Continuous positive airway pressure therapy restores bradyarrhythmia with 10-second asystole in hypertensive obese patient with obstructive sleep apnea

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Introduction

Obstructive sleep apnea (OSA) serves as a risk factor for cardiovascular diseases, including arrhythmias.[1] Sleep-disordered breathing (SDB) is associated with greater incidence of bradycardia, and the severity of SDB correlates with duration and severity of bradycardia.[2] Patients with OSA develop nocturnal arrhythmias in 24.4% cases, while sinus bradycardia is the most frequent arrhythmia in OSA patients, developing in 79.8% of cases.[3] The incidence of arrhythmias in patients with SDB may be related to several pathophysiologic pathways such as repetitive hypoxia and reoxygenation, increased oxidative stress, inflammation and sympathetic activation, and/or autonomic dysregulation.[1]

On the other hand, the majority of patients requiring cardiac pacing have undiagnosed sleep apnea.[4] Right atrial overdrive during sleep has been suggested to reduce apneic events by decreasing the autonomic dysregulation; however, it did not prove to be effective in treating SDB.[5] According to the guidelines of the European Society of Cardiology, pacing is not indicated for patients with reversible causes of bradycardia such as OSA and for patients with asymptomatic rhythm disorders.[6] Whether patients with SDB and sinus arrest of more than 3 seconds during nighttime may benefit from an implantable pacemaker to avoid extreme arrhythmias and possible cardiac arrest is unknown.

We present a case of a middle-aged male patient with 10-second asystole in the setting of newly diagnosed OSA.

KEYWORDS Asystole; Bradycardia; Continuous positive airway pressure; Hypertension; Nocturnal arrhythmia; Obesity; Obstructive sleep apnea
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Case report

On April 12, 2016, the 48-year old male patient at very high cardiovascular risk was emergently admitted to our center from the Department of Functional Diagnostics owing to the severe bradyarrhythmia shown by 24-hour Holter monitoring. The results demonstrated 20 asystole episodes with a duration of 3047 to 10,521 milliseconds (average 4105 ms) and 20 episodes of significant bradycardia during the nighttime (Figure 1).

Earlier, in August 2011, sinus node dysfunction (second-degree transient sinoatrial block) was diagnosed and considered to be related to the prior inferior myocardial infarction followed by urgent revascularization. Since then, the patient complained of angina-like chest pain, low exercise tolerance, and persistent nocturnal bradyarrhythmia increasing in quantity and duration (Figure 2). Importantly, no syncopes occurred in the daytime. The other comorbidities included third-degree hypertension, congestive heart failure NYHA II, type 2 diabetes mellitus, morbid obesity (body mass index = 40.85 kg/m^2), and dyslipidemia. The patient received the following medications: angiotensin II receptor blocker (losartan), imidazoline receptor agonist (moxonidine), lipid-lowering drugs (simvastatin/ezetimibe), dipeptidyl peptidase-4 inhibitor (vildagliptin), and antiaggregant (acetylsalicylic acid).

Owing to the predominance of nocturnal bradyarrhythmias, presence of excessive daytime sleepiness (Epworth sleepiness scale: 15 points), morbid obesity, and witnessed sleep apneas, OSA was suspected to be the underlying cause of the heart rhythm disorder. This hypothesis was supported by nocturnal and early morning hypertension according to the results of 24-hour electrocardiography and blood pressure monitoring (March 29 and April 12, 2016). To exclude SDB, the diagnostic polygraphy study (Embletta, Natus, Pleasanton, CA) was conducted on April 12, 2016, (Figure 3) and showed 287 obstructive apnea-hypopnea episodes during 7 hours 7 minutes sleep time (apnea-hypopnea index [AHI],

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KEY TEACHING POINTS

- Obstructive sleep apnea can increase the risk of bradyarrhythmias in patients at high cardiovascular risk owing to the destabilization of cardiac autonomous regulation.
- Continuous positive airway pressure (CPAP) therapy for obstructive sleep apnea may be helpful to eliminate even severe bradyarrhythmias in patients at high cardiovascular risk. Therefore, CPAP therapy may be recommended as a bradyarrhythmia treatment approach before considering pacemaker implantation in patients with comorbid obstructive sleep apnea.
- Large randomized controlled studies are required to define the efficacy, reliability, and safety of CPAP therapy for bradyarrhythmia treatment in patients with comorbid obstructive sleep apnea.

