Concomitant Brugada syndrome substrate ablation and epicardial abdominal cardioverter-defibrillator implantation in a child

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Introduction

Brugada syndrome (BrS) is a primary electrical disease of autosomal dominant inheritance, characterized by coved-type ST-segment elevation in the right precordial leads and increased risk of sudden cardiac death.[1] Although the initial description included 3 children in a series of 8 patients,[2] the prevalence of BrS in pediatric populations was extremely low (0.0098%) in subsequent studies compared to adults in the fourth or fifth decade of life (range 0.14%–0.7%).[3] We report the case of a 3-year-old boy with highly symptomatic BrS, focusing on the feasibility and safety of combined epicardial substrate ablation of the right ventricular outflow tract (RVOT) and implantation of an epicardial implantable cardioverter-defibrillator (ICD).

Case report

A 3-year-old boy (height 103 cm, weight 14 kg, body surface area 0.63 m^2) presented for the first time at the emergency department of another center with dyspnea, diaphoresis, and cyanosis. Electrocardiography (ECG) showed a sustained monomorphic ventricular tachycardia (MVT) at 250 bpm (Figure 1A). The tachycardia was successfully cardioverted to sinus rhythm with a 50-J direct current shock after failure of intravenous procainamide. Cardiac magnetic resonance imaging ruled out myocardial structural disease and coronary arteries anomalies. The patient was treated with intravenous amiodarone (at a loading dose) and later discharged on oral maintenance dose of 25 mg/Kg. Three months after the initial presentation, the patient was readmitted to the emergency department with a feverish upper respiratory system infection, and ECG showed fast MVT with markedly broader QRS complexes. The sustained fast ventricular tachycardia (VT) degenerated into ventricular fibrillation (VF), and an external direct current shock was immediately delivered to restore sinus rhythm. The diagnosis of BrS was established at that time, based on type 1 Brugada pattern on the 12-lead ECG record post shock (Figure 1B). A proarrhythmic effect of amiodarone was considered, so amiodarone was replaced by quinidine, which was gradually titrated from 2 mg/kg to 20 mg/kg over a 7-day period. The patient was referred to our center in Brussels for further investigation because medical treatment with quinidine failed to prevent VT recurrences. Given this electrical instability, an epicardial substrate RVOT ablation was performed via a left thoracoscopic approach as previously reported.[4] Because of the small size of the child's thorax and the presence of 3 ports on the left hemithorax used for thoracoscopic access, surface ECG leads V_4 through V_6 could not be placed during the procedure; therefore, a complete 12-lead ECG could not be obtained not available in the perioperative setting. Before the ablation was started, neither VT nor VF could be induced. The programmed electrical stimulation protocol that we adopted, previously reported by Brugada et al,[5] consists of 3 basic pacing cycles of 8 beats (at 600, 500, and 400 ms [S1]) with 1–3 ventricular extrastimuli (S2–S4), from a single site of stimulation in the right ventricular apex. The minimum coupling interval of S2–S4 was set to 200 ms. The target area

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KEY TEACHING POINTS

- Symptomatic Brugada syndrome (BrS) occurring during a young age is a rare but malignant condition related to a very high risk of future arrhythmic events and sudden cardiac death.
- Concomitant epicardial right ventricular outflow tract ablation and implantable cardioverter-defibrillator implantation with epicardial leads can be a safe, feasible, and effective approach for symptomatic BrS patients.
- This novel combined procedure seemed to be safe, feasible, and effective in a 3-year old child.

