Substrate modification via epicardial ablation in a patient with long QT syndrome type II

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Introduction

The treatment of patients with congenital long QT syndrome (LQTS) is based on several therapeutic pillars. Conservative measures such as avoidance of hypokalemia and triggers depending on the underlying subtype, as well as medical therapy with beta-blockers and genotype-specific therapies, are usually powerful to avoid malignant ventricular arrhythmias (VA). Furthermore, implantable cardioverter-defibrillator (ICD) implantation can prevent sudden cardiac death in patients with a high risk for VA after an individual risk assessment or after malignant arrhythmias. Bailout strategies such as left cardiac sympathetic denervation have been studied and recommended for patients who are still symptomatic under beta-blocker therapy or when an ICD is declined or contraindicated.[1]

Pappone and colleagues[2] described distinct electrophysiological changes of epicardial signals in a case series of 11 patients with LQTS undergoing an electrophysiological study (EPS) and consecutive successful epicardial catheter ablation of pathologic signals.

We report a case of a patient with LQTS undergoing epicardial ablation after multiple ICD shocks for torsades de pointes (TdP) tachycardia and ventricular fibrillation.

KEY TEACHING POINTS

- Primary electrical diseases may have an underlying substrate that is not visible in conventional imaging, such as cardiac magnetic resonance imaging, but rather is seen in an electrophysiological study displaying abnormal local voltage and signals.
- Epicardial mapping and consecutive catheter ablation may be a future bailout strategy in patients with long QT syndrome and frequent arrhythmia events refractory to guideline-directed therapy.
- All conventional therapies and measures, such as trigger avoidance and beta-blockers, should be continued after catheter ablation.
- A careful assessment of whether guideline-directed therapies are maxed out and informed consent about new therapies are necessary before offering epicardial ablations to patients with long QT syndrome.

Case report

We report a case of a 27-year old female patient with diagnosed LQTS type II. Starting at the age of 8 years, she presented to the pediatric emergency department on a regular basis owing to seizures and syncopes of unknown origin, finally leading to her LQTS diagnosis with an initial QTc duration of 530 ms at a heart rate of 60/min. Genetic testing confirmed LQTS type II (*KCNH2* mutation), with several female family members on the maternal side also being affected by LQTS. There were no other mutations or other features identified that could suggest an overlap syndrome. The patient did not have any other comorbidities. All echocardiographic parameters were reported to be normal.

Nevertheless, the patient was treated with propranolol in an initial dose of 2 mg per kg daily. She showed a persistent prolonged QTc duration of 500–560ms but no malignant VA in initially repeatedly carried out 24-hour electrocardiograms (ECGs). Moreover, she was free of syncopes and symptoms for several years under this therapy. At the age of 14 years, syncopes recurred. One year later, she was admitted to the pediatric ward for a further check-up after another episode.