42.8/h) with average saturation 88.8%. Average episode duration was 15.8 seconds, maximal 46.5 seconds. Continuous positive airway pressure (CPAP) therapy in auto mode (pressure, 10.4 cm H_2O) was prescribed and was effective, resulting in residual AHI of 8.9/h. The patient was highly compliant (daily usage 9 hours 34 minutes) and reported an increase in sleep quality. The repeated 24-hour Holter monitoring during CPAP therapy showed asystole episodes below 5 seconds (Figure 2). Multidisciplinary arrhythmology consultation confirmed that there were no indications for emergent cardiac pacing, but planned surgery was recommended.

At 3-month follow-up after the discharge, the CPAP device–based report showed good compliance (88% of nights, 5.2 hours nightly on average; AHI <10/h). Repeated polysomnography with CPAP therapy demonstrated mild OSA (AHI 12.8/h) without significant cardiac pauses.

Later, in September 2016, the patient was invited for cardiac pacing, but the patient refused the surgery since he had no complaints. No arrhythmias were registered by 24-hour Holter monitoring. Therefore, the patient had no indications for cardiac pacing, and the surgery was canceled.

Since then the patient continued CPAP therapy. He was completely asymptomatic, experiencing no episodes of dizziness or syncope and taking no medications, at the end of 3-year follow-up (Figure 2). At that moment polysomnography demonstrated mild OSA (AHI 9.4/h), and electrocardiography recordings were normal.

Discussion

This case illustrates that CPAP therapy can be successfully applied in patients with OSA-related nonsymptomatic sinus node dysfunctions, even severe ones.

The need for pacemaker implantation in patients with severe bradyarrhythmia comorbid with OSA is still under debate.[7] The effectiveness of CPAP therapy in the treatment of bradyarrhythmia comorbid with OSA was shown in controlled clinical trials.[8,9] CPAP therapy decreased the incidence of sinus bradycardia and sinus arrest from 57.4% and 7.4% to 4.6% and 0.0%, respectively, in patients with comorbid OSA and arrhythmia.[8] The decline in overall cardiovascular mortality following CPAP therapy was also reported in patients with OSA.[10] Besides, CPAP therapy is characterized by the lower risk (13%) and severity of complications (mouth dryness, skin allergies, vasomotor reactions, nasal obstruction, nasal bleeding, etc) in comparison with pacemaker implantation, which may be associated with electrode dislocation and dysfunction, myocardial perforation, pneumothorax, etc (10%–35% of cases).

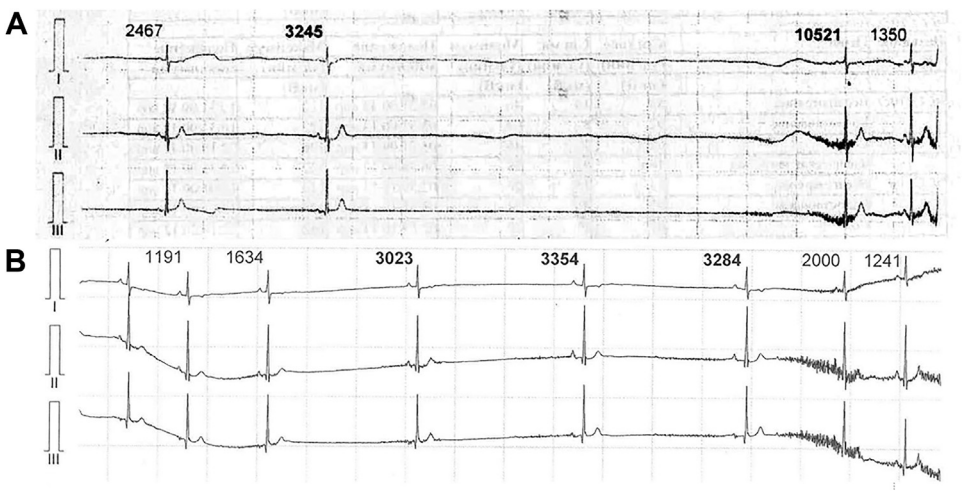

Figure 1 Holter monitoring on April 12, 2016, shows asystoles of **A:** 10,521 ms and **B:** 3023–3284 ms. The P wave to P wave is lengthening, suggestive of reduced sinoatrial node automaticity from enhanced vagal tone.

