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CASE REPORTS

Treatment of Cardiomyopathy with PAP Therapy in a Patient with Severe Obstructive Sleep Apnea

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Obstructive sleep apnea is common in patients with heart failure. This case illustrates that treatment with PAP therapy can improve cardiac function in patients with both conditions. CPAP-emergent central apnea, as seen in this patient, has multiple etiologies. It is commonly seen in patients with severe sleep apnea, usually resolves over time, and does not need treatment with adaptive servoventilation.

Keywords: Heart failure, obstructive sleep apnea, PAP therapy, CPAP-emergent central sleep apnea

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Obstructive sleep apnea (OSA) is a common condition with high rates of morbidity and mortality.[1] The prevalence of this disease has increased substantially, along with the cost of diagnosing and treatment of this condition.[2] Despite its association with cardiovascular diseases, sleep apnea remains underdiagnosed in patients with heart disease.[3,4] Meanwhile, there has been increased development and promotion of new, advanced, and more expensive devices by industry to treat sleep apnea despite the lack of any evidence that these devices have superior clinical outcomes.[5] Following is a case which highlights both these issues.

REPORT OF CASE

TC, a 44-year-old obese African American male with a BMI of 41, longstanding history of hypertension, non-smoker, with no history of alcohol use, and a 2-3 year history of progressively increasing shortness of breath and cough, was diagnosed with New York Heart Association (NYHA) class III heart failure (HF) in July 2008. Electrocardiogram (ECG) findings were notable for biatrial abnormality and borderline left ventricular (LV) hypertrophy, with no evidence of heart block. Echocardiogram showed severe dilation and global hypokinesis of LV with a LV ejection fraction (LVEF) of 10% and moderately reduced right ventricular (RV) function. Left heart catheterization did not show any occlusive coronary artery disease. Right heart catheterization showed elevated right atrial (RA) pressure at 17 mm Hg, pulmonary capillary wedge pressure (PCWP) of 30 mm Hg, pulmonary artery (PA) pressure of 74/30 mm Hg, and severely reduced right ventricular (RV) function. Cardiopulmonary exercise test showed maximum oxygen consumption (VO_2) of 12 cc/kg/minute. His clinical presentation was consistent with idiopathic dilated cardiomyopathy of unknown etiology. An endomyocardial biopsy was not performed to rule out any treatable causes of heart failure, in keeping with current recommendations by the American Heart Association/American college of Cardiology (AHA/ACC).[6] He was treated with aspirin and maximal tolerated doses of ACE receptor inhibitor, β-blocker, and a diuretic. An ICD (implantable cardioverter-defibrillator) was placed, and he was evaluated and placed on the cardiac transplant list.

Due to his longstanding history of snoring, witnessed apneas, and excessive daytime sleepiness (Epworth Sleepiness Scale [ESS] score of 17), he was evaluated for OSA in December 2008. Polysomnography, performed with a split-night protocol revealed an apnea-hypopnea index (AHI) of 68 with a SaO_2 nadir of 58%. Respiratory events were all obstructive in nature with no central apneas. Continuous positive airway pressure (CPAP) titration to a maximum pressure of 20 cm H_2O was unsuccessful in controlling the obstructive respiratory events. He was also noted to develop central apneas, not present on diagnostic polysomnography, along with a high leak with increasing pressures. He was prescribed a bilevel device, set at a maximum pressure of 25/21 cm water pressure, after a retitration study in the sleep laboratory, during which a pressure of 28/23 cm water was insufficient to control obstructive apneas and hypopneas. This was again associated with central apneas on increasing the pressures (so called CPAP-emergent central apnea). Significantly, he had evidence of high leak on both titration studies.

On subsequent follow-up appointments, he demonstrated fairly good compliance of > 80% with his bilevel device, despite complaints of dry mouth. He continued to have a high leak, along with an elevated AHI of 15-17 on download of smart card data. The patient had difficulty tolerating the high pressures, and at one point tracheostomy was considered for control of apneas but rejected by the transplant team due to fear of infection following transplant, as the patient would be on immunosuppressants.

He underwent an adaptive servoventilation (ASV) titration study in October 2009. Expiratory positive airway pressure (EPAP) was titrated to 18 cm water pressure with elimination of all obstructive apneas and hypopneas. During this study he had minimal leak and no evidence of central apneas as EPAP

pressures were being increased. He was prescribed an ASV machine, set with a minimum EPAP of 18 cm, maximum inspiratory positive airway pressure (IPAP) of 25 cm, minimum pressure support (PS) of 0, maximum PS of 7, and a backup respiratory rate of 10.

Despite all the problems with PAP therapy during this year, his symptoms of OSA and heart failure improved. NYHA functional class improved from Class III to Class I over the next year. VO_2 increased from 12 cc/kg/min at initial evaluation to 20 cc/kg/min two years later. Repeat echocardiograms at periodic intervals showed gradually improving cardiac function. Echocardiogram with Doppler done in June 2011 showed mild global LV dysfunction, with a LVEF at 45% to 50%. There was mild LA and LV enlargement. RA and RV were normal with significant reduction of estimated PA systolic pressure to 30 mm Hg. Daytime sleepiness was no longer present, with improvement of ESS to 5. He no longer required a cardiac transplant.

