

Upper Airway Resistance Syndrome—Report of Three Cases

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Abstract

Introduction: Patients with the upper airway resistance syndrome are frequently overlooked, and even if clinically suspected, often escape identification by polysomnographic monitoring. **Clinical Picture:** Three cases (2 women and a man) with excessive daytime sleepiness and fatigue were confirmed to have the upper airway resistance syndrome after undergoing polysomnography with oesophageal pressure monitoring. **Treatment:** Nasal CPAP during sleep was prescribed for 2 cases but 1 case refused all available treatment options. **Outcome:** After one month of CPAP therapy, the 2 cases reported improved symptoms and Epworth sleepiness scores. Lower daytime blood pressures were also recorded. **Conclusions:** Oesophageal pressure monitoring and EEG arousal analysis can greatly enhance the diagnostic accuracy in the upper airway resistance syndrome. Accurate diagnosis and effective treatment of this condition is important because of its sequelae of hypersomnolence and association with other disorders like systemic hypertension.

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Introduction

Sleep-related breathing disorders are widely recognised as important causes of morbidity and mortality over the past 3 decades.¹ The obstructive sleep apnoea syndrome² (OSAS) and the sleep hypopnoea syndrome³ are well-known and well-described breathing disorders during sleep. In contrast, the upper airway resistance syndrome^{4,5} (UARS) is a recently recognised clinical entity and its position in the pathophysiologic continuum of sleep-disordered breathing (SDB) is currently still unclear. Previously labelled as “idiopathic hypersomniacs” or “symptomatic snorers”, cases of UARS are characterised by excessive daytime sleepiness (EDS) resulting from numerous brief arousals caused by repetitive increases in resistance to airflow within the upper airway during sleep.⁵ Unlike OSAS, in which hypopnoeas, apnoeas and oxygen desaturation resulting from narrowing or closure of the upper airway during sleep are apparent during polysomnography (PSG), the transient increases in airway resistance in UARS are not readily detectable by standard sleep studies. Hence, the diagnosis of UARS is a difficult one to make with certainty.

Three cases of UARS are described and the challenges faced in the recognition of this condition are discussed.

Case Reports

Case 1

A 50-year-old Chinese man with a history of hypertension of one year's duration presented with the problems of EDS and loud habitual snoring of more than 10 years' duration. His Epworth Sleepiness Score⁶ (ESS) was 22 out of a maximum of 24 points. There were no symptoms suggestive of narcolepsy or restless legs syndrome. He spent at least 7½ hours in bed each night but often complained of non-restorative sleep with at least 3 awakenings for nocturia each night. Physical examination revealed a body mass index (BMI) of 26.2 kg/m² and a neck circumference of 40.5 cm. He had a narrow and high-arched hard palate and the oropharynx was narrow due to a low soft palate. He had micrognathia and retrognathia with increased overbite. An initial PSG did not detect any significant obstructive sleep apnoea (OSA) as the apnoea-hypopnoea index (AHI) was 4.3 and there was no significant oxygen desaturation. PSG with oesophageal pressure (Pes) monitoring using a paediatric feeding catheter and a continuous water-filled system as previously described⁷ was performed. The second PSG showed a sleep efficiency of 76% with no delta sleep and 9.5% of rapid eye movement (REM) sleep. The AHI was 0.3 and the minimum oxygen saturation during sleep

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C3A2 and O2A1 are EEG electrodes; LOC: left oculomyogram; ROC: right oculomyogram; Chin EMG: submental electromyogram; ECG: electrocardiogram; L Leg: left leg electrode; R Leg: right leg electrode; Airflow: airflow by oro-nasal thermistery; Chest: chest movements; Abdomen: abdominal movements; Snore Mic: microphone; O2 Sat: oxygen saturation; Pes: oesophageal pressure

Fig. 1. An epoch from the PSG of Case 1 showing a crescendo Pes arousal. Progressively negative Pes is seen until a Pes nadir (arrow) is reached followed directly by an arousal (arrowhead) and less negative Pes. Note that airflow measured by oro-nasal thermistors does not change significantly prior to the arousal.

