An unexpected finding by epicardial mapping: Atrial fibrillation in a 14-month-old patient with short QT syndrome

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Introduction

Short QT syndrome (SQTS) is a very rare channelopathy accompanied by familial clustering and sudden cardiac death.[1] It has an estimated prevalence ranging from 0.02% up to 2% in the adult population, but only 0.05% among pediatric patients.[2–6] To date, 9 mutations in 6 different genes have been identified, including *KCNH2*, *KCNQ1*, *KCNJ1*, *CACNA1C*, *CACNB2*, and *CACNA2D1*. In pediatric patients, SQTS is characterized by shortening of the corrected QT interval (QTcB <316 ms, J-Tpeak cB <181 ms, and the presence of early repolarization) on the surface electrocardiogram (ECG).[7] The underlying pathophysiological features involve shortening of myocardial repolarization due to potassium and calcium channelopathies, which creates at a very early age the electrical substrate for not only bradyarrhythmia but also atrial and ventricular tachyarrhythmia, including atrial fibrillation (AF).[2,8,9] This case report presents a 14-month-old female patient with SQTS scheduled for an epicardial pacemaker implantation indicated by bradyarrhythmia and chronotropic incompetence in which epicardial high-density mapping revealed an unexpected and unique finding.

KEY TEACHING POINTS

- Atrial fibrillation (AF) may occur in very young patients with short QT syndrome.
- AF in these patients can be sustained with an excessively high rate of the fibrillatory process (25 ms).
- In pediatric patients with arrhythmias undergoing cardiac surgery, epicardial mapping could be used as an additive diagnostic tool to guide therapy.

Case report

A 14-month-old female patient was hospitalized for elective epicardial pacemaker implantation for chronotropic incompetence. There was no family history of seizures, syncope, arrhythmias, or sudden unexplained deaths. The patient was born with a sinus bradycardia (72 beats/min [bpm], QTc 391 ms, as illustrated in Figure 1) and was therefore hospitalized. A 24-hour Holter recorded 2 days after birth revealed sinus rhythm with bradycardia (67–148 bpm), frequent ventricular ectopic beats, and a nodal escape rhythm. A heart rate increase to 100 bpm resulted in prolongation of the QTc to >400 ms. A 24-hour Holter was repeated after 1 month, revealing sinus node dysfunction with a ventricular escape rhythm.

After 4 months, there was an increase in left ventricular (LV) and left atrial dilation, LV hypertrophy, mitral regurgitation, and LV dysfunction in combination with an open ductus arteriosus. The ECG showed changes in T-wave morphology with a QTc of 330 ms (Figure 1). The open ductus arteriosus was successfully percutaneously closed in the following month. Thereafter, the patient remained in a ventricular escape rhythm (60–70 bpm), alternating with sinus rhythm (110 bpm). The next 24-hour Holter revealed sinus rhythm or ectopic atrial rhythms with frequent ventricular escape rhythm (57–93 bpm) and occasionally second-degree atrioventricular block type II. In the seventh month, genetic evaluation revealed a de novo pathogenic variant in the *KCNQ1* gene (Chr 11: NM_000218.2(KCNQ1):c.421G>A (p.Val141MET), class

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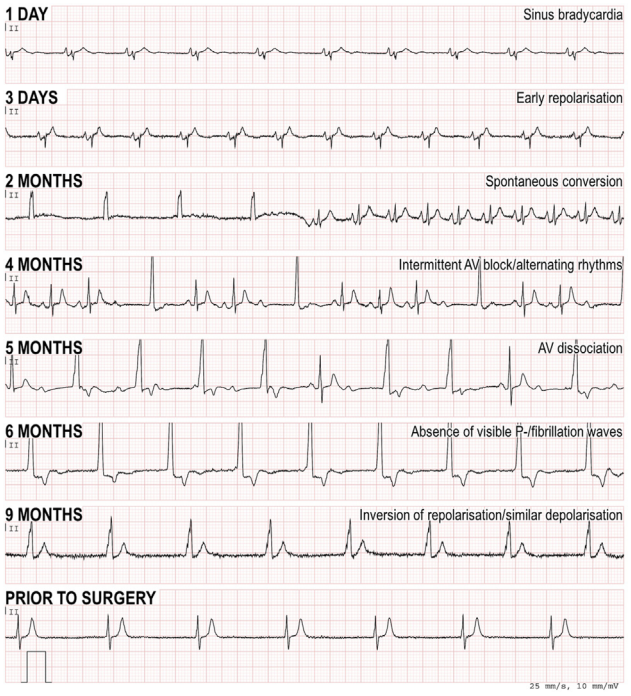