was identified with the patient under ajmaline infusion, as described by Nademanee et al,[6] using a decapolar catheter (ViaCath NG 10, standard [curve D], Biotronik, Berlin, Germany) connected to an EnSite Cardiac Mapping System (St. Jude Medical, Minneapolis, MN), and a voltage map was obtained. At 0.5 mg/kg ajmaline dose, fractionated, low-voltage, and delayed potentials appeared on the anterior wall of the RVOT (Figure 2A). Ablation of the entire region was performed using a bipolar unidirectional radiofrequency linear device (Coolrail, AtriCure Inc, West Chester, OH) until all substrate abnormal low-voltage fractionated signals had been eliminated (Figure 2B and Supplemental Video 1). The right bundle branch block morphology of the clinical VT on the surface 12-lead ECG (Figure 1A) could have suggested a different origin site rather than the RVOT.[7] However, the epicardial voltage map showed a unique area of low and

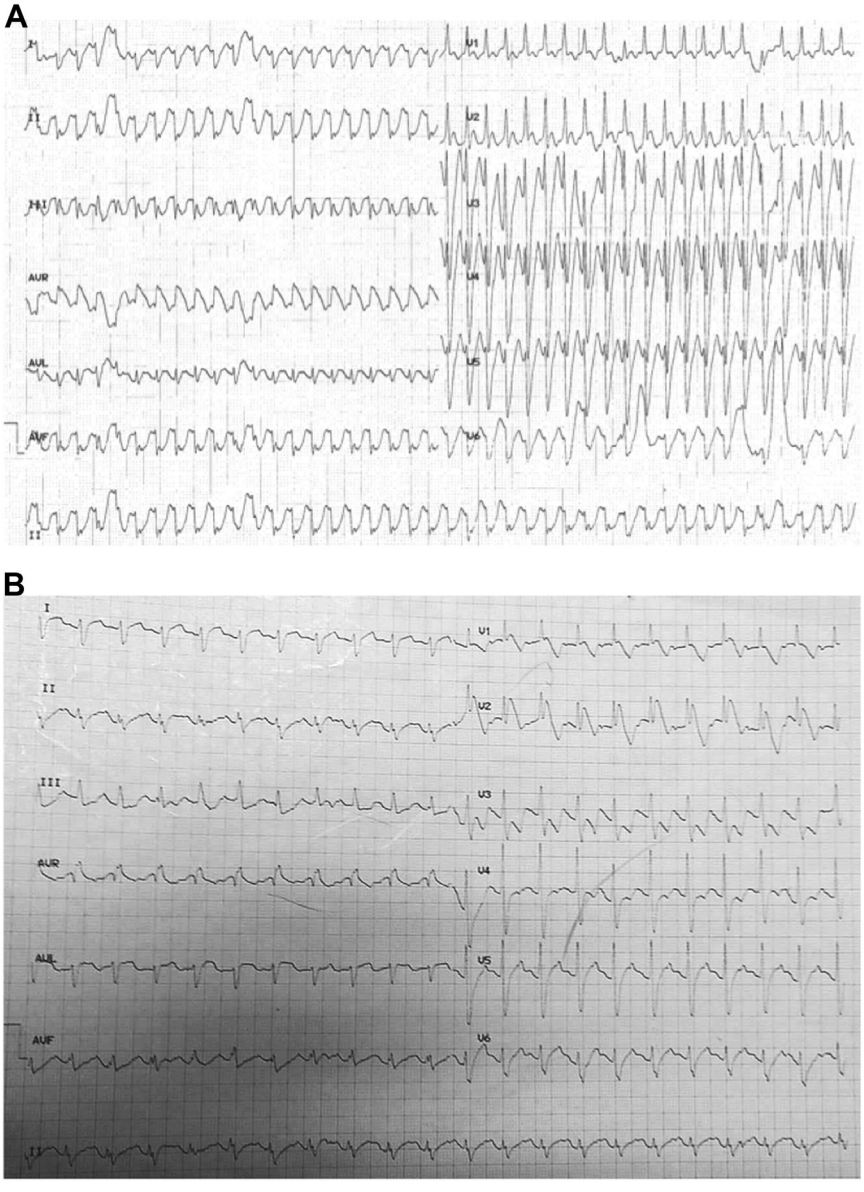

Figure 1 **A:** Twelve-lead electrocardiogram shows a ventricular tachycardia at 250 bpm. **B:** Twelve-lead ECG shows type 1 Brugada pattern evident in lead V_2 after direct current shock.

