More: Recognizing and Treating Excessive Sleepiness in Primary Care

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The Super Sleeper CME

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Disclosures

History of Present Illness

Mr. Adams is a 23-year-old man who was referred to our tertiary care sleep clinic for persistent sleepiness despite adequate treatment of his medical and psychiatric comorbidities.

He relates that throughout his life he has always had difficulty waking up in the morning. The problem became more concerning during adolescence when he was frequently late to school. Subsequently, his difficulty awakening has cost him several jobs . At night, he stays awake worrying that he won't be able to get up in the morning. He has repeatedly slept through the rings of multiple alarm clocks. Even when awakened, he has been amnestic for conversations with his wife and even for eating breakfast; coworkers have awakened him by phone, but he falls back to sleep soon after speaking with them.

He reports that he typically falls asleep within 10 to 15 minutes of lying down, and he never wakes up during the night. His wife has not witnessed any snoring, pauses in breathing, or excessive leg movement during sleep. During the day, he drinks at least 4 cups of coffee to keep him going, but even so, if he is engaged in sedentary work, he may fall asleep and stay asleep for 2 to 4 hours. His current job is in jeopardy for this reason. These daytime sleep episodes are usually not refreshing, and the patient usually feels exhausted afterwards. He denies any symptoms of muscle weakness or sleep paralysis.

Recent History

Mr. Adams was first evaluated by his primary care physician almost 7 years previously. No confirmatory diagnosis was made for his sleep complaint at that time, but he was found to have hypothyroidism, and this was treated with thyroid hormone supplementation. Later on, after complaining of feeling depressed and losing interest in activities of daily life, he was formally evaluated by a psychiatrist. After trials of sertaline, paroxetine, and citalopram, which exacerbated his sleepiness, he was stabilized on venlafaxine. A trial of modafinil initially provided moderate relief , but the effect receded .

Medical History

Mr. Adams is known to have migraine headaches, hypothyroidism, and depression. He is currently taking levothyroxine , venlafaxine, and verapamil for his headaches. His family history is not significant for any sleep disorders. He is married and works an afternoon job as a computer programmer. He denies nicotine and alcohol abuse.

Clinical Evaluation

Mr. Adams is a well built young man with a body mass index (BMI) of 28 kg/m². He has Mallampati class I oropharyngeal airway, indicating a relatively normal oropharyngeal passage (the higher the Mallampati class [1-4], the greater the risk for obstructive sleep apnea). His Epworth Sleepiness Scale score (Figure 1) is 20. Otherwise, his physical and neurologic examinations are normal. His affect is appropriate.

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Use the following scale to choose the most appropriate number for each situation:-
0 = would never doze
1 = Slight chance of dozing
2 = Moderate chance of dozing
3 = High chance of dozing

Situation	Chance of dozing
Sitting and reading	3
Watching TV	3
Sitting, inactive in a public place (e.g. a theatre or a meeting)	4
As a passenger in a car for an hour without a break	2
Lying down to rest in the afternoon when circumstances permit	3
Sitting and talking to someone	1
Sitting quietly after a lunch without alcohol	3
In a car, while stopped for a few minutes in the traffic	1
Total	20

Score:
0-10 Normal range
10-12 Borderline
12-24 Abnormal

Figure 1. An Epworth Sleepiness Scale score of 20 provides subjective evidence of extreme sleepiness.

We scheduled him for standard overnight polysomnography (PSG) with multiple sleep latency test (MSLT) the following day. PSG showed an excellent sleep efficiency of 93% but shortened sleep latency of 6 minutes. There was no evidence of apneas or hypopneas, no significant oxygen desaturation, and no periodic limb movements of sleep. Hypnogram of the patient showed excellent sleep efficiency with no arousals; no evidence of sleep apnea or periodic limb movement disorder of sleep; no snoring recorded. His total sleep time including REM sleep latency and duration was within normal limits. MSLT showed reduced mean sleep latency of 5.5 minutes, indicative of pathologic hypersomnolence. No sleep-onset REM was noted, which argued against the diagnosis of narcolepsy (Figure 2).

