Pediatric radiofrequency ablation of cardiac parasympathetic ganglia to achieve vagal denervation

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Introduction

Syncope is a common presenting complaint in pediatric cardiology outpatient referrals. While some causes of syncope such as ventricular tachyarrhythmias or bradyarrhythmias are inherently cardiac in nature, neutrally mediated syncope (NMS) can also occur owing to an imbalance of sympathetic and parasympathetic tone. Enhanced parasympathetic tone via the vagus nerve can cause slowing of the sinus or atrioventricular (AV) nodes, resulting in sinus pauses or AV block, respectively.[1] At times, these patients will require pacemaker implantation if medical treatment fails.[2–5] However, pacemaker implantation in infants and small children is more invasive than in adults, as placement of transvenous leads may result in more complications and a higher risk for development of venous stenosis.[6] Adult-sized patients with transvenous pacemakers still have risks of infection, cardiac perforation, or pneumothorax during the procedure. Over time, there is additional risk of needing reintervention on a transvenous device owing to lead failure secondary to dislodgement, fracture, or insulation break.[7] A novel therapy for NMS is cardioneuroablation of parasympathetic substrate from the endocardium.[8] The targets of the procedure are epicardial ganglionic plexuses.[9] This can be performed via a minimally invasive percutaneous procedure, and no hardware needs to remain inside the body. We present a case of a pediatric patient with vagally mediated neurocardiogenic syncope due to paroxysmal high-grade AV block treated with parasympathetic ganglia cardioneuroablation.

KEYWORDS Ablation; Electrophysiology; Parasympathetic ganglia; Pediatrics; Syncope; Vagal denervation

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KEY TEACHING POINTS

- Neurally mediated syncope (NMS) is caused by an imbalance of sympathetic and parasympathetic input to the sinoatrial (SA) or atrioventricular (AV) nodes. This is a common cause of syncope, especially in pediatric patients.
- Endocardial parasympathetic ganglia that provide input to the SA and AV nodes could serve as targets for cardioneuroablation in order to prevent NMS.
- Pediatric patients can derive significant benefits from the use of cardioneuroablation to treat NMS by avoiding both the short- and long-term effects of pacemaker implantation.

Case report

The inpatient cardiology team was initially called to consult on a 16-year-old boy with congenital thoracic scoliosis who was noted to have an asystolic event on cardiac telemetry overnight following spinal fusion surgery (posterior spinal fusion, T4-L2 with instrumentation (autograft, and allograft bone) and Ponte osteotomies at T6-T7 and T7-T8). His rhythm during this event was a 6-second period of high-grade AV block with no ventricular escape. During the episode, he recalled trying to drink water and having difficulty swallowing. He had previous syncopal events associated with getting up too quickly from a supine position and climbing stairs. Family history was notable for maternal cardiomyopathy of unknown etiology.

The patient's initial 12-lead electrocardiogram demonstrated normal sinus rhythm at a rate of 74 beats per minute and normal intervals. There were no periods of AV block. An echocardiogram showed a structurally normal heart with an intact atrial septum. A limited inpatient Holter monitor revealed episodes of paroxysmal AV block and asystole with maximum pause duration of 3.3 seconds (Figure 1a). Given his previous syncopal episodes without

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prodrome, a LINQ implantable cardiac monitor (Medtronic, Mounds View, MN) was implanted to assess his rhythm during future syncopal events, given his previous history of presyncope and syncope.[10]

The patient was then followed regularly as an outpatient. He continued to have intermittent periods of high-grade AV block on subsequent Holter monitors and remote monitoring tracings (Figure 1b) without actual syncope. He was noted to have intermittent ventricular ectopy on some Holter monitors. Stress testing revealed a normal AV nodal conduction response to exercise. Our patient underwent cardiac magnetic resonance imaging looking for signs of structural heart disease (myocardial scarring) given his family and personal history; however, late gadolinium enhancement was negative. Multiple treatment options were presented to the family after 51 months of observation and continued symptoms, including pharmacologic treatment with anticholinergic medications, pacemaker implantation, or neurocardiac ablation. The patient and family elected to pursue ablation.

