Case Report
Which Condition Leads to Enuresis Nocturna? Seizures or Sleep Apnea?
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Abstract

A 52-year-old woman with a history of enuresis nocturna had admitted to the outpatient clinic of sleep disorders. Patient had complaints of increased daytime sleepiness, morning headaches, sialorrhoea, nocturia and nocturnal enuresis for four years. Her background history revealed partial complex seizures, sometimes with secondary generalization, which have started when she was 23 years old. Her seizures often happened to occur at daytime with a frequency of once in 3 months, but rarely could occur at nighttime. For four years she had nocturnal enuresis once in six months, and the frequency of enuresis increased in the last month. She used to have complaints of muscle and jaw pain, when she awaked after nocturnal enuresis attacks. We have performed a full night polysomnography, which has revealed heavy obstructive sleep apnea syndrome; with an apnea-hypopnea index of 107 events per hour. The conclusion was drawn that the patient had epileptic seizures and ictal enuresis during nighttime, caused by obstructive sleep apnea leading to deep deoxygenation. The treatment with nasal continuous positive airway pressure device was started. Four-month follow-up period showed very good compliance, elimination of seizures, and diminished daytime sleepiness.

ABBREVIATION S
OSA: Obstructive Sleep Apnea; SDB: Sleep-Disordered Breathing; BMI: Body Mass Index; MRI: Magnetic Resonance Imaging; EEG: Electroencephalography; EOG: Electrooculography; EMG: Electromyography; PSG: Polysomnography; AHI: Apnea-Hypopnea Index; REM: Rapid Eye Movement; n-CPAP: Nasal Continuous Positive Airway Pressure; ANP: Atrial Natriuretic Peptide; AASM: American Academy of Sleep Medicine

INTRODUCTION

Epilepsy and sleeping have significant influences on each other. Clinicians may have difficulty distinguishing abnormal sleep events from epileptic seizures and the two disorders are likely to have detrimental effects on each other.

Studies reported that, seizures were nocturnal in 13.4- 21 %, diurnal in 41.5-42 % and diffuse or random in 37- 45.1 % of the cases [1,2]. There is increasing evidence that obstructive sleep apnea (OSA) coexists with epilepsy (in 10 % of unselected adult epilepsy patients, 30 % of drug- resistant epilepsy patients) [3].

Nocturnal enuresis is defined as “voiding that occurs during sleep” [4]. It is classified as primary or secondary according to onset time [5]. Nocturia is an important factor for nocturnal enuresis. It may be due to excessive intake of water during the day, congestive heart failure, renal functional impairment, depressor over activity, bladder outlet obstruction and urinary infection [6]. Arousal problems occurring in deep slow wave sleep and in fragment sleep, such as sleep apnea, are associated with enuresis nocturna [7]. Nocturia is the one of the commonest symptoms of sleep-disordered breathing (SDB). Pathological nocturia, defined as two or more urinations per night, occurred in 47.8 % of the subjects with sleep apnea syndrome (OSAS), and the frequency was higher in women [8].

The aim of our case report was to discuss the nocturnal enuresis in a patient who had epilepsy diagnosis, and determine the factors related to nocturnal urination.

CASE PRESENTATION

A 52-year-old woman had admitted to the outpatient clinic of sleep disorders with complaints of enuresis nocturna occurring with a frequency of 2-3 times per month. She also suffered from snoring and apnea during sleep.

In her past history, she had history of seizures that began when she was 23 years old. Her birth and delivery history was normal with normal developmental milestones. She had been...
followed for hypertension for 14 years and insulin resistance for 2 years. She had history of tobacco usage, half a pack per day, for 30 years. She had no history of polyuria, polydypsia, dysuria and alcohol intake.

Her seizures were focal motor on left side and secondary generalized tonic clonic when she was on sleep. Carbamazepine therapy was started at a dose of 400 mg per day after the first seizure. Her seizures were seen often during the day, had experience of nocturnal seizures only 2-3 times since the beginning with a duration of 1-2 minutes, without micturation. Her last diurnal seizure occurred 3 months ago and nocturnal seizures occurred 20 years ago in the routine progress of her disorder.

She began to have habitual snoring when she was 37 years old and witnessed apnea for four years. She had concomitant bed wetting episodes since the beginning of sleep apnea. Bed wetting occurred with a frequency of once every 5-6 months in the beginning. The frequency of enuresis has gradually increased and she experienced enuresis nocturna 2-3 times per month, for the last 4-5 months. Also she complained from increased daytime sleepiness, morning headaches, sialorrhoea, nocturia for four years. She also experienced muscle pain, 1-2 times tongue biting in the mornings following nights with micturation.

