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SLEEP MEDICINE PEARLS

Is It Mild Obstructive Sleep Apnea?

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A 63-year-old woman was referred to the sleep center complaining of daytime sleepiness, snoring, and insomnia. She was single and never married but, on a recent business trip, was noted by a colleague to snore loudly. There was no report of witnessed apnea. She slept 8 to 8.5 hours per night but complained of daytime drowsiness and mental fogginess, particularly in the afternoons. She occasionally dozed off during small-group meetings. She also complained of nighttime awakenings, which she attributed to work stress. If she woke up and had trouble falling back to sleep, then she would take either zolpidem or alprazolam.

The patient had gained 25 to 30 pounds over the past 3 to 5 years, up to a current maximum of 198 pounds, and had been on antihypertensive medications for 2 years. Her past medical history included knee and foot surgery, tonsillectomy, gastroesophageal reflux disease, irritable bowel, and postmenopausal status. Medications were amlodipine 2.5 mg daily, plus zolpidem 10 mg or alprazolam 1 mg as needed. She reported allergies to penicillin, some antidepressants, ibuprofen, and eszopiclone. Family history was negative for sleep apnea.

Physical examination showed an obese woman in no distress. Blood pressure was 126/86. Airway exam revealed Mallampati class 1 (normal soft palate), small uvula, no tonsils, and no retrognathia. Exam was otherwise unremarkable, including normal heart and lung exam.

Polysomnography was performed without hypnotic medication. See summary graph (Figure 1).

What is Your Diagnosis?

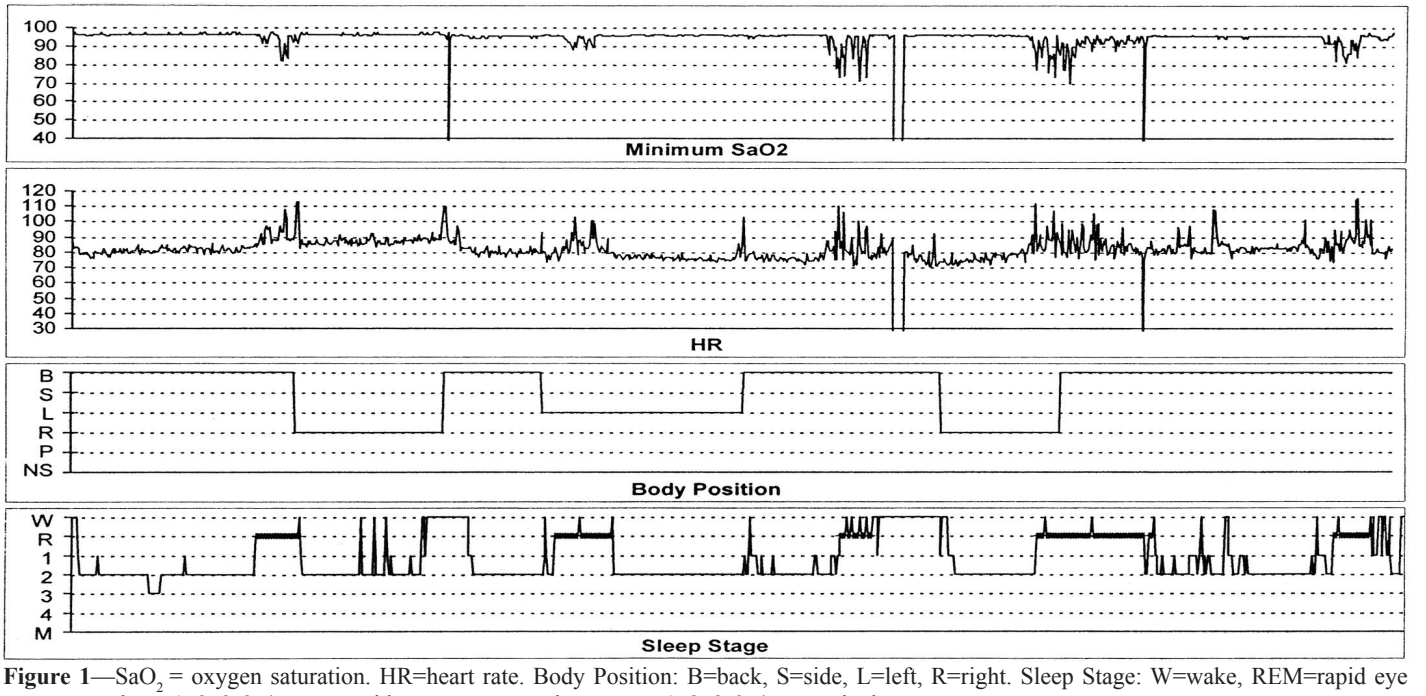

Figure 1—SaO_2 = oxygen saturation. HR=heart rate. Body Position: B=back, S=side, L=left, R=right. Sleep Stage: W=wake, REM=rapid eye movement sleep; 1, 2, 3 & 4 = non rapid eye movement sleep stages 1, 2, 3 & 4 respectively.

