Evaluation of arrhythmias associated with sudden cardiac death in paediatric patients

Mark Walsh
Graham Stuart
Rob Martin

Abstract

In the last decades we have seen an increased focus on the prevention of sudden cardiac death (SCD). There is much controversy regarding the most appropriate screening programs where we attempt to balance potentially preventable cases of SCD with the cost of screening programs in addition to the anguish caused by false positive results. Recent events have also demonstrated to us the danger of strenuous exercise in people who have a genetic susceptibility to SCD, whatever the mechanism may be. Also, the barrage of genetic testing now available to us provided us with a new clinical problem, those who are genotype positive but yet do not show any manifestations of the disease. Syncope is very common in the paediatric age group and its evaluation is the cause of much anxiety. As physicians, we would rather not over investigate what is probably a benign condition; however, a missed diagnosis has potentially catastrophic consequences. In this review we will outline the various cardiac pathologies involved, how they are diagnosed, what the potential implications are for the patient and the best available therapeutic options.

Keywords arrhythmias; long QT syndrome; paediatric electrophysiology; sudden cardiac death

Clinical presentation

Unfortunately for patients who have a genetic predisposition to SCD, the most common presentation is a fatal event. The first step in dealing with a case of SCD is to ascertain the exact cause of death. Once this has been established, our aim should be to appropriately investigate first degree relatives and prevent further episodes. The presence of a protocol greatly facilitates this process, ensures that the appropriate specialists are contacted and that due diligence is carried out.

Mark Walsh *MD is a Consultant Cardiologist in the Bristol Congenital Heart Centre, Bristol Royal Hospital for Children, Bristol, UK. Conflict of interest: none declared.*

Graham Stuart *MD is a Consultant Cardiologist in the Bristol Congenital Heart Centre, Bristol Royal Hospital for Children, Bristol, UK. Conflict of interest: none declared.*

Rob Martin *MD is a Consultant Paediatric Cardiologist in the Bristol Congenital Heart Centre, Bristol Royal Hospital for Children, Bristol, UK. Conflict of interest: none declared.*

The first point of contact will be the coroner who in most circumstances will request that a post mortem be performed. Pathologists involved in the process should liaise with all of the appropriate specialities including a physician with an interest in electrophysiology. Where there is no identifiable structural cause found, a molecular autopsy should be preformed, screening for all of the known channelopathies. Identification of a gene mutation from any of the major channelopathies greatly facilitates screening first degree relatives for the same mutations. In the absence of any identifiable structural cause, it is reasonable to conclude that death was most likely due to a malignant arrhythmia of some kind: a condition often referred to as sudden arrhythmic death syndrome (SADS). Where there is no identifiable genetic cause, investigation of first degree relatives is more difficult. Specialist review, including a complete history, physical examination and an ECG should occur in all cases. Preexisting conditions, the presence of symptoms, a complete family pedigree and drug ingestion may point towards causative factors. A baseline ECG may diagnose long QT, Brugada, or Arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC); however a normal ECG does not exclude the aforementioned conditions. Other diagnostic tests that should always be carried out where the diagnosis is not clear include a signal averaged ECG (ARVC), a drug challenge with a sodium channel blocker (ajmaline, flecainide or procainamide) to test for the Brugada syndrome and an exercise test to look for catecholamine sensitive polymorphic ventricular tachycardia (CPVT). These tests are not expensive; the ECG and the drug challenge have the highest diagnostic yield (35% and 49%, respectively). Genetic testing is usually performed where clinically indicated such as an ECG that is suspicious for long QT syndrome.

Unfortunately the number of patients who present having survived an out of hospital cardiac arrest is still very small. These patients should always have a complete diagnostic work up and most people would advocate an internal cardiac defibrillator (ICD).

Neurocardiogenic syncope

Many paediatric patients present to our clinic with syncope and fortunately the majority of this is neurocardiogenic. Triggering factors often include stressful or emotional events, standing for long periods of time and exposure to noxious stimuli; it is commonly seen in teenage girls. A complete history of the events leading up to, during and afterwards by a physician with some expertise in this area will usually determine whether syncope is neurocardiogenic in origin. Factors in the history that point towards a neurocardiogenic cause include presence of a prodrome, awareness of the event throughout, ability to protect themselves during a fall or avoid falling altogether by sitting down. Exercise related syncope is usually pathological. It is important to be specific as to whether syncope occurred during maximum exertion or whether it happened afterwards, when neurocardiogenic syncope is common. Wherever there is any doubt an exercise test or a tilt table test can be useful.

Screening for sudden cardiac death

There has been increased interest in targeting certain high-risk populations, such as children who participate in competitive

sports. Published evidence suggests that the history and physical examination have limited value in identifying causes of sudden cardiac death. Most cases of SCD do not have a positive family history. The European Society of Cardiology has recommended a complete family/personal history, examination and a 12-lead ECG for all children participating in competitive sports. The American Heart Association have not recommended performing a 12-lead ECG. A large proportion of young athletes due to physiological conditioning demonstrate changes on the 12-lead ECG consistent with hypertrophic cardiomyopathy hence these ECGs often need to be reviewed by cardiologists familiar with physiological versus pathological changes. The positive predictive value of any screening test is very low by virtue of the fact that most of these conditions are fortunately quite rare; also, sensitivity and specificity are often variable.