was 93.9%. There were 115 arousals scored using established criteria⁸ and most of these were related to increasingly negative Pes (crescendo Pes arousals). Typically an arousal followed a period of progressively negative Pes, with the Pes nadir being the lowest (i.e. most negative) during the breath immediately preceding the arousal followed by an instant return of Pes to baseline values upon arousal (Fig. 1). The most negative Pes recorded during sleep was -50.3 cmH₂O. No periodic limb movements that might cause the frequent arousals were detected during the PSG. A multiple sleep latency test⁹ (MSLT) showed a mean sleep latency of 8.2 minutes and one sleep-onset REM period (SOREMP) out of the 5 study periods. Nasal continuous positive airway pressure (CPAP) titration was performed during sleep using the AutosetTM (ResMed, Sydney, Australia) self-setting CPAP device on a separate night. A conventional CPAP machine set at a fixed pressure of 9 cmH₂O was prescribed. This pressure was chosen as it was the pressure that was exceeded only 5% of the time, after first excluding periods in which the total leak (reported by the software) exceeded 0.4 L/s, during Autoset night. After one month of being on nasal CPAP during sleep, the patient reported marked improvement in daytime sleepiness and his ESS had dropped to 7. He no longer had nocturia or frequent awakenings at night. Daytime blood pressure decreased to 120/80 mmHg from a baseline of 170/100 mmHg prior to initiation of CPAP. The patient refused a repeat sleep study performed on nasal CPAP to document improved sleep efficiency as he was no longer symptomatic.

Case 2

A 51-year-old Chinese woman had excessive daytime fatigue and tiredness for 4 to 5 years. She also complained of poor memory, lack of concentration and difficulty coping with her job as a teacher during the same period. She was on follow-up and treatment with a gynaecologist for menopausal symptoms and had consulted a psychiatrist as well as a cardiologist for her symptoms of daytime fatigue. She had also consulted at least 2 other specialists for a suspected sleep disorder. A previous PSG had shown an AHI of 6.9 with no significant oxygen desaturation, multiple arousals and diminished delta and REM sleep. MSLT showed a mean sleep latency of 8.3 minutes and 1 possible SOREMP out of 4 naps. A diagnosis of possible UARS had been made based on these results and bi-level positive airway pressure via a nasal mask had been empirically prescribed. She could not tolerate this therapy and further consultation was made. When seen at our centre, she complained of daytime tiredness despite an average of 9 hours of sleep daily and her ESS was 10. She also had frequent awakening from sleep because of nocturia (ranging from 1 to 3 times per night) and difficulty breathing. According to her husband, she had occasional snoring which was not loud. He also described her as a very restless sleeper. Physical examination revealed a slim woman with a BMI of 20.6 kg/m². She had retrognathia and prominent overjet of the front teeth. Her uvula and oropharynx appeared normal. Neck circumference was 32.5 cm. A repeat PSG with Pes monitoring confirmed the diagnosis of UARS and the results were as follows: sleep efficiency was 81.4% with 1.9% delta and 13.3% REM sleep. Arousal index was 11.8 and there were multiple crescendo Pes arousals. The minimum (most negative) Pes during sleep was -55.2 cmH₂O. AHI was 4.5 and minimum oxygen saturation during sleep was 93.4%. Periodic leg movements were not detected.

The patient refused treatment for her condition as the various treatment options were not acceptable to her. Nonetheless she was satisfied with the knowledge of a diagnosis that could account for her symptoms.

Case 3

Perturbed by complaints of loud habitual snoring which was threatening her marital harmony and EDS that was affecting her job as a secretary, a 53-year-old woman sought medical attention. She also had a history of hypertension of 20 years' duration.

Her BMI was 23.8 kg/m² and neck circumference was 34 cm. She had slightly enlarged tonsils, a low-lying soft palate and an elongated uvula. Her jaw occlusion was normal and she did not have any obvious retrognathia. An initial PSG had not detected any significant OSA with an

AHI of 4.8. A repeat PSG with Pes showed a sleep efficiency of 75.6% with 16.8% delta and 3.2% REM sleep. Arousal index was 17.7. The most negative Pes recorded during sleep was $-69.3 \text{ cmH}_2\text{O}$. AHI was 4.6 with no significant oxygen desaturation during sleep. A MSLT confirmed her daytime hypersomnolence as the mean sleep latency was 7.3 minutes with one SOREMP out of 5 nap periods. Nasal CPAP at $10 \text{ cmH}_2\text{O}$ was prescribed after a night of CPAP titration using an autotitrating system as in Case 1. After one month of using nasal CPAP during sleep, the patient reported improved sleep quality. She no longer complained of EDS and the ESS had dropped from 21 before treatment to 3 after one month of nasal CPAP. Blood pressure was recorded at 130/90 mmHg after one month of CPAP therapy, having decreased from a previous recording of 160/100 mmHg. As in Case 1, this patient also refused a repeat sleep study performed on nasal CPAP as she was no longer symptomatic after one month of treatment.