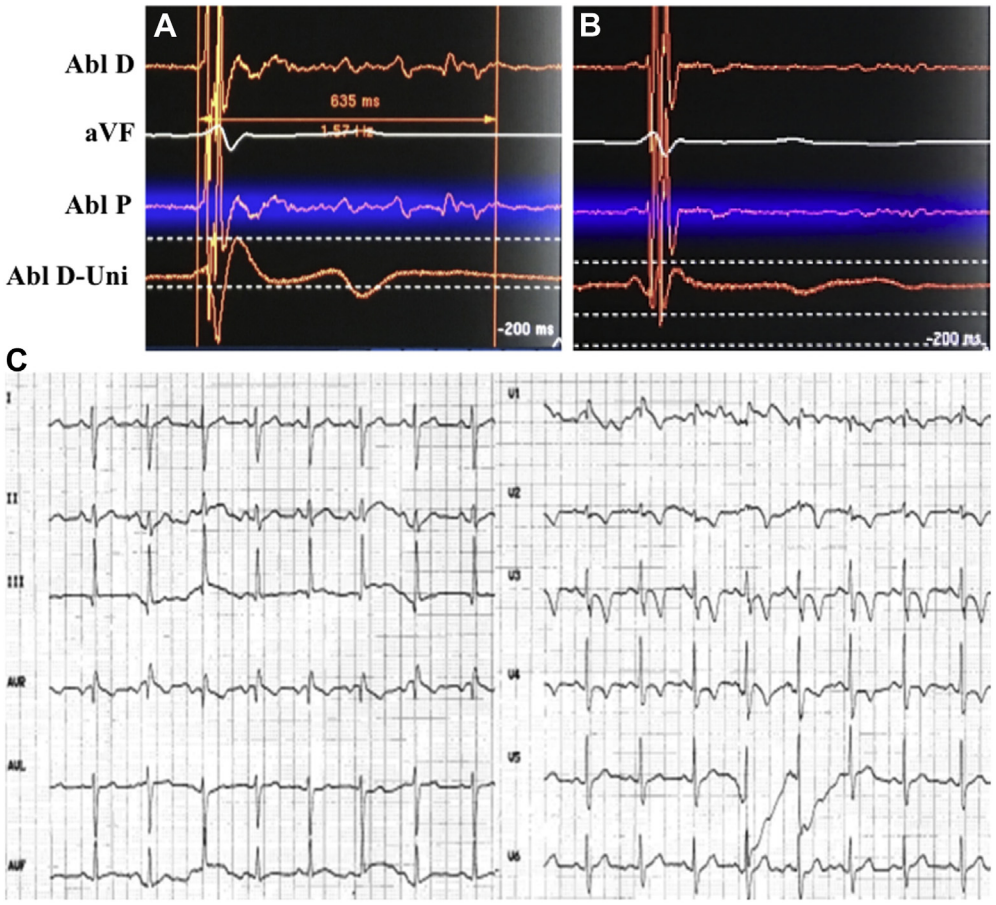

Figure 2 **A:** Abnormal prolonged low-voltage fractionated electrogram (EGM) recorded from the anterior wall of right ventricular outflow tract epicardium before ablation. **B:** EGM recorded from the same site after ablation shows disappearance of the mid and late components of the fractionated potentials recorded before ablation. **C:** Twelve-lead electrocardiogram recorded during ajmaline challenge (1 mg/kg) after ablation was performed is negative for Brugada pattern. Abl D = bipolar ablation distal; Abl D-Uni = unipolar ablation distal; Abl P = bipolar ablation proximal.

