Successful bilateral thoracoscopic sympathectomy for recurrent ventricular arrhythmia in a pediatric patient with hypertrophic cardiomyopathy

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Introduction

Hypertrophic cardiomyopathy (HCM) is the most common monogenic cardiac disorder and remains a significant cause of sudden cardiac death in children and young adults. Sudden cardiac death is a serious complication of HCM and is the result of malignant ventricular arrhythmias. Currently, beta blockade, antiarrhythmic therapies, and insertion of an implantable cardioverter-defibrillator (ICD) represent the standard of care in patients with ventricular tachyarrhythmia (VT) in HCM.[1]

The autonomic nervous system plays a critical role in the initiation and maintenance of ventricular arrhythmias.[2] Cardiac sympathetic denervation (CSD) has been demonstrated to increase the ventricular fibrillation (VF) threshold.[3] Left CSD has an established role in the treatment of some forms of congenital long QT syndrome and catecholaminergic polymorphic ventricular tachycardia.[3,4] However, bilateral CSD may provide additional benefit by further decreasing sympathetic nervous system output to the heart, although the role of the right stellate ganglion is controversial.[5–7]

The utility of CSD in the treatment of VT of HCM is not as well defined, especially in the pediatric population. We report a case of successful treatment of recurrent VT with bilateral sympathectomy in a child with HCM.

KEY TEACHING POINTS

- The autonomic nervous system plays a critical role in the initiation and maintenance of ventricular arrhythmias in hypertrophic cardiomyopathy.
- Cardiac sympathetic denervation (CSD) has become increasingly accepted as a therapy for ventricular tachyarrhythmias refractory to maximal antiarrhythmic medications.
- Bilateral CSD can be safely and successfully performed in pediatric patients with hypertrophic cardiomyopathy and ventricular tachyarrhythmias refractory to maximal antiarrhythmic medications.

Case report

A previously healthy 9-year-old female child collapsed while walking at the airport in the early morning. A bystander emergency room physician confirmed that she was pulseless and initiated cardiopulmonary resuscitation. She responded to a single defibrillation and had regained pulses by the time emergency medical technicians arrived on scene. A 12-lead electrocardiogram revealed biventricular hypertrophy. An echocardiogram and magnetic resonance imaging were performed, revealing asymmetric left ventricular hypertrophy with the midventricular inferoseptal wall measuring 17 mm (Z-score +6.7), no left ventricular outflow tract obstruction, normal left ventricular systolic function with no delayed enhancement, and diastolic dysfunction with biatrial dilation and markedly low early diastolic velocities by Doppler. On cardiac catheterization, the right ventricular end diastolic pressure was 16 mm Hg, while the left ventricular end diastolic pressure was 22 mm Hg, with depressed cardiac index (2.3 L/min/m^2) and normal pulmonary vascular resistance. Her imaging was consistent with HCM but lacked the classic high-risk findings. In addition, rhythm strips of the automatic external defibrillator during her collapse were not available for review (she was in sinus rhythm by the time emergency services had arrived). Given the lack of clarity of her presentation, a cardiac exercise test was performed. This resulted in VF arrest after 90 seconds of exercise. After successful resuscitation, she underwent placement of a

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dual-chamber, single-coil ICD, and medical therapy was started with verapamil and atenolol.

Genetic testing (GeneDx, Gaithersburg, MD) identified a mutation in the tropomyosin gene *TPM1*, c.550G>C (p.Glu184Gln), that was classified as a variant of uncertain significance. This was a de novo mutation for our patient, which remains unpublished to our knowledge, and is not observed in large population cohorts. In silico (using computational predictive software programs) analysis, which includes protein predictors and evolutionary conservation, supports a deleterious effect.

Our patient had no further events for the 5 years following. She gradually gained weight to the point she became obese, but did not complain of any cardiac-related symptoms. She underwent annual exercise testing, where she demonstrated blunted heart rate response while on beta blockade, but no arrhythmia. Echocardiographic evaluation remained stable, without further progression of the hypertrophy or development of left ventricular outflow tract obstruction.

