First report of concomitant subcutaneous defibrillator and phrenic nerve stimulator implantation in a patient with severe central sleep apnea and left ventricular systolic dysfunction

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Introduction

There is a clinically significant association between central sleep apnea (CSA) and heart failure with reduced ejection fraction (HFrEF).[1,2] The presence of CSA has been associated with an increased risk of decompensated heart failure and death[3] and the prevalence of CSA increases in parallel with the severity of HFrEF. Phrenic nerve stimulation (PNS) using the remedē system (Respicardia, Minnetonka, MN) is a new therapeutic modality to treat CSA that involves placing transvenous leads to stimulate the phrenic nerve and activate the diaphragm. Since many patients with severe HFrEF have implanted defibrillators, a clinical scenario where concomitant CSA and defibrillator therapy are necessary is likely to occur. However, data are lacking concerning potential interaction between these devices. We present a case report of a patient with severe ischemic cardiomyopathy with a pre-existing subcutaneous implantable cardioverter-defibrillator (S-ICD) who was later diagnosed with severe CSA and underwent successful remedē system implantation.

Case report

A 54-year-old man with poorly controlled type 1 diabetes mellitus, end-stage kidney disease on hemodialysis, paroxysmal atrial fibrillation, and ischemic cardiomyopathy with HFrEF (left ventricular ejection fraction 30%) underwent a primary prevention Emblem S-ICD insertion (Boston Scientific, St. Paul, MN) in December 2015. The sensing vector was secondary. Conversion testing of ventricular fibrillation

KEY TEACHING POINTS

- The prevalence of central sleep apnea (CSA) is relatively high in patients with heart failure with reduced ejection fraction and can lead to significant morbidity and mortality if left untreated. Phrenic nerve stimulation (PNS) is a desirable option in patients with systolic dysfunction, as continuous positive airway pressure is not effective in treating CSA.

- The artifact generated during impedance testing by the remedē device (Respicardia, Minnetonka, MN) could theoretically interfere with subcutaneous implantable cardioverter-defibrillator function but is not demonstrated in this case despite rigorous testing.

- Because up-titration of pacing output and/or pacing pole reprogramming is often needed after PNS implant, potential device-device interaction should be assessed at implant and during follow-up using maximum pacing output in all available PNS pacing configurations.

was successfully performed with 65 J shock and the shock impedance was measured as 46 ohms.