fragmented voltages on the anterior wall of the RVOT, whereas the remaining myocardial tissue was found to be normal. Moreover, QRS vector and morphology in a 3-year-old child might not follow the same criteria as those of an adult because pediatric thorax surface and heart size and axis are smaller and completely different. Because of this, we targeted our ablation specifically on the abnormal substrate area detected with the electroanatomic/voltage map. Immediately after ablation, we proceeded with ICD implantation with epicardial leads via a subxiphoid access. A double shock coil lead was positioned on the atrium through the sinus transversus of the pericardium, and a pace-sense bipolar lead was positioned on the right ventricle as previously described.[8] Both were connected to an abdominal generator (Figure 3). After the epicardial RVOT ablation, programmed electrical stimulation and ajmaline challenge (1.0 mg/kg administered over a period of 5 minutes) were repeated, and both were negative for VT/VF induction and ECG Brugada pattern, respectively (Figure 2C). No complications related to the procedure occurred. The patient was discharged after 5 days on sotalol 3 mg/kg/d, which was maintained for 3 months after the ablation and then discontinued. The patient was followed with a remote monitoring system. Two months after ablation, the patient experienced fever with multiple VT episodes, with a heart rate that was slower than the naïve one. The episodes were treated with appropriate ICD therapies. This recurrence of VTs probably can be attributed to scar homogenization during the healing process of the surrounding vital intramyocardial tissue, which may have provided the substrate for a transient slower reentrant circuit after radiofrequency ablation. No other VTs subsequently occurred, and the Brugada ECG pattern was not observed during 1-year follow up, not when the patient experienced fever. Family screening revealed the mother was affected by BrS (i.e., positive ajmaline test) but thus far she has been asymptomatic. Based on genetic analysis, the boy was heterozygous for the following SCN5A gene mutation: cDNA mutation NM_198056(SCN5A):c.903G>A; protein-level amino acid sequences mutation: p.Trp301*.[9]

Discussion

Here we report the case of a 3-year-old boy with BrS, SCN5A gene mutation, and recurrent MVTs. To the best of our knowledge, this is the first case of a symptomatic drug-refractory BrS patient treated with concomitant epicardial RVOT ablation and ICD implantation with epicardial leads and the first time this procedure was performed in a child.