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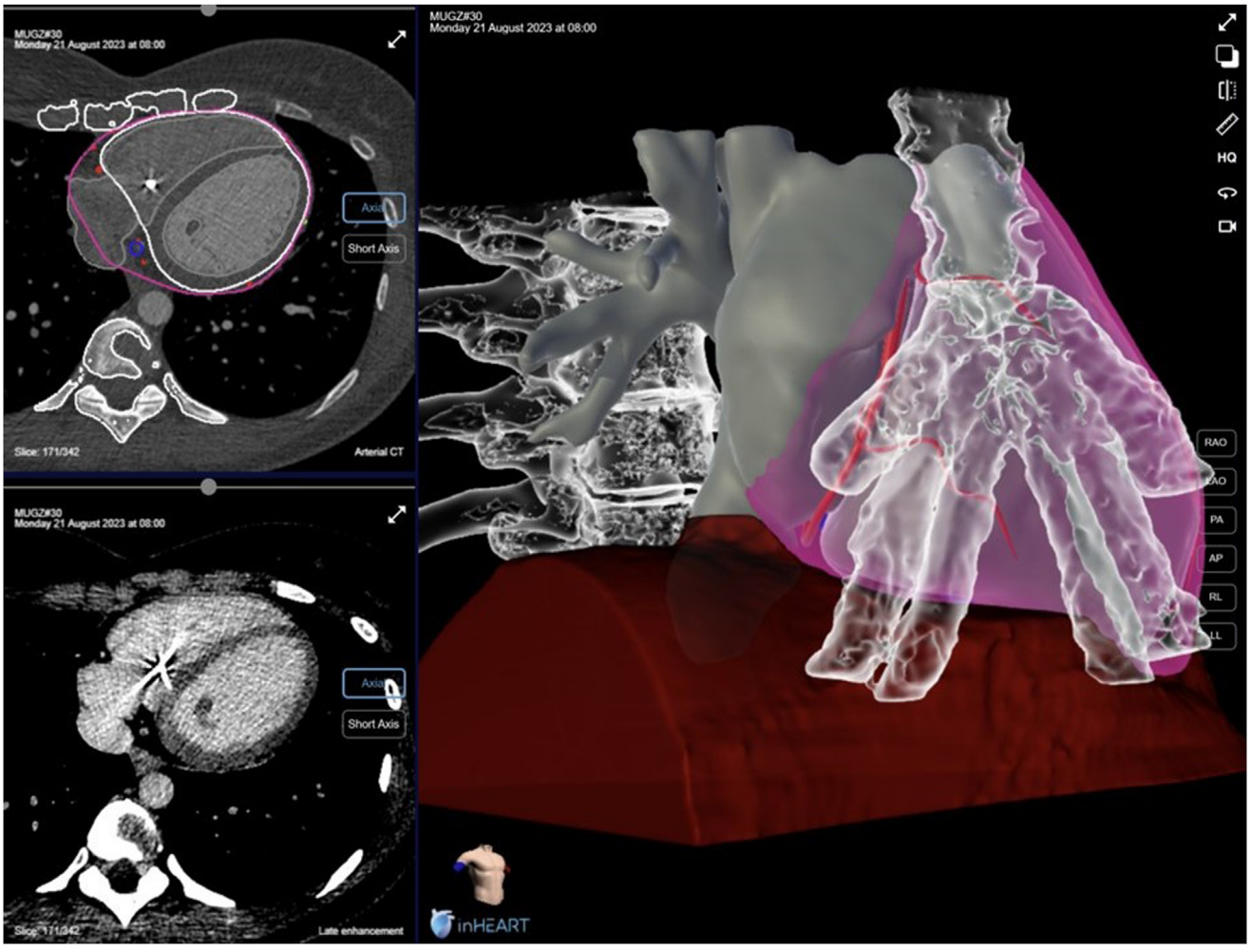

Figure 1 InHEART (Pessac, France) reconstruction of the patient's cardiac computed tomography.

ECG monitoring revealed short episodes of TdP tachycardia, which led to implantation of a single-lead ICD in 2011 at the age of 15. During the following years, she experienced multiple ICD shocks for TdP tachycardia while still on beta-blockers and under potassium as well as magnesium supplementation, and 2 ICD box changes (2016 and 2021). Her potassium levels ranged between 3.7 and 4.0 mmol/L (reference range 3.5–5.0 mmol/L) while she was mainly under control by her general practitioner.

At the age of 27, she was in regular routine check-ups at our ICD outpatient clinic and presented with remote alarms for ICD discharges owing to frequent TdP tachycardia (21 shocks since the last box change in 2021), with all of them clinically resulting in syncope (Supplemental Figure 1).