Download of smart card data on subsequent appointments showed no leak, with complete control of apneas at an EPAP average device pressure of 18 cm for ≤ 90% of time and average PS of 2. All breaths were patient triggered. In other words, this device was functioning as a CPAP machine set at a fixed pressure of 18 cm (minimum EPAP was set at 18), with no leak and complete control of apneas.

DISCUSSION

This case is interesting because it highlights a number of important points. First is the association of obstructive sleep apnea with heart failure. Sleep disordered breathing (OSA and central sleep apnea) is common in patients with heart failure, but the diagnosis is frequently missed, as the typical symptoms of OSA may not be present.[7] The prevalence can be as high as 50% in patients with reduced ejection fraction.[8] In the Sleep Heart Health Study, a large prospective, multicenter observational cohort study over 9 years, obstructive sleep apnea was associated with an increased risk of incident heart failure in both middle-aged and elderly males and reduced survival in younger males.[9] There was also a dose-response relationship, with a higher AHI being associated with a greater risk of developing heart failure as well as increased mortality. In one observational study of 296 patients with severely reduced cardiac function (median LVEF of 33%), patients with severe sleep disordered breathing had a 2-fold increased risk for death, which improved in the patients who were treated with CPAP.[10]

OSA may worsen cardiac function by increasing afterload due to the negative intrathoracic pressure generated during respiratory efforts against an occluded upper airway.[11] Sleep apnea has also been shown to cause progression of heart failure possibly due to intermittent hypoxia.[12,13] It is well known that cardiac function improves with PAP therapy.[14,15] This is not only as a consequence of positive intrathoracic pressure reducing transmural pressure, which reduces afterload, but preload is also reduced. Both lead to improvement in ejection fraction.[16,17] In a retrospective study of over 30,719 Medicare beneficiaries with heart failure, those who were tested, diagnosed, and treated for OSA had a better 2-year survival rate than subjects with heart failure who were not tested for OSA. Similarly, among subjects who were tested and diagnosed with OSA, those who were treated had a better 2-year survival rate than those who were not treated.[18]

It is now recommended that physicians caring for patients with heart failure need to be aware of the presence of OSA and its effect on causing progression of heart failure, along with the role of treatment of sleep apnea and other therapies for heart failure.[19,20] An expert consensus statement from the AHA/ACC recommends that with the current epidemic of obesity, hypertension, and heart failure, the prevalence and consequences of OSA are likely to increase. There needs to be an increased interaction between sleep specialists and cardiologists in diagnosing and treating this condition.[21]

Second, this case also highlights a possible etiology of CPAP -emergent central apnea. Several hypotheses have been proposed to explain CPAP-emergent central apnea; most of these hypotheses suggest that CPAP -emergent central apnea resolves over time.[22] It has been shown in one study of patients with both OSA and CHF to be related to a high respiratory controller gain prior to application of CPAP.[23] A high leak leading to CO_2 washout could also be responsible. It may be due to the changes in CO_2 excretion that occur with relief of the upper airway, leading to a fall in pCO_2 below the apneic threshold.[24] Sleep fragmentation with frequent sleep-wake transitions occurring with initiation of CPAP can lead to central apneas.[25] Adaptive servoventilation (ASV) has been shown to be superior to CPAP in treating central sleep apnea, but there have been no long-term studies showing superior clinical outcomes.[26,27] There are currently two ongoing multicenter, randomized controlled trials, ADVENT-HF and SERVE-HF,[31] to evaluate the cost effectiveness and efficacy of ASV in treating patients with heart failure and central sleep apnea.

It is my view that this patient developed a dilated non-ischemic cardiomyopathy, most likely due to severe untreated OSA, with hypertension and hypoxemia, present for many years. It is possible that other etiologies of heart failure such as viral myocarditis, sarcoidosis, and rare conditions like amyloidosis and hemochromatosis may have been present, and an endomyocardial biopsy would have better elucidated the cause of heart failure.[6] However, the clinical scenario presented strongly suggests that the cause of heart failure in this patient was obstructive sleep apnea. Treatment of OSA with PAP therapy, along with the associated improvement in hypoxemia, in conjunction with medical therapy for hypertension and heart failure contributed significantly to improved cardiac function to the extent that he did not require a cardiac transplant.

With PAP therapy, he developed central apneas, possibly due to a high leak. Over time, central apneas were no longer present as evidenced by smart card data with no use of PS (PS of 2 being insignificant) and all breaths being patient triggered. PAP requirements to keep the upper airway open were reduced to a much lower level along with minimal leak. This may have been due to increased compliance and volume of the upper airway,[28] partly due to improved ejection fraction, with reduced congestion of the upper airway. Reduced CPAP pressures requirements may also be due to reduced collapsibility of the upper airway with increasing lung volume from continued CPAP use,[29] loss of weight, and decreased heart size. It is possible that reduced inflammation of the upper airway over time with CPAP use may have played a role.[28,30] It is important to note that this patient

was treated with an ASV device, which eventually functioned as a CPAP machine.

In conclusion, this case should heighten the awareness of the association of heart failure and OSA. It also illustrates the improvement in cardiac function with positive pressure therapy. CPAP-emergent central apnea has multiple etiologies, and in most patients resolves over time, and does not need to be treated. Finally, pressure requirements to treat severe OSA may decrease over time.

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