Successful endocardial catheter ablation of a drug-resistant monomorphic ventricular tachycardia in a child with Brugada syndrome

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Introduction

Brugada syndrome (BrS) is an inherited arrhythmia that may cause fatal ventricular tachyarrhythmias in mainly males between their fourth and fifth decade of life.[1] Recently, epicardial radiofrequency (RF) ablation of right ventricular outflow tract (RVOT) arrhythmias has been performed to eliminate the arrhythmogenic substrate in cases not responding to first-line medications such as bepridil, and a favorable outcome has been reported in adults.[2] In pediatric patients, however, an epicardial approach is still uncommon and endocardial ablation is often initially attempted. Further, published data on RF ablation targeting children and adolescents with BrS and arrhythmic events are limited.

Here, we report a female child with BrS who demonstrated a novel *SCN5A* mutation and in whom a successful endocardial RF ablation was achieved for frequent occurrences of monomorphic ventricular tachycardia (VT).

KEY TEACHING POINTS

- *SCN5A* mutations are related to various conditions such as Brugada syndrome, long QT syndrome, atrial and ventricular tachycardias, sick sinus syndrome, progressive cardiac conduction defect, and cardiomyopathy, as in this patient.
- Symptomatic Brugada syndrome at a young age is rare but may be accompanied by a progressive conduction disturbance and life-threatening ventricular tachycardias.
- Radiofrequency ablation targeting a reentrant circuit and/or the endocardial substrate may become a feasible option for treating drug-resistant ventricular tachycardia in children with Brugada syndrome.

Case report

A 9-year-old girl (height 126.8 cm, weight 23.3 kg, and body surface area 0.9 m^2) was referred to our hospital to control recurrent appropriate and inappropriate implantable cardioverter-defibrillator (ICD) shocks due to atrial tachycardia (AT) and VT. Her parents called for an ambulance when she was 2 years old for convulsions associated with a fever. While she was being transported, an electrocardiogram monitor documented a sustained monomorphic VT (300 beats/min [bpm]), which was terminated by an automated external defibrillator (Figure 1A). She was then admitted to the hospital. Episodes of AT were recorded during the admission (Figure 1B), and she was transferred to another hospital to control the ATs. ATs from 5 foci of the right and left atria were successfully treated by RF ablation. Her father lost consciousness owing to ventricular fibrillation when he was explaining the daughter's condition and was diagnosed with BrS. She was also diagnosed with BrS based on a positive pilsicainide provocation test (Figure 1E). They were proven to have a novel *SCN5A* mutation causing a splicing error at exon 13 (c.IVS13-1 g/c). She was implanted with a retrosternal ICD lead and epicardial ventricular leads 1 month later. At the age of 3, she had a recurrence of AT episodes and 30 mg per day of bepridil was started; however, the ATs and VTs were not controlled, so RF ablation of the ATs was performed when she was 5 years old. Owing to several appropriate ICD shocks for VTs documented despite increasing the dose of bepridil up to 50 mg per day, she was referred to our hospital for a third session of RF ablation.

KEYWORDS Brugada syndrome; Children; Endocardial ablation; Monomorphic ventricular tachycardia; Pediatrics; Progressive cardiac conduction defect; *SCN5A* mutation

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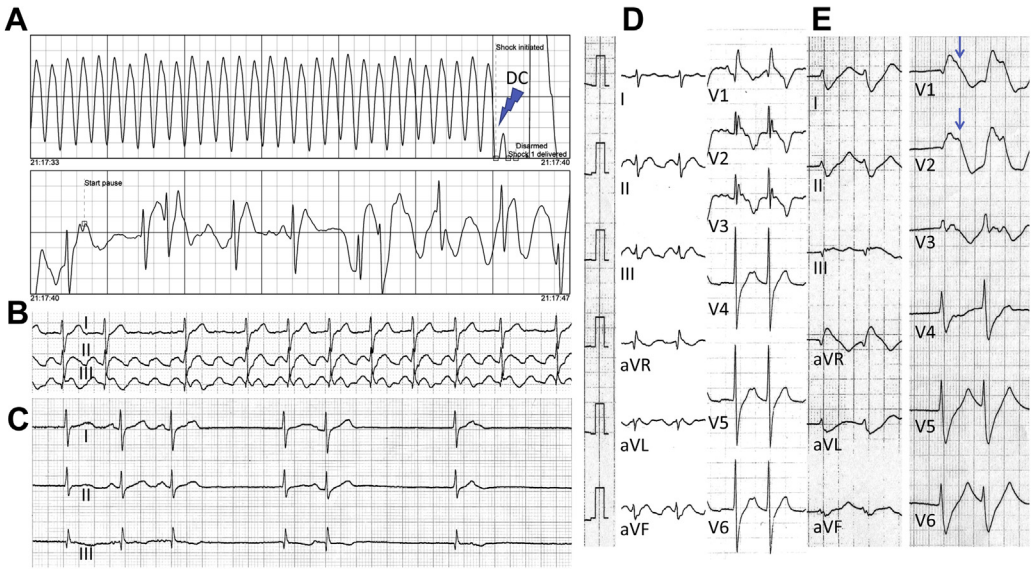

