CASE REPORT

Sleep-related psychosis

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SUMMARY

We report the case of a 19-year-old male student with a Kleine-Levin syndrome who was referred to our sleep laboratory during an episode of hypersomnia, hypersexuality, cognitive impairment and bizarre behaviour. Owing to similar clinical symptoms, he had been misdiagnosed with schizophrenia. This had led to a placement in a facility for persons with chronic schizophrenia, antipsychotic pharmacotherapy for 4 years and side effects, including substantial weight gain and hypertension. After cessation of the antipsychotic medication, the weight and blood pressure normalised. We started a prophylactic treatment with lithium under which the patient had become asymptomatic and had been able to begin a vocational training since treatment.

BACKGROUND

Kleine-Levin syndrome (KLS) is considered a rare disorder, presenting with characteristic changes in sleep regulation, food intake, sexual drive, cognitive abilities, perception, behaviour and the vegetative system.¹ It is difficult to diagnose because it can present like more common psychic disorders (eg, bipolar disorder, schizophrenia). It is important to consider KLS when presented with a case of episodic hypersomnia with cognitive and behavioural changes to select the best treatment.

CASE PRESENTATION

A 19-year-old student was referred to our sleep laboratory presenting with a rapidly progressive feeling of derealisation, depressed mood and increased sleep requirement. During monitoring, additional symptoms occurred, including bizarre manners, for example, the excessive use of a blow-dryer for hours and unusually frequent masturbation. Extended hospitalisation was indicated due to acute suicidal tendencies. During hospitalisation, he undertook several disorganised suicidal attempts, such as trying to asphyxiate himself with a pillow in the presence of staff members.

The history revealed several similar episodes with a sudden onset after febrile influenza for 7 days in 2006. Simultaneously with the normalisation of the temperature, several mental changes occurred. In the following weeks, he presented episodes of hypersomnia, derealisation and a depressive syndrome as well as episodes of insomnia. In addition, various cognitive impairments occurred, affecting speech, concentration, orientation and memory. Furthermore, a disinhibition, including hypersexuality, echopraxia and echolalia, were observed. The patient reported compulsions, such as obsessive singing of a certain verse taken from a famous song by the punk band 'Bloodhound

Gang'. Overall, the symptoms were unstable with rapid changes emerging over a course of 1.5 years. Several extended hospitalisations were needed. In the end, the patient had been moved to an assisted living group for chronically ill or mentally disabled adolescents.

Under the hypothesis of schizophrenia, the patient had been treated with different antipsychotic medications, including chlorprothixen (25 mg), haloperidol (10 mg), olanzapine (10 mg) and finally clozapine (400 mg) for almost 4 years. Clozapin treatment had led to a weight gain of 40 kg and consecutive arterial hypertension. Under antipsychotic treatment, there were no episodes of altered behaviour, but episodes of excessive hypersomnia and cognitive impairment remained.

Under the suspicion of KLS, all medication had been stopped 7 months prior to admission to our hospital. During this period, the patient had been able to reduce his overweight (−40 kg) and restore a normal blood pressure. He had been free of all symptoms until the onset of the reported episode.

INVESTIGATIONS

His Family history reported four cousins with a schizophrenia spectrum disorder. The analysis of cerebrospinal fluid showed a slight increase in the amount of protein without further alterations. There were no onconeural (anti-Hu, Yo, Tr, Ri, CV2, Amphiphysin) or anti-neutrophile (NMDAR, AMPAR, GABAR, LGI1, CASPR2) antibodies or any sign of infection. HLA-DQB1*02 was detected²
³ Repeated drug screenings, MRIs of the brain +/− contrast medium, ECGs, extended blood analyses, copper concentration in the urine, as well as microbiological, viral, rheumatological and metabolic screening tests showed no abnormalities. The EEG exhibited frontal decelerations and dysrhythmias. In the reported episode, polysomnography showed a total sleep time of almost 16 h followed by a short waking period of 5 h before going to bed for the second night (figure 1). The sleep architecture was normal. No signs for an organic sleep disorder occurred (apnea-hypopnea-index 1.1/h; periodic-leg-movement-index 0.4/h).

DIFFERENTIAL DIAGNOSIS

Main differential diagnoses include mental disorders, like bipolar or schizophrenia spectrum disorders. Both disorders have been suspected during the course of the reported case. Mainly, the characteristic episodes of hypersomnia in combination with the occurrence of typical symptoms and the favourable clinical course point to the diagnosis of KLS.

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Figure 1 Hypnogram recorded during the described episode of Kleine-Levin syndrome. Note the hypersomnic sleep pattern with an increased total sleep time of 954 min. The depicted sleep period was followed by a waking time of 5 h, followed by another extended sleep period.

Other differential diagnoses comprise epileptic disorders of the temporal lobe, the Kluever-Bucy syndrome or metabolically or genetically induced encephalopathies which were ruled out at the onset.^{1 4}

TREATMENT

Following the reviews of the current literature⁴⁻⁶ and due to the patient's preference, a treatment with lithium (900 mg) and risperidone (4 mg) was started in the acute episode.

