

Menstruation-Related Hypersomnia Treated with Hormonal Contraception: Case Report and Review of Literature

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Menstrual-related hypersomnia (MRH) is a rare disorder consisting of recurrent hypersomnia that is temporally linked with menses. An unusual case of an 18-year-old female with repeated episodes of hypersomnia was referred to a psychiatrist and a neurologist. A review of the literature was done so that an accurate diagnosis could be made, thereby enabling the development of an appropriate treatment plan. Making an effective diagnosis was a challenge because of the similarity of the symptoms of MRH with other psychiatric disorders. As additional clinical features were identified and treatments were ruled ineffective, further diagnoses were proposed. The patient's symptoms ceased with oral contraceptive treatment. Hormones play a role in the menstrual cycle and frequently affect behavior (such as sleep patterns). This case underlines the importance of multidisciplinary evaluation and treatment in unusual cases. The potential role of hormone fluctuation in patients with psychiatric conditions should be considered when diagnosing and treating those who are unresponsive to traditional pharmacological treatments. [P R Health Sci J 2016;35:40-42]

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Menstrual-related hypersomnia (MRH) is a rare disorder that consists of recurrent hypersomnia temporally linked with menses (1). During the last days of the menstrual cycle, when hormone levels are at their lowest, is when women are most likely to experience negative somatic and mood-related symptoms. Excessive daytime sleepiness can occur during the last days of the menstrual cycle, usually disappearing shortly after the cycle begins again (1). It has been established that there are gender differences in sleep disorders, especially after the onset of puberty, to the degree that in women, menstrual cycles, pregnancy, and menopause can alter sleep patterns (2). Significant hormonal changes in women are associated with a high incidence of sleep disorders (3, 4). Oral contraceptives have been associated with mood alterations (4).

Symptoms of other psychiatric conditions can also be identified in this sleep disorder. A study identified 18 cases of MRH from a total of 339 cases of recurrent hypersomnia. Just over 35% of the 18 patients verified to have MRH presented episodes of depression (5). As is the case with Kleine-Levin Syndrome (KLS), significant weight gain is reported in women with MRH. In addition, similarities were found between all forms of recurrent hypersomnia (MRH and KLS, included) and 2 mood disorders. In all of them, similar symptoms may be presented, including significant weight gain, hypersomnia, and episodes of depression.

We present, herein, the unusual case of an 18-year-old Puerto Rican girl with MRH who was effectively treated with oral contraceptives. This case highlights the importance of taking into account the role of hormone fluctuations in psychiatric diagnoses and advances the possibility that there is another medical use for oral contraceptives.

Case Report

An 18-year-old Puerto Rican female had a first episode of cephalalgia, hypersomnia, lethargy, and disorientation that persisted for several days. The patient was taken first to a psychiatrist and then referred to a neurologist. No prior history of psychiatric treatment was reported.

Initially, the patient was diagnosed with major depressive disorder and prescribed fluoxetine (10 mg, increased to 20 mg based on symptoms). An electroencephalogram showed zeta

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waves and epileptiform wave discharges suggestive of epileptic foci. The patient had amnesia of both the events during the episodes and the episodes themselves. However, further evaluation yielded no alarming findings.

After 3 months of being asymptomatic, the episodes returned. She was also depressed because she had gained 21 pounds over the course of those 3 months. After a few weeks, her symptoms started to ameliorate. The patient and her mother insisted on reducing the medication doses because of the weight gain. She started on a carbohydrate-free diet. Additionally, other forms of alternative medicine were tried, such as those employed by a chiropractor.

After several weeks the patient reported experiencing excessive daytime sleepiness, which she would occasionally treat with Ritalin. The patient was instructed to keep a record of her menstrual cycle, which record showed that her symptoms lasted for 13 days of her cycle. The patient was referred to an obstetrician/gynecologist, who prescribed Ortho Tri-Cyclen Lo (norgestimate/ethinyl estradiol); nevertheless, her symptoms did not improve. A second ob/gyn was consulted, and this one prescribed Ortho-Cyclen (ethyl estradiol 35mg/norgestimate 0.25mg), without the placebo. This treatment has so far been effective and has kept her asymptomatic for the last 2 years. The patient was able to lose weight and reestablish normal activities.

Discussion

There are several causes of excessive sleepiness, and multiple factors should be considered. The common causes of excessive sleepiness are psychiatric comorbidities, the side effects of psychotropic medications, or both. Additionally, sleep disorders such as obstructive sleep apnea (OSA), narcolepsy, and Kleine-Levin Syndrome should be considered.

Possible side effects of any current medical treatment were ruled out since the patient was not using any medication. Given the clinical presentation of anhedonia, hypersomnia, lethargy, unusual weight gain, decreased energy for at least 2 weeks, and occasional disorganized and erratic behavior, we considered major depressive disorder with psychotic features as the primary diagnosis.

