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Left Cardiac Sympathetic Denervation in a Pediatric Patient with Hypertrophic Cardiomyopathy and Recurrent Ventricular Fibrillation

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INTRODUCTION

Initially performed for angina in the early 1900's [1], left cardiac sympathetic denervation (LCSD) has become an important therapeutic option in patients with long QT syndrome (LQTS) and catecholaminergic polymorphic ventricular tachycardia (CPVT) [2-5]. For these heritable channelopathies, LCSD has filled the therapeutic gap between daily medications (i.e. beta blockers) and implantable cardioverter-defibrillator (ICD) therapy. LCSD's anti-fibrillatory properties have been demonstrated clearly for patients with LQTS where there is an estimated 90% reduction in LQT-triggered cardiac events post-denervation [2, 4].

Hypertrophic cardiomyopathy (HCM) is one of the most prevalent heritable cardiovascular disease and the most common cause of sudden cardiac death in young athletes [6]. Clinically, HCM is characterized by unexplained and unequivocal cardiac hypertrophy in the absence of hypertrophy-inducing conditions such as hypertension and aortic stenosis.

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Besides the underlying genotypic heterogeneity, HCM is characterized by profound clinical heterogeneity as well [6, 7]. Patients can display extremely varying degrees of hypertrophy, fibrosis, and left ventricular outflow tract obstruction, and have an increased propensity for potentially life-threatening ventricular arrhythmias [6].

A recent article reported success using neuraxial modulation, either LCSD or thoracic epidural anesthesia (TEA), in adult patients with refractory arrhythmias, including 3 patients with HCM [8]. Herein, we report a pediatric patient with HCM who underwent LCSD for his malignant, ventricular fibrillation-prone HCM substrate, in hopes of delaying cardiac transplantation.

CASE REPORT

Clinical History

A 3-year-old previously healthy male presented with an out-of-hospital cardiac arrest to an outside institution. He had gotten out of bed and woken up his parents, concerned that he wasn't feeling well, when he suddenly collapsed. Emergency services were activated and when paramedics arrived, they found him to be in ventricular fibrillation (VF). He was defibrillated successfully with two shocks using an automated external defibrillator. He was admitted to the pediatric intensive care unit for observation, and remained in sinus rhythm. His family history was unremarkable, lacking any history of premature sudden death. On evaluation by echocardiography, severe HCM was documented. An epicardial ICD was placed subsequently and he was started on beta-blocker therapy with atenolol (12.5 mg once daily, 0.75 mg/kg/day). He was discharged uneventfully from the hospital, although was readmitted four days later with pericarditis. This resolved with a 6-week course of aspirin.

Our patient was symptom free for 8 months after his sentinel event, at which point he experienced a single appropriate VF-terminating ICD shock. He was not active at the time of the shock, and was conscious. ICD interrogation verified the presence of VF. He received a second shock one month later while playing at the playground. He again was conscious without collapse at the time of his appropriate VF-terminating, single ICD discharge. His third appropriate shock occurred one month later while playing soccer in the backyard with his father, again requiring only one single ICD discharge (Figure 1). At that time, his medication was switched from atenolol to sotalol (42.5 mg twice daily, ~100 mg/m²/day). Two months after the medication change, the patient had his fourth appropriate VF-terminating ICD discharge, while running through the house at the time of the shock. He had his fifth shock two weeks later, again while running through the house. During this event, he became acutely short of breath and clutched his abdomen. He became limp and collapsed. His parents activated emergency response, but he had recovered by the time they arrived. ICD interrogation confirmed an appropriate VF-terminating ICD therapy.

Due to the frequency of his appropriate VF-terminating shocks, further interventions were discussed and a transplant evaluation was initiated. He was referred to our institution for consideration of alternate therapies, including the possibility of LCSD in hopes to postpone cardiac transplantation. Prior to coming to our institution, in fear of another ICD discharge, his parents restricted his activity.

On repeat echocardiography at our institution, the patient was noted to have marked anterior and septal left ventricular hypertrophy (LVH), including a ventricular septum measuring 20 mm (normal 6-8 mm) with a reversed septal curvature pattern. He had no evidence of left ventricular outflow tract obstruction, and had moderate left atrial enlargement (Figure 2). His left ventricular systolic longitudinal strain was abnormal, with an average value of -15% (normal being more negative than -18%). An electrocardiogram (ECG) revealed

normal sinus rhythm, biatrial enlargement, left axis deviation, and LVH with a strain pattern. Due to the concern for refractory recurrent VF despite pharmacotherapy and in an effort to potentially postpone cardiac transplantation, LCSD was advised.

Surgical Intervention with Videoscopic LCSD

The patient had an LCSD performed as previously described [2] using the video-assisted thorascopic surgery (VATS) technique. This involved removal of the lower half of the left stellate ganglion (T1) and the T2-T4 sympathetic ganglia. The dissected materials were sent to pathology and read by frozen section to ensure accurate anatomic dissection. There were no complications of the surgical procedure. While ready for discharge the day after the procedure, he remained in the hospital for a total of 3 days in order to transition from sotalol to nadolol pharmacotherapy.

Clinical Follow-up

After discharge, the patient was maintained on nadolol pharmacotherapy (10 mg twice daily, 1 mg/kg/day, titrated up to 20 mg twice daily, 2 mg/kg/day). The patient was shock-free for the first 5 months following LCSD. At that point, he was playing in a hotel swimming pool when he received a single appropriate VF-terminating ICD discharge. He also was noted to have a fever at that time, and was ultimately diagnosed with H1N1 influenza the following day. Four months after this, he received two more single appropriate VF-terminating shocks. The first shock occurred while roller skating during a class trip (Figure 3). The second occurred while playing on the furniture at home, just 24 hours after his previous shock. Since that time, he has not had any further shocks. Now 24 months since LCSD (censored 3/2011), he has gone over a year without an appropriate discharge. Furthermore, parental anxiety for ICD-shocks has diminished, and he has now been allowed to resume his active lifestyle, thereby significantly increasing the quality of life for him as well as his parents.

