Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT)

