generally have behavioural and cognitive problems in the intervals between these sleep episodes. The patient may experience insomnia once the symptomatic phase ends. This condition might linger for one-to-many days.

Confusion, hallucinations, trouble speaking or concentrating, memory problems, and sensations of unreality are just a few of the cognitive anomalies these people encounter. Additionally, there is a sense of apathy that might outweigh the other cognitive deficiencies. Patients occasionally say they don't necessarily find it difficult to accomplish things, but that they aren't interested in completing them. Another symptom of Kleine-Levin syndrome that is frequently reported is the sensation of unreality. Patients who experience this feeling frequently say they are unsure of whether what they are feeling is real or just a dream. Every single one of the 108 patients in the series experienced derealization.

Patients with Kleine-Levin syndrome exhibit a variety of behavioural disorders, with hypersexuality, irritability, aggression, and hyperphagia being the most prevalent. Contrary to extreme drowsiness and cognitive problems, not all individuals have behavioural abnormalities. Upon waking after extended durations of sleep, more than half of patients frequently engage in binge eating. When patients are awakened from a sleep episode in the midst, they may become agitated and hostile. Male patients are more likely to experience hypersexuality, which shows itself as frequent masturbation and improper sexual practises. There may be a variety of other symptoms, such as depression, anxiety, regressive habits, headaches, photophobia, and phonophobia. [2]

AETIOLOGY:

The crucial function of the hypothalamus in controlling sleep, hunger, and sexual behaviour raises the possibility of an underlying illness; yet, no persistent abnormalities of the hypothalamus have been found. Cerebrospinal fluid analysis, structural brain imaging, and serological inflammatory marker examination are unremarkable. In the majority of instances, electroencephalographic slowing during episodes is noticeable without epileptic activity. There have been reports of diffuse cerebral hypoperfusion, primarily affecting the thalamus and frontotemporal regions. On the basis of the numerous reports of flu-like symptoms at the outset and the most common precipitating event (70%) viral and autoimmune causal factors have been proposed. Inflammatory lesions in the thalamus, diencephalon, and midbrain in postmortem neuropathology have been reported in a small number of case reports, which suggests a viral infection. It was found that in rare cases there is increased frequency of the human leukocyte antigen DQB1 * 0201 allele. In few cases, abnormalities in serotonin and dopamine metabolism have been reported, suggesting a neurotransmitter imbalance in the serotonergic or

dopaminergic pathway. The eventual, spontaneous disappearance of the syndrome is as mysterious as the mechanisms determining its periodicity, and should prompt future investigation. [3]

PRECIPITATING FACTORS:

The first episode of Kleine-Levin syndrome peaked in December (14.8%) and most frequently occurred in the autumn (31.1%) or winter (31.1%). Infections were most frequently remembered by patients (89%), followed by alcohol use (23%), sleep deprivation (22%), unusual stress (20%), physical exertion (19%), travel (10%), head trauma (9%), and marijuana use (6%). Eighty-nine percent of patients remembered an event closely associated with onset. [4]

DIAGNOSIS

Diagnosis of Kleine–Levin syndrome is very difficult since there are no symptoms that allow for a positive diagnosis. Kleine–Levin syndrome is instead a diagnosis of exclusion, where a doctor must first eliminate a long list of other conditions that could mimic the symptoms. The diagnosis is entirely clinical. According to the International Classification of Sleep Disorders Diagnostic criteria A to E must be met:

A. The patient experiences at least two recurrent episodes of excessive sleepiness and sleep duration, each persisting for 2 days to 5 weeks.

B. Episodes recur usually more than once a year and at least once every 18 months.

C. The patient has normal alertness, cognitive function, behavior, and mood between episodes.

D. The patient must demonstrate at least one of the following during episodes: 1. Cognitive dysfunction 2. Altered perception 3. Eating disorder (anorexia or hyperphagia) 4. Disinhibited behaviour (such as hypersexuality)

E. The hypersomnolence and related symptoms are not better explained by another sleep disorder, other medical, neurologic, or psychiatric disorder (especially bipolar disorder), or use of drugs or medications

MRIs can determine if the symptoms are caused by certain brain disorders, stroke, and multiple sclerosis. Lumbar puncture can determine if encephalitis is the cause. Kleine–Levin syndrome must be differentiated from substance abuse by toxicology tests.The use of electroencephalography can exclude temporal status epilepticus from consideration. EEGs are normal in about 70% of Kleine–Levin syndrome patients, but background slowing may sometimes be detected. In addition, low-frequency high-amplitude waves can be observed during waking hours. [5]

PATHOPHYSIOLOGY:

Kleine-Levin syndrome's pathophysiology is not fully understood. Since flu-like symptoms are described during disease initiation, viral and autoimmune mechanisms may possibly be involved in the pathophysiology of Kleine-Levin syndrome. On SPECT, diffuse cerebral hypoperfusion has been identified, primarily in the thalamic and frontotemporal regions. Functional neuroimaging during the symptomatic stage of Kleine-Levin syndrome indicated frequent transitory hypoactivity in the thalamus, with less severe hypoactivity identified in the hypothalamus, frontal, and temporal areas. However, during the asymptomatic intervals, the thalamic hypoperfusion that was seen during acute illness episodes fully disappeared.