In November 2018, an in-laboratory polysomnogram was obtained to evaluate for obstructive sleep apnea owing to complaints of daytime sleepiness, fatigue, and difficulty initiating and maintaining sleep. At that time his body mass index was 20.4 kg/m^2. His most recent echocardiogram demonstrated further worsening of heart function with a left
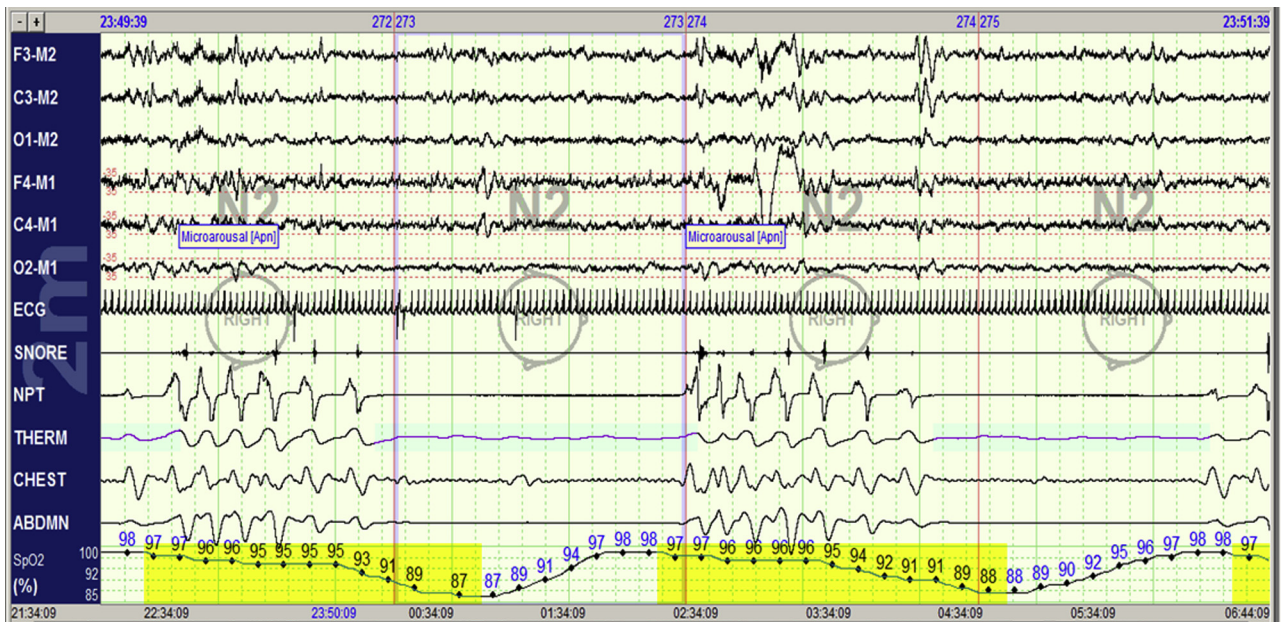
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Figure 1   Polysomnogram showing central apneas. Two-minute window from overnight polysomnogram demonstrating frequent central apneas with Cheyne-Stokes respiration. There are 2 central apneas during the representative 2-minute window recorded during stage 2 non–rapid eye movement (N2) sleep based on the 6 electroencephalography leads (F3-M2, C3-M2, O1-M2, F4-M1, C4-M1, O2-M1) with the patient in the right lateral decubitus position. Each central apnea lasts approximately 30 seconds and is characterized by a lack of airflow on the nasal pressure transducer (NPT) and the oronasal thermistor (Therm), no effort on the chest and abdominal respiratory inductance plethysmography belts, followed by a 10% oxygen desaturation (in yellow). Each cycle, from the beginning of an apnea to the end of the next apnea, lasts approximately 60 seconds and the microarousals occur at the peak of ventilatory effort, consistent with central sleep apnea with Cheyne-Stokes respiration pattern.
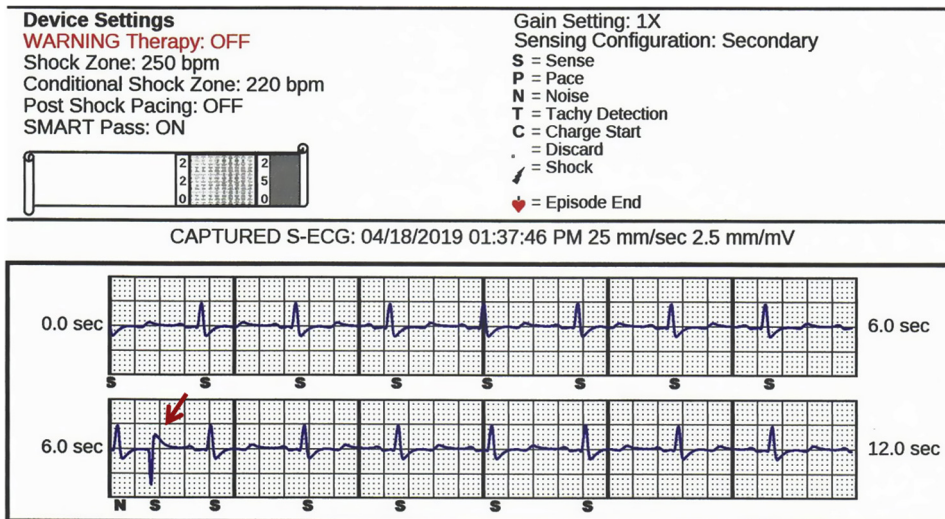
ventricle ejection fraction of 14%. The polysomnogram revealed severe sleep-disordered breathing with predominant CSA. The total apnea-hypopnea index was 61 events per hour (normal: less than 5 events per hour; severe: more than 30 events per hour). The central apnea index was 42 events per hour and the obstructive apnea-hypopnea index was 19 events per hour. Sleep-disordered breathing was also accompanied by significant sleep hypoxemia. Figure 1 illustrates a representative 2-minute window from the overnight polysomnogram demonstrating central apneas. After failing continuous positive airway pressure (CPAP) titration, the patient underwent bilevel positive airway pressure spontaneous-timed (PAP-ST) titration in the sleep laboratory and was prescribed home PAP-ST therapy with settings of 25/16 cm H_2O with a backup respiratory rate of 16 breaths per minute with an oronasal mask. Adequate adherence was shown during the first 30 days of therapy, as obtained by downloading data from the patient's device. The device-estimated residual apnea-hypopnea index was 22 events per hour (residual central apnea index of 14 and hypopnea index of 8). He did not feel any improvement in his symptoms despite adequate adherence to bilevel PAP-ST therapy. Given the persistence of symptoms and persistent CSA despite bilevel PAP-ST therapy, he was referred for phrenic nerve stimulator implantation.