Discussion

UARS is a clinically significant sleep disorder largely because of its sequelae of daytime somnolence and its association with systemic hypertension. By definition, EDS is a component of UARS and may be as severe as that found in OSAS.⁵ Perhaps more important than sleepiness with regard to the long-term sequelae are the haemodynamic changes that can result from UARS. Guilleminault et al¹⁰ recorded increases in systolic and diastolic blood pressure during transient arousals in patients with UARS. In addition, pulsus paradoxus and leftward shift of the interventricular septum as demonstrated by echocardiography have also been recorded during periods of most negative Pes nadirs. The exact nature of the association between SDB and daytime hypertension is currently unresolved but in an extensive review of the literature regarding hypertension and SDB, it was concluded that most cases of “essential hypertension” are caused by increased upper airway resistance during sleep from either OSAS or UARS.¹¹

UARS is a commonly overlooked sleep-related breathing disorder. A likely reason for this is that cases of UARS do not share the typical characteristics of OSAS that are familiar to many physicians. UARS does not show the typical male dominance reported in OSAS. In large reported series, there are roughly as many male as female individuals with UARS.⁵ Contrary to what is seen in OSAS, UARS patients are typically non-obese, with a mean BMI of $\leq 25 \text{ kg/m}^2$ and they are also frequently younger than OSAS patients.⁵ As previously observed⁴ and as in Case 2, not all patients were regular snorers and thus differential diagnoses of UARS include disorders associated with unexplained daytime fatigue and sleepiness such as chronic fatigue syndrome and idiopathic central nervous system

hypersomnia.

Interestingly, 2 of these 3 cases complained of nocturia. Nocturia and enuresis have been well-documented in patients with OSAS¹² and nocturia is thought to occur as a result of increased secretion of atrial natriuretic peptide (ANP) in response to the increased venous return resulting from the generation of negative intrathoracic pressure during episodes of upper airway obstruction. To our knowledge, there have been no reports of nocturia in patients with UARS thus far.

Definitive diagnosis of UARS may be difficult and, as was the situation in these 3 cases, patients with this clinically significant disorder often escape identification by polysomnographic monitoring. Oesophageal pressure monitoring (an approximation of respiratory effort) and pneumotachographic airflow measurements (an indication of upper-airway resistance) taken during PSG are the “gold standard” techniques for diagnosis.⁵ While Pes monitoring is well tolerated and does not cause any clinically important changes to sleep architecture, the use of tight-fitting full-face masks to record tidal volume during sleep often disturbs sleep quality and is difficult to conduct in the standard diagnostic setting. As with these 3 cases, Pes monitoring and EEG arousal analysis can greatly improve diagnostic accuracy in the absence of quantitative resistance measurements. The use of nasal cannula attached to a sensitive pressure transducer for airflow measurements, obviating the need for an intrusive tight-fitting facemask is promising, but its accuracy compared to the face mask/pneumotachograph has not been assessed.⁵ Although patterns of snoring, arousals, airflow by thermistery and abdominal/thoracic plethysmography from conventional PSG may, at times, suggest the diagnosis of UARS, they are by no means definitive or confirmatory measurements.

Besides the difficulties in the use of measurement techniques, the diagnosis of UARS is also plagued by the lack of standardisation in nomenclature and diagnostic criteria. The polysomnographic criteria that were used in the 3 cases described above as well as routinely in our centre for the diagnosis of UARS are as follows: AHI < 5 and > 10 Pes arousals per hour of sleep. A Pes arousal consists of a transient (3 to 15 seconds) EEG arousal scored according to established rules with the Pes nadir of the breath preceding the arousal being more negative by at least 50% of baseline values measured during quiet supine wakefulness. The Pes nadir had to be the most negative of the breaths preceding the arousal and had to decrease in magnitude with the breath immediately following the arousal as shown in Figure 1. This criteria is quite similar to the one used by the Stanford group in their 1993 study.⁴ It is not as stringent as the original clinical definition of the syndrome using both Pes and pneumotachographic airflow

assessments¹³ but is more rigorous than the simplistic criteria used in a later study on the surgical management of UARS.¹⁴

Conclusions

UARS has often been considered as a “subtle” form of OSAS. This may be true inasmuch as UARS is a more challenging condition to diagnose and manage. With regard to symptoms, both conditions can result in equal degrees of severity. More so than in cases of OSAS, the diagnosis, treatment and follow-up of patients with UARS require close attention of health care professionals in order to maximise treatment outcomes.

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