An electrophysiology study was performed with the patient under general anesthesia. Two sheaths were placed in the right femoral vein (8F and 6F), and 2 sheaths were placed in the left femoral vein (8.5F and 5F). A 7.5F 3.5-mm-tip SmartTouch irrigated ablation catheter (Biosense Webster, Diamond Bar, CA) was inserted into the right femoral vein and advanced to the heart. A 3-dimensional electroanatomic map of the right atrium was created using FAM and the CartoSound module of the CARTO mapping system (Biosense Webster). A 5F quadripolar catheter was inserted into the right ventricle, and another 5F quadripolar catheter was positioned at the bundle of His. The baseline AH interval was 74 ms. A corrected sinus node recovery time was calculated to be 327 ms with a paced cycle length (CL) of 750 ms. Rapid atrial pacing and atrial extrastimulatory testing demonstrated a Wenckebach CL of 340 ms and an antegrade AV nodal effective refractory period (AVNERP) of 260 ms at a paced CL of 600 ms. The 8F sheath was exchanged for an 8.5F SL1 long sheath in order to obtain left atrial

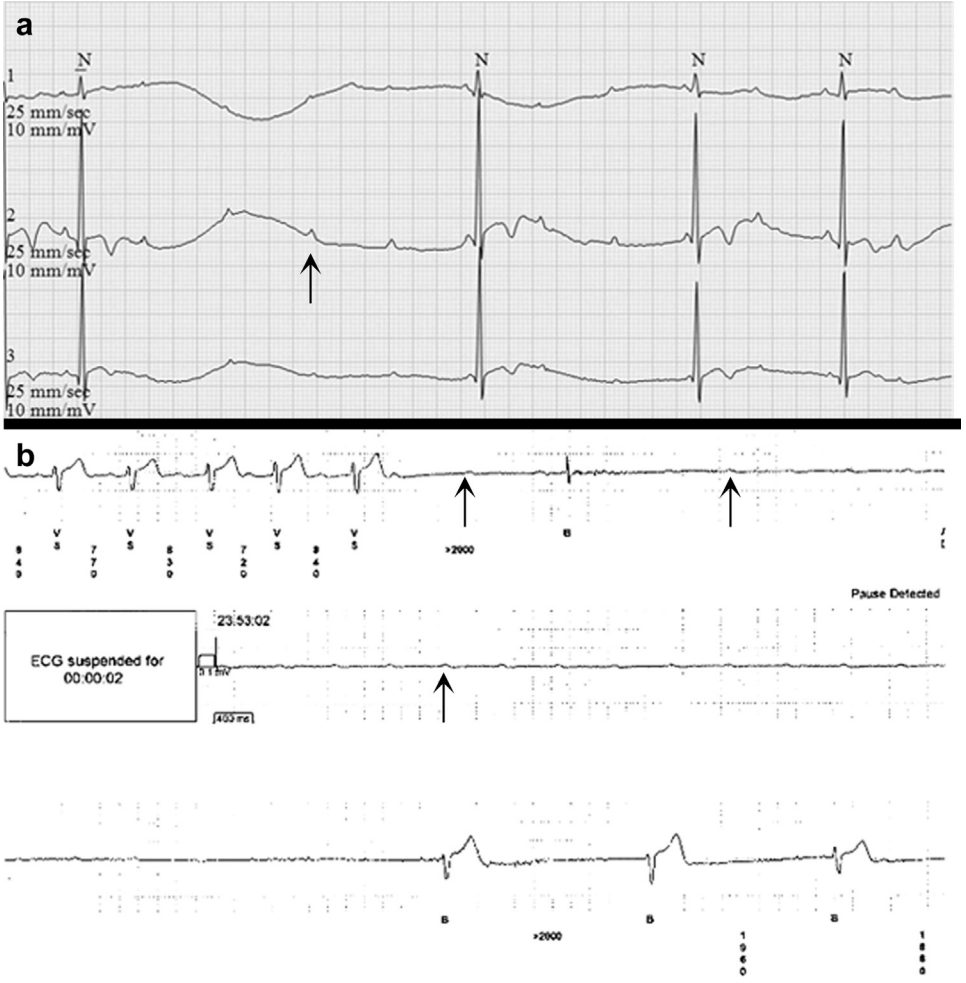

Figure 1 **a:** A 3.3-second period of high-grade atrioventricular (AV) block without ventricular escape on the patient's initial inpatient Holter monitor. **b:** High-grade AV block with a fascicular escape rhythm noted after 18 seconds from his implanted cardiac monitor. Vertical arrows refer to representative P waves that are not conducted.

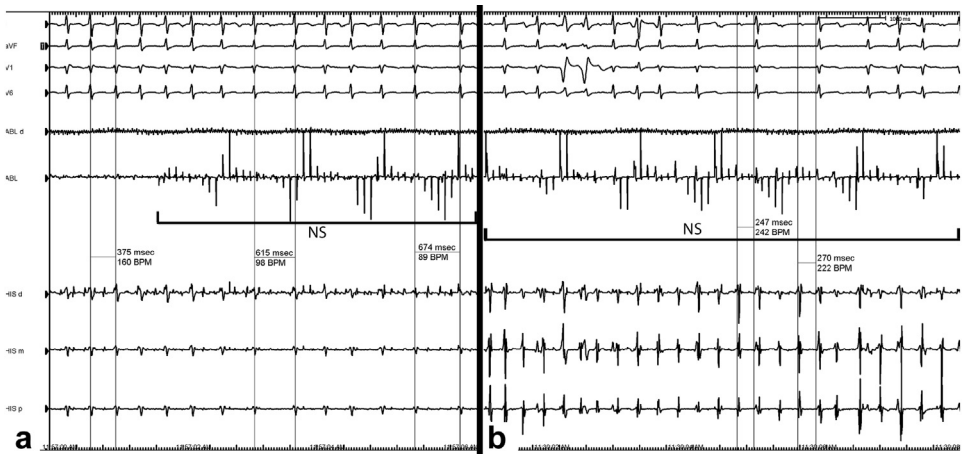

Figure 2 Two examples of neurostimulation of the atrioventricular (AV) node parasympathetic ganglion delivered via the ablation catheter. **a:** Slowing of AV conduction during atrial fibrillation. **b:** Neurostimulation resulted in atrial tachycardia with marked PR prolongation. (NS depicts the duration of neurostimulation in each snapshot).