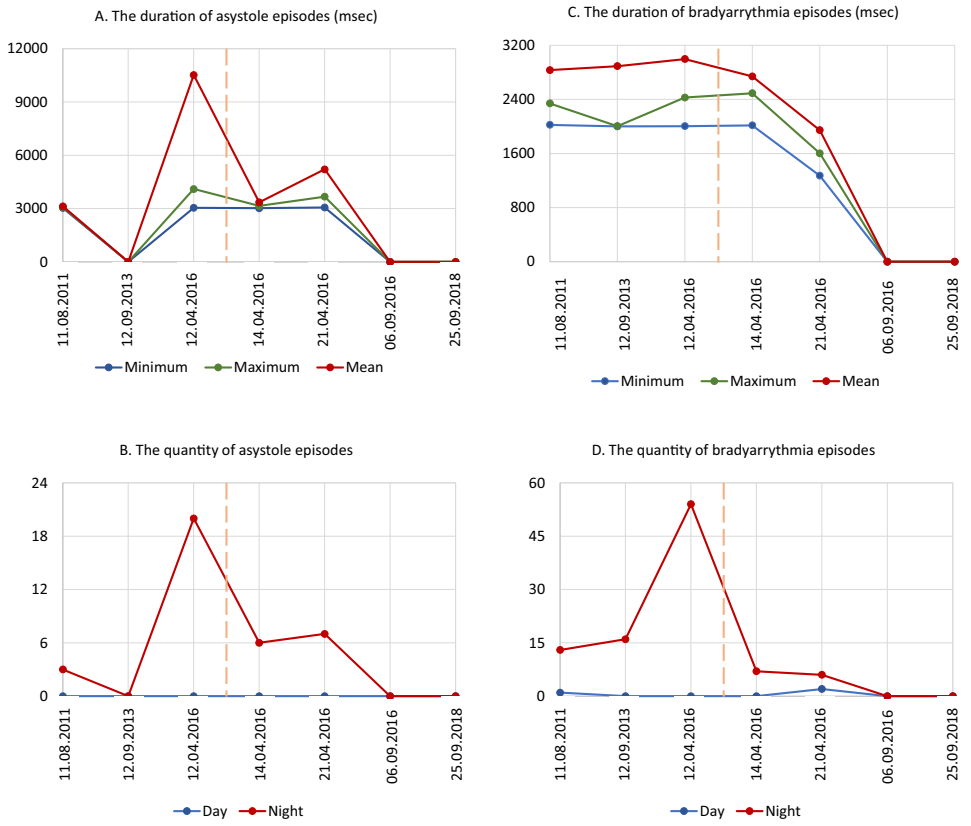

Figure 2 The results of Holter monitoring throughout the observation period. **A:** Duration of asystole episodes, in milliseconds. **B:** Duration of bradyarrhythmia episodes, in milliseconds. **C:** Quantity of asystole episodes. **D:** Quantity of bradyarrhythmia episodes. Continuous positive airway pressure therapy was initiated on April 13, 2016 (dotted lines).

However, some issues should be addressed in future studies, including the maximum duration of sinus arrest to be prevented by CPAP therapy, the frequency of follow-up sleep studies, and the AHI threshold to be achieved.

To our knowledge, this case is unique in illustrating the utility of CPAP therapy in the treatment of highly severe bradyarrhythmia with sinus arrest lasting up to 10 seconds, while the majority of case studies report the opportunity of

