CLINICAL VIGNETTE

The Case of Recurring Nighttime Palpitations

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Case Report

A 67-year-old man with past medical history significant for paroxysmal atrial fibrillation presented to his primary physician with complaints of episodic nighttime palpitations. He also reported daytime fatigue, but denied daytime sleepiness, and continued to work full time. Four years prior, the patient underwent radio-frequency ablation after a confirmed diagnosis of paroxysmal atrial fibrillation (AF) with subsequent resolution of the palpitations. Approximately a year after the ablation was performed, the palpitations returned. The patient reported the events occurred only at night and awakened him from sleep. The patient was referred to the cardiac electrophysiologist.

Evaluation by the cardiac electrophysiologist confirmed the history of nocturnal palpitations. The physical exam was unremarkable. EKG revealed sinus rhythm, intact AV conduction without QRS abnormalities and left atrial enlargement. During prior treadmill stress test, the patient achieved the target heart rate response without ischemic ST segment or T wave changes. Laboratory data showed normal chemistries and normal complete blood count. An echocardiogram was ordered and showed normal left ventricular size and ejection fraction with a mildly enlarged right atrium (4.38 cm), without evidence of pulmonary hypertension. Cardiac stress testing (Myoview) was normal. Holter monitoring showed baseline sinus rhythm with multiple episodes of AF with rates of 100 to 169 beats per min. All of the AF episodes were nocturnal and correlated with the symptom diary. Episodes ranged in duration from 45 min to 2 hours. The patient's wife reported to the cardiologist that the patient snored loudly and had occasional episodes of apnea. The consulting cardiologist referred the patient for a fully attended polysomnogram (PSG).

The PSG demonstrated severe obstructive sleep apnea (OSA) with an overall apnea hypopnea index (AHI) of 36/hr with oxygen desaturation nadir to 72%. Apnea was more frequent and severe during rapid eye movement (REM) sleep (REM AHI 69/hr), and sleep in the supine position (supine AHI 80/hr). There were occasional short runs of atrial fibrillation on the night of the study correlating with decreased air flow. CPAP at 10 cm H2O effectively treated the sleep disordered breathing and normalized the oxygen saturation, including during REM sleep in the supine position. Based on the abnormal polysomnogram results, the patient was referred to sleep medicine for further evaluation and management.

Sleep Medicine Consultation

A detailed sleep history was obtained, and the patient denied waking up with symptoms of shortness of breath or gasping for air. He reported occasional morning headaches, but stated that he felt fairly rested when awakening in the mornings. He reported that he typically took Excedrin several times a day to help him stay alert at work and during the late afternoon drive home. He denied any episodes of falling asleep while driving. Additional history was notable for correction of a deviated nasal septum in 2006. The only medications were simvastatin 20 mg daily, and Excedrin Extra Strength (acetaminophen 250 mg/aspirin 250 mg/caffeine 65 mg) 2 pills, 3 to 4 times daily. Physical examination was notable for Mallampati class IV airway (unable to visualize uvula or soft palate), but was otherwise unremarkable.

After discussing the polysomnogram results and treatment options, the patient was prescribed continuous positive airway pressure (CPAP) at 10 cm H2O. At the first follow-up visit, the patient was using CPAP nightly and reported that his sleep was more restful and the nighttime palpitations had resolved. His main complaint was that the pressure setting of 10 cm H2O felt like "too much air." He was advised to continue with the prescribed setting of 10 cm H2O.

The patient decreased the pressure to 8 cm H2O after he learned how to program the CPAP on-line. With

reduction in the CPAP setting, the patient experienced recurrent episodes of nocturnal palpitations and AF. He was discouraged that this occurred despite using CPAP. After further discussion with the sleep medicine physician, he was transitioned to an auto-titrating PAP device which he found much more comfortable.

Diagnosis: Obstructive sleep apnea induced atrial fibrillation

Discussion

Obstructive Sleep Apnea is associated with Atrial Fibrillation

Obstructive sleep apnea (OSA) affects 5-9% of the general US population and a large proportion of the population remains undiagnosed. While a history of excessive daytime sleepiness, snoring, paroxysmal nocturnal dyspnea and episodes of apnea are classically suggestive of OSA, other symptoms can be subtle and include nocturia, cognitive impairment, depression, and hypertension or diabetes resistant to medical management. OSA is diagnosed by either a monitored or an unmonitored polysomnogram. AF is the most common chronic arrhythmia in the general population affecting over 2 million individuals in the US and contributes to significant morbidity and mortality. Data from the Sleep Heart Health Study show a clear association between OSA and arrhythmias. Patients with OSA had a four-fold increased risk of developing atrial fibrillation when compared to patients without sleep disordered breathing[1]. There is also evidence that the arrhythmias are temporally related to respiratory disturbances[2].

Further investigation by Altmann used a validated home based sleep study to screen for sleep disordered breathing in patients with non-valvular paroxysmal or persistent AF, found a prevalence of 43%. Patients with sleep apnea did not differ from patients without sleep apnea in regards to age, gender, BMI, prevalence of hypertension, diabetes, smoking status, LVEF, left atrial enlargement or antiarrhythmic drug therapy. The patients with sleep apnea were more likely to have concomitant coronary artery disease (CAD) than patients without sleep apnea. Interestingly, the patients with sleep apnea did not have significant daytime sleepiness (as measured by the Epworth Scale Score). Patients that screened positive for at least moderate OSA were informed of the results and the association of sleep apnea with cardiovascular disease. They were offered to undergo a fully attended polysomnogram and treatment with CPAP. The authors note that only 15% of the AF cohort that screened positive for sleep apnea agreed to undergo polysomnogram and only 5% were treated with CPAP. The authors attribute this low percentage to the lack of significant daytime sleepiness in the sleep apnea group[3].