access. A fluoroless transseptal puncture was performed using a Baylis RF needle (Baylis Medical, Montreal, Canada) under intracardiac echocardiography guidance via an 8F Soundstar intracardiac echocardiography catheter (Biosense Webster) via the left femoral vein.[11] Known areas of AV nodal parasympathetic ganglia were targeted, and a neurostimulator was used at 15 Hz with 15 V at 0.15 ms pulse width to map ablation targets. We targeted areas that resulted in high-grade AV block (Figure 2) without sinus bradycardia. This ensured that we were targeting only AV nodal ganglia as opposed to sinus node ganglia. Multiple ablation lesions were performed in the targeted areas in the inferomedial left atrium near the right inferior pulmonary vein (RIPV). The fat pad underlying parasympathetic control of the AV node is located at the junction of the RIPV and the coronary sinus (CS). Transmural lesions were attempted due to the epicardial location of the fat pads. Additional lesions were placed on the right atrial side near the os of the CS. The median power and duration of lesions were 34 watts and 45 seconds, respectively. A 3-dimensional map of all ablation lesions is shown in Figure 3. The endpoint target was a decrease in AH interval and AVNERP by 20% each. Following ablation, the antegrade Wenckebach CL and AVNERP had decreased to 310 ms and 210 ms, respectively, at a paced CL of 600 ms, indicating acute procedural success. The resulting AH interval was also shortened to 54 ms. Moreover, there was no change in AH interval, Wenckebach CL, or AVNERP with administration of atropine. The entire procedure was performed without fluoroscopy. The patient was taken to the recovery room and discharged after a 6-hour observation period in stable condition.