In July 2023, another ICD shock appeared as a remote alarm. In this specific case all established therapies like trigger avoidance and beta-blockers (apart from nadolol, which is not available in Austria) did not prove to reduce her arrhythmia burden and shock rate, and more established bailout strategies like left cardiac sympathetic denervation were clearly declined by the patient. An upgrade to a 2-chamber device was not considered useful, as episodes were not associated with bradycardia or pause-dependent (Supplemental Figure 2a and 2b). Furthermore, she expressed that she plans to have children in the near future. As LQTS type II is reported to have an increased arrhythmia burden in the peripartum and postpartum period,[3] epicardial ablation was offered before a potentially planned pregnancy. After an extensive and long discussion about all options, her planned pregnancy, and potential bail-out-strategies, she decided to undergo epicardial ablation, fully aware that the data on this option are scarce.

Prior to the procedure, cardiac computed tomography (CT) including late iodine enhancement, a transthoracic echocardiography, a laboratory examination, and a 12-lead ECG were performed. All tests were unremarkable; the QTc duration was known to be extensively prolonged to 590 ms (Supplemental Figure 3). In order to look for an overlap with another cardiac syndrome (Brugada syndrome, BrS) or disorder or another underlying pathology (infiltrative disease, arrhythmogenic right ventricular cardiomyopathy, etc) as alternative explanation for this presentation, all examinations were reviewed thoroughly and excluded the before-mentioned.