The hypoperfusion seen on SPECT may be brought on by a potential autoimmune-induced inflammatory response. In contrast to between episodes, no differences in serum cytokine levels were found during episodes of Kleine-Levin syndrome. There have also been reports of inflammation in the thalamus, diencephalon, and midbrain, as well as various abnormalities in the hypothalamus, amygdala, and grey matter of the temporal lobe.

When compared to normal patients, functional neuroimaging has also revealed lower striatal dopamine transporter binding potential in asymptomatic Kleine-Levin syndrome patients. The thalamus and putamen showed hypermetabolism of cerebral glucose during symptomatic Kleine-Levin syndrome episodes. In contrast, during symptomatic Kleine-Levin syndrome episodes, there was evidence of relatively decreased glucose metabolism in the bilateral occipital gyri, the left lingual gyrus, the right angular, middle, and superior temporal gyri. The notion that an underlying thalamic disease contributing to Kleine-Levin syndrome is supported by similarities between the clinical presentation of Kleine-Levin syndrome and that observed in patients with hypothalamic or third ventricle malignancies.

Derealization is a common feature of the Kleine-Levin syndrome presentation, which may indicate underlying parieto-temporal dysfunction. The cross-modal connection of somatosensory (body knowledge), auditory, and visual information occurs in the parieto-temporal junction. Derealization could therefore result from malfunction and/or hypoperfusion in the junction. Hypoperfusion in the right medial prefrontal cortex and the orbitofrontal cortex may be the causes of apathy, as shown in Kleine-Levin syndrome, and lesions in the orbitofrontal cortex may also lead to irregular eating habits. There have also been reports of abnormalities in the metabolism of the neurotransmitters dopamine and serotonin.

Since more than 90% of narcolepsy patients have lower-than-normal hypocretin concentrations in their cerebrospinal fluid, hypocretin has received considerable attention in the context of Kleine-Levin syndrome. However, hypocretin levels have been reported to fluctuate between normal and lowered in the cerebrospinal fluid of patients with Kleine-Levin syndrome. Since episodic reductions in Kleine-Levin syndrome may not be as severe as those in narcolepsy-cataplexy, examination of cerebrospinal fluid hypocretin levels in Kleine-Levin syndrome needs to be carefully considered. [6]

TREATMENT:

The aetiology of Kleine-Levin syndrome is currently unknown, hence there is no proven cure. Some symptoms of the illness, such extreme daytime sleepiness, have been treated with medications like stimulants. Other medications, like lithium, have been reported to lessen the intensity and frequency of the episodes. Many different drugs, such as stimulants, amantadine, To determine if pharmaceutical treatment for Kleine-Levin syndrome was efficient and secure, the Cochrane epilepsy group made an effort to thoroughly analyse randomised control studies. Unfortunately, the researchers found no randomised control studies for steroids, clarithromycin, antipsychotic drugs, antidepressants, or antiepileptic drugs. Some progress has been seen, but because to the condition's rarity, long-term participant follow-up is difficult.

Management of patients with Kleine-Levin syndrome requires both knowledge and assistance. Additionally, for the majority of people with Kleine-Levin syndrome, reassurance and upholding a basic cleanliness regimen with home management are typically highly beneficial. It is crucial to give patients a secure and comfortable place to sleep, to refrain from driving, and to keep an eye out for any medical or psychological problems. Sadly, there is no proof that further therapeutic approaches, like as light therapy, melatonin, or vitamin supplements, are effective. [7]

EPIDEMIOLOGY

Although the precise prevalence of Kleine-Levin syndrome is unknown, it is considered to be a highly rare condition that may afflict one person in a million. With a mean age of onset of 15 years (range 4-82 years), patients are primarily male (68–78% of cases) and young adults (81% of patients). [8]

PROGNOSIS:

The prognosis is generally positive, with the majority of individuals experiencing fewer frequent and severe episodes as they age and the syndrome disappearing about 30-35 years old. About 20 to 30 percent of individuals experience minor attentional or memory problems during asymptomatic times. Fewer patients have persistent psychiatric illnesses than other patients.

CONCLUSION:

Intermittent hypersomnolence, behavioural and cognitive problems, hyperphagia, and in certain cases hypersexuality are the key characteristics of the unusual sleep disease known as Kleine-Levin syndrome. Due to the rarity of the illness, determining the underlying biological reason and the best course of treatment is challenging. To assist in the creation of disease-specific targeted therapeutics, extensive research into the aetiology, pathophysiology, inquiry, and treatments is needed.

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