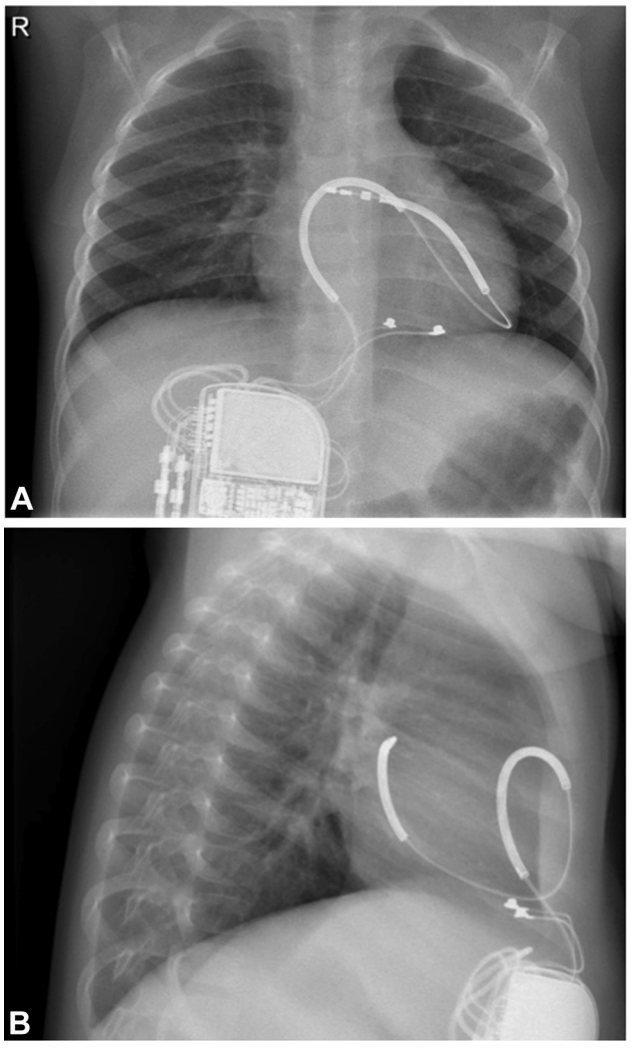

Figure 3 **A:** Radiograph of the thorax in the anteroposterior view shows the positions of the epicardial leads and the abdominal implantable cardioverter-defibrillator. **B:** Radiograph of the thorax in the lateral view better shows the position of the distal coil in the transverse sinus of the pericardium.

We aimed to outline the safety, feasibility, and effectiveness of this combined approach at mid-term follow-up. The diagnosis of BrS is extremely rare in pediatric populations, with a low penetrance rate (<20%) even in known SCN5A mutation carriers.[3] Despite its rarity, symptomatic BrS during a young age is a malignant condition related to a very high risk of future arrhythmic events and sudden cardiac death.[10] Any episode of VT occurring in a pediatric patient should be highly suspicious for BrS and the syndrome systematically considered in the differential diagnosis. MVT triggered by fever in infants with SCN5A mutations has already been reported in the literature[7]; however, the current literature has not provided sufficient information to determine an association between MVT and the SCN5A mutation because of the rarity and inconsistency of the available data.[7] The incidence of MVT described in a large cohort of patients with BrS implanted with an ICD was 4.2%.[7] The efficacy of ICDs in preventing sudden cardiac death is well established for patients with symptomatic BrS.[1,11] However ICD-related complications, such as endocardial lead fractures or dislodgments and device infections, occur more frequently in the pediatric population than in the adult population.[3] For our pediatric patient, we chose to implant epicardial ICD leads using a minimally invasive approach that has shown to be feasible and may be safer than an transvenous approach.[8] The lead insertion technique and the final lead positions need to accommodate the child's growth in order to keep the device functional as long as possible. Implantation of epicardial leads, which avoids the tricky passage below the clavicle through the subclavian vein, seems to be better for children and young men because a wider range of movements and physical activities are allowed, and the risk of fractures and dislodgments may be reduced.[8] Consensus that the epicardial RVOT is the arrhythmogenic substrate for BrS was reported in the last 10 years.[4] The anterior wall of the RVOT epicardium in symptomatic BrS patients was found to be characterized by low-voltage, prolonged, and fractionated potentials.[4,6,12–14] In particular, Nademanee et al[6] reported the importance of sodium channel blocker infusion during the procedure in order to identify the entire epicardial area involved and ablate it completely. Radiofrequency epicardial ablation of these clustered potentials could normalize the type 1 Brugada ECG pattern and make VT/VF noninducible.[4,6,13] RVOT substrate ablation had never previously been performed in a child. Today, this procedure is indicated as a last possible therapeutic treatment to manage symptomatic BrS patients with recurrent ventricular arrhythmias refractory to medical treatment. It seems to be a safe and feasible procedure, effective during short-term follow-up in restoring electrical stability and improving quality of life. However, the therapeutic impact of epicardial RVOT substrate ablation during the entire natural course of BrS is not known yet because long-term data are not available, and even less is known about the syndrome in the pediatric population. This first pediatric case shows the feasibility of the combined approach of epicardial RVOT ablation and ICD implantation with epicardial leads in a 3-year-old child and the persistence of good clinical outcome 1 year after the procedure. However, data regarding the overall effect during the patient's lifetime are not available, and in particular nothing is known about the possible different long-term results between children and adults.

Conclusion

Combined substrate epicardial ablation of RVOT and ICD implantation with epicardial leads seems to be a safe, feasible, and effective procedure in a 3-year-old child with symptomatic BrS.

Appendix

Supplementary data

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.hrcr.2017.12.004.

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