Figure 1 Series of electrocardiograms from the first admission when the patient was 2 years old. **A:** Automated external defibrillator monitor. Monomorphic ventricular tachycardia during the first onset in this patient successfully terminated by a direct current (DC) shock. **B:** Atrial tachycardia after admission. **C:** Atrial standstill after termination of the atrial tachycardia. **D:** Electrocardiogram on admission. **E:** Pilsicainide provocation test. After a pilsicainide injection, a marked ST-segment elevation in the right precordial leads was noted.

Electrophysiological study findings and details of RF ablation

The bepridil was discontinued 3 days prior to the ablation. All the procedures were performed under general anesthesia with dexmedetomidine hydrochloride, propofol, and fentanyl by an anesthesiologist. Her basic rhythm was junctional rhythm without any atrial beats with a heart rate under 40 bpm. The back-up ventricular pacing rate of the ICD was set up at 60 bpm before the electrophysiological study. Pacing from the proximal and distal coronary sinus did not capture the atrium, and we concluded that she had atrial standstill. Burst pacing from the right ventricular (RV) apex provoked nonsustained polymorphic VT, which terminated spontaneously. The configuration of the VT changed from a right bundle branch block pattern with an inferior axis to a left bundle branch block pattern with a superior axis. A voltage map of the RV endocardium was obtained by the Rhythmia Mapping System (Boston Scientific, Washington, DC) using an Orion catheter (Boston Scientific, Washington, DC). A low voltage area on the RVOT anterior wall and fragmented late potentials in the same area were acquired (Figure 2B). After a small dose of pilsicainide (13.2 mg) was slowly administered, VT1 (tachycardia cycle length [TCL]: 427 ms) was induced (Figure 2A). Because the QRS duration widened, isoproterenol was administered and VT1 changed to VT2 (TCL: 472 ms) (both of them had RVOT origins; see Figure 2A). A propagation map of VT2 suggested 2 types of reentry existed concurrently, which were a spiral wave reentry in the center of the RVOT and a counter-clockwise macroreentry around the RVOT (Figure 3A and Supplemental Video). We performed a linear ablation from the pulmonary valve annulus to the central core of the spiral wave reentry. Furthermore, substrate modification of the RVOT anterior wall was performed from the endocardium, where a low voltage and late potentials were obtained. Subsequently, another VT (VT3, TCL: 307 ms) originating from the RV inferior wall was induced by RV burst pacing (Figure 2A). Because of a hemodynamic deterioration, it was terminated by a DC shock. A low voltage area from the left ventricular (LV) septum to the apex (Figure 3B and C) and reduced ventricular wall motion especially at the LV apex were observed. However, pace mapping from the LV did not resemble VT3 at all. Since there was no low voltage area in the RV endocardium other than in the RVOT, pace mapping from the RV endocardium did not resemble VT3, and access to the epicardium could be limited by the epicardial ventricular leads, we suspected the epicardial VT was from the crux. The pace map from the middle cardiac vein was almost identical to VT3 and activation mapping during VT3 illustrated that the area was the earliest ventricular activation site. After several ablation applications in the middle cardiac vein and coronary sinus ostium, no further VT was induced.

As shown in Figure 3B and C, a wide area of the LV demonstrated a low voltage, which might have suggested the development of some kind of cardiomyopathy caused by the *SCN5A* mutation. A coronary angiogram revealed a torturous left anterior descending artery (Figure 3D), but there were no stenotic lesions in the left and right coronary arteries (Figure 3D and E), indicating that ischemic heart disease was not an etiology of her condition.

Discussion

There were some unique findings in this patient. First, she presented with typical symptoms of BrS despite her young age, such as atrial standstill, AT, and VT from multiple foci.

According to a recent large cohort targeting BrS patients under 20 years old,[3] there were marked differences in the symptoms between the pediatric group (under 12 years old)

