CLINICAL VIGNETTE

Idiopathic Hypersomnia: A Rarer Case of Hypersomnia in Young Patients

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Introduction

Daytime sleepiness is a frequent complaint among adolescents and young adults. The most common cause of daytime sleepiness in this age group is insufficient sleep. Other possible causes include mood disorders such as depression, medical conditions such as hypothyroidism, medication side effects and substance use. When a patient is referred to a sleep specialist due to persistent daytime sleepiness, their insufficient sleep is further evaluated to see if it is related to insomnia or having a delayed sleep-wake phase disorder. Obstructive sleep apnea (OSA) is also considered given increased obesity in our population. If the cause remains elusive, sleep providers then consider central disorders of hypersomnolence. These include narcolepsy and idiopathic hypersomnia. Idiopathic hypersomnia is rare, estimated to be less than half as prevalent as narcolepsy.[1] We present a young female patient with daytime sleepiness, who was eventually diagnosed with idiopathic hypersomnia.

Case

A 19-year-old female with no significant past medical history presented to sleep clinic for persistent daytime sleepiness despite sleeping up to 11 hours at night and napping daily. She was regularly late for work due to oversleeping and fell asleep while at work. Other symptoms included snoring, sleep paralysis once a month, and vivid dreams. She denied cataplexy, a form of muscle weakness triggered by strong emotion. Her Epworth Sleepiness Scale score was 24 out of 24, consistent with excessive daytime sleepiness. Labs were within normal range, including a TSH of 1.5 mIU/L, hemoglobin of 13.5 g/dL, and vitamin B12 of 680 pg/mL. She underwent two-week actigraphy to monitor her sleep pattern. It revealed a mild delayed sleep phase and an average of 7.8 hours of sleep per night.

The first step in her sleep evaluation was to perform a polysomnogram (PSG) to evaluate for OSA given her history of snoring. Her PSG revealed no evidence of OSA with a normal Apnea Hypopnea Index (AHI) of 3.0 events/hr. With a sleep breathing disorder ruled out, the next step was to evaluate for central disorders of hypersomnolence. She underwent a PSG followed by a Multiple Sleep Latency Test (MSLT). Repeat PSG revealed a normal AHI of 1.3 events/hr, a sleep duration of 465 minutes, and a REM onset latency of 67 minutes. Her MSLT revealed a reduced mean sleep latency of 6.3 minutes (abnormal if </= 8.0 minutes) and zero sleep onset REM periods (SOREMPs). To be thorough, she underwent HLA genetic testing for narcolepsy markers HLA-DQA*1*0102 and HLA-DQB1*0602 which returned negative. Her clinical history along with her PSG and MSLT results met the International Classification of Sleep Disorders (ICSD) criteria for idiopathic hypersomnia[2] (Table 1).

Discussion

Idiopathic hypersomnia is a rare sleep disorder, with estimated prevalence of 20 to 100 cases per million.[2] Men and women are thought to have similar prevalence, though one review reported a higher rate in women.[3] Typical symptoms include excessive daytime sleepiness, increased sleep inertia, and un-refreshing naps that are often longer than one hour. Some patients may also report more than 10 hours of total sleep time per day, sleep paralysis, hypnagogic or hypnopompic hallucinations, vivid dreams, and autonomic dysfunction (such as headaches, orthostasis, temperature dysregulation, or Raynaud's). Mean age of symptom onset ranges from 16 to 22 years.[2] To meet criteria for diagnosis of idiopathic hypersomnia, other medical, psychiatric, and sleep disorders must be ruled out first. Consequently, the age at which the diagnosis of idiopathic hypersomnia is finally made is often delayed to when patients are in their 30s.[3]

Objective data which supports the diagnosis of idiopathic hypersomnia come from PSG followed by MSLT, 24-hour PSG, or one-week actigraphy.[2] The 24-hour PSG is logistically difficult to carry out at sleep centers and actigraphy is not reimbursed by insurance, so are omitted by many sleep providers. If a 24-hour PSG or one-week actigraphy is performed, a diagnosis of idiopathic hypersomnia is supported by a total sleep time of equal to or more than 660 minutes. The PSG followed by MSLT is most commonly done. Prior to performing a PSG followed by MSLT, patients are asked to complete a sleep log (or actigraphy) for two weeks to ensure adequate sleep prior to the study. Patients are titrated off REM suppressing medications, such as SSRIs/SNRIs/TCAs/benzodiazepines, and stimulant medications two weeks prior to the study, if it is safe to do so. It is recommended that patients abstain from other common substances such as alcohol, caffeine, and nicotine during the day of and if possible, days leading up to the study. A PSG is done the night before the MSLT to ensure the patient has at least six hours of sleep prior to the MSLT. It is also done to ensure

no other sleep disorders such as OSA are present if a sleep study had not been done previously. If there is insufficient sleep or evidence of OSA on the preceding PSG, the MSLT is no longer carried out the following day. Patients with idiopathic hypersomnia often show a high sleep efficiency of >/= 90% on their PSG. The MSLT is started 1.5 to 3 hours after the patient wakes up from their PSG. It consists of five naps, each separated by two hours, with each nap lasting up to 35 minutes.[4] The objective is to determine a patient's sleep onset latency and whether there is any REM sleep within 15 minutes of falling asleep (sleep onset REM period, SOREMP). Patients with idiopathic hypersomnia have a mean sleep latency </= 8 minutes and one or fewer SOREMP on the PSG and MSLT. In contrast, narcoleptics have a mean sleep latency </= 8 minutes and two or more SOREMPs, or clinical cataplexy along with a SOREMP on the nocturnal PSG.[2]

