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CASE REPORT
Electrophysiology

Cardioneuroablation for the treatment of ictal-associated cardiac asystole: case report and literature review

Jian Liang Tan[1], Timothy M Markman[1], Pasquale Santangeli [2], and Matthew C. Hyman [1]*

[1]Section of Cardiac Electrophysiology, Hospital of the University of Pennsylvania, Philadelphia, PA, USA; and [2]Section of Cardiac Pacing and Electrophysiology, Heart and Vascular Institute, Cleveland Clinic Foundation, Cleveland, OH, USA

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Background Ictal-associated bradyarrhythmia or asystole can be a manifestation of malignant seizure syndromes. In patients with ictal-associated hypervagotonia and asystole, cardioneuroablation may provide a promising alternative to permanent pacemaker implantation.

Case summary We present a case of a 47-year-old female with a 1.5-year history of ongoing uncontrolled seizures with multiple semiologies despite multiple antiepileptic drugs who had episodes of symptomatic severe sinus bradycardia (15–30 b.p.m.) and sinus pauses (15–16 s). She underwent a successful cardioneuroablation for ictal-induced asystole with complete resolution of bradyarrhythmias.

Discussion This case highlights the utility of cardioneuroablation in patient with ictal-induced cardiac bradyarrhythmia and asystole. Cardioneuroablation may be an approach to avoid permanent pacemakers in this population.

Keywords Asystole • Cardioneuroablation • Case report • Ictal-associated asystole • Syncope • Case report

ESC curriculum 9.9 Cardiological consultations • 5.7 Bradycardia • 5.2 Transient loss of consciousness

Learning points

- To understand the mechanism of ictal-induced bradyarrhythmia or asystole.
- To recognize the management options of ictal-induced bradyarrhythmia or asystole in whom the epilepsy could not be controlled despite multiple antiepileptic drugs.
- To highlight the potential role of cardioneuroablation procedure in patients with profound ictal-induced asystole.

Introduction

Symptomatic ictal-associated bradyarrhythmia or asystole is a rare, though potentially life-threatening phenomenon.[1] Patients with ictal asystole are frequently managed with permanent cardiac pacemaker implantation though this practice remains controversial. While the precise mechanism of ictal asystole and ictal bradyarrhythmias is unclear, hypervagotonia has been implicated as a contributing factor.[2] Cardioneuroablation (CNA) has recently emerged as a promising tool to treat excessive vagal stimulation of the heart through parasympathetic denervation.[2] Here, we present a case of a successful CNA procedure to treat ictal-associated cardiac asystole.

