

# Inherited Arrhythmia Syndromes

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Inherited primary arrhythmia syndromes include long-QT syndrome, catecholaminergic polymorphic ventricular tachycardia, and Brugada syndrome. These syndromes are most commonly caused by single-gene mutations. Genetic alterations can also result in primary cardiomyopathy disorders that can be associated with arrhythmias. Cardiomyopathies include arrhythmogenic cardiomyopathy, hypertrophic and dilated cardiomyopathy, and LV noncompaction. Genetic results aid in diagnosis, can help guide counseling and in certain diseases, can guide management of patients.

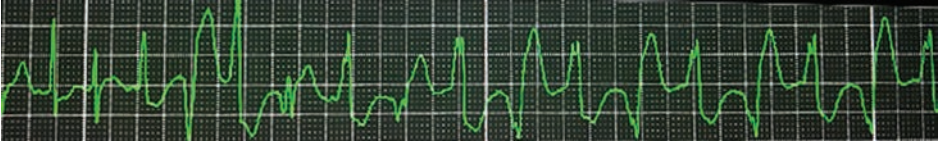
Patients with suspected primary inheritable arrhythmia syndromes or patients with a history of aborted cardiac arrest should undergo thorough evaluation including clinical history, ECG, echocardiogram, and a 3-generational pedigree. Patients with suspected or potential Brugada syndrome should undergo a modified Brugada ECG and ECGs should be obtained during any fever. Workup and genetic testing should be guided by the Electrophysiology Team.

## Long-QT Syndrome

This syndrome is a genetic condition most commonly caused by heterozygous mutations in cardiac potassium- (*KCNQ1*, *KCNH2*) or sodium-channel (*SCN5A*) genes. These mutations result in delayed repolarization and risk of a specific form of ventricular tachycardia called torsade de pointes.

Management of patients with known long-QT syndrome or those with marked QT prolongation include:

- Patients should be monitored.
- Avoid all QT-prolonging drugs (refer to [crediblemeds.org](http://crediblemeds.org)) particularly in patients with long-QT syndrome.
- In patients with QT prolongation without known long-QT syndrome, the risks and benefits of QT prolonging drugs need to be weighed.
- If a QT-prolonging drug must be administered (e.g., cancer treatment), the ECG and QTc must be followed during initiation of the medication and when the steady-state level of the drug is reached. If the QTc exceeds 480 msec, the drug should be held and cardiology consulted.
- Continue beta-blocker therapy while admitted.
- Maintain electrolytes in the normal range, particularly potassium, calcium, and magnesium. Hypokalemia, hypocalcemia, and hypomagnesemia can exacerbate arrhythmias.
- In case of torsade de pointes, give magnesium 25-50 mg/kg IV, esmolol, and defibrillation if necessary. Avoid any antiarrhythmic that can prolong the QTc such as amiodarone and sotalol.



**Figure 35-1.** Bidirectional ventricular tachycardia seen on patient bedside monitor. This pattern is pathognomonic for CPVT when seen only during adrenergic stimulation.

### Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT)

CPVT is most commonly caused by heterozygous mutations in the cardiac ryanodine receptor (*RYR2*) gene although there is a rare form caused by homozygous mutations in *CASQ2*. These genes are responsible for calcium handling in the cardiac cell. Adrenergic stimulation (such as exertion or emotional stress/anxiety) results in abnormal calcium release during diastole, which triggers life-threatening ventricular arrhythmias. Arrhythmias include polymorphic and bidirectional ventricular tachycardia (Figure 35-1) as well as ventricular fibrillation. Atrial arrhythmias are also common. Both supraventricular and ventricular arrhythmias only occur under adrenergic stimulation. In the hospital setting, this may include agitating or causing pain to the child during routine care (e.g., blood draws, peripheral IV placement).