General physical and neurological examination and an MRI scan of the brain were normal. Her body mass index (BMI) was 35 kg/m². Her blood pressure was 150/90 mm/Hg. She had no retro position of mandibula, and the sizes of her tonsils and uvula normal. Her neck was thick (36 cm) and short. Laboratory studies showed no abnormality for thyroid hormones, electrolytes and serum creatinine. Her routine electroencephalography (EEG) was normal. Video EEG revealed sharp-theta activity on left fronto-central and temporo-central region with amplitude of 30-50 µV.

Whole night video-EEG-polysomnography (PSG) study was performed with computerized PSG machine, 16 channel-EEG, electrooculography (2-channel), electromyography (2-channel), electrocardiography (1-channel), nasal/oral airflow, abdominal/thoracic respiratory movement censors and pulse oximetry with finger probe (SaO₂: 1-channel). Sleep stages were visually scored according to AASM 2007 standard criteria [9]. In the whole night evaluation; there were detected 645 obstructive sleep apnea episodes with an apnea and hypopnea index (AHI) of 107/h. The minimum oxygen saturation was 61 % and the total time spent with low oxygen saturation (< % 88) was 9.29 minutes. The sleep architecture showed a reduction of rapid eye movement (REM) and absence of deep sleep stage (Figure 1). The majority of sleep consisted of stage 3 sleep and there was prolonged REM latency (Table 1). The nasal continuous positive airway pressure (n-CPAP) device was started for nighttime after titration. Her previous anti-epileptic treatment was continued with n-CPAP treatment. After n-CPAP treatment, hypnogram showed significant improvement (Figure 2). Nocturnal seizures, diurnal seizure and enuresis completely disappeared after n-CPAP treatment. Four-month follow-up period showed very good compliance, no seizures, no nocturnal enuresis and diminished daytime sleepiness.

**DISCUSSION**

Nocturia is defined by the International Continence Society as the interruption of sleep one or more times at night for micturation. Pathological nocturia, defined as two or more urinations per night. It is relatively uncommon among younger adults, the prevalence rises to 80 to 90 % in both men and women.
by 80 years of age [10]. The presence of nocturia disrupts sleep, leading to daytime somnolence, depressive symptoms, cognitive dysfunction, and a reduced sense of well-being and reduced quality of life [11]. Moreover, nocturia is associated with an increased risk of morbidity and even mortality in OSAS cases. Obstructive sleep apnea syndrome is associated with nocturia and nocturnal enuresis, which means voiding during deep sleep. Nocturnal enuresis was noted in 7% of 120 adult patients with OSAS in one series [12]. Enuresis is encountered infrequently in the clinical practice of adult sleep medicine.

The mechanism for nocturnal enuresis is not totally clear and may be multifactorial. Such as hypoxemia, sleep fragmentation, and inspiratory effort have been reported. A major hypothesis of this proposal is that nocturia may actually be a result of the diuretic hormone response to obstructive respiratory events. The generation of negative pressure in the thorax caused by partial or total obstruction of upper airway and sustained ventilatory effort stimulates atrial natriuretic peptide (ANP) release from cardiac muscle cells. This mechanism also causes to increase urine production and this explains nocturia in OSA patient [13].

Obstructive sleep apnea can cause sleep deprivation and fragmentation, intermittent hypoxia, autonomic dysregulation, and increased systemic inflammation [14]. As a result of sleep deprivation, prolonged REM latency and decreased REM stage can cause cortical excitement and interictal EEG discharges in epileptic patients. All of these changes decrease the threshold of epileptic seizure generation. In many cases, this epilepsy-OSAS interaction has important implications for the diagnosis and treatment of seizures [14].

In our patient, we thought that enuresis related with nocturnal seizures was mostly related to OSA according to her medical history and PSG findings. Nocturnal ictal enuresis was the main diagnosis. Polysomnography revealed increased sleep fragmentation, prolonged REM latency and decreased REM stage with frequent intermittent hypoxemia (Figure 1). Frequency of seizures has increased after complaints of snoring and especially after apneas. And the semiology of seizures also changed in time.

A few lines of evidence suggest that, CPAP treatment for OSA in epilepsy patients improves seizure control, cognitive performance and quality of life [3,14]. In our case, nocturia and enuresis nocturna episodes diminished after CPAP therapy. This good response to CPAP therapy confirmed our diagnosis of nocturnal seizures associated with enuresis nocturna, which exacerbated by OSA. Four-month follow-up period showed very good compliance, no seizures, and diminished daytime sleepiness.

Secondary enuresis is an uncommon symptom in adults, so we should always remember that when an epileptic patient admitted with complaints of nocturnal enuresis this can be related with nocturnal epileptic seizures triggered by OSAS. Continuous positive airway pressure treatment can be useful for controlling seizures and nocturia symptoms. Polysomnography can help to identify seizures related with apnea and also permits the clinician to provide the best medical care.

REFERENCES