* Corresponding author. Tel: +215 662 7652, Email: matthew.hyman@pennmedicine.upenn.edu
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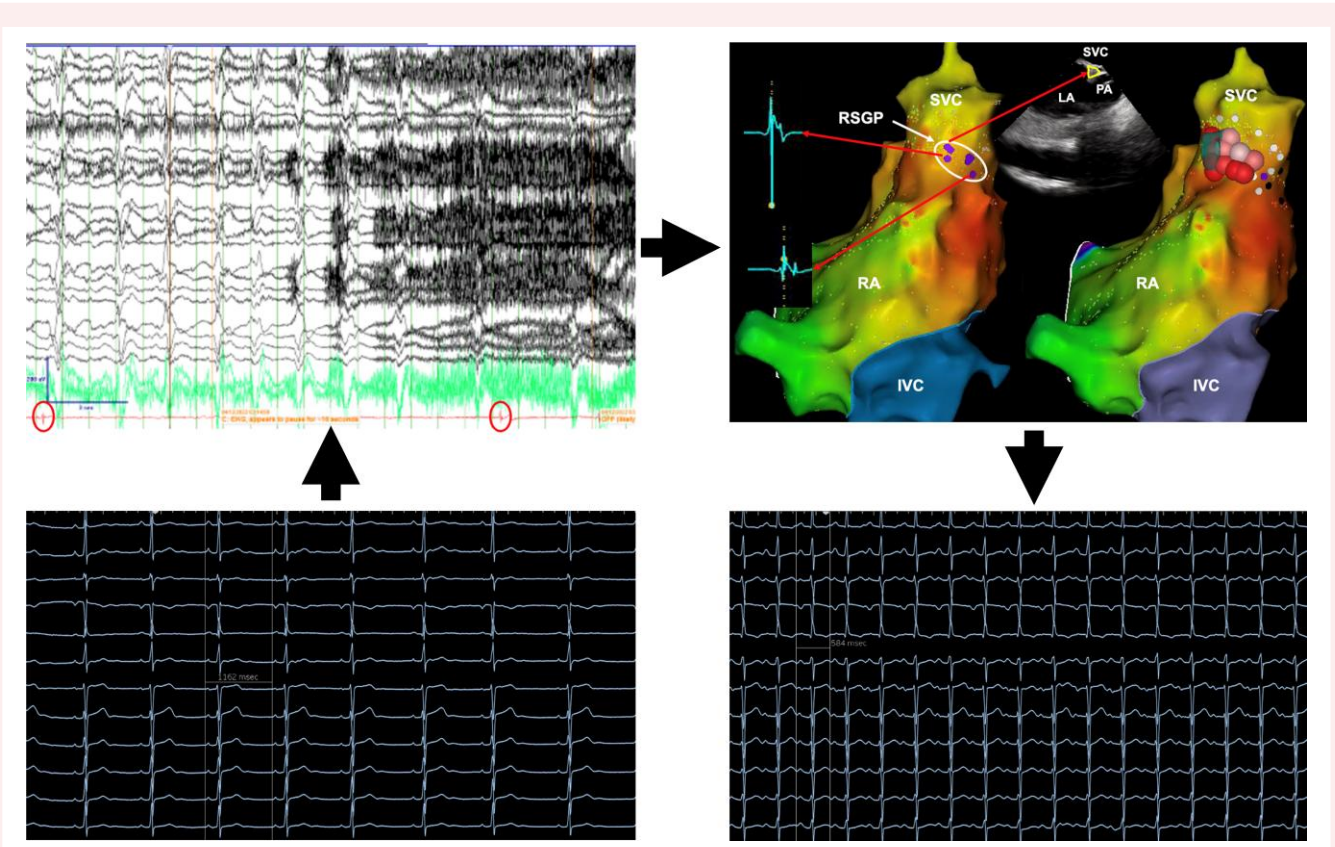
Summary figure



Case presentation

A 47-year-old female with a medical history notable for focal impaired awareness seizures (FIAS) was admitted to the Epilepsy Monitoring Unit for seizure classification and management of antiepileptic medications. She started having multiple episodes of uncontrolled seizures, despite multiple antiepileptic drugs following a mild COVID-19 infection.

Electroencephalogram (EEG) and magnetic resonance imaging of the brain revealed right temporal onset seizures without structural lesions. Her seizure descriptions included spells of incoherent speech, followed by impaired awareness, dissociated sensation, and eventual loss of consciousness, with post-ictal urinary incontinence, crying, fatigue, and headache.

The patient's other past medical history included hypertension, type II diabetes mellitus, hypothyroidism, depression, and obstructive sleep apnoea. She did not report history of smoking or illicit drug use.

Baseline neurological and cardiorespiratory examinations were unremarkable. Her baseline electrocardiogram (ECG) demonstrated normal sinus rhythm with a heart rate of 60 b.p.m. Other laboratory results including full blood count, thyroid function level, and biochemistry assay were all unremarkable.

All the antiepileptic drugs were temporarily withheld during the 3-day inpatient continuous video-EEG monitoring. During this period, she developed four episodes of FIAS with right temporal onset. Seizures manifested by facial twitching, oral automatism, and left gaze preference, followed by loss of body tone and unresponsiveness. During the late offset of each FIAS, she developed profound ictal bradycardia with the lowest heart rate of 15 b.p.m. (*Figure 1A*), and asystole with the longest duration lasted up to 21 s (*Figure 1B*). Telemetry monitoring demonstrated PP interval slowing with PR interval prolongation prior to the pauses consistent with a vagally mediated mechanism.