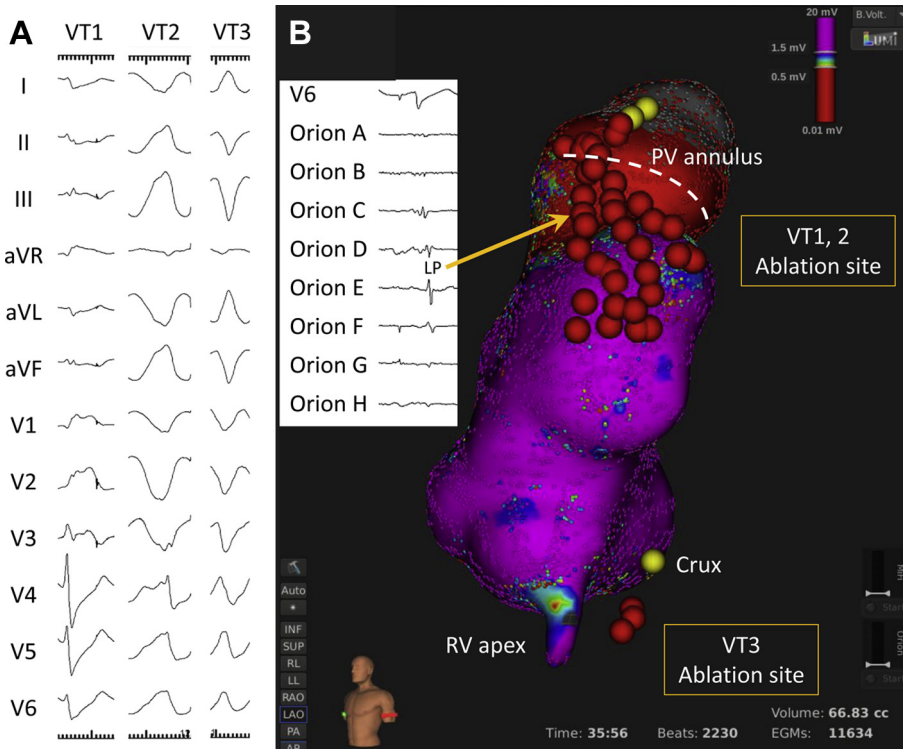

Figure 2 Induced ventricular tachycardias (VT) and voltage map of the right ventricular outflow tract (RVOT) and left ventricle. **A:** Induced VT1, VT2, and VT3. **B:** A voltage map of the RVOT (left anterior oblique [LAO] view). The late potentials in the RVOT and the ablation site are shown. A low voltage area with an amplitude below 0.5 mV is shown in the red area. Note the area is restricted to the RVOT area. See the text for further discussion. LP = late potential; PV = pulmonary valve.

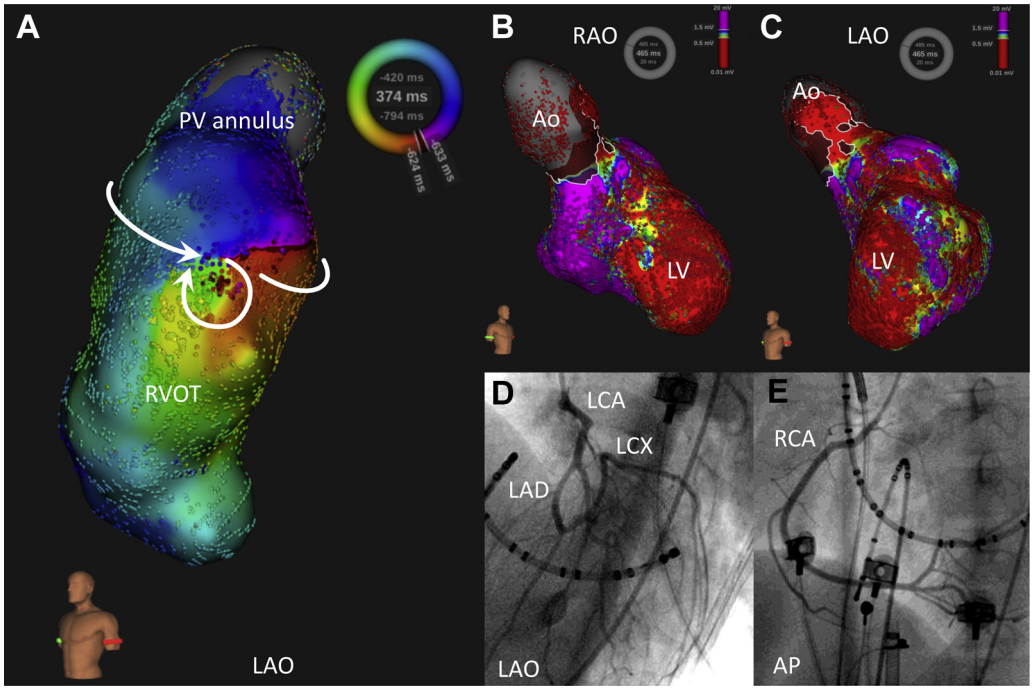

Figure 3 **A:** A propagation map of ventricular tachycardia (VT) 2. A reentrant circuit within the right ventricular outflow tract (RVOT) endocardium is shown. The slow conducting zone is located on the RVOT anterior wall. **B:** A voltage map of the left ventricle (LV), right anterior oblique (RAO) view. **C:** A voltage map of the LV, left anterior oblique (LAO) view. A low voltage area with an amplitude below 0.5 mV is shown in red. A wide area including the septum and apex of the LV demonstrated a low voltage area. **D:** Left coronary angiogram. The left coronary angiogram revealed a torturous left anterior descending artery, and the left circumflex artery diverged from the distal part of the torturous left anterior descending artery. **E:** Right coronary angiogram. The right coronary artery is normal. Ao = aorta; AP = anteroposterior view; LAD = left anterior descending artery; LCA = left coronary artery; LCX = left circumflex artery; PV = pulmonary valve; RCA = right coronary artery.