At age 14, she presented with an episode of syncope while walking at school. Interrogation of her device noted polymorphic VT that degenerated to VF, prompting a successful shock from her ICD (Figure 1). An echocardiogram did not note any change to her baseline ventricular function. She was transitioned from atenolol to nadolol, but owing to several recurrent appropriate shocks over a 3-month period, medical management was altered several times, eventually to a combination of amiodarone, nadolol, and mexiletine. Despite maximal medical management, she had another episode of polymorphic VT and syncope with minimal activity. A transplant evaluation was then initiated, and after multiple discussions among the team members and the family, the decision was made to perform a bilateral sympathectomy for cardiac denervation. The procedure consisted of video-assisted thoracoscopic sympathectomy, as previously described.[8] The patient was intubated with a double-lumen endotracheal tube to facilitate lung isolation. Left CSD was performed first, followed by right CSD. The procedure was successful but was complicated by mild left-sided ptosis, which was successfully treated with left internal mullerectomy.

Since the procedure, she has been maintained on amiodarone, mexiletine, and bisoprolol. Our plan is to wean her off her medical management over time. However, given her age, her wish to pursue an active life, and past refractoriness of her arrhythmia, we decided to proceed with liberalization of her activities first, followed by slow and gradual weaning of her medications.

With 33 months of follow-up, she has had no further episodes of VT or VF, despite returning back to regular levels of activity, including school, gym class, tennis, and ziplining. She still does not pursue highly competitive or contact sports.

Discussion

Left CSD is an established procedure that has become increasingly accepted as a therapy for VT in long QT and catecholaminergic polymorphic VT refractory to maximal antiarrhythmic medications. It has been reported to decrease arrhythmia load in patients with refractory VT due to other conditions as well, including HCM, although it has not become an established standard-of-care treatment to date.[9,10]

Initial animal reports had suggested that right CSD may lower the VF threshold and therefore possibly confer additional arrhythmogenesis. More recently, however, bilateral CSD has been postulated to bring additional benefit to arrhythmia control compared with left CSD alone, as it appears that the right stellate ganglion accounts for significant innervation to the ventricles.[5–7] Clinical case series in adult patients with refractory arrhythmias suggest that bilateral cardiac sympathectomy is at least not inferior, and is potentially superior, to traditional left-sided denervation for ventricular arrhythmias.[8] A recent retrospective review of 121 adult patients with a variety of structural heart diseases and recurrent VT attempted to evaluate long-term outcomes after both left and bilateral CSD.[11] After a mean follow-up of 1.5 years, there was an 88% reduction in the number of ICD shocks overall. Patients with bilateral CSD had longer ICD-shock-free, transplant-free survival compared to patients who underwent a left-only procedure ($P = .014$).[11] The study included 3 patients with HCM but no pediatric patients.

When CSD had been considered in the past, left CSD was usually performed for medication-refractory ventricular tachycardia, followed by right CSD for further recurrences. Recent reports, however, support earlier application of bilateral CSD in adults with refractory arrhythmias.[5,12] Our patient had received multiple appropriate shocks (5) within a period of 3 months despite maximal medication therapy. The arrhythmic events occurred with minimal exertion (walking a few steps), to the point that she was afraid to move. Given the multiple shocks, and family and patient anxiety, after multiple team meetings the decision was made to proceed with bilateral sympathectomy rather than proceed in a stepwise fashion.

Sudden death from ventricular arrhythmias is a major cause of death in young people with HCM. The occurrence of malignant VT in HCM may be associated with increased global cardiac sympathetic nerve stimulation.[13] Despite this, CSD has rarely been performed in the past in children with HCM. Left CSD has, to our knowledge, only been reported in 2 children with HCM, with resulting decrease in frequency of shocks but incomplete resolution of the arrhythmia.[10,14] A single prior case of bilateral CSD in a child with HCM has been reported in a teenager, performed by minimally invasive posterior extrapleural thoracic sympathectomy.[15] As with our patient, this patient was maintained on antiarrhythmic medications after the surgery and remained symptom free on follow-up, which was, however, shorter than that of our patient. It is unclear if he was allowed to pursue physical activity, as was our patient.

Pediatric heart disease with associated near–sudden death and/or life-threatening arrhythmias untreatable with medications or an implantable defibrillator is an indication for