The cardiac electrophysiology team was consulted for the ictal bradyarrhythmias. Due to the suggestion of a vagally mediated mechanism for the bradyarrhythmias, the decision was made to offer CNA as an alternative to the implantation of a permanent pacemaker. The patient provided written informed consent for the CNA procedure. This procedure was performed under monitored anaesthesia care with midazolam, propofol, and fentanyl boluses. The right atrium (RA) and left atrium (LA) three-dimensional electroanatomical map was constructed using a CARTO 3 fast anatomical mapping system (Biosense Webster, Diamond Bar, CA, USA). A three-dimensional voltage mapping of the atria was performed in sinus rhythm with a high-density mapping catheter (PentaRay®) at filter settings of 100–500 Hz and facilitated by a SoundStar intracardiac echocardiography. Fractionated electrograms indicative of the right superior ganglionated plexus (RSGP) were identified and tagged in the anatomic map along the lower posteroseptal aspect of the superior vena cava (*Figure 2A*). This location correlated to the location on the anterior aspect of the right superior pulmonary vein, where fractionated electrograms were identified and tagged during LA mapping. Initial ablation was performed in the targeted areas of RSGP from the RA using a 3.5 mm irrigated-tip catheter (ThermoCool

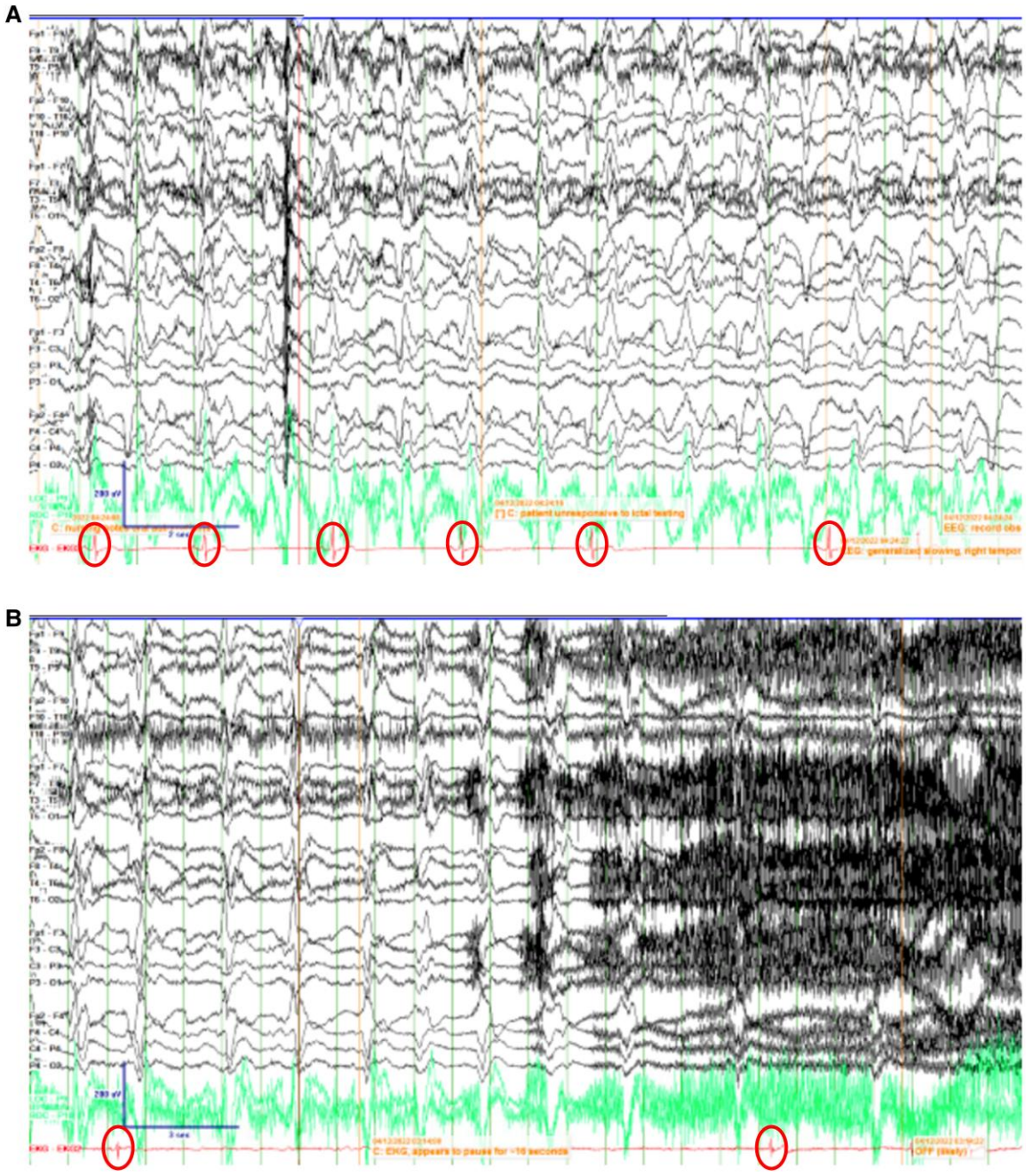


Figure 1 (*A*) Electroencephalogram recording demonstrated epileptic episode with ictal bradyarrhythmia (heart rate of 15–30 b.p.m., red circles indicated QRS complexes on an electrocardiogram tracing). (*B*) Electroencephalogram recording demonstrated an epileptic episode with ictal sinus arrest/asystole (16 s, ovals indicated QRS complexes on an electrocardiogram tracing). The asystole resulted in syncope with cerebral hypoperfusion.