Following this procedure, the patient did not have any further episodes of presyncope or syncope, and no periods of high-grade AV block were noted on his LINQ or subsequent Holter monitors. Of note, a month after the procedure, the patient presented with new palpitations from atrial fibrillation and atrial tachycardia (paroxysmal atrial fibrillation) with rapid AV conduction. Echocardiogram at that time did not reveal any evidence for pericardial effusion. Initially we attempted to suppress his atrial arrhythmia with

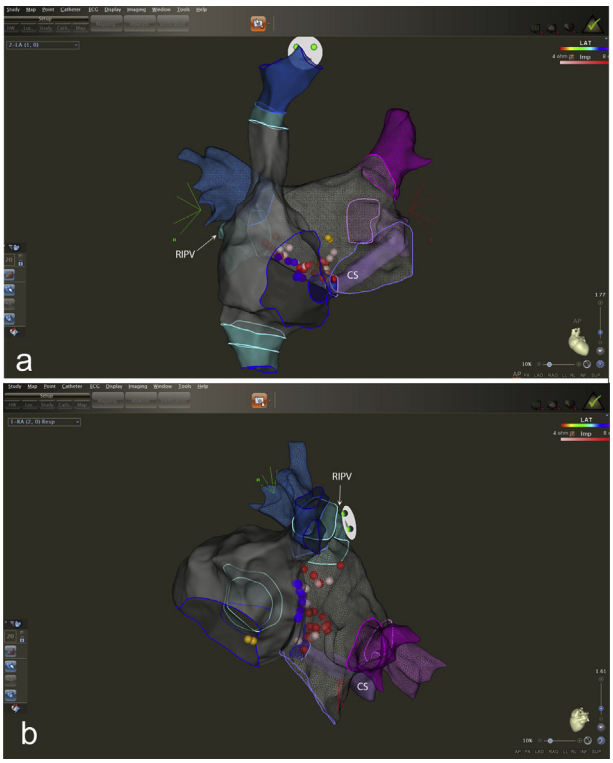

Figure 3 Three-dimensional CARTO (Biosense Webster, Diamond Bar, CA) maps depicting ablation lesions in the (**a**) anteroposterior (AP) projection and (**b**) left anterior oblique (LAO) and cranial projections. Outline of the right atrium (RA) is solid with some transparency. Left atrium (LA) is mesh. RA lesions are colored blue, while LA lesions are colored white, pink, or red. Yellow dots represent the area of the His bundle. The coronary sinus (CS) is colored purple, and the right inferior pulmonary vein (RIPV) is light blue.

flecainide, which was unsuccessful. Once sotalol was administered, his arrhythmia resolved after 3 months of treatment. In the 6-month period prior to the ablation procedure, the patient had 7 documented episodes of paroxysmal AV block recorded by the Implanted Cardiac Monitor. We have now followed him for 12 months post procedure and he continues to remain free of AV block and atrial fibrillation.

Discussion

We present a report of neurocardiac ablation of parasympathetic ganglia in a pediatric patient. The first study to describe cardioneuroablation for treatment of functional bradycardia was described in 2005 by Pachon and colleagues.[12] Since that time, this approach has been used in carefully selected patients to treat NMS without the use of a pacemaker.[2] However, no large-scale studies have been done in either pediatric or adult patients. The majority of reports are either single case reports or small observational studies, as the practice has not become widespread as of yet.[2]

We have described previous animal work in which enhancement of parasympathetic tone via the right inferior fat pad ganglion selectively slows AV nodal conduction to provide rate control for atrial fibrillation or junctional ectopic tachycardia.[13] Our strategy for treatment of this patient's high-grade AV block was to use this connection to create the opposite effect. Eliminating this specific fat pad ganglion resulted in enhanced AV nodal conduction by reducing parasympathetic tone to the AV node. The primary fat pad target was in the inferomedial left atrium, between the RIPV and CS. Since the fat pad is epicardial in location, we attempted to create transmural lesions with an irrigated ablation catheter. However, we also added supplemental lesions on the right atrial side in order to achieve the desired effect, transmural injury to the right inferior AV node fat pad.