Figure 1 Lead II of surface electrocardiography (ECG) demonstrating various rhythms. At the first day after birth, the ECG demonstrates a sinus bradycardia. At day 3, early repolarization can be seen. At 2 months, ventricular escape rhythms without visible P wave spontaneously converted to sinus rhythm. After 4 months, there is a Mobitz type I atrioventricular (AV) block with ventricular escape. At the fifth month, there is predominantly AV dissociation. P waves or fibrillation waves are not visible at the sixth month. After 9 months, there is an inversion of repolarization, but without change in depolarization. Prior to surgery, there is a nodal rhythm without visible P waves or fibrillation waves.

V, heterozygous); variants in the KCNQ1 gene were not found in any family members after genetic testing. The ECG at this moment demonstrated a ventricular escape rhythm (60 bpm) with early repolarization and significant shortening of QTc (285 ms), and the patient was therefore diagnosed with SQTS.

From the seventh month, LV systolic and diastolic function further deteriorated with progressive LV dilatation, which was routinely measured on echocardiography. At the 12th month it was therefore decided to implant an epicardial DDD-pacemaker. At the age of 14 months, the patient underwent surgery. The preoperative ECG demonstrated a nodal rhythm (Figure 1). The patient participated in the FANTASIA study (MEC-2019-0543), in which epicardial high-density mapping of the atria was performed.[10] Immediately after mini-sternotomy, a 128-electrode array (0.28 mm^2, interelectrode distance 2.12 mm) was placed on the right atrium perpendicular to the caval veins and epicardial electrograms were recorded for 5 seconds. These electrograms, unexpectedly, revealed continuous AF with an average cycle length as short as 25 ms (Figure 2). Fibrillation waves could, however, not be identified on the surface ECG. The surgeon observed a mechanical standstill of the atria. Because of the presence of persistent AF and limited literature supporting cardioversion in young patients with SQTS and persistent AF,[9,11,12] electrical cardioversion was not performed. Consequently, only an epicardial VVI pacemaker was implanted. Postoperatively, anticoagulation therapy with aspirin was started.

Discussion

Atrial fibrillation in pediatric patients

Although AF is the most common cardiac arrhythmia among adults, it is an extremely rare entity in the pediatric population. The global prevalence of AF in the under-5-years age group is approximately 3 per 100,000.[13] The vast majority of AF cases in the youngest age groups in epidemiological studies are often associated with coexisting congenital heart disease or channelopathy. Owing to their rarity, there has been minimal investigation of atrial excitation and mechanisms of AF in the youngest patients. Epicardial mapping during pediatric cardiac surgery provides a unique opportunity to study atrial excitation at a high resolution in various congenital defects and channelopathies. Recently, epicardial mapping revealed that local conduction disorders are already present in pediatric patients (<1 year) with congenital heart disease.[14] In this case report, we now demonstrated that epicardial mapping also has a direct value for real-time diagnosis in daily clinical practice. If (epicardial) atrial electrograms during cardiac surgery had not been recorded using a dedicated mapping system, AF could not have been confirmed, and possibly not have been diagnosed for many years.[12]

Short QT syndrome and atrial fibrillation

Patients with SQTS often present with AF, even at a very young age. Several genetic mutations have been linked to SQTS, including the *KCNQ1* gene, which codes proteins that produce a membrane channel that conducts I_{Ks}. Mutations in the *KCNQ1* gene cause either gain or loss of function in the channel and its current. Loss-of-function variants typically cause long QT syndrome, but gain-of-function variants, with increased I_{Ks} current, have been associated with SQTS. However, the mechanisms underlying the increased atrial arrhythmogenesis and impaired cardiac pacemaker activity arising from increased I_{Ks} remain unclear. Computer modeling demonstrated that the Val141MET KCNQ1 mutation increased dispersion of action potential duration. Furthermore, the model showed that atrial action potential duration indeed shortened by a large instantaneous outflux of potassium upon membrane depolarization, thereby prematurely abolishing the action potential plateau phase.[15] Interestingly, an extremely short cycle length was observed in our patient, indicating that the refractory period could be <25 ms. Reduction of the effective refractory period in combination with spatial dispersion in refractoriness can therefore result in a high number of fibrillation waves exciting the atria at a very high rate even within the small atria of young pediatric patients.

