Venoarterial extracorporeal membrane oxygenation and implantable cardioverter-defibrillator implantation in a hemodynamically unstable infant with ventricular tachycardia from multiple cardiac rhabdomyomas

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Introduction
Tuberous sclerosis complex (TSC) is a neurocutaneous disorder characterized by benign tissue hamartomas in multiple organ systems, including cardiac rhabdomyomas.1 Though prevalent in TSC, cardiac tumors are rare in children, occurring in about 0.03%–0.17%. Rhabdomyomas are the most common, accounting for 45%.2,3 When present, they are multiple and in the ventricular myocardium.4 Frequently, they regress and surveillance is all that is required until spontaneous regression.5 Intervention is necessary when life-threatening obstruction or hemodynamically significant refractory arrhythmias occur. This case highlights the course of a 6-month-old infant with TSC and cardiac rhabdomyomas who presented in refractory ventricular tachycardia (VT) with decompensation and cardiac arrest necessitating venoarterial extracorporeal membrane oxygenation (VA-ECMO), complex antiarrhythmic therapy, and ultimately implantable cardioverter-defibrillator (ICD) implantation.

Case report
Our patient was found to have intracardiac tumors by a fetal echocardiogram at 34 weeks gestation. Postpartum, an echocardiogram and electrocardiogram (ECG) were completed. The ECG showed normal sinus rhythm with normal intervals and voltages, with J point and ST elevation in the inferolateral leads, consistent with benign early repolarization. His echocardiogram confirmed multiple rhabdomyomas along the interventricular septum and left ventricular myocardium, and in the anterior outlet septum extending into the right ventricular outflow tract, but without inflow or outflow obstruction of either ventricle (Figure 1). Additionally, a head ultrasound was concerning for intracranial tumors. These findings raised high suspicion for TSC and he was referred for further testing. He developed infantile spasms and was started on vigabatrin for management. At 3 months of age, his ECG was unchanged and echocardiogram displayed minimal regression of the tumors. At that visit, a 6-month cardiac follow-up with repeat testing was recommended.

At 6 months of age, he awoke from a nap crying and lost consciousness for 2 minutes, described as “unlike his infantile spasms.” On emergency medical services arrival, he was alert but upset. A cardiac monitor revealed a wide complex tachycardia (WCT) with a heart rate of 300 bpm. At the local emergency department he was given 3 doses of adenosine (single dose of 0.1 mg/kg and 2 doses of 0.2 mg/kg), without any effect on the WCT. His ECG (Figure 2) was consistent with monomorphic VT and an esmolol infusion (50 mcg/kg/min) was initiated at the recommendation of the on-call pediatric cardiologist. The patient was then transferred to our center and during transport remained stable on room air with appropriate capillary refill (<2 seconds). Upon arrival, an emergent echocardiogram showed no evidence of obstruction or pericardial effusion, with inability to comment on systolic function secondary to the heart rate. He remained in VT at 280–330 bpm and his esmolol drip was titrated to 150 mcg/kg/min. An additional dose of adenosine (0.2 mg/kg) was administered without notable change. He received 7 mg of ketamine and 7 mg of rocuronium. Calcium chloride (100 mg) was given prior to an amiodarone bolus (5 mg/kg) in an attempt to chemically cardiovert the rhythm. His rhythm suddenly deteriorated into ventricular fibrillation (VF) and cardiopulmonary resuscitation was initiated. Two 15 J shocks were administered with conversion to sinus, but rhythm immediately reverted back into VT with a palpable pulse. He was intubated and...
place on a ventilator. His perfusion worsened, with evidence of cardiogenic shock. The decision was made to place him on VA-ECMO for continued support (flow started at 100 mL/kg). After cannulation, he went into VF (total time about 5 minutes after full extracorporeal membrane oxygenation [ECMO] flows) and was defibrillated with 15 J and successfully cardioverted to sinus rhythm.