OUTCOME AND FOLLOW-UP

About 3 weeks after the onset and under treatment with the aforementioned drugs, a fast remission of all described symptoms could be observed. The administration of risperidone was discontinued. Lithium treatment (daily dose 900 mg, plasma level 0.73 mmol/L) was continued with the aim to prevent a possible relapse or, at least, to decrease the frequency of episodes. Since then, the patient has been able to start a vocational training and has shown no sign of any residues.

DISCUSSION

There are a limited number of case reports describing patients with this rare disorder which have been summarised by Arnulf *et al.*¹ The same research group conducted a 1-year worldwide search for additional cases and analysed this sample for various parameters.⁴ The authors identified 100 new cases in 1 year and concluded that KLS might be more common than originally assumed and might have a high number of undiagnosed and unreported cases.

With regard to the clinical manifestation during an episode, several typical symptoms could be identified.⁴ The sleep requirement appears to be largely increased, averaging 18 h, and to be accompanied with intense dreaming, hypnagogic hallucinations and a dreamy wake state. All patients reported cognitive impairments and an amnesia for the episodes as well as an altered perception. Almost all patients showed altered eating behaviour with an increased overall intake and either a pattern of 'eating what is presented' or a preference for sweets or atypical food choices. Hypersexuality was observed in half of the patients. Although abnormal behaviour seems to be common, the overall impression was that of apathy and depression. In between episodes, patients did not differ significantly from a healthy control group.⁴

In their study, Arnulf *et al.*⁴ showed that patients with KLS sustained an average of 19 episodes of 13 days each. The mean course of disease persisted for 14 years, with a longer duration in men and when beginning with a late onset. In the course of

the disorder, the episodes tended to decrease in incidence and intensity, until in most cases the disease totally ceased.

In retrospect, our patient matched the typical symptoms of KLS very well. Nevertheless, it is a diagnostic challenge to distinguish KLS from a schizophrenia spectrum disorder when presented with cognitive impairment, bizarre behaviour and hypnagogic hallucinations. The slight EEG changes are not specific for KLS, but could be regarded as a sign for any kind of organic brain disease.

There are several hints suggesting an autoimmune context, such as the regularly reported flue-like symptoms prior to the first episode and the increase in specific HLA-types.⁷ A possible defect in the hypocretin/orexin system is discussed,⁸ but the underlying pathophysiology still needs to be elucidated.

In terms of treatment, the most consistent reports exist for lithium which seems to reduce the risk for relapse, to shorten the mean duration of an episode and to decrease the occurrence of behavioural changes during the episodes.⁶ Arnulf *et al.*⁴ found a relevant benefit for treatment with lithium, amantadine or valproate. However, there is a clear need for further reports or, if possible, systematic trials, because today, no therapy with a higher level of evidence is available.⁵

Learning points

- ▶ Kleine-Levin syndrome is a rare disorder presenting with typical episodes of hypersomnia, increased food intake, disinhibited sexual drive, cognitive impairment and alterations of perception, behaviour and the vegetative system.
- ▶ Kleine-Levin syndrome is often misdiagnosed. Inadequate treatment can lead to significant side-effects.
- ▶ Although there is currently no evidence-based treatment, several authors report benefits under treatment with amantadine, lithium or valproate.

Contributors LF, BS and CN were responsible for the clinical evaluation and the treatment, discussed the case and conceptualised the manuscript. LF and CN wrote the manuscript.

Competing interests None.

Patient consent Obtained.

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REFERENCES

- 1 Arnulf I, Zeitzer JM, File J, *et al.* Kleine-Levin syndrome: a systematic review of 186 cases in the literature. *Brain* 2005;128(Pt 12):2763-76.

- 2 Huang CJ, Liao HT, Yeh GC, *et al.* Distribution of HLA-DQB1 alleles in patients with Kleine-Levin syndrome. *J Clin Neurosci* 2012;19:628–30.
- 3 Dauvilliers Y, Mayer G, Lecendreux M, *et al.* Kleine-Levin syndrome: an autoimmune hypothesis based on clinical and genetic analyses. *Neurology* 2002;59:1739–45.
- 4 Arnulf I, Lin L, Gadoth N, *et al.* Kleine-Levin syndrome: a systematic study of 108 patients. *Ann Neurol* 2008;63:482–93.
- 5 Oliveira MM, Conti C, Saconato H, *et al.* Pharmacological treatment for Kleine-Levin syndrome. *Cochrane Database Syst Rev* 2009;(2):CD006685.
- 6 Poppe M, Friebe D, Reuner U, *et al.* The Kleine-Levin syndrome—effects of treatment with lithium. *Neuropediatrics* 2003;34:113–19.
- 7 Billiard M. The Kleine-Levin syndrome: a paramedian thalamic dysfunction? *Sleep* 2005;28:915–16.
- 8 Ganjavi H, Shapiro CM. Hypocretin/Orexin: a molecular link between sleep, energy regulation and pleasure. *J Neuropsychiatry Clin Neurosci* 2007;19:413–19.

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