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	Sleep Onset	REM Onset
Nap 1	11 min.	none
Nap 2	3 min.	none
Nap 3	4.5 min.	none
Nap 4	2.5 min.	none
Mean (min.)	5.25 min.	0/4

Figure 2. Multiple sleep latency test shows a mean sleep latency of 5.25 minutes with no sleep-onset REM periods, providing objective evidence of pathologic hypersomnolence.

Based on clinical and diagnostic interpretations, Mr. Adams is given the diagnosis of idiopathic hypersomnia (IH) with long sleep time.

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Management and Clinical Course

After an extensive discussion about our diagnostic impression with Mr. Adams and his wife, we note that they are greatly relieved to finally have a diagnosis. His condition is quite disruptive to his life at this time and efforts to manage it are certainly warranted. In terms of current medications, venlafaxine is a good choice for him because of its unique alerting effect. Most other antidepressants are sedating . We advise him to take it during the daytime. He will continue thyroid supplementation with close monitoring of thyroid stimulating hormone. In addition, we prescribe dextroamphetamine spansules (extended release) 10 mg to be taken first thing in the morning with additional doses of immediate-release dextroamphetamine, 5 mg, 5 times daily spaced 2 hours apart . He will follow-up with the sleep clinic in 3 months.

Patients with IH typically take 2 to 3 naps during the day .The immediate-release stimulants are taken 2 hours apart throughout the day to improve daytime functioning (some patients sleep 19 hours). Patients usually take both the extended-release and initial dose of the immediate-release agent the first thing in the morning. Extended-release formulations are probably not a good choice later in the afternoon.

At the follow-up visit, Mr. Adams is pleased about his overall clinical improvement. His job performance has improved markedly. His only concern is about the persistent difficulty with morning awakening. We advise him to use modafinil 200 mg at bedtime, which has proved helpful in this patient population (personal communication, Rodney Radtke, MD, January 2008)).

This approach is based entirely on anecdotal experience and may not achieve a universal response. Modafinil does not inhibit the initiation of sleep at bedtime, and the agent has helped some patients in this population to wake up in the morning. In fact, sleep drunkenness does not typically respond well to pharmacotherapy, and clinicians usually recommend behavioral methods (placing the alarm clock far away from the bed, using multiple alarm clocks at different places in bedroom, friends making repeated wake-up calls).

Discussion: Idiopathic Hypersomnia With Long Sleep Time

IH is probably one of the most frequently misdiagnosed sleep disorders, and thus an accurate understanding of this unique disorder is essential for primary care physicians to make timely referrals.

The nomenclature has evolved considerably during the 4 decades since it was first recognized by Dement in 1966.[1] Roth and coworkers further extended the spectrum by classifying monosymptomatic and polysymptomatic forms.[2] The monosymptomatic form is manifested by excessive daytime sleepiness alone, whereas the polysymptomatic form shows abnormally long nocturnal sleep and signs of sleep drunkenness on awakening, apart from the excessive daytime sleepiness. This entity has been called essential narcolepsy, non-REM narcolepsy,[3] hypersomnia

The American Academy of Sleep Medicine (AASM) accepts IH as a separate nosologic entity and places it among the hypersomnias of central origin (Table 1). In the current diagnostic classification, 2 variants have been recognized based on the duration of nocturnal sleep (10 hours of sleep vs more than 10 hours of sleep).[5]

Table 1. Hypersomnias of Central Origin[5]

Narcolepsy with cataplexy
Narcolepsy without cataplexy
Narcolepsy caused by medical conditions
Idiopathic hypersomnia with long sleep time
Idiopathic hypersomnia without long sleep time
Recurrent hypersomnia
Kline-Levin syndrome
Menstruation-related syndrome
Behaviorally induced insufficient sleep syndrome
Hypersomnia caused by medical condition, drugs, or substance
Hypersomnia not caused by substance or known physiologic condition
Physiologic (organic) hypersomnia, not otherwise specified

The onset of the disease is usually before 25 years of age with no gender preference.[6] The prevalence of IH in the general population is unknown. The only available data are the ratios of IH to narcolepsy, with wide variations. Earlier studies hinted that IH may be less prevalent than narcolepsy (1:6 by Bassetti and Aldrich, 1997[7]; 1:10 by Billiard and Basset, 1994[8]) subsequent to improved identification of sleep disorders that were formerly diagnosed as IH. Recently Anderson and colleagues[9] reported a study in which IH occurred 40% more frequently than narcolepsy.