Once cardioverted, he was cooled and placed on morphine and dexmedetomidine infusions to decrease metabolic demand. A repeat echocardiogram showed severely reduced biventricular systolic function, prompting initiation of calcium chloride (5 mg/kg/hr) and milrinone (0.5 mcg/kg/min). He was loaded with oral amiodarone through a nasogastric tube at 20 mg/kg/day with frequent ECG monitoring. His mean arterial pressures (MAP) increased, necessitating a gastric tube at 20 mg/kg/day with frequent ECG monitoring.

At his last postdischarge follow-up visit, at 9 months of age, he has remained stable, free from recurrent VT.

Discussion

Cardiac tumors (even rhabdomyomas) are rare in children, and they typically do not cause symptoms or hemodynamic compromise in the majority of patients. However, they can become symptomatic, depending on the number, position, and size of the tumors. Some may obstruct blood flow and lead to ventricular or valvular dysfunction with subsequent heart failure. They may also compress or interrupt the conduction system, leading to arrhythmia, heart block, sinus node dysfunction, and/or preexcitation. In this report, we detail a patient with rhabdomyomas with abrupt development of significant arrhythmogenesis and hemodynamic collapse. With aggressive treatment including hemodynamic bridging with VA-ECMO, antiarrhythmic therapy, and long-term protection with an ICD, the patient was stabilized and is doing well with outpatient management.
in 17% of the children and significant arrhythmias were found in 16%. These arrhythmias included VT (6%), ventricular preexcitation with sustained supraventricular tachydardia (SVT) (2%), ventricular preexcitation without SVT (8%), and sustained SVT (5%) without underlying preexcitation. Additionally, ventricular ectopic beats and couplets and brief nonsustained SVT were found in 12% and various other arrhythmias were found in 28% of the patients. Józwiak and colleagues evaluated 154 patients with TSC and found that of the 74 with cardiac rhabdomyomas, the main clinical manifestations of the tumors that did not remain silent were arrhythmias (23%), murmurs (14.9%), and heart failure (5.4%). Based on published literature, arrhythmia remains the most common symptomatic cardiac manifestation in individuals with TSC. Frequently, they are successfully treated with antiarrhythmic medications as an adjunct to careful follow-up, with eventual tumor regression, as seen in a retrospective single-center study conducted from 1968 to 2010. Our patient presented with sustained intractable monomorphic VT that culminated in cardiac arrest from degeneration into VF. His management required early recognition of his
rhythm and transfer to a center with pediatric subspecialty care. With intensive care, defibrillation on VA-ECMO, numerous antiarrhythmic medications, and epicardial ICD implantation, the child was able to survive and is doing well in follow-up.

The workup of wide complex tachycardia can be challenging in young patients, particularly if hemodynamically tenuous. Pediatric patients can have extremely fast ventricular rates compared to adults, and the QRS complexes may not be recognized as wide by standard ECG machines or providers who are unfamiliar with pediatric ECGs. The majority of wide complex tachycardias in pediatric patients are due to aberrant SVT, and therefore adenosine is part of the Pediatric Acute Life Support algorithm for wide complex tachycardia if the patient is stable. The ECG showed right bundle branch morphology with an inferior axis that is also rightward (negative in leads I and aVL), suggesting the VT was from the left ventricular outflow tract. There was no concordance in the precordial leads to make VT more likely, but using the aVR criteria, there is an initial R wave that made VT more likely. The historic clues to making the diagnosis were knowing the patient had a normal ECG at 2 months of age and he had significant rhabdomyomas in his ventricular myocardium. With no change in tachycardia cycle length or QRS morphology with adenosine administration, VT was the most likely rhythm.

The mechanism of the VT was presumed to be triggered activity as well as reentry, but not definitively proven. After defibrillation (prior to ECMO cannulation), the patient would shortly revert back into VT after a sinus beat. After placement of the ICD, the tachycardia would terminate with ATP in the ventricle, supporting reentry as a contributing mechanism. The patient’s history and known presence of rhabdomyomas in the ventricles made verapamil-sensitive (fascicular) VT unlikely.

