KLEINE-LEVIN SYNDROME

Interface between neurology and psychiatry

Luís Pereira Justo¹, Helena Maria Calil², Sílvia A. Prado-Bolognani³, Mauro Muszkat⁴

ABSTRACT - We report the first episode of Kleine-Levin (KLS) syndrome in a 17-year-old male. The illness onset, clinical features, neuropsychological evaluation and polysomnographic recording are described. Typical symptoms hypersomnia, hyperphagia and sexual disinhibition were observed besides behavioral disturbances, polysomnographic and neuropsychological alterations. Behavioral disturbances similar to a manic episode including psychotic symptoms were relevant. The pharmacologic treatment included lithium, methylphenidate and risperidone. The introduction of risperidone aimed the control of psychotic symptoms and the persistent manifestations of hypersexuality after sleepness control and to the best of our knowledge there are no other report regarding risperidone use for KLS in the literature.

KEY WORDS: Kleine-Levin, neuropsychology, polysomnography, risperidone, sleep disorders.

The Kleine–Levin syndrome (KLS) is characterized by episodes of recurrent hypersomnia, hyperphagia or megaphagia and behavioral alterations, mainly sexual disinhibition; the prognosis is benign, since the episodes often decrease in frequency and intensity with age, finally reaching spontaneous remission¹². This syndrome has its typical onset during the second decade of the patients’ life, and is more prevalent among men³. The diagnosis was first described and formalized in the first half of 20th century⁴⁶. There were approximately 500 cases described all over the world until the year 2000⁷. A recent published systematic review found 186 different cases reported in 195 articles in Medline ranging from 1962 to 2004⁸. This review shows that men were 68% of the cases, the median age of onset was 15 years (range 4-82 years, 81% during the second decade) and the mean duration of syndrome was 8 years⁹.

We report the first episode of KLS in a young man.

CASE

A 17-years-old male student, had no history of previous behavioral alterations or illnesses, except for those that are common in childhood; no use of alcohol or drugs and without family history of mental illness. He perpetrated a sexual attack on a stranger woman in a public place. Minutes later, he presented sleepiness and disorganized thought. He was taken to a hospital and remained there for 3 days. He went through several exams, among them resonance imaging of the head and exam of cerebrospinal fluid; all of them did not show any alterations.

The behavioral alterations became more pronounced; he was discharged from the hospital and referred to a psychiatrist, with a provisional diagnosis of schizophreniform disorder. Due to his excessive sleepiness (he slept approximately 21 hours a day on the first days), the psychiatrist referred the patient to another neurologist, who postulated the hypothesis of KLS. A polysomnography was carried out and revealed a pattern of low voltage rhythm, with reduced sleep latency and REM latency, and a reduc-
tion of the elements characteristics of the sleep phases II, III and IV (Table 1).

When awake, he was irritable and had hypersexualized behavior directed to women. His liquids intake was also remarkable (polydypsia) and in a few days later he manifested hyperphagia. The psychiatric assessment revealed disorientation regarding time, but not space, nor self, agitation, pressured speech, discreet thought disorder, delusional ideation with grandiose and sometimes persecutory content and auditory hallucinations. There were outbursts of verbal aggressiveness. He would make occasional references to his experiences as if they were the result of some kind of health problem, suggesting some degree of “awareness of illness”. Although there were variations in the intensity and predominance of symptoms, his condition remained almost the same for approximately 50 days after beginning treatment. The disappearance of his symptoms was gradual, and when recovered the patient resumed the same behavior he had before the onset of the syndrome, showing a quite adequate notion of having gone through a period of behavioral alterations, with abundant though unclear recollections of the sensations and situations he had experienced. He remarked he had lived that period as if he was in a dream from which he could not awake completely. Following the diagnosis of KLS, lithium (600 mg initially, adjusted according to the blood level, to 900 mg/day, in order to reach 0.6 µMol/L) and methylphenidate (10 mg/day in the first fortnight) were introduced. In the 23rd day of treatment, when the patient had already had a significant reduction of hypersomnia, the psychotic symptoms, hyperphagia and hypersexuality began to prevail. Then methylphenidate was interrupted and risperidone was initiated (2 mg/day, later increased to 4 mg/day). A neuropsychological evaluation was carried out two months after the beginning of treatment, and its results are in Table 2.