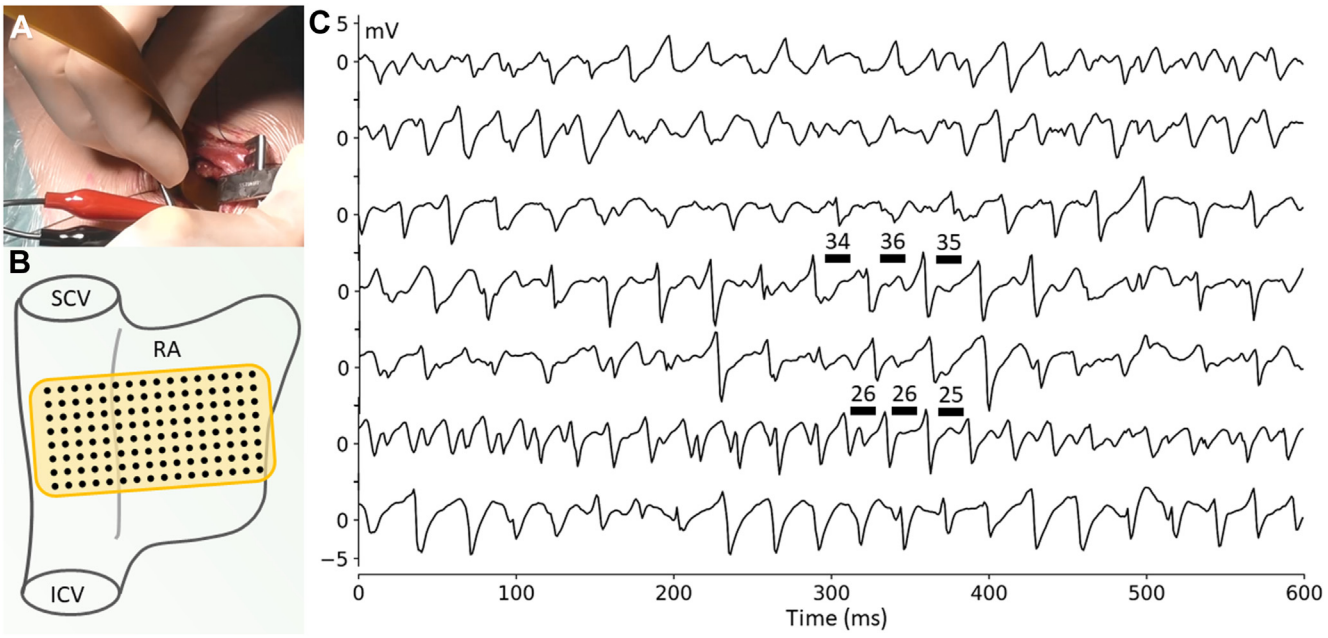

Figure 2 Unexpected atrial fibrillation at the right atrium. **A:** Positioning of electrode array using the pacemaker incision. **B:** Schematic representation of the position and orientation of the 128-electrode array (2.15 mm interelectrode distance) at the middle of the right atrial free wall. **C:** Unipolar epicardial electrograms recorded from the middle of the right atrium demonstrating beat-to-beat variation in electrogram morphology and cycle length, indicating atrial fibrillation. ICV = inferior caval vein; RA = right atrium; SCV = superior caval vein.

Conclusion

Even in very young patients with SQTS, AF can be sustained with an excessively high rate of the fibrillatory process, which is not visible as fibrillation waves on the surface ECG. In pediatric patients with arrhythmias undergoing cardiac surgery, (epicardial) mapping could be used as an additive diagnostic tool to guide therapy.

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