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Monozygotic Twins Affected with Kleine-Levin Syndrome

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Kleine-Levin syndrome (KLS) is the most frequent and typical form of recurrent hypersomnia.[1] KLS includes recurrent episodes of hypersomnia diversely associated with behavioral symptoms such as compulsive eating, sexual disinhibition, and odd behaviors; cognitive symptoms such as a feeling of unreality, confusion, delusions/hallucinations, and less dramatic symptoms such as impaired speech, concentration, memory; mental symptoms such as depression and anxiety; physical signs such as dysautonomic features and weight gain; and transient symptoms such as amnesia, elation, and insomnia for one or two days at the end of episodes.[1-3] The simultaneous occurrence of all these symptoms is the exception rather than the rule. Standard laboratory tests are not informative. Between episodes, the patient is presumably totally normal.[1,2]

Nine cases of familial KLS have been identified in one series,[3] two with more than two affected relatives,[4,5] and five in another series[6] including two of the previous series; no cases of twins have been previously reported. We report here the first case of twins affected with KLS.

CASE REPORTS

The twin brothers were seen at the Gregorio Marañón University Hospital Sleep Unit outpatient clinic by one of us (RPA) in October 2010. After obtaining the patients' consent, the study was approved by the local Ethics Committee.

They underwent a thorough clinical work-up and laboratory tests including magnetic resonance imaging, HLA class II typing, and genetic marker analysis.

The twin brothers were born on 2.10.1977. Neither of the twins had a history of psychiatric disorders.

Case # 1 (GLG) was the first-born twin. His first attack occurred at the age of 16 years, in the context of rhinitis, and his last attack at 29 years. Clinical features included recurrent hypersomnia, decreased eating, odd behaviors (beating his own legs against the wall to know if he was awake or sleep), irritability, feeling of unreality, illusions (persisting impression of wet hands), depression and anxiety, transient insomnia, and partial amnesia at the end of episodes. Onset and end of episodes were progressive. Mean duration of episodes was 15 days at the beginning and progressively shorter. Cycle length (time from onset of one episode to the next one) was 40 days. The patient was strictly normal between episodes. He was given lithium carbonate for 5 years, despite poor response and weight gain up to 11.2 kg during attacks. The increase of weight was not acute, associated with the episodes of hypersomnia, but progressive as a side-effect of sustained treatment with lithium

Case # 2 (ALG) was the second-born twin. His first attack occurred at the age of 17 years, after the break-up of his first love affair, and his last attack at the age of 31 years. Clinical features included recurrent episodes of hypersomnia associated with compulsive eating and drinking during most episodes; sexual disinhibition; irritability; confusion, feeling of unreality; altered tactile, gustative, and olfactory perceptions; apathy, impaired speech, impaired memory; depression and anxiety; profuse sweating; and transient amnesia, moderate elation, and insomnia at the end of episodes. Onset and end of episodes were progressive; mean duration of episodes was 2 weeks, with cycle length 40 days at the beginning of condition and 180 days thereafter. The patient was normal between episodes. He was prescribed lithium carbonate for 4/5 years without much benefit and weight gain up to 9 kg during attacks.

Clinically the second-born twin showed typical clinical features of Kleine-Levin syndrome, while the first-born twin showed a less typical form, in which there was no compulsive eating, but instead decreased eating.

Brain magnetic resonance imaging was normal. Genetic markers (HLA and 7 additional highly polymorphic markers on chromosome 11 and 15) revealed identical results, confirming monozygosity. HLA typing revealed heterozygosity: *DRB1*04, DRB1*15/DRB4*01, DRB5*01, DQB1*03:02, DQB1*06:01*.

This is the first report of monozygotic twins in KLS. The twins were concordant for KLS, although the first-born twin showed a less typical form of KLS. Interestingly enough, the documented allele, *DQB1*06:01*, was at variance *with DQB1*02:01* previously reported to be associated with KLS in 28.3% of cases.[7] Although familial cases of KLS are relatively rare (9 out of 239 cases, 3.7%),[3] our observation raises the possibility of genuine genetic forms of KLS. This is supported by monozygosity, similar age at onset of the condition (16 and 17 years), and close similarities in symptoms (except for compulsive eating). Future assessment should include CSF hypocretin-1 measurement, and a complete genetic work-up including linkage analysis and the new generation exome sequencing to identify a potential pathogenic mutation.

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DISCLOSURE STATEMENT

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