The patient was placed on antidepressant and antipsychotic medications. Since these medications were not effective and her clinical presentation started to include different pathologies, other causes had to be considered. The patient didn't present any of the symptoms associated with OSA, such as obesity, snoring, episodes of breathing cessation during sleep, or a morning headache. Nor did she present the symptoms that are often seen in narcolepsy, such as cataplexy and sleep paralysis.

People with KLS are often misdiagnosed with a psychiatric disorder. It was thought that this clinical entity was in part responsible for the patient's clinical presentation. This diagnosis (i.e., KLS) describes a patient with similar symptoms but is not associated with the menstrual cycle.

Once the association between the patient's menstrual cycle and the symptoms was identified, MRH was considered. MRH is a rare disorder consisting of recurrent hypersomnia that is temporally linked to menses. Although there is little information about this entity or about the role that hormones play during the menstrual cycle, it seems probable that hormones are responsible for the symptomatology (including demeanor and behavior) that this particular patient presented. The response of the patient to oral contraceptives sheds some light on why she was exhibiting such conduct. Although treatment with triphasic oral contraceptives did not cause any differences in her symptoms, treatment with monophasic contraceptives did. We were able to associate her symptoms with the secretory phase of her menstrual cycle. When ovulation was inhibited, the hypersomnia ceased.

It has been established that the peaks of depression in women occur at times of hormonal fluctuations in the premenstrual phase (6). High-dose estrogen has been used effectively to treat patients with chronic relapsing depression. In previous studies it has been found that treatments that inhibit ovulation in the patients with MRH stop its symptoms (7, 8). A more recent study reported on a young female and her brother, both with sleep disorders that manifested during adolescence. His KLS was effectively treated with low dose carbamazepine, while her particular disorder (determined to be MRH) responded positively to oral contraceptives (9). Undoubtedly, there is more to learn about MRH and its effects on the body.

Oral contraceptives played a key role in ameliorating our patient's symptoms and improving her quality of life. Furthermore, this case shows that multidisciplinary evaluation and treatment are important in medical diagnosis, especially in unusual cases. In order to effectively diagnose a patient with one or more psychiatric conditions who is otherwise unresponsive to traditional pharmacological treatments, the possible effect of hormone fluctuations on that patient's outcome must be considered by the clinician. Doing so might shed new light on research exploring MRH, thereby furthering our understanding of how to treat patients with this rare disorder.

Resumen

La hipersomnia relacionada a la menstruación es un trastorno raro de hipersomnia recurrente temporalmente ligado al ciclo menstrual (1). Un caso inusual de una mujer puertorriqueña de 18 años fue referida a un psiquiatra y a un neurólogo principalmente a causa de episodios de hipersomnia. Una revisión de literatura se llevó a cabo para alcanzar un diagnóstico adecuado para un tratamiento efectivo. El diagnóstico fue un reto debido a semejanzas entre los síntomas presentados con otros trastornos psiquiátricos. Al identificarse síntomas adicionales y tratamientos inefectivos, se continuó con la búsqueda del tratamiento adecuado. Los síntomas de la paciente cesaron al tratarla con anticonceptivos. Las hormonas tienen

un rol durante el ciclo menstrual y afectan el comportamiento (como patrones de sueños). Este caso brinda la importancia de la evaluación y tratamiento multidisciplinario en casos inusuales. El rol potencial de la fluctuación de hormonas en casos de condiciones siquiátricas deben ser consideradas en el diagnóstico y tratamiento de pacientes que no responden a tratamientos fármacos tradicionales.

References

1. Baker FC. Menstrual-Related Hypersomnia. In: Thorpy MJ, Billiard M. eds. *Sleepiness: Causes, Consequences and Treatment*. Cambridge, UK; Cambridge University Press; 2011:147–153.
2. Krishnan V, Collop NA. Gender differences in sleep disorders. *Curr Opin Pulm Med* 2006;12:383–389.
3. Regal AR, Amigo MC, Cebrián E. Sleep and women [in Spanish]. *Rev Neurol* 2009;49:376–382.
4. Kurshan N, Neill Epperson C. Oral contraceptives and mood in women with and without premenstrual dysphoria: a theoretical model. *Arch Womens Ment Health*. 2006;9:1–14.
5. Billiard M, Jaussent I, Dauvilliers Y, Besset A. Recurrent Hypersomnia: A Review of 339 Cases. *Sleep Med Rev* 2011;15:247–257.
6. Studd J, Panay N. Hormones and depression in women. *Climacteric* 2004;7:338–346.
7. Billiard M, Guilleminault C, Dement WC. A menstruation-linked periodic hypersomnia. Kleine–Levin syndrome or new clinical entity? *Neurology* 1975;25:436–443.
8. Sachs C, Persson HE, Hagenfeldt K. Menstruation-related periodic hypersomnia: A case study with successful treatment. *Neurology* 1982;32:1376–1379.
9. Rocamora R, Gil-Nagel A, Franch O, Vela-Bueno A. Familial recurrent hypersomnia: two siblings with Kleine–Levin syndrome and menstrual-related hypersomnia. *J Child Neurol* 2010;25:1408–1410.