It is particularly important to highlight that this technique may have even more utility in pediatric patients owing to greater risks of pacemaker implantation. Whereas an adult patient with a transvenous lead may or may not need an extraction in the future, a patient in his or her teens may require pacemaker therapy for the rest of their life. This obligates the patient to undergo multiple surgeries for generator replacements. Also, it is unreasonable to expect a pacing lead to last more than 30 years, and so this patient would have likely had to undergo at least 1 extraction during his lifetime in order to replace the lead. Lead extraction is a procedure that carries significant morbidity and mortality, so this approach could avoid having to take this major risk.

The advent of leadless pacing has been proposed as a potential solution to this problem, as the complications associated with leads are no longer present.[7] However, the battery life of the only approved device on the market is no longer than 15 years. Although this may be sufficient in an older adult patient, in a teenager the device will not last long enough. Multiple devices may be required, but there are no long-term studies on the effects of multiple devices within the right ventricular endocardium. Moreover, there is no current method to extract the device, so we do not consider this a viable solution at the moment.

There were no complications during our procedure, and neurocardiac ablation achieved our chosen endpoint of shortening the AH interval and AVNERP by approximately 20% each. In future cases, using transjugular vagal nerve stimulation might provide a more objective potential endpoint, ie, blocking the effect of acute vagal stimulatory effects on AV nodal conduction.[12] The medium-term primary outcome was excellent, as the patient has not had any further presyncope or syncope episodes or AV block documented by his implanted monitor in the 12 months following the procedure. Our patient did develop atrial arrhythmias (paroxysmal atrial fibrillation with rapid conduction) within a month following the procedure that subsequently resolved on medical therapy. We propose that the rapid AV conduction response was partially secondary to elimination of tonic parasympathetic control of AV conduction following fat pad ablation. The paroxysmal atrial fibrillation may have been owing to either a proarrhythmic effect of ablation lesions in the atria or an imbalance between sympathetic and parasympathetic tone, or potentially from pericarditis following the procedure. This arrhythmia was well controlled on medical therapy, and subsequently resolved. Previous reports in the literature have suggested inappropriate sinus tachycardia as a consequence of neurocardiac ablation, but none have mentioned paroxysmal atrial fibrillation.

We felt justified in proceeding with some medical treatment option of our patient despite 51 months of observation, conservative management, and continued symptoms. We believe the first step in management of vagally mediated / neurally mediated syncopal events should always be conservative management. However, in the authors' experience this will only work in 30%–50% of pediatric patients (that come to a specialized electrophysiology clinic) and additional medical interventions are necessary in the others. Many physicians underestimate the psychological and quality-of-life impact that syncopal events have on pediatric patients and their families.[14,15] Resolution of syncopal events, while not life-saving, frequently improves the patients' quality of life and improves their functionality. We discussed with the patient and family different treatment options such as continued observation, pharmacologic treatment with anticholinergics, neurocardiac ablation, and pacemaker implantation; the family decided on neurocardiac ablation.

Although this was an adolescent patient, we were able to locate his parasympathetic ganglia via neurostimulation, differentiating spots within the atria using a 3.5-mm-tip radiofrequency ablation catheter. We speculate that this may be more difficult in smaller children owing to the changes in geometry expected from navigating smaller cardiac structures.

Conclusion

Cardioneuroablation is a potential therapy for NMS in pediatric patients that can provide definitive therapy without the need for an implantable device. Further large-scale studies

are needed to study the medium- and long-term effects of parasympathetic ganglia ablation.

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