Clinical Features

The main symptom of IH is a more or less constant daytime sleepiness. Along with this background of excessive sleepiness, patients have episodes of daytime sleep. Daytime naps are less refreshing; less irresistible, and of longer duration compared with the sleep of people with narcolepsy. Nighttime sleep lasting typically longer than 10 hours is the hallmark of IH. Sleep efficiency on PSG testing is usually above 85%, with no frequent arousals as seen in narcolepsy. For this reason, patients with IH are sometimes called "super sleepers." Awakening is often a daunting task for these patients; they usually use sophisticated alarm clocks or devices to wake up and often report postawakening confusion, a phenomenon referred to as "sleep drunkenness." These patients describe morning disorientation in time and space, slowing of thought and speech, and inappropriate behavior lasting from several minutes to an hour or more.[10,11]

An intriguing feature of this disease is the presence of dysautonomic symptoms in a minority of patients. These symptoms are characterized by the following: (1) orthostatic hypotension and syncope, (2) headaches that usually include migrainous features, and (3) peripheral vascular complaints such as Raynaud's phenomena, with cold hands and feet.[5]

Pathophysiology

As the name suggests, no definite cause of the disorder has been identified to date. Neurochemical studies looking into cerebrospinal fluid monoamine metabolites and hypocretin levels have so far been unrevealing. Because of some familial cases, a genetic basis has been suggested with autosomal dominant mode of inheritance. In contrast to narcolepsy, there are no specific human leukocyte antigen (HLA) haplotypes or an animal model for IH.[12]

Diagnosis

The diagnosis of IH is primarily based on clinical features. However, PSG and sometimes MSLT are necessary to exclude sleep and medical disorders, along with physiologic variants that cause excessive daytime sleepiness (Table 2).

Table 2. Differential Diagnosis of Idiopathic Hypersomnia

Narcolepsy without cataplexy
Hypersomnia with depression
Upper airway resistance syndrome
Post-traumatic hypersomnia
Postinfectious hypersomnia
Delayed sleep phase syndrome
Chronic pain disorders
Long sleepers (healthy hypersomniacs)

The following International Classification for Sleep Disorders criteria have been formulated by the American Academy of Sleep Medicine (Table3) for diagnostic purposes.[5]

Table 3. International Classification of Sleep Disorders Criteria for Idiopathic Hypersomnia With Long Sleep

Complaint of EDS for > 3 months
Prolonged sleep time > 10 hours with laborious awakening in the morning or from naps
Nocturnal PSG excludes other causes of EDS
PSG findings: a major sleep period > 10 hours in length with a short sleep latency
MSLT findings: mean sleep latency < 8 minutes and < 2 SOREMP
Hypersomnia is not better explained by another sleep disorder, medical or neurological disorder, mental disorder, medication use, or substance abuse

EDS = excessive daytime sleepiness; PSG = polysomnography; MSLT = multiple sleep latency test; SOREMP = sleep-onset REM periods

HLA typing is not helpful. Neuroimaging including magnetic resonance imaging of the brain may sometimes be required if a structural lesion is suspected. Psychiatric consultation may be necessary if an underlying mood disorder is considered.

Management

The treatment of IH is mainly symptomatic largely because the etiology of the disorder is unknown. The mainstay of treatment is stimulant medications such as methylphenidate, dextroamphetamine, and modafinil. Behavioral and sleep hygiene techniques have little if any effect.[13] Earlier studies showed marginal benefit with these medications in patients with IH compared with patients with narcolepsy; however, the recent study by Anderson and colleagues[10] found that 61% of their patients who were treated with some form of stimulant medication experienced a significant improvement in their symptoms. These medications should be titrated slowly to achieve the desired clinical benefit and to avoid adverse side effects.

Complications

IH is usually a chronic lifelong disorder with significant implications for social, professional, and employment-related aspects of the patient's life.[5] Rare case reports of spontaneous improvement provide some hope for a better prognosis than previously thought.[7]