and adolescent group (13 to 20 years old). In the pediatric group, the mean age of the onset was 3 years and they were characterized by a greater prevalence of females (42%) and a high morbidity from a fever (52%) during arrhythmic events. On the other hand, in the adolescent group, the mean age of onset was 18 years, and its features were less prevalent in females (13%), and they had a lesser occurrence of a fever (6.5%) during the arrhythmic events, which seems to be analogous to that of the adult BrS group. The authors added that those patients with *SCN5A* mutations and a young age were at high risk of a progressive conduction delay and recurrence of ventricular tachyarrhythmic events.

This finding was reinforced by another recent report of a large pediatric cohort of *SCN5A* genotype–positive patients under the age of 16,[4] stating that cardiac conduction disorders are the most prevalent phenotype. According to the report, 55.7% of patients were symptomatic. The details of the phenotypes were isolated progressive cardiac conduction defects (25.6%), isolated LQT3 (10.6%), isolated BrS (1.8%), isolated sick sinus syndrome (1.4%), and an overlap of any of them (15.6%). Symptomatic individuals and LQT3 patients, especially under 1 year old at the time of the diagnosis in probands, have the worst prognosis. Mostly, these symptomatic patients need an ICD implantation, as we performed in our case.[5]

Moreover, as we observed in this case, some patients had a sign of a potential cardiomyopathy caused by the *SCN5A* as well. Wilde and colleagues[6] illustrated the mechanistic link between *SCN5A* mutations and dilated cardiomyopathy. They implied that the disruption of the normal depolarization or cytoskeleton caused by functional and mechanical degeneration of NaV 1.5 can be a trigger of developing cardiomyopathy.

Interestingly, her father, who had the same mutation causing a splicing dysregulation of *SCN5A*, did not have any symptoms other than syncope. The relatively benign clinical course might be explained by a variation in the single nucleotide polymorphism between individuals[7] or post-transcriptional gene modifications.[8]

Secondly, unlike the previous reports,[2,9] we could record a low voltage area and fragmented late potentials on the RVOT endocardium, and an ablation of this area achieved further noninductivity of the VT from the RVOT origin. One possibility is that a relatively thin cardiac wall enabled us to record the epicardium potentials from the endocardium. However, as illustrated in another report,[10,11] we were confident that the substrate was located in the endocardium as well, because propagation mapping of the endocardium fulfilled the entire cycle length of the monomorphic VT, and RF ablation targeting the slow conduction zone in the endocardium terminated the reentrant VT. Although there was no information about the RVOT epicardium in this patient, we concluded that the observed reentry circuit in the endocardium was not a bystander, and the substrate in the endocardium was crucial for sustaining VT2.

A monomorphic VT in BrS patients is a rare symptom. According to a retrospective observational study,[12] 4.2% of patients with BrS with an ICD presented with monomorphic VT, which is mostly from the RVOT, but is also from the LV and bundle branch reentry. Of note, many of them are successfully eliminated by endocardial ablation.

In this case, the first 2 VTs (VT1 and VT2) were reentrant VTs around the RVOT. VT1 was induced during a slow pilsicainide injection and a change in the reentry circuit (from VT1 to VT2) was observed during an isoproterenol administration. This phenomenon suggested that the conducting properties of the RVOT were changed dynamically by the Na channel blockade. Although we could not record the epicardial electrocardiograms, the thickness of the RVOT in this age of children is less than 5 mm, and therefore it may be possible that a transmural lesion may have been created in this patient.

Interestingly, the last VT (VT3) was a focal VT originating from the epicardium of the RV inferior wall. Because of the scarce information on the epicardium, we could not determine the entire mechanism of the VTs; however, one could speculate that she had multiple substrates both in the endocardium and in the epicardium, and there was a possibility that a vast majority of her myocardium was potentially degenerated by the *SCN5A* mutation.

Conclusion

Symptomatic BrS at a young age is rare, but it often is accompanied by a conduction delay and results in a poor prognosis. When young patients with BrS develop drug-resistant VT, RF ablation targeting the reentrant circuit and substrate modification of the RVOT endocardium may become a safe and feasible option.

Appendix

Supplementary data

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.hrcr.2020.06.011.

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