DISCUSSION

LCSD has been shown to be a safe and effective treatment option to reduce the frequency of life threatening ventricular arrhythmias in patients with heritable channelopathies [2, 4, 5] and in a couple of adult patients with HCM [8]. To the best of our knowledge, this is the first report of a potential anti-fibrillatory effect of LCSD for a child with HCM.

Bourke *et al.* recently reported a series of 14 patients who underwent neuraxial modulation, by either LCSD or TEA, as treatment for refractory ventricular arrhythmias [8]. This report included 3 patients with HCM including a 66-year-old and 44-year-old male with ventricular-tachycardia (VT) storms and a 57-year-old male with incessant VT. Two of these patients underwent LCSD, of whom one had a good response with no further VT. The other died 3 days after LCSD due to VT recurrence. The HCM patient who underwent TEA had a 38% increase in arrhythmias after the procedure and this patient ultimately underwent urgent cardiac transplantation. It is important to note that these were all adult patients, and many were in extremis due to VT/VF storms [8]. Thus, the poor outcomes reported after LCSD in this study may not refute the potential benefits of LCSD in patients with HCM. Further research is needed to delineate the potential role of LCSD in patients with HCM and refractory arrhythmias.

There are numerous effects of LCSD that contribute to its clinical efficacy. LCSD raises the threshold for VF in subjects with ischemia, making it more difficult for the heart to fibrillate [9, 10]. LCSD reduces the arrhythmia burden after acute myocardial ischemia in anesthetized and conscious animal models [9] of sudden death. LCSD does not reduce heart rate and does not impair myocardial contractility because the right-sided stellate ganglion

and sympathetic chain provide adequate compensation [10]. These known experimental effects of LCSD make it tempting to speculate a potential utility in HCM patients with frequent ventricular arrhythmias.

Although his episodes of VF have not been eliminated, our patient has had a marked reduction in the frequency of his events, especially over the last year. Compared to 5 ICD shocks that he had during the 13 months prior to LCSD and on medical therapy alone, he has had only 3 shocks in the 24 months after LCSD. This apparent attenuation in VF events may be attributed to several factors. It is important to note that the ventricular arrhythmogenic substrate is markedly different in patients with LQTS/CPVT and patients with HCM. Myocardial fibrosis in particular, is distinctly a HCM-specific finding, and the resultant potential re-entrant arrhythmias will not be ameliorated by performing an LCSD. In our experience, patients with LQTS who have had breakthrough events after an LCSD are expectedly over-represented by those who had LCSD performed as part of an adjunctive secondary prevention strategy. Thus, the fact that our patient had events prior to LCSD undoubtedly placed him at higher risk of having events post-LCSD. Adjustments were also made in his beta-blocker therapy, both in choice of drug and dose, after his LCSD. This may be significant, as high-dose beta-blockade may also improve survival in pediatric patients with HCM [11].

Cardiac transplantation is an important therapeutic option in patients with end-stage HCM, both due to severe structural and hemodynamic compromise and heart failure as well as due to refractory ventricular arrhythmias. However, the average 10-year survival rate for pediatric patients undergoing transplant in the modern era is still only around 65% [12]. Although transplantation may be the best ultimate option, it should be delayed for as long as possible. In patients being considered for transplantation because of malignant ventricular arrhythmias, LCSD may provide a bridge to transplant and if its anti-fibrillatory effect is realized, denervation therapy might even delay or prevent cardiac transplantation altogether.

Limitations

While this patient has had a clear attenuation in the frequency of ICD shocks since his LCSD, there are numerous other factors other than LCSD that may have affected the outcome. These factors include the change of beta-blocker medications ultimately to nadolol after the procedure [11], the natural variability in the disease substrate, or a combination of factors.

CONCLUSION

To our knowledge, this is the first report of LCSD in a pediatric patient with HCM. When cardiac transplantation is being considered in pediatric patients with HCM solely due to refractory ventricular arrhythmias, LCSD may provide an alternative treatment option that might delay or prevent cardiac transplantation.

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Abbreviations used

CPVT	Catecholaminergic polymorphic ventricular tachycardia
ECG	Electrocardiogram
HCM	Hypertrophic cardiomyopathy
ICD	Implantable cardioverter-defibrillator
LCSD	Left cardiac sympathetic denervation
LQTS	Long QT Syndrome
LVH	Left ventricular hypertrophy
TEA	Thoracic epidural anesthesia
VATS	Video-assisted thoracic surgery
VF	Ventricular fibrillation
VT	Ventricular tachycardia

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Figure 1.

Interrogation of our patient's ICD after his third appropriate VF-terminating shock, demonstrating (A) VF and (B) subsequent conversion to a ventricular paced rhythm after a single device therapy.

Figure 2. Two-dimensional echocardiographic image from the patient's initial evaluation at our institution. A parasternal long-axis view demonstrates severe septal hypertrophy without evidence of left ventricular outflow tract obstruction.

Figure 3. Interrogation of our patient's ICD after his first appropriate VF-terminating shock occurring after his LCSD. The rhythm (A) is consistent with VF and subsequent conversion (B) to a ventricular paced rhythm after a single device therapy.