SmartTouch SurroundFlow Bi-Directional, Biosense Webster, Diamond Bar, CA, USA). The ablation settings used were power control of 25 W in RA for a duration up to 60 s, targeted contact force between 10 and 40 g, and maximum temperature of 40°C. The targeted ablation index (Biosense Webster, Diamond Bar, CA, USA) was between 400 and 550. The baseline heart rate was 52 b.p.m., and the QTc pre-CNA procedure was 435 ms (*Figure 3A*). During the ablation of RSGP in the RA, the heart rate increased to 103 b.p.m. (*Figure 3B*). A total of 11 lesions (660 s) were delivered from the RA (*Figure 2B*). Additional lesions (290 s) were delivered opposite this region along the interatrial septum from the LA (*Figure 2C*). With no further increase in heart rate noted, the ablation procedure was stopped. The final heart rate was 103 b.p.m. and the QTc post-CNA procedure was 487. The procedure duration was 124 min and the fluoroscopy time was 9.8 min (dose–area product 6.27 Gycm^2).

An implantable loop recorder (Reveal Linq Medtronic, Minneapolis, MN, USA) was implanted to monitor for additional bradyarrhythmia or asystole post-CNA. During a follow-up of 12 months, the patient has

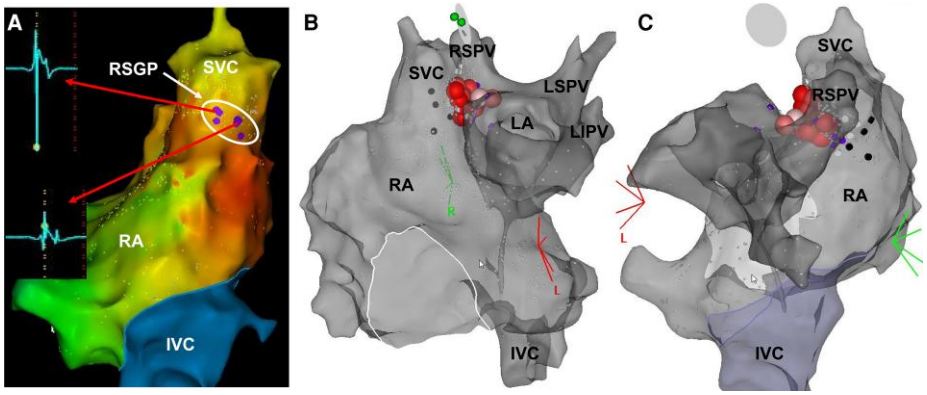


Figure 2 (*A*) A posteroanterior view of three-dimensional electroanatomical mapping of the right atrium. Dots along the interatrial septum represent the region where the right superior ganglionated plexus is located. Fragmented electrograms were recorded along the lower posteroseptal region of the superior vena cava using a high-density mapping catheter (PentaRay®) with the filter settings set at 100–500 Hz. (*B*) and (*C*) showed a left lateral view and posterolateral view of three-dimensional electroanatomical mapping of the right atrium and left atrium. Red dots represent the radiofrequency ablation lesions along the posterior interatrial septum from both the right atrium and left atrium. Purple dots represent the region where the right superior ganglionated plexus is located. Black dots represent the phrenic nerve course. IVC, inferior vena cava; LA, left atrium; RA, right atrium; RSGP, right superior ganglionated plexus; SVC, superior vena cava.

