

Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT)

What is CPVT?

Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT) is an inherited arrhythmia (heart rhythm disorder). CPVT is sometimes known as a channelopathy. This is because CPVT is caused by an abnormality of ion channels which allows calcium to accumulate in the heart muscle cell. This can lead to abnormal heart beats – usually during exercise or when adrenaline is released in stressful situations. These extra beats can arise from the top collecting chambers of the heart (atrial ectopic beats) or, more frequently, from the bottom pumping chambers of the heart (ventricular ectopic beats). If there are runs of fast beats from the atria or ventricles these are known as atrial or ventricular tachycardia. In CPVT the heart usually has a normal structure. It is thought that about 1 in 10,000 people have CPVT, although the exact numbers are unknown.

Symptoms

Episodes of ventricular tachycardia (VT) can cause light-headedness, dizziness and loss of consciousness (syncope). Symptoms usually start in childhood but can appear in young adults for the first time.

Most syncopal episodes in childhood are benign, however those who suffer syncope during exercise or in response to an adrenergic stimulus should be further investigated. Sometimes these episodes can be mistaken for a fit/epilepsy as they can look very similar and as a consequence many children are treated with anti epileptic drugs.

In a child not responding to anti epileptic drugs a diagnosis of CPVT should be considered. Unfortunately, sometimes the first presentation can be sudden cardiac arrest– an episode of VT cannot be sustained for a long period of time and may result in the heart completely stopping (cardiac arrest). Atrial tachycardia usually causes

a sensation of inappropriate racing of the heart (palpitations). This is not usually dangerous but can be unpleasant.

Diagnosis

In patients presenting with sudden cardiac arrest in the absence of structural cardiac disease, CPVT should be considered in the differential diagnosis. Clinical diagnosis is made based on family history, exercise or emotional stress-induced symptoms and, significantly, response to exercise or catecholamine (adrenaline) infusion, however not all episodes are triggered by adrenaline.

The cardiac ultrasound test (echocardiogram) and resting ECG are usually normal.

Genetics

The most common cause of CPVT results from mutations in the cardiac ryanodine receptor gene (RYR2). Less common causes are in other genes such as Calsequestrin, Calmodulin and Triadin. These genes code for proteins that handle calcium which helps maintain a regular heart beat.

Familial inheritance has been seen in about a third of cases of CPVT. RYR2 causes autosomal dominant inheritance meaning if you inherit the abnormal gene from only one parent, you can get the disease.

First-degree relatives should be evaluated with ECG, Holter monitoring and exercise stress testing. Genetic testing can sometimes be helpful. Identification of a genetic abnormality that is the definite cause of the condition (a “pathogenic” mutation) can allow other family members to be tested.

analysis might identify silent carriers of CPVT-related mutations, and it may be recommended that even symptom-free carriers are treated with medication such as beta blockers. Sometimes, a genetic change is discovered and it is unclear if this is the definite cause. This is known as a "variant of unknown significance" or VUS. A VUS cannot be used for family screening.

Treatment

Once diagnosed, treatment is usually with a beta blocker. Beta blockers decrease the activity of the heart by blocking the action of hormones such as adrenaline, which would normally increase in times of exercise or emotional stress. Subsequently, the number of episodes of VT is reduced. A high dose is often required.

Flecainide works on the sodium channel and may inhibit cardiac ryanodine receptor-mediated calcium release. Flecainide appears to work very well in many people and is rapidly becoming a preferred drug in many people with CPVT

Missing even a single dose of beta blocker can be potentially dangerous. Internal defibrillators (ICD) are sometimes fitted in addition to medication to 'shock' the heart back into normal rhythm if VT occurs. Survivors of cardiac arrest or high-risk patients with a strong family history of sudden death are more likely to be offered an internal cardioverter defibrillator. ICD treatment without use of beta blockers is not advised as a shock from the defibrillator can lead to an adrenaline surge and multiple runs of ventricular tachycardia known as an 'electrical storm'.

A left cervical sympathectomy may be offered to some patients, eg those in whom beta blockers are contraindicated, when an ICD cannot be fitted, or where there is recurrent VT in patients with an ICD despite maximal medical treatment. A cervical sympathectomy is an operation carried out through a small incision under the arm. This blocks a group of nerves that produce and deliver adrenaline to the heart. These nerves are not essential to normal heart function but sympathectomy can be very helpful in preventing serious arrhythmias.

Additionally some sports may be restricted, eg competitive swimming, compliance can result in an episode of tachycardia.

Acknowledgments: Arrhythmia Alliance would like to thank all those who helped in the development and review of this publication. In particular, thanks are given to Dr Jan Till, Dr Charlotte D'Souza and Dr Graham Stuart.