The analysis revealed reduced attentional span, reduced immediate retention for verbal and visual stimuli, but good acquisition and retrieval capacities. The patient demonstrated normal intellectual efficiency, with a significant discrepancy between the verbal and executive functions, showing satisfactory performance in tasks based on language and abstract thinking. However he presented major difficulties regarding motor-visual speed and precision, as well as visuospatial planning strategies. The executive functions evaluated by the Wisconsin test (6 categories were carried out) showed satisfactory performance. After, he remained stable for approximately 3 months the medication was gradually reduced until its complete withdrawal.

The patients signed the informed consent for this publication.

**DISCUSSION**

The KLS is a challenge to the physician, since its causes are not yet clear, its symptoms are a mix of manifestations of neurological illnesses and psychiatric disorders, and also because of the uncertainties regarding its treatment. Although the psychiatric symptoms associated to the KLS have been reported, they seem hardly understood.

This case illustrates the similarities between some of the KLS symptoms and those of a manic state which, in spite of being typical of bipolar disorder, might also occur in several diseases. Such similarity has been previously mentioned. Additionally, it is also noteworthy that the drug treatments most frequently used to treat the KLS are the same used in the treatment of bipolar disorder such as lithium. The choice of risperidone among the antipsychotic medications was due to the fact that it has a weak sedative property, a small potential to produce extrapyramidal adverse reactions at low doses, and mainly because it quickly increases the levels of prolactin, which seems to be associated to the reduction of the libido and possibly to the control of manifestations of hypersexuality (our patient had simultaneous increase of prolactin and reduction of hypersexuality). To the best of our knowledge there are not reports in the literature of the risperidone use in the KLS treatment. The diagnosis of KLS is purely clini-

<table>
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<th>Function (Test)</th>
<th>Percentile/Score</th>
<th>Conclusion</th>
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<tr>
<td>Verbal attention (WMS)</td>
<td>9</td>
<td>Marked difficulty</td>
</tr>
<tr>
<td>Visual attention (Coding (WAIS-R))</td>
<td>25</td>
<td>Moderate difficulty</td>
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<tr>
<td>Language (FAS)</td>
<td>80</td>
<td>Good performance</td>
</tr>
<tr>
<td>Vocabulary (WAIS-R)</td>
<td>50</td>
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<td>Verbal IQ (WAIS-R)</td>
<td>97</td>
<td>Verbal-execution discrepancy</td>
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<td>Executive IQ (WAIS-R)</td>
<td>75</td>
<td>Moderate difficulty</td>
</tr>
<tr>
<td>Executive function (WCST)</td>
<td>6 categories</td>
<td>Good performance</td>
</tr>
</tbody>
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WMS, Wechsler memory scale; WAIS-R, Wechsler adult intelligence scale-revised; WCST, Wisconsin card sort test.
In conclusion, even though there is often suggestion of neurological and neurophysiologic abnormalities, leading physicians to think of dysfunction in the diencephalic areas, mainly in hypothalamus. Therefore, physicians can observe polysomnographic alterations such as a reduction of the REM sleep latency, REM latency and superficial sleep with a reduction of stages III and IV, as were observed in this case. The neuropsychological examination seems to corroborate the hypothesis of integrity of prefrontal areas, since his executive functions were preserved. His visual-constructive difficulties, the discrepancy between his non-verbal intellectual functioning and use of language, on the other hand, could be related to the involvement of associative areas of the non-dominant hemisphere, important for the balance and modulation of the functions related to the attentional control, the affective/emotional modulation and the impulses control, including the inhibitory sexual behavior. The clinical polymorphism and the significance of the psychiatric manifestations during the KLS episodes highlight the need for neurologists and psychiatrists to work together when taking care of these patients.

REFERENCES