CLINICAL VIGNETTE

Severe Primary Central Sleep Apnea in a Patient with Multiple Sclerosis

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Introduction

Central sleep apnea is a disorder characterized by a reduced drive to breathe during sleep. This manifests as repetitive pauses in breathing associated with an absence of effort to breathe. Underlying pathophysiology varies to some degree, however, unstable ventilatory drive is the key underlying mechanism. Central sleep apnea is significantly less prevalent than obstructive sleep apnea. When both central and obstructive sleep apnea are present, the central form is considered to be primary when greater than fifty percent of apneas are central during testing. Certain groups have a higher risk of developing central sleep apnea compared to the general population. These include patients with congestive heart failure, patients who are post-acute stroke, chronic opiate users, and patients treated for obstructive sleep apnea with continuous positive airway pressure (treatment emergent-central sleep apnea). Structural neurologic conditions such as tumors and Arnold-Chiari malformations are also risk factors for central sleep apnea but multiple sclerosis has not traditionally been included as a risk factor.

Case

The patient is a 65-year-old male with multiple sclerosis (MS) who presents with polycythemia and sleep maintenance insomnia. He falls asleep without difficulty but wakes up in the middle of the night and is unable to return to sleep. He lives alone and does not know if he snores, however, frequently wakes up with a dry mouth. He denies any symptoms of excessive sleepiness. Hs Epworth sleepiness scale is 4/24.

He has one cup of coffee in the morning without other caffeine intake and has one glass of wine with dinner without other alcohol intake.

Chronic medications include Diroximel fumarate. Exam included normal vital signs with BMI 24.7, TSH 2.5, Hgb/Hct 17.6/52.8. No significant abnormalities were noted and he was scheduled for home sleep apnea testing. Home testing suggested mixed obstructive and central sleep apnea.

Home Sleep Apnea Test Results

Respiratory event index (REI) 29.8 events per hour
Supine REI 36.7 events per hour
Non-supine REI 26.6 events per hour
Obstructive apnea index (OAI) 7.5 events per hour
Central apnea index (CAI) 10 events per hour
Mixed apnea index 0.7 events per hour
Unclassified apnea index 7.9 events per hour.
A follow up, attended polysomnogram revealed severe primary central sleep apnea, without obstructive events.

Baseline Polysomnogram
Apnea-hypopnea index (AHI) 62 events per hour
Apnea index 59 events per hour
Central Apnea Index 59 events per hour
Obstructive apnea index 0 events per hour
Hypopnea index 3 events per hour
Supine AHI 80 events per hour
REM AHI 5 events per hour

Split protocol CPAP treatment was attempted during the polysomnogram but the patient was unable to tolerate CPAP. At home auto-CPAP was attempted. Despite significant effort by the patient he was unable to tolerate therapy. Patient was then referred for a polysomnogram with BiPAP titration to determine optimal therapy.

Polysomnogram with BiPAP Titration
BiPAP pressures of 8/4 cmH2O to 12/4 cmH2O did not reduce respiratory events. Adaptive-servo ventilation (ASV) Titration was successfully conducted with settings of EPAP 4 cmH2O and Pressure support ranging between 3 and 15 cmH2O.

A home adapted severe ventilation device was well tolerated. It effectively controlled his sleep apnea and improved his symptoms.

Discussion

Risk factors for central sleep apnea (CSA) include age greater than 65, male sex, and co-morbidities of heart failure, and chronic opioid use.[1] Neurologic disorders affecting brain stem function are also risk factors for CSA including tumors, stroke, and Arnold-Chiari Malformations.[2] Typical symptoms are similar to those of the more common obstructive sleep apnea – disrupted sleep, excessive daytime sleepiness, poor sleep quality, and difficulties with daytime concentration. Patients with known risk factors for CSA should be preferentially referred for in-laboratory polysomnography rather than ambulatory home sleep apnea testing, as the majority of home testing devices have not been validated for CSA.

Patients with MS have higher rates of sleeping difficulties than the general population[3]. Causes of these sleep disturbances include pain, spasms, and bladder dysfunction. However, SDB is also a significant cause of poor sleep. Available literature on rates of SDB in MS is limited. Reported prevalence also varies significantly (0-87%). Questionnaire studies report prevalence varying between 36% and 56%. While MS patients tend to be female and not obese these values are higher than seen in the general population, suggesting different risk factors specific to MS.[3] Symptoms of SDB can also overlap with those of MS including fatigue and difficulty concentrating, and may compound one another if both disorders are present.

There are multiple potential mechanisms by which lesions in MS could precipitate SDB. Demyelinating lesions could affect upper airway muscle responsiveness which could contribute to obstructive events.[4] Studies have shown that treatment with anti-inflammatory therapy can improve OSA severity in the general population.[5] As MS is an auto-immune disorder with increased cytokine levels,[6] this may be a poorly understood but potential mechanism of OSA.

Demyelinating lesions may also trigger central sleep apnea via impairment of ventilatory drive. Brainstem lesions can affect primary central respiratory drive. Spinal cord lesions may impair motor neurons that innervate respiratory muscles. MS patients with known brain stem lesions have higher rates of both obstructive and central sleep apnea events than MS patients without known brain stem lesions.[7] One study of 21 patients with MS, found only CSA.[8] Poor sleep quality and daytime sleepiness were common symptoms in this cohort.

SDB may also exacerbate symptoms of MS. Both conditions are associated with chronic inflammation. Intermittent hypoxia from SDB may also contribute to progression of MS lesions. Given the overlap of symptoms and potential for a bi-directional relationship it is important to consider SDB in MS patients.

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