Once a diagnosis of idiopathic hypersomnia is made, deciding on treatment is next. Stimulants are the first line medication. The preferred stimulants are modafinil or armodafinil, which are dopamine reuptake inhibitors. They are preferred due to their favorable side effect profile compared to other stimulants. Women of child bearing age should be educated that modafinil and armodafinil increase the metabolism of oral contraceptives. They should use other contraceptive methods while on these medications. Other possible stimulants prescribed are methylphenidate and amphetamines. More caution is used with these stimulants due to their cardiovascular and abuse risks. In 2021, the FDA approved the low sodium formulation of sodium oxybate, mixed-salt sodium oxybate, for the treatment of idiopathic hypersomnia in adults. The medication can be dosed once or twice nightly. The active particle of sodium oxybate is gamma hydroxybutyrate (GHB). There are a host of side effects to monitor for, including respiratory depression, weight loss, nausea, worsening mood disorders, and abuse. The medication is only available through one national pharmacy. To monitor for adverse medication effects, the FDA mandates patients taking sodium oxybate participate in a Risk Evaluation and Mitigation Strategy (REMS) program. Many patients find difficulty adjusting to the stringent monitoring and lifestyle changes to use sodium oxybate, such as avoiding alcohol. As a result, this medication is not a preferred choice for many providers or patients. Our patient initially tried methylphenidate rather than modafinil since she did not want to stop her oral contraceptive. However, while on methylphenidate, she experienced adverse effects of vision changes and facial numbness and weakness. She was then switched to amphetamine/ dextroamphetamine 15 mg BID PRN and has been managing her daytime sleepiness well.

In summary, this patient highlights the process involved in evaluating patients with daytime sleepiness and eventually arriving at diagnosis of idiopathic hypersomnia. Her case reminds us of the differential diagnoses, the diagnostic steps, and the risks and benefits of treatment to consider in treating patients with idiopathic hypersomnia.

Table 1: ICSD-3-TR diagnostic criteria for idiopathic hypersomnia

Criteria A-F must be met

A. The patient has daily periods of irrepressible need to sleep or daytime lapses into drowsiness or sleep occurring for at least 3 months.
B. Cataplexy is absent.
C. Polysomnography and Multiple Sleep Latency Test (MSLT) findings are not consistent with a diagnosis of narcolepsy type 1 or 2.
D. The presence of at least one of the following:
    1. The MSLT, performed in accordance with current recommended protocols, shows a mean sleep latency of </= 8 minutes.
    2. Total 24-hour sleep time is >/= 660 minutes (typically 12-14 hours) on 24-hour polysomnographic monitoring (performed after correction of chronic sleep deprivation), or by wrist actigraphy in association with a sleep log (averaged over at least seven days with unrestricted sleep).
E. Insufficient sleep syndrome is ruled out (if deemed necessary, by lack of improvement of sleepiness after an adequate trial of increased nocturnal time in bed, preferably confirmed by at least a week of wrist actigraphy).
F. The symptoms and signs are not better explained by a circadian rhythm sleep-wake disorder or other current sleep disorder, medical disorder, mental disorder, or medication/substance use or withdrawal.

REFERENCES

1. **Anderson KN, Pilsworth S, Sharples LD, Smith IE, Shneerson JM**. Idiopathic hypersomnia: a study of 77 cases. *Sleep*. 2007 Oct;30(10):1274-81. doi: 10.1093/sleep/30.10.1274. PMID: 17969461; PMCID: PMC2266276.
2. American Academy of Sleep Medicine. *International Classification of Sleep Disorders, 3rd ed* - text revision. American Academy of Sleep Medicine, 2023.
3. **Ali M, Auger RR, Slocumb NL, Morgenthaler TI**. Idiopathic hypersomnia: clinical features and response to treatment. *J Clin Sleep Med*. 2009 Dec 15;5(6):562-8. PMID: 20465024; PMCID: PMC2792973.
4. **Krahn LE, Arand DL, Avidan AY, Davila DG, DeBassio WA, Ruoff CM, Harrod CG**. Recommended protocols for the Multiple Sleep Latency Test and Maintenance of Wakefulness Test in adults: guidance from the American Academy of Sleep Medicine. *J Clin Sleep Med*. 2021 Dec 1;17(12):2489-2498. doi: 10.5664/jcsm.9620. Erratum in: *J Clin Sleep Med*. 2022 Aug 1;18(8):2089. PMID: 34423768; PMCID: PMC8726366.