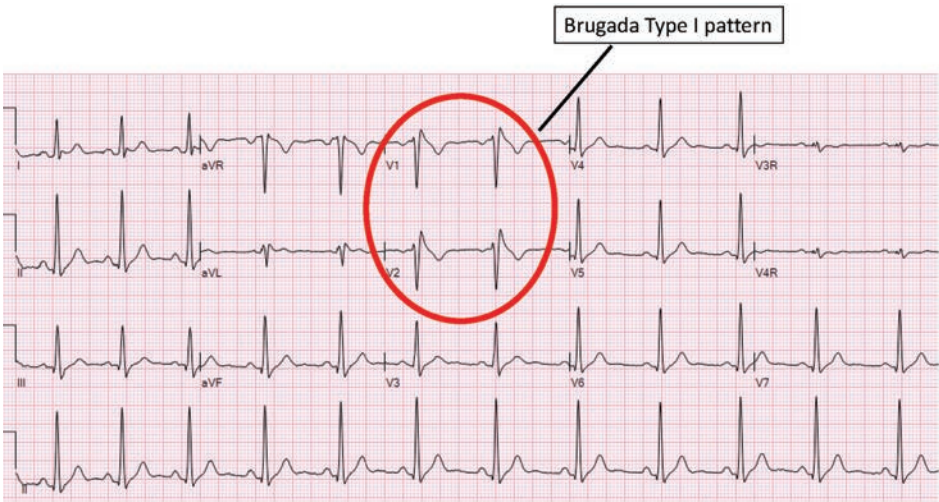
Although CPVT is rare, the mortality rate is the highest of all inherited arrhythmia disorders with a risk of cardiac event occurring in up to 30-50% by the age of 30 years. The most common age at presentation is 8-12 years and thus any child with exertional or emotional syncope should be evaluated for possible CPVT.

Treatment of patients with CPVT include:

- Make efforts to minimize catecholamine surges including painful stimuli during routine care, if possible. Avoid adrenergic inotropes or boluses such as epinephrine, if possible.
- Monitor for ventricular ectopy, couplets, or bidirectional ventricular tachycardia with stimulation (this can be diagnostic if seen in patients in whom the diagnosis is not yet known).
- Treat acute ventricular arrhythmias with esmolol and sedation, if needed. Oral nadolol or flecainide can also be used to prevent arrhythmias during adrenergic stimulation.

### Brugada Syndrome

Brugada syndrome results in ventricular arrhythmias most commonly triggered by sleep, fever, overheating, large meals, or specific medications. The most common age at presentation is 20-40 years and the most common presentation is death during sleep. Children, and even infants, can be affected at an early age. In children, arrhythmias are commonly seen during fever. Male patients are most likely to be affected. The most common genetic mutation is a heterozygous loss of function mutation in the *SCN5A* gene. Treatment of these patients include:



**Figure 35-2.** ECG of patient with Type-I Brugada pattern seen in right precordial leads (V1 and V2). There is ST elevation with T-wave inversion. This pattern can come and go and, in children, is most commonly brought out during a fever.

- Aggressively treat fever with antipyretics and avoid overheating (such as Bair Hugger™).
- Avoid Brugada-provoking drugs (refer to [brugadadrugs.org](http://brugadadrugs.org)), including diphenhydramine (Benadryl®), fexofenadine (Allegra®), amiodarone, amitriptyline, clomipramine, desipramine, lithium, loxapine, nortriptyline, oxcarbazepine, trifluoperazine, bupivacaine, procaine, propofol, disopyramide, lidocaine, propranolol, verapamil, vernakalant, bupropion, carbamazepine, clothiapine, cyamemazine, dosulepine, doxepine, fluoxetine, fluvoxamine, imipramine, lamotrigine, maprotiline, paroxetine, perphenazine, phenytoin, thioridazine, ketamine, tramadol, demenhydrinate, diphenhydramine, edrophonium, indapamide, and metoclopramide.
- Diagnosis is made by presence of a type-I Brugada pattern on ECG (Figure 35-2). This pattern can come and go and a normal ECG does not rule out disease. A specific modified-Brugada ECG protocol should be performed. ECG obtained during fever can help.
- In case of ventricular tachycardia, treatment options include isoproterenol or esmolol. If recalcitrant, sedation and intubation are recommended.

### Workup for Cardiac Arrest

In cases of cardiac arrest, a complete workup should be performed. An ECG should be obtained to look for prolongation of the QTc, Brugada changes, abnormal repolarization pattern (such as inverted T waves in the right precordial leads [V1-V3] in an adolescent), and ischemia. A Brugada protocol ECG should be performed. Because the QTc is often prolonged after an arrest, multiple ECGs are recommended to follow ECG changes over time.

An echocardiogram should be performed to evaluate hypertrophic/dilated cardiomyopathy, LV noncompaction, coronary anomalies, and pulmonary hypertension. The echocardiogram should also include protocols to evaluate the RV for arrhythmogenic cardiomyopathy, which must include measurements of the RV outflow tract in the parasternal long and short axis.

Some additional considerations are:

- A history of drowning in a patient who can swim should warrant investigation of long-QT syndrome.
- A thorough patient history with exact details of the arrest and 3-generation pedigree should be obtained.
- All rhythm strips from the arrest should be reviewed. If an automated external defibrillator (AED) was used, the AED should be brought with the patient and the rhythm strips reviewed.
- An electrophysiology consult is warranted for further evaluation and for potential genetic testing, particularly if a definitive cause is not identified.