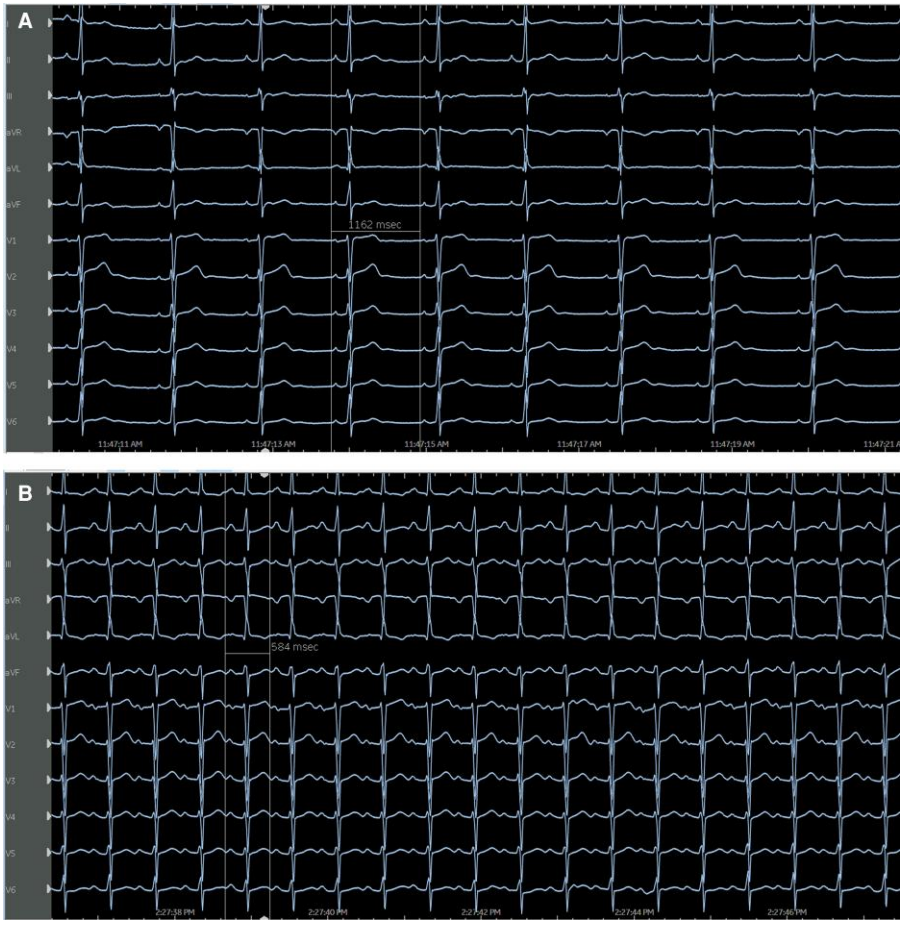


Figure 3 (*A*) Twelve-lead electrocardiogram demonstrated sinus bradycardia (heart rate of 52 b.p.m.) prior to cardioneuroablation procedure. (*B*) Twelve-lead electrocardiogram demonstrated sinus rhythm (heart rate of 103 b.p.m.) post-cardioneuroablation procedure.

had multiple episodes of recurrent focal epilepsy. Over that interval, interrogation of her loop recorder has revealed no bradyarrhythmia or asystole. Her resting ECG showed sinus rhythm and her resting heart rates during the follow-up period were between 70 and 110 b.p.m. She remains under evaluation for possible surgical treatment for drug-resistant FIAS.