Long QT syndrome

Congenital long QT syndrome is one of the main cardiac channelopathies. It affects approximately one in 5,000 people and often the first presentation is sudden death at a young age. It has a marked phenotypic and genotypic heterogeneity. Historically, the two types that have been described are Jervell—Lange-Nielsen and Romano-Ward syndrome. The former is autosomal recessive, associated with congenital deafness, and represents the most severe spectrum of the disease; due to the high risk of events most of these patients have an ICD implanted. Romano-Ward is more common, it is autosomal dominant, although inheritance is often more complex than this and sporadic mutations are often seen. The most common types are LQT1 (KCNQ1: delayed potassium rectifying current), LQT2 (KCNH2: rapid potassium rectifying current) and LQT3 (SCN5A: delayed deactivation of sodium channel current: Figure 1). There are other types of long QT syndrome that are associated with a typical phenotype such as Anderson-Twail syndrome. Also called long QT type 7, this syndrome consists of a typical facial appearance consisting of micrognathia, low set ears, clinodactylies in association with features of long QT syndrome. These patients can also present with ventricular tachycardia and are often mistaken for cases of CPVT.

LQTS is diagnosed using criteria outlined in Table 1. A corrected QT interval of over 440 ms in boys and 460 ms in girls is considered abnormal. There is however considerable variation in the QT interval during the first weeks of life and in the presence of structural heart disease. Factors which put patients at high risk include a corrected QT interval of >500 ms, presence of T-wave alternans and the presence of sinus pauses which are often a precipitating event for torsade de pointes. Sometimes, long QT syndrome can present with 2:1 block on ECG: this will usually require placement of an ICD or pacemaker. There is some evidence to suggest that up to 11—13% of cases classified as sudden infant death syndrome, are actually due a channelopathy, most commonly long QT syndrome.

Treatment for long QT1 syndrome is primarily with B-blockade: propranolol in infants and nadolol in older children which allows daily administration due to its longer half-life. Clear evidence suggests that β-blockers are extremely effective in LQT1; they are usually tried in other types however the data is less conclusive. Placement of an ICD is a class I indication for patients who have had documented cardiac arrest. By contrast, there is considerable variation in practice with respect to other indications. The relatively low incidence of sudden death in this condition sometimes makes it difficult to implant an ICD, especially when the morbidity from such devices is so much higher in children.

Brugada syndrome

Brugada syndrome is a relatively recently described condition consisting of ST segment elevation in the anterior precordial

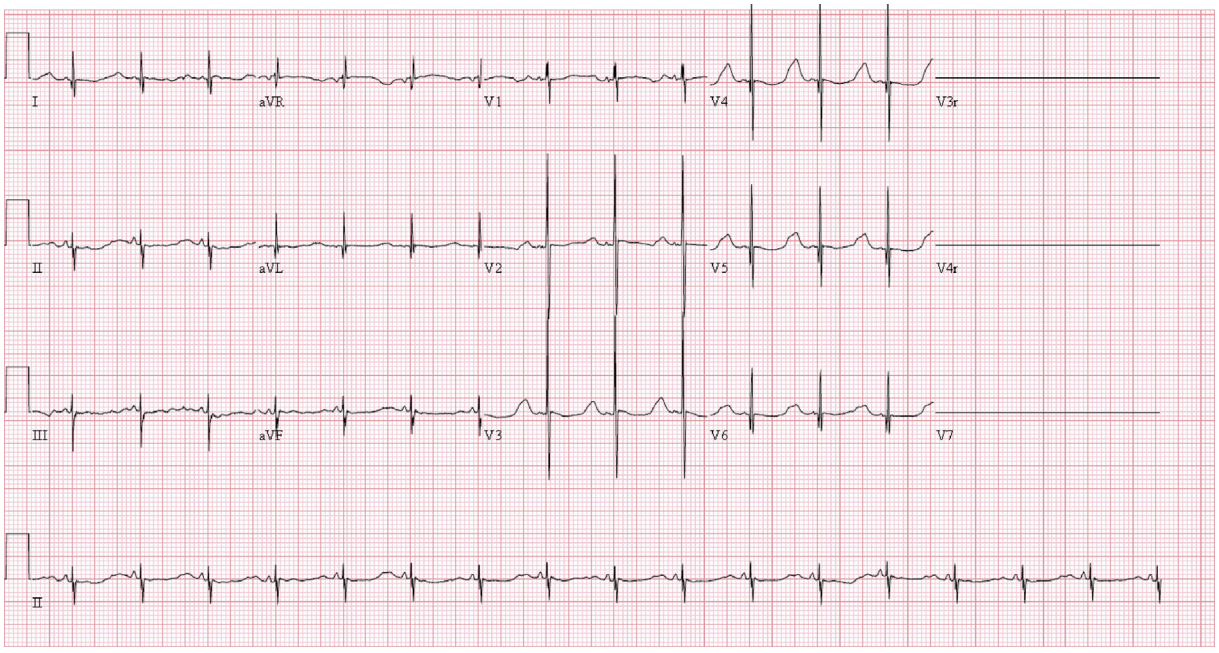

Figure 1 This patient presented at birth with bradycardia. The QT interval is markedly prolonged and genetic work-up demonstrated long QT3. They had an ICD implanted at 2 months of age.