This is the first report of hemodynamically significant VT due to cardiac rhabdomyomas in a pediatric patient leading to VA-ECMO and ICD implantation. The natural history of these tumors would suggest that observation is prudent in most cases; however, our patient required significant antiarrhythmic therapy and an ICD owing to his arrest from VT. The patient’s case was discussed at our combined surgical/cardiology conference after he was on ECMO and transferred to a pediatric quaternary center where we have an established partnership for care of patients. Tumor resection was not an option owing to the extensive nature of the masses and extension into the crux of the heart and proximity to the coronary arteries. Resection of the left ventricular free wall was not feasible. Antitumor medications, such as sirolimus, were considered, but the duration of treatment would be long and there was no guarantee a smaller tumor would equate to less or no VT. The risks of ICD implantation in a young patient were weighed carefully (frequent shocks as well as inappropriate shocks, infection risk, and future invasive procedures for generator changes/lead revisions). Transplantation was considered, but he was weaned successfully from ECMO and the decision was made to place an ICD after all possible options were considered.

For now, the patient is doing well and thriving on flecainide and amiodarone with close outpatient monitoring. Knowing that patients with TSC and cardiac rhabdomyomas can have life-threatening arrhythmias, it is worth considering more frequent ambulatory outpatient monitoring with pediatric cardiologists or electrophysiologists to survey for life-threatening rhythms. If sustained arrhythmias are seen, intervention might be warranted sooner than careful observation and waiting for regression of the masses.

References
1. Ajay V, Singhal V, Venkateshwarlu V, Rajesh SM. Tuberous sclerosis with rhabdomyoma. Indian J Hum Genet 2013;19:93–95.
2. Delmo Walter EM, Javier MF, Sander F, Hartmann B, Ekkernkamp A, Hetzer R. Primary cardiac tumors in infants and children: surgical strategy and long-term outcome. Ann Thorac Surg 2016;102:2062–2069.
3. McAllister HA Jr. Primary tumors of the heart and pericardium. Pathol Annu 1979;14 Pt 2:325–355.
4. Hinton RB, Prakash A, Romp RL, Krueger DA, Knilans TK. Cardiovascular manifestations of tuberous sclerosis complex and summary of the revised diagnostic criteria and surveillance and management recommendations from the International Tuberous Sclerosis Consensus Group. J Am Heart Assoc 2014;3:e001493.
5. Birnbaum SE, McGahan JP, Janos GG, Meyers M. Fetal tachycardia and intramyocardial tumors. J Am Coll Cardiol 1985;6:1358–1361.
6. Bryant R 3rd, Aboutalebi A, Kim JJ, Kertesz N, Morales DL. Epicardial implantable cardioverter-defibrillator system placed in a 4.9-kg infant. Tex Heart Inst J 2011;38:421–423.
7. Shaher RM, Mintzer J, Farina M, Alley R, Bishop M. Clinical presentation of rhabdomyoma of the heart in infancy and childhood. Am J Cardiol 1972;30:95–103.
8. Van der Hauwaert LG. Cardiac tumours in infancy and childhood. Br Heart J 1971;33:125–132.
9. Miyake CY, Del Nido PJ, Alexander ME, et al. Cardiac tumors and associated arrhythmias in pediatric patients, with observations on surgical therapy for ventricular tachycardia. J Am Coll Cardiol 2011;58:1903–1909.
10. Józwiak S, Kotulska K, Kasprzyk-Obara J, et al. Clinical and genotype studies of cardiac tumors in 154 patients with tuberous sclerosis complex. Pediatrics 2006;118:e1146–e1151.
11. Kleinman ME, Chameides L, Schexnayder SM, et al. Part I4: pediatric advanced life support: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation 2010;122:S876–S908.
12. Barnes BT, Procaccini D, Crino J, et al. Maternal sirolimus therapy for fetal cardiac rhabdomyomas. N Engl J Med 2018;378:1844–1845.
13. Breathnach C, Pears J, Franklin O, Webb D, McMahon CJ. Rapid regression of left ventricular outflow tract rhabdomyoma after sirolimus therapy. Pediatrics 2014;134:e1199–e1202.
14. Castro-Monsalve J, Alvarado-Socarras JL, Mantilla KA, Forero L, Moreno A, Prada CE. Cardiac rhabdomyomas in tuberous sclerosis complex. J Pediatr 2018;192:264–264.e1.