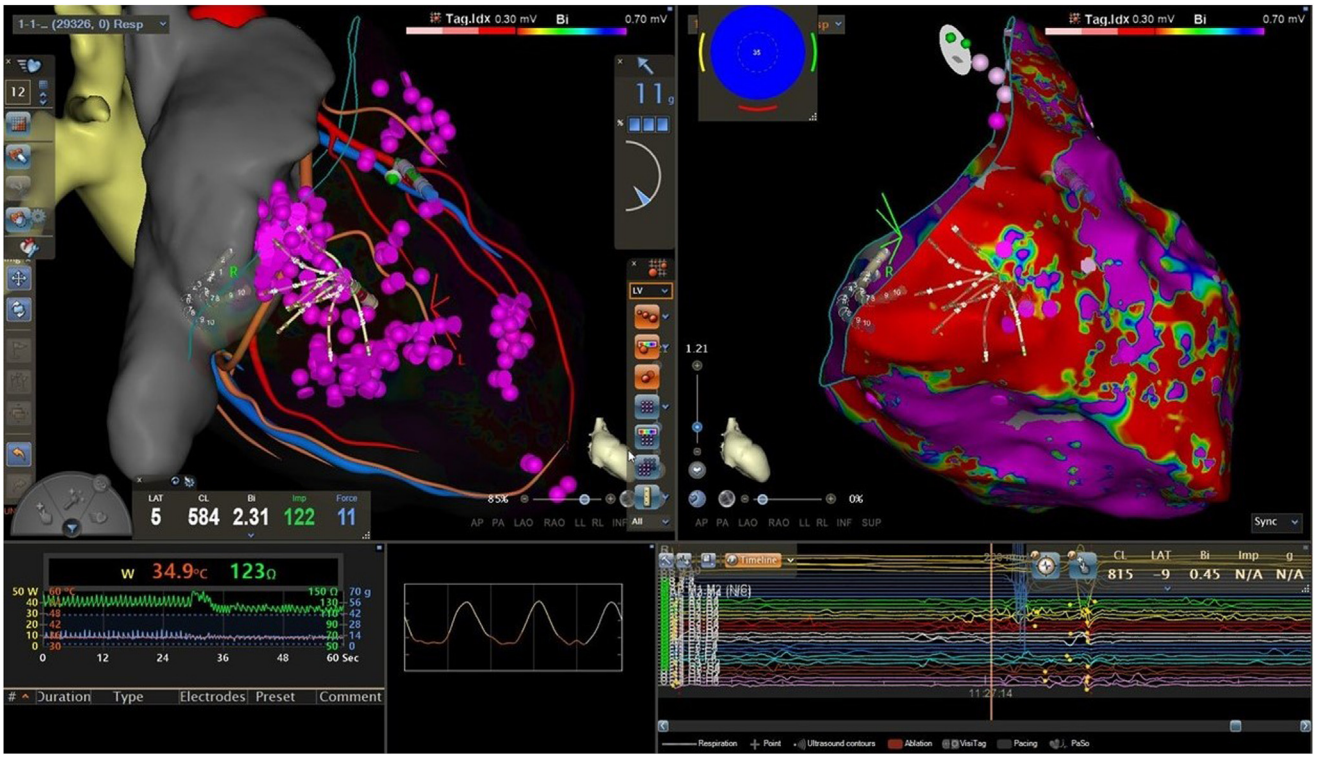

Figure 2 The epicardial 3D electroanatomical map showed extensive low-voltage areas at the apical as well as the inferobasal aspect reaching into the outflow tract of the right ventricle (pink is normal voltage, red is low voltage, pink location points indicate fractionated low potentials as seen in the right picture).

The cardiac CT did not show any abnormalities and was modeled with inHEART (Pessac, France) technology for usage in the mapping program (Figure 1).

The EPS was performed under processed electroencephalogram-guided general anesthesia with propofol and remifentanil and the patient was intubated. The epicardial access was achieved without complications under fluoroscopic guidance and a 3D electroanatomical map was done and aligned with the InHEART reconstructed CT. The 3D electroanatomical map showed extensive low-voltage areas at the right ventricular outflow tract (RVOT), especially if cut-offs were reduced from 0.5–1.0 mV to 0.3–0.7 mV. The most remarkable low-voltage areas were identified at the inferobasal aspect of the right ventricle (RV) extending to the RVOT and a small area at the apex of the RV. Few late potentials and several fragmented potentials were identified in the above-mentioned low-voltage areas. To identify potential targets the electrogram criteria (low amplitude <1 mV and duration of >80 ms with ≥ 3 deflection components; or distinct double potential, or delayed component extending beyond the end of the QRS complex) proposed by Pappone and colleagues[2] were applied.

In addition to a thorough alignment of the reconstructed CT, a coronary angiogram was performed to assess proximity of the planned lesions to coronary arteries. The voltage of the left ventricle as well as the voltage of the endocardial RV were unremarkable (Supplemental Figure 4).

After mapping in sinus rhythm under normal conditions, isoprenaline was administered to assess whether premature

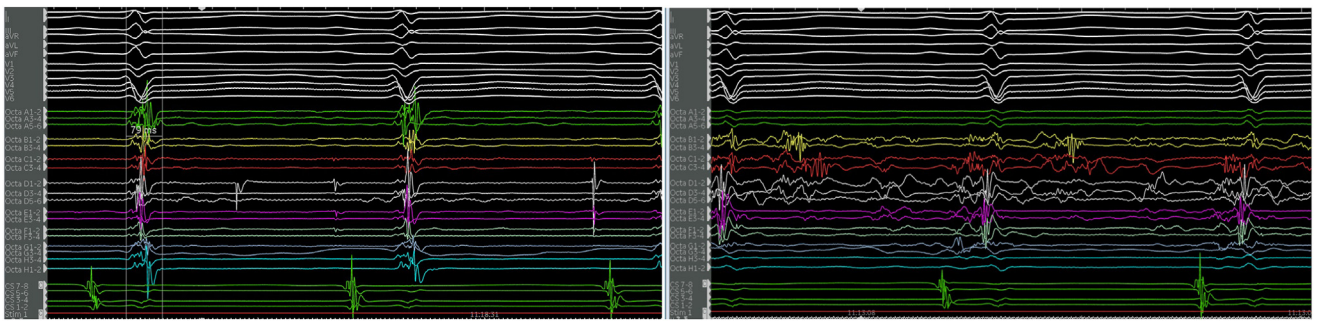

Figure 3 Low-voltage QRS fragmentation without provocation (left side) and under provocation with isoprenaline (right side): 12-lead surface electrocardiogram, white signals; a multipolar mapping catheter (OctaA1-2 to OctaH1-2) and a coronary sinus catheter (CS7,8-1,2) in bright green; recorded at a speed of 200 ms/s.

ventricular contractions could be triggered as possible ablation targets. The patient showed an adequate increase in heart rate without having any premature ventricular contractions. As an incidental finding, a massive fragmentation of the epicardial ventricular signals was seen in the previously identified low-voltage areas. The most conspicuous signals were noted in the basolateral aspect extending to mid lateral aspect and a smaller area at the RVOT (Figures 2 and 3).