Implantation of the remedē system was performed in the electrophysiology laboratory under moderate sedation via the right subclavian vein access. The S-ICD was temporarily disabled to allow for electrocautery. The implantation technique of the remedē system has been described previously[4]

but in short, we inserted a multipolar pacing lead Respistim LQS model 4065 (Respicardia, Minnetonka, MN,) into the left pericardiophrenic vein, which courses over the lateral border of the epicardium and runs parallel with the left
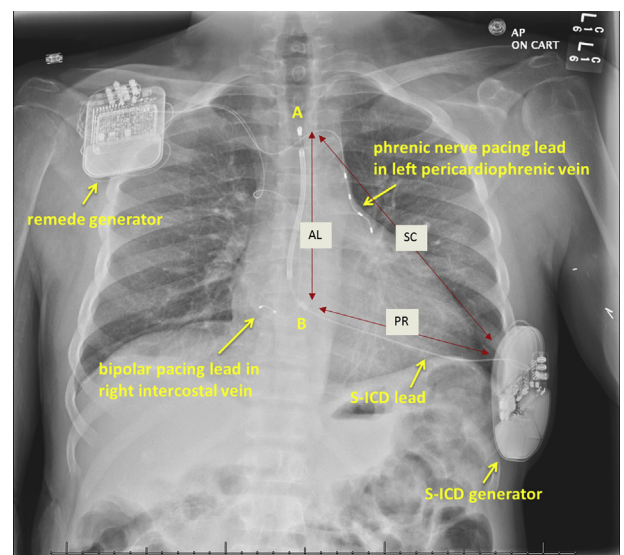
Figure 2   Chest radiograph showing implanted hardware. Anteroposterior (AP) chest radiograph of right pectoral position of phrenic nerve stimulator with multipolar pacing lead in left pericardiophrenic vein and sensing lead in low right intercostal vein via the azygos vein. Subcutaneous implantable cardioverter-defibrillator (S-ICD) is in its usual position on the left lateral thorax with corresponding suprasternal lead. A = distal electrode; AL = alternate S-ICD vector; B = proximal electrode; PR = primary S-ICD vector; SC = secondary S-ICD vector.

Device Settings
WARNING Therapy: OFF
Shock Zone: 250 bpm
Conditional Shock Zone: 220 bpm
Post Shock Pacing: OFF
SMART Pass: ON

Gain Setting: 1X
Sensing Configuration: Secondary
S = Sense
P = Pace
N = Noise
T = Tachy Detection
C = Charge Start
. = Discard
/ = Shock
♥ = Episode End

CAPTURED S-ECG: 04/18/2019 01:37:46 PM 25 mm/sec 2.5 mm/mV

Figure 3　Subcutaneous electrocardiography signals recorded from the subcutaneous implantable cardioverter-defibrillator during phrenic nerve stimulation impedance testing. During impedance testing by the remedē device (Respicardia, Minnetonka, MN), the stimulus (*red arrow*) was recorded and labeled as a sensed event (S). The preceding sinus beat (which is on time with the patient's intrinsic rhythm) was labeled as noise (N). This finding was reproducible during implant but not evident at the follow-up visit.

phrenic nerve. A second lead, Medtronic Attain Ability model 4196 (Medtronic, Minneapolis, MN), was inserted into a low right intercostal vein via the azygos vein. This lead is used for monitoring transthoracic impedance, which is a surrogate for respiration. The generator was placed in a pectoral pocket (Figure 2).