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REM Sleep-Specific Obstructive Sleep Apnea

The polysomnogram showed an overall apnea-hypopnea index (AHI) of 8.3 events per hour, but, in rapid eye movement (REM) sleep, the AHI was 52.7 events per hour. Although her overall AHI was only mildly elevated, the patient's clinical symptoms of sleepiness and hypertension clearly indicated the need for treatment. Continuous positive airway pressure (CPAP) titration was performed, with CPAP 6 to 8 cm H_2O reducing the REM AHI to 2.0 and overall AHI to 4.1. After 1 month of CPAP, the patient reported more daytime alertness and mental acuity, plus a reduction in her nighttime awakenings. Her blood pressure was stable, and she was working to reduce her use of zolpidem and alprazolam.

REM sleep-specific obstructive sleep apnea (OSA) is an important diagnosis to consider in a patient who has a mildly elevated AHI accompanied by substantial daytime sleepiness. The overall AHI may be only "mildly" elevated, but predominance in REM sleep with the markedly elevated REM AHI can account for clinically significant symptoms. A differential diagnosis in cases of excessive sleepiness in the setting of a mildly elevated AHI would also include upper airway resistance syndrome, inadequate sleep duration, periodic limb movements of sleep, narcolepsy, idiopathic hypersomnia, depression, and drug side effects. The polysomnographic findings in this case combined with the clear improvement on CPAP established the diagnosis of REM sleep-specific OSA.

The purported mechanism for REM-specific OSA to cause clinical symptoms is by fragmentation of REM sleep. Kass et al[1] described a clinical series of 17 patients who only had OSA in REM sleep. In this study, the overall AHI in the REM OSA group was 7.1 events per hour; all 17 patients had a REM AHI >15 events per hour. Multiple sleep latency testing in these patients showed a reduced mean sleep latency of 8.3 minutes. A control group of patients who had a normal AHI in both REM and non-REM (NREM) sleep demonstrated a normal mean sleep latency by Multiple Sleep Latency Test of 14.5 minutes. When the REM OSA group was compared with the control group, the mean sleep latency was significantly shorter in the REM OSA group. There was no treatment intervention. Kass concluded that the REM-concentrated sleep-disordered breathing was associated with a short sleep latency.

O'Connor et al,[2] in a larger retrospective review of a Canadian referral population, found that women were more likely than men to show REM-predominant OSA. In the 838 patients described, the REM AHI was similar in men and women, but the NREM AHI was significantly lower in women compared with men. Sixty-two percent of women were found to have REM-predominant OSA, whereas only 35% of women showed more-typical OSA that occurred in all sleep stages and sleep positions. In men, 24% showed REM-predominant OSA, and 62% showed more-typical OSA. Since these sex differences did not appear to be due to age or weight, the authors speculated that differences in upper-airway control may account for these sex differences.

Investigators have observed erratic breathing patterns in patients during REM sleep. To investigate the possible contribution of a decrease in airway-dilating muscle activity, Wiegand et al[3] studied the airway and ventilation in a small group of male subjects (n=6) and observed a decrease in genioglossus and alae nasi electromyogram (EMG) activity specifically during phasic REM sleep when compared with NREM and tonic REM sleep, and this was associated with decreased ventilation, tidal volume, and mean inspiratory airflow in phasic REM. Muscle activity in tonic REM was similar to that observed in NREM sleep.

White and colleagues have investigated sex differences with interesting yet inconclusive results. Popovic and White[4] studied genioglossus EMG activity in 11 male versus 11 female subjects during wakefulness. Waking genioglossus activity was higher in women than in men, which might make women more susceptible to sleep-related decreases in genioglossus activity, but no data were obtained during sleep. A follow-up study in 12 premenopausal versus 12 postmenopausal women showed the highest waking genioglossus activity in the luteal phase of the menstrual cycle, which decreased in the follicular phase and was lowest in postmenopausal women.[5] In a subset of postmenopausal women, hormone replacement for 2 weeks increased genioglossus EMG activity during wakefulness, supporting the concept that female hormones affect airway-muscle activity. Pillar et al[6] compared genioglossus and tensor palatini EMG activity during NREM sleep in male versus female subjects and showed similar levels of muscle activity during inspiratory resistive loading, but no data were obtained during REM sleep. Malhotra et al[7] showed that male predisposition to collapse may also be related to increased length of the upper airway in men compared with women. Finally, Shea et al[8] showed a somewhat paradoxical response, whereby negative pressure, which typically leads to activation of pharyngeal dilator muscles during wakefulness and to a less extent during NREM sleep, led to a decline in dilator muscle activity during REM sleep. These data suggest an impairment in protective pharyngeal reflexes during REM sleep, which may contribute to vulnerability of the pharyngeal airway. However, these intriguing results have yet to provide a clear explanation for sex-related differences in REM-predominant OSA. The paucity of data specific to REM sleep suggests this is an important area for future research.

CLINICAL PEARLS

1. Patients with substantial REM OSA may have only a mildly elevated overall AHI, but, if an elevated REM AHI is accompanied by marked sleepiness or other sleep symptoms, then a trial of treatment should be considered.
2. Women appear to have REM-predominant OSA more frequently than men.
3. A trial of CPAP treatment should be given to patients suspected of having REM OSA, since a response to CPAP supports the diagnosis.

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