Three areas of fragmented signals (low amplitude <1 mV and duration of >80 ms with ≥ 3 deflection components) at the basal and mid lateral segment of the RV as well as the RVOT were identified as potential targets during mapping (Supplemental Figure 5), while few late potentials were identified and no double potentials were seen in this case. After careful identification and consideration of all vulnerable structures and a reasonable size of the targeted area for ablation, ablation was performed epicardially using a steerable sheath (Agilis EPI; Abbott, Abbott Park, IL) and an irrigated ablation catheter (QDOT Micro; Biosense Webster, Irvine, CA) with radiofrequency applications at 30–40 W over 30–60 seconds. After a few ablation points the QTc duration showed a decrease from initial 600 ms to 460 ms (both were recorded at approximately 70 beats/min heart rate and under deep anesthesia) (Supplemental Figure 6).

As a specific endpoint of this procedure is not defined so far, the procedure was stopped after a remap did not reveal any further fragmented signals and after the acute QTc shortening. After having targeted all pathologic signals with ablation, a control coronary angiogram was performed and did not show any pathologic alterations. Programmed ventricular stimulation did not induce ventricular fibrillation either before or after the procedure. As standard of care, a pigtail catheter was placed in the epicardium and triamcinolone was administered. The patient was observed at the cardiac care unit for 1 night and could be discharged free of symptoms after 2 days. Regular follow-ups in our outpatient clinic as well as remotely were scheduled. In December 2023, the 3-month follow-up was scheduled and the patient was free of any symptoms and ICD shocks since the procedure. The follow-up ECG on the day after the ablation procedure, as well as all other 12-lead ECGs, showed a persistent prolonged QTc duration of around 550 ms. She currently takes propranolol on a low dose (10 mg twice daily), which she tolerates well.

Discussion

An EPS and ablation of pathologic epicardial signals in LQTS patients has not been mentioned in the current European Society of Cardiology guidelines.[1] LQTS patients having a high arrhythmia burden under guideline-directed therapy are rare; bailout strategies are scarce and come with a relevant rate of potential complications. This patient had a high arrhythmia burden, with an even higher burden to be expected during her planned pregnancy, as described in LQTS type II, which is why this strategy was exceptionally offered in a center with extensive expertise with catheter ablation.

This case report shows the course of this young but highly symptomatic patient and helps to identify open questions that need to be studied. One question that is of high interest is how to determine ablation targets and which signals are relevant for the long-term outcome. Furthermore, the long-term implications and long-term effect of ablation procedures in these patients have not been studied before. As a surrogate parameter for the ablation effect, the ECG showed a disappearance of the typical ST-segment elevation in BrS patients. Pappone and colleagues,[2] on the other hand, reported a persisting QTc shortening in 11 patients. In this case the QTc shortening was only a transient phenomenon, with no clear evidence for a causal relationship with the epicardial ablation, and could also be multifactorial (sedation, isoprenaline).

Nevertheless, an interesting finding is the location of the low-voltage areas that seem to be similar to BrS and to the locations described in the cohort of Pappone and colleagues.[2]

The electrophysiological changes seem strictly epicardial and focused on the RV and/or RVOT, with case reports suggesting potential overlaps of these 2 syndromes. Moreover, the identification of eligible patients will be a challenge until further data either confirm or reject the success of epicardial ablation in LQTS patients.

This bailout strategy will be reserved for highly symptomatic patients in expert centers until further data are available, and more patients have to be treated to understand the underlying mechanisms, to determine ablation strategies, and to see a long-term effect and long-term follow-ups.

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Appendix

Supplementary Data

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.hrcr.2024.05.015.

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