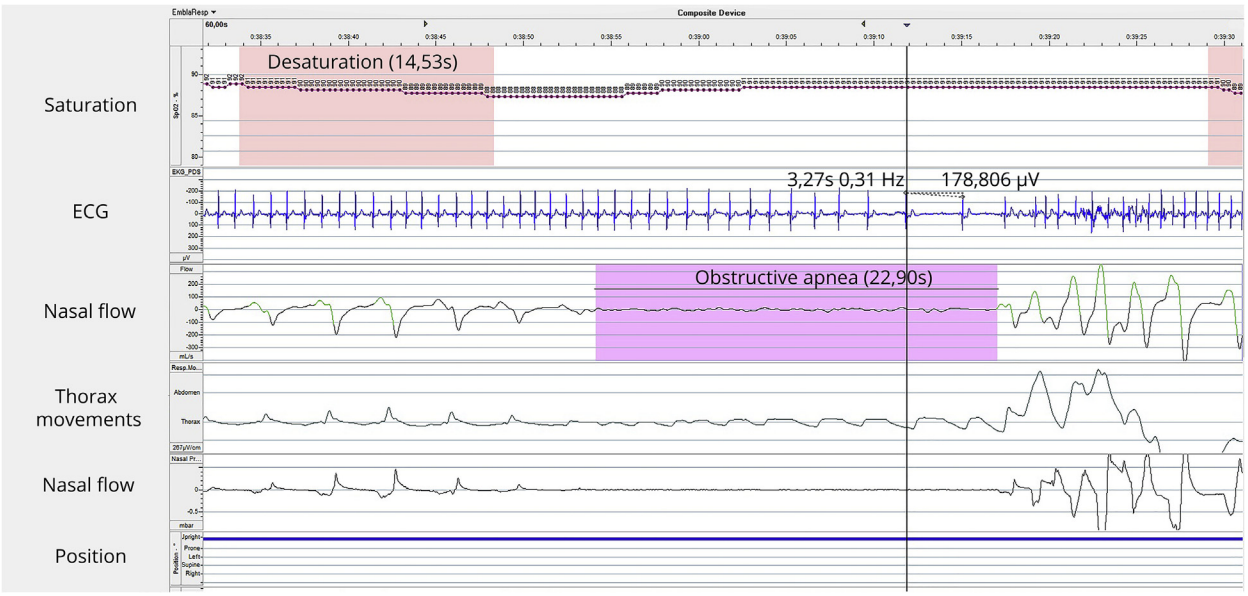

Figure 3 Polygraphy (60-second epoch) from April 12, 2016. A 3.27-second asystole at the end of the episode of obstructive sleep apnea before the onset of the further reduction in O_2 saturation.

CPAP therapy to normalize bradyarrhythmia with up to 7- to 8-second pauses.[11,12] In 1 case report, the authors emphasized that even though the body mass index of the patient with morbid obesity remained unchanged after several weeks of CPAP therapy, no asystoles were registered on the follow-up.[12] Obesity seems to be important, since the patients with apnea-associated bradyarrhythmia are more overweight than patients without bradyarrhythmia[13] and hypertensive obese patients with OSA demonstrate 4-fold higher incidence of heart rhythm and conduction disturbances than subjects without SDB.[14] However, we assume that the decrease in AHI index associated with CPAP therapy plays a more significant role for elimination of bradyarrhythmias compared to weight reduction. In our case the patient's weight has also been stable during 2.5-year follow-up. Thus, CPAP therapy had a long-term beneficial outcome on rhythm normalization despite the presence of coexistent severe hypertension and ischemic heart disease.

Nevertheless, the need for pacemaker implantation should be considered in case of low CPAP effectiveness, compliance, or intolerance owing to the subjective or objective causes. The pacemaker implantation should be applied in patients with cardiac conduction system abnormalities and daytime symptoms (syncope, presyncope), since the latter could hardly be related to SDB. In patients with severe bradyarrhythmia, we would recommend full polysomnography (or cardiorespiratory monitoring) to exclude SDB and esophageal electrophysiological study to exclude organic conduction disorder. However, electrophysiological study might not be helpful to distinguish the level of conduction system dysfunction related to functional causes, including transient sleep-related heart rhythm disorders. Grimm and colleagues[15] demonstrated the absence of electrophysiological abnormalities in the majority of OSA subjects with severe bradyarrhythmias during wakefulness. Electrophysiological study is technically difficult to perform in normal sleep, while the use of sedatives results in abnormal sleep structure and can affect heart rhythm. Consequently, we hypothesize that bradyarrhythmia observed in our case might have had a functional vasovagal origin due to a neurally mediated cardioinhibitory reflex that led to depressed sinoatrial node automaticity and sinus arrest. OSA can be equally viewed as a reversible cause of bradyarrhythmia in patients at low cardiovascular risk with minor clinical manifestations of OSA.

Conclusion

In conclusion, despite the limitations, our case study demonstrates that the treatment of OSA should be considered first in severe comorbid bradyarrhythmia. CPAP treatment leads to the stabilization of autonomous regulation of cardiac rhythm, helping to eliminate bradyarrhythmias. Larger, randomized controlled studies are required to define the efficacy, reliability, safety, and appropriate patient selection criteria for arrhythmia treatment in CPAP users; as well, the frequency of follow-up sleep studies and AHI threshold to be achieved need further elucidation.

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