Discussion

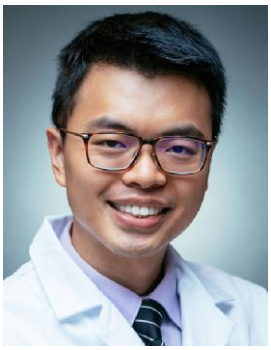
Ictal-induced bradyarrhythmia or asystole is rare occurring in <0.5–2% of patients with pharmacoresistant epileptic seizures undergoing prolonged video EEG monitoring.[3,4] The precise mechanism of ictal-induced bradyarrhythmia or asystole remains unclear, though it is postulated that the epileptic seizures may trigger a circuit comprising the insula and the limbic system (amygdala, hypothalamus, thalamus, and hippocampus).[5] This circuit interconnects the brainstem (dorsal vagal nucleus, nucleus ambiguous, and nucleus of the solitary tract) and the spinal cord nuclei that help to regulate the cardiac functions.[6] Stimulation of the central autonomic network during the ictal episode may trigger a burst of hypervagotonia. Prolonged episodes of ictal-induced bradyarrhythmia or asystole may result in syncope or even death due to impairment of cerebral perfusion. Thalamic seizures are particularly associated with ictal-induced asystole and temporal lobe surgery results in diminished autonomic modulation of the heart.[4,7]

There are no current guidelines that specifically discuss the management of patients with drug-resistant ictal-induced bradyarrhythmia or asystole. Historically, a permanent pacemaker has been considered for patients with significant sinus pauses of ≥6 s during seizures, but practice patterns are heterogeneous.[3] This may be due to the fact that the patients at greatest risk for ictal asystole are younger, with greater implications for lifetime cardiac implantable electronic device-associated morbidity. Given the enhanced vagal tone of ictal bradycardias and the recent growth of the CNA field, it is possible that autonomic modulation may become a viable alternative to pacemaker implantation for these individuals. Recent non-randomized studies have demonstrated that CNA is a promising treatment for cardioinhibitory neurocardiogenic syncope.[8,9] Further, recent work by Gopinathannair *et al.*[10] reported similar effectiveness and comparable safety of CNA vs. permanent pacing in select patients with recurrent cardioinhibitory vasovagal syncope. In this case report, we extend this prior work by describing the successful catheter ablation of cardiac parasympathetic ganglia to eliminate asystolic episodes in a patient with a malignant seizure syndrome. As compared with a prior report by Antolic *et al.*,[2] we performed partial parasympathetic denervation of the sinoatrial node by targeting only the RSGP from both the RA and LA. A sufficient endpoint in the form of resting heart rate modulation was met and achieved without the need to perform additional ablation of the inferior paraseptal GP. The follow-up interval of the current study is twice the duration of the prior work. We primarily targeted the RSGP as it was the presumed main GP with predominant parasympathetic fibres firing on the sinoatrial node via the right vagus nerve.[11,12] Hence, the ablation of RSGP from both the RA and LA is thought to be sufficient in patient with neurocardiogenic syncope.[11] Together, these data suggest that modulation of cardiac parasympathetic innervation by targeting the RSGP may be a successful way to treat ictal bradycardias much as it is for the management of bradyarrhythmia associated with neurocardiogenic syncope.

Conclusions

Our case highlights the potential role of CNA in a patient with drug-resistant, malignant seizure syndrome and profound ictal-induced asystole. Cardioneuroablation is an emerging therapy that may one day be used to treat patients with ictal-induced bradyarrhythmias to avoid permanent pacemaker implantation.

Lead author biography



Jian Liang Tan is currently an electrophysiology fellow at the Hospital of the University of Pennsylvania in Philadelphia, PA, USA. His research interests include sudden cardiac death and cardiac sarcoidosis.

Consent: The authors confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: T.M.M. received speaking honoraria from Boston Scientific, research grants from the Harlan Batrus EP Research Fund, the Mark Marchlinski EP Research Fund, and the National Institutes of Health National Heart, Lung, and Blood Institute (K23HL161349) and M.C.H received speaking honoraria from Biosense Webster and Abbott. J.L.T. and P.S. report no conflict of interest.

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Data availability

The data underlying this article are available in the article and in its online supplementary material.

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