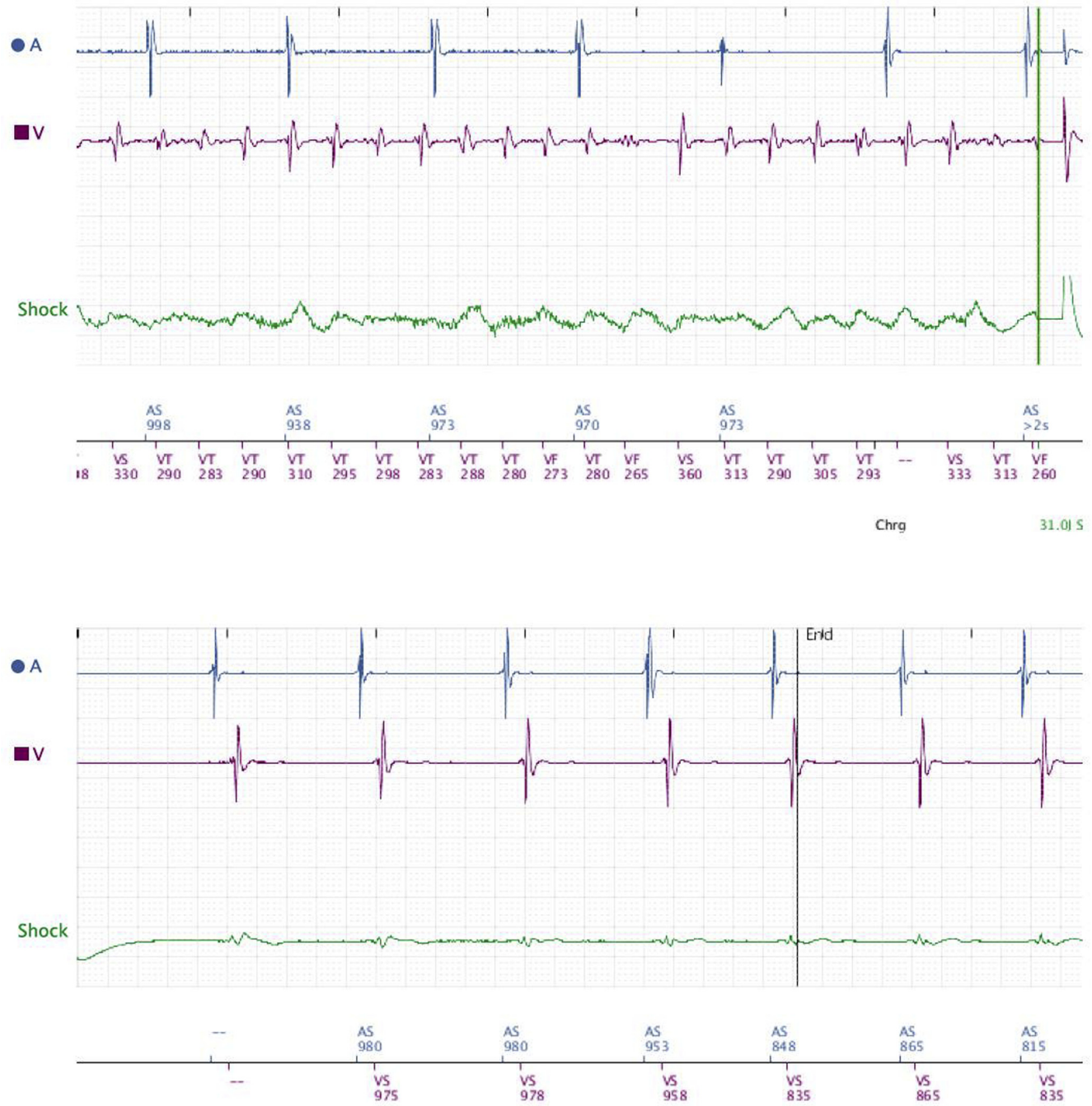

Figure 1 Intracardiac electrograms from the patient's implantable cardioverter-defibrillator. Polymorphic ventricular tachycardia successfully terminated with a 31 J shock.

cardiac transplantation. Given the shortage of organ donors, effective treatments prior to transplantation would be a welcome addition to the treatment repertoire. As our patient displays, it is possible that CSD could be considered as an adjunct treatment option to delay or even prevent transplantation in pediatric patients with refractory arrhythmias from HCM.

Cardiac sympathectomy carries the risk of occasional complications, such as Horner syndrome, facial flushing, alterations in sweating patterns, and neuropathic pain. Our patient experienced ptosis, which is a known possible adverse event. It is unclear if bilateral CSD carries a different risk of complications than left CSD alone. Our patient's ptosis persisted but improved to the point that the cosmetic effect was minimal. Our teenage patient desired further cosmetic improvement and underwent internal mullerectomy, with excellent result, which may make sympathectomy more acceptable to this age group.

In this report, we demonstrate the successful use of bilateral cardiac denervation to suppress refractory ventricular tachycardia and fibrillation in a pediatric patient with HCM. The bilateral CSD has resulted in no further ICD

shocks with over 30 months of follow-up. Larger studies are required to better understand the utility of bilateral CSD and how to select which patients are best suited for this procedure.

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