Because of this patient's pre-existing S-ICD, the potential for device-device interaction was systematically assessed. The S-ICD was re-enabled. With maximum Respistim LQS bipolar pacing output (10 mA, 300 microseconds, 20 Hz) from all 4 pacing electrodes, subcutaneous signals were recorded from all 3 S-ICD vectors. Pacing artifact was evident in the primary and secondary vectors but absent in the alternate. While the pacing artifact was visible, it was not sensed as noise. During the remedē impedance check, 4 0.5-mA pulses were delivered and the resultant artifact was recorded on the subcutaneous signal. The sinus beat preceding the impedance check stimulus was labeled as noise and the stimulus was sensed (Figure 3). The S-ICD sensing vector was programmed as secondary. The leads were connected to the generator and the system was implanted in a right pectoral pocket with the aid of a TYRX antimicrobial envelope (Medtronic, St. Paul, MN). The remedē system was not activated, as is recommended, to allow for the leads to settle in and stabilize. The patient was discharged the next day and 6 weeks later was brought back for remedē system activation. With S-ICD sensing programmed to secondary vector, device-device interaction was assessed in the same fashion as at the time of the initial implant. There was no noise detected with up-titration of pacing output. With impedance testing, artifact similar to what was seen during implant was present, but this finding was not sensed reproducibly. The remedē system was activated. After 6 weeks of PNS, he is feeling better and S-ICD interrogation has not revealed any shocks. A repeat polysomnogram is scheduled in 2 months.

Discussion

To our knowledge, this is the first report of concomitant S-ICD and phrenic nerve stimulator implantation. The prevalence of sleep apnea, both obstructive and central, is high among patients with congestive heart failure, approaching 50%–75% in some studies.[1,5] Untreated sleep apnea is associated with high morbidity and mortality.[6,7] Obstructive sleep apnea is more commonly recognized and is usually treated with positive pressure therapy such as CPAP. Prior to PNS, there were no effective treatments for CSA, as CPAP does not effectively treat central apneas[8] and adaptive servoventilation has been associated with a higher mortality in patients with HFrEF,[9] particularly in patients with an ejection fraction below 30%.[10] PNS with the remedē system has been shown to improve symptoms and reduce central apneas and is currently indicated for patients diagnosed with moderate-to-severe CSA.[11,12] Both sensing and pacing leads of the remedē system are programmable. The quadripolar left lead can be programmed in multipolar pacing configuration to deliver output between 0.1 and 10 mA at a pulse width of 60–300 microseconds. Most patients require up-titration of PNS pacing output during follow-up, which is why it is important to test for interaction at maximum output and with all available pacing options.

There are 3 sensing vectors available on the S-ICD that are used for detecting malignant ventricular arrhythmias (primary, secondary, and alternate) (Figure 2). The S-ICD algorithm automatically chooses one based on subcutaneous signal amplitude, morphology, and quality.[13] A different sensing vector can be selected by the implanting physician if desired. Although an artifact was detected on primary and secondary vectors during pacing and impedance testing of the remedē system, the alternate vector was spared, as it senses signals from an area outside the PNS (ie, between distal and proximal lead electrodes; Figure 2). While it may

seem desirable to manually select the alternate vector in these cases, it is often the one least chosen by the S-ICD algorithm owing to poor signal quality.[13] Regardless, even with maximum pacing output from the PNS, there was no noise or pacing artifact sensed. While artifact was recorded and intermittently sensed during PNS impedance testing, this finding was not reproducible. Because the S-ICD has limited storage capability, impedance testing artifact, even if it occurred during auto–impedance testing by the remedē device, would not likely be saved and available for review.

Conclusion

Our case is the first example of concomitant PNS and S-ICD implantation. Given the relatively high prevalence of CSA in the HFrEF population, situations where these 2 therapies could be utilized concurrently will become more commonplace. We did not see any significant interactions, but our follow-up is short. More data are needed before we can definitively say that concomitant PNS and S-ICD therapy is safe.

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