Refractory or recurrent Atrial Fibrillation may be due to untreated Obstructive Sleep Apnea

Refractory or recurrent AF may be related to untreated OSA. Patients with co-morbid OSA are less likely to have the AF controlled with medications, and are less likely to remain free of recurrent AF post cardioversion or electophysiologic ablation.

Monahan prospectively studied the impact of OSA severity on treatment of symptomatic AF treated with antiarrhythmic drugs. Treatment success was defined as > 75% reduction in symptomatic AF episodes on the same regimen over a period of 6 months. Patients were divided into responders and non-responders. Patients with paroxysmal AF were more likely to respond to drug therapy than patients with persistent AF. Patients with severe OSA were half as likely to respond to antiarrhythmic drug therapy for AF as patients with mild or no OSA[4].

Kanagala found a significant increase in recurrence of AF after cardioversion in patients with untreated OSA, compared with those with treated OSA or no history of OSA. In addition their study not only illustrated the association of OSA and AF, but demonstrated that CPAP therapy decreases the risk of recurrent AF to less than that of patients without sleep disordered breathing[5].

Patients with untreated OSA have an increased recurrence of AF after catheter directed ablation. Effective treatment with CPAP in patients with OSA decreases the rate of recurrent AF[5]. A recent meta-analysis evaluating the impact of obstructive sleep apnea on the recurrence of atrial fibrillation after catheter ablation looked at six studies involving a total of 3995 patients (958 with OSA) with a follow-up period up to 32 months, and found a 25% greater risk of recurrent AF after catheter ablation in patients with OSA compared to controls[6].

Pathophysiology linking Obstructive Sleep Apnea and Atrial Fibrillation

The exact pathogenic mechanisms linking OSA and AF have not been established. Heart failure severity does not seem to be the only factor. Bitter found an increased incidence of AF in patients with sleep disordered breathing and normal systolic left ventricular function, suggesting that heart failure itself does not account for the correlation and an independent pathophysiologic mechanism exists[7].

Theories for the mechanism relating OSA to AF include cyclical hypoxemia, increased atrial pressures, sympathetic activation and atrial remodeling. Obstruction of the upper airway during sleep results in a number of adverse physiologic consequences including: hypoxemia, hemodynamic stress and activation of pro-inflammatory pathways. Repetitive respiratory efforts against a collapsed upper airway result in large swings in intra-thoracic pressure. This requires the heart to pump against intermittent increases in opposing thoracic forces and sympathetically induced increased afterload. The combination of increased myocardial wall stress and increased myocardial oxygen demand in the setting of intermittent hypoxemia, over time, may contribute to atrial remodeling[8].

Supporting the concept of OSA contributing to cardiac remodeling, Dimitri found increased atrial volumes, conduction disturbances, and regions of altered electrical activity in the hearts of patients with OSA[9]. Additionally, Alonzo-Fernandez found a correlation between nocturnal arrhythmias in patients with OSA and elevated urine catecholamine levels[10]. Hypoxemia is also of clinical significance as confirmed by studies by both Kanagala and Gami. Each group independently demonstrated that OSA predicts the diagnosis of AF and the degree of nocturnal desaturation was an independent predictor of AF[5,11]. There are also data suggesting the perfusion-reperfusion injury pattern contributes to the development of free radicals and transcription of pro-inflammatory, hypoxia induced genes[8].

Treatment of co-morbid OSA improves clinical outcomes in AF

Naruse evaluated the clinical impact of CPAP treatment in patient with OSA on the rate of recurrent AF after catheter ablation and found that patients with recurrent AF had a greater prevalence of untreated OSA. A multivariate regression analysis revealed that concomitant OSA (HR 2.61), left atrial volume (HR 1.11) and CPAP use (HR 0.41) were the factors most strongly associated with AF recurrence during the follow-up period. Concomitant OSA and left atrial size were independent predictors of recurrent AF after catheter ablation. CPAP treatment of OSA was associated with a lower rate of recurrent AF after ablation[12].

Patel investigated the safety and efficacy of an ablation strategy including pulmonary vein antral isolation (PVAI) and found that OSA was independently associated with PVAI failure and that patients treated with CPAP had higher PVAI success rates than patients not on CPAP[13].

Clinical Course

This patient had symptomatic, nocturnal, lone AF coupled with nightly snoring and witnessed apnea which prompted an evaluation for sleep apnea. After an attended polysomnogram confirmed the diagnosis and an effective treatment setting was determined, the patient was prescribed CPAP at 10 cm H2O. The patient reported that he rarely slept supine and preferred sleeping in the lateral positions. He was transitioned to an auto-titrating PAP device. His tolerance improved on the Auto-PAP. At 3 years of follow-up, the patient continued to use Auto-PAP nightly and remained free of symptomatic AF episodes. Repeat Holter monitoring showed NSR without episodes of AF. This case demonstrates the importance of obtaining a sleep history in cardiovascular patients to identify potential co-morbid sleep disorders and that focused, effective treatment of OSA can improve cardiovascular outcomes.

Clinical Pearls

- *OSA is a common disease and is highly associated with cardiovascular comorbidities.*
- *Patients with atrial fibrillation, especially recurring after cardioversion or refractory to medical therapy should be evaluated for OSA.*
- *OSA is treatable with CPAP, compliance may be poor and needs to be monitored.*
- *Effective treatment for OSA can significantly reduce cardiovascular co-morbidities, including a reduction in adverse cardiovascular events and*

burden of dysrhythmia in patients with atrial fibrillation.

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