Case Report

Combination of Obstructive and Central Sleep Apnea as a Non-Sleepy Phenotype of Obstructive Sleep Apnea (OSA): A Case Report and Literature Review

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Abstract

Background and Objective: Co-occurring central sleep apnea (CSA) and obstructive sleep apnea (OSA) are a developing apprehension because many patients referred to sleep studies have co-morbidities such as cardiovascular and/or neurological disorders which increase the possibility of central and obstructive episodes. Here, we report a patient without excessive daytime sleepiness and a combination of CSA and OSA.

Case Report: We present a 16-year-old boy with a history of snoring, poor quality of sleep, nightmare, sleep walking, and sleep talking since he was two-years old. His STOP-Bang score was 7. Standard attended polysomnography (PSG) with audio-video monitoring was performed**.** The PSG results contained Apnea Hypopnea Index (AHI): 30.2 (number of OSAs was 50 and number of CSAs was 49 during sleep). Then, a titration study was performed and continuous positive airway pressure (CPAP) setting as low as eight cmH_2O was effective in eliminating obstructive events, but there was emerging CSAs in favour of Treatment Emergent CSA (TCSA).

Conclusion: This case represents a non-sleepy phenotype of OSA in combination with many CSAs in PSG. We suggest that further studies be performed on the association between the concomitant presence of CSA and OSA among non-sleepy patients with OSA.

Keywords: Central sleep apnea; Continuous positive airway pressure; Polysomnography; Obstructive sleep apnea

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Introduction

Obstructive sleep apnea (OSA) is a common condition represented by a normal breathing pattern when awake but repeated episodes of upper airway obstruction during sleep (1). These events (apneas or hypopneas) are owing to an imbalance between upper airway load (soft tissue and bone structures which can decrease the diameter of the throat) and the tone of the upper airway dilator muscle induced by sleep (2).

Central Sleep apnea (CSA) is described as the absence of stimulation for breathing during sleep from centre of respiratory-regulation for a time of at least 10 consecutive seconds (3). Polysomnography (PSG) shows the absence of any activity in airflow, chest, and abdominal movements (3, 4). Clinical presentation of CSA is difficulty in breathing during night and insomnia or poor sleep efficiency (3).

Individuals with a low arousal threshold (i.e., easily excitable) are prone to an instability of sleep state and central sleep apnea. It may be sufficient to cause a repetitive CSA when the individual oscillates between wakefulness and sleep, leading to a likely combination of CSA and OSA (5). Here, we report a patient with combined obstructive and central sleep apneas.

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Case Report

Our patient was a 16 year-old boy referred to our sleep clinic with a history of several years of snoring, sleep talking and walking, poor quality of sleep, sleep eating disorder, and abnormal movements during sleep since he was two-years old. He was treated for asthma, but his symptoms did not improve. His weight was 117 kg and height was 175 cm. He was not a smoker or an alcohol user. He denied taking opium or any other substance. He was being treated with clonazepam according to the symptoms of restless leg syndrome. He had not recently travelled to a high altitude. The STOP-Bang, Insomnia Severity Index (ISI), Epworth sleepiness scale (ESS), and Beck Depression Inventory II (BDI-II) scores were 7, 3, 3, and 19, respectively. Echocardiography was normal and left ventricular ejection fraction (LVEF) was 60%. He had not past medical history of cardiac or neurologic disorders.

Sleep study with attended full night PSG was performed with audio-video monitoring (MINI screen, Lowenstein, Germany). Electrocardiography was normal on the PSG and he had a sinus rhythm.

The PSG results are summarized in table 1. In physical examination and laboratory evaluation for approach to central apneas, evaluation of neurologic and heart disorders and arterial blood gas (ABG) test was performed. The brain magnetic resonance imaging (MRI) was normal and the neurologic examination was also completely normal. Toxicology (urine drug screen) and thyroid function tests were normal; PCO_2 was 57 in venous blood gas (VBG) analysis and 43.7 in the ABG test. The patient then underwent a titration study and continuous positive airway pressure (CPAP) settings as low as 8 cmH2O was effective in eliminating obstructive events, however there were a lot of CSAs that could suggest treatment emergent CSA. The patient refused using CPAP and lost follow up visits albeit intermittent calls from sleep clinic.

Discussion

This case presents a non-sleepy phenotype of OSA with many CSAs, but did not meet sufficient criteria for CSA as defined by International Classification of Sleep Disorders 3rd (ICSD3), so according to age and absence of underlying comorbidity that could explain the presence of CSA, we hypothesized that it could be mentioned as a phenotype of non-sleepy OSA combined with CSAs.

Our patient was an obese non-sleepy phenotype of severe OSA who had both obstructive and central events in his PSG. The patient's sleep efficiency and sleep stages were in the quite normal range for his age and gender. To assess his arousal threshold and explore low arousal threshold as a mechanism for OSA-CSA, we used clinical predictors [Apnea Hypopnea Index (AHI), Nadir SPO_2, and hypopneas] and the covariates [age, sex, and body mass index (BMI)] formula; and the result "-15.9" was obtained, which indicated a high arousal threshold (6).

Table 1. Polysomnography (PSG) parameters of the patient

PSG parameter	Diagnostic study	Titration study
Time in bed (minutes)	479.9	455.0
TST (minutes)	403.8	395.0
Sleep efficiency (%)	84.1	86.8
Stage N1 (%/minute)	9.91	10.51
Stage N2 (%/minute)	54.98	58.1
Stage N3 (%/minute)	20.56	25.57
REM (%/minute)	14.61	5.95
Number of obstructive apnea	50	8
Hypopneas	99	44
Number of central apnea	49	100
Mixed apneas	7	4
Time below 90% saturation (%) (minutes)	46.51	29.54
AHI	30.2	23.7
Arousal index (per hour)	11.6	15.0
Oxygen desaturation index (per hour)	15.9	16.5
Periodic Leg Movements Index (per hour)	20.0	0.6
Lowest desaturation (%)	85	89
Snoring Index (per hour)	204.4	45.1
Stage shifts	123	110

PSG: Polysomnography; TST: Total sleep time; AHI: Apnea Hypopnea Index

Nowadays, phenotyping has become more prominent in the management of patients with OSA.

Multiple studies have been conducted over the last two decades to find out why some individuals with OSA generate daytime symptoms associated to sleep disordered breathing and others do not, because the prevalence of OSA without sleepiness in the community is so high. Compared to non-sleepy types, sleepiness has been linked to higher cardiovascular and metabolic comorbidity, and many studies have attempted to explore whether CPAP treatment leads to better outcomes, in addition to improving quality of life (QOL), mainly by reducing excessive daytime sleepiness (EDS) (7). However, this may not be true for all patients, as some such as our patient had a combination of obesity and non-sleepy OSA that may affect cardiovascular outcomes in the future. Despite the differences between studies, patients with OSA and sleepiness are more prone to have a higher BMI, are older, and have more metabolic disorders than those with OSA and without EDS (7). Given the studies, patients without EDS, compared to those with it have less total sleep time (TST), sleep latency, Apnea Hypopnea Index (AHI), arousal index (ARI), habitual snoring, cardiovascular disease (CVD), asthma, chronic obstructive pulmonary disease (COPD), and lower BMI. Our patient also was a young non-sleepy phenotype of OSA although his BMI was 38.2 (non-consistent with available studies that reported lower BMI in non-sleepy phenotypes) (7). OSA is manifested by intermittent narrowing or collapse of the upper airway muscles during sleep and leads to blood gas disorders that is often associated with a brief awakening which may interfere with sleep continuity (7).

The coexistence of OSA and CSA is important because the majority of patients referred for sleep studies have comorbidities such as cardiovascular and/or neurological disorders that increase the possibility of obstructive and central events. Treating these complex sleep-related breathing disorders is challenging because understanding the basic pathophysiological mechanisms is critical to understanding why obstructive and central events overlap and to provide the most appropriate type of ventilation support (8). The three-factor interactions predispose a person to ventilatory instability, central sleep, and apnea hypopneas: Decreased CO_2 reserve ($PaCO_2$ eupneic minus $PaCO_2$ apneic), high or low loop gain (including of plant, controller, and mixing gains), and sleep stage instability (9).

Anything that causes multiple transitions between sleep and wake, such as maintenance insomnia, sleep breathing disorders, insufficient adherence to CPAP, or sleep movement disorder, can increase the tendency to ventilatory exceeding, periodic breathing, and central sleep apneas, markedly in a context of high chemosensitivity (9).

Our patient had an OSA and high number of CSAs accompanied by obesity. Obesity is a well-known risk factor for obstructive sleep apnea, but association of central sleep apnea with obesity-related OSA is less explored. It is also an issue that seems overlooked in comparing patients with non-sleepy phenotype of OSA to sleepy ones as non-sleepy ones may have a higher number of CSA albeit not meeting criteria of ICSD3 for CSA, such as our patient. However, literature indicates that CSA is associated with abdominal obesity and fat mass in children. In obese patients, increased soft tissue volume in the upper airways could change neuromuscular activity or weaken the response of the respiratory center, which is responsible for maintaining muscle tone in the upper airways (10).

The rapid transition from sleep to wake arousal induces a sudden change in the homeostatic control of the cardiorespiratory system. The ventilatory response leads to a rapid decrease in $PaCO_2$ so that CSA can occur during subsequent sleep if the hypocapnia is sufficient to exceed the apnea threshold. As in our patient, CSA was frequently accompanied by OSA in the form of mixed sleep apnea (central and obstructive events) (11).

Another form of sleep-disordered breathing is the complex sleep apnea syndrome, which central apneas persist or appear when obstructive events vanish with positive airway pressure (PAP) therapy. According to the last accepted definition, the number of central apneas or hypopneas must consist of more than half of breathing events that occur during sleep or cause periodic breathing that becomes prevalent and disturbing on PAP therapy and the central apnea index must be more than five events/hour (12). This pattern may be another explanation of CSAs in our patient.

Conclusion

This case represents a non-sleepy phenotype of OSA in combination with many CSAs in PSG. Cardiologic evaluations and laboratory examinations were normal. The patient was an obese non-

sleepy phenotype in adolescence, not described yet in the literature. Patients with non-sleepy OSA because of CO_2 level changes may have more CSAs, although this characteristic of non-sleepy ones has not been discussed yet and requires more investigation among non-sleepy phenotypes of OSA. It is recommended that further studies be performed on the association of mix presentation of CSA and OSA among non-sleepy patients with OSA.

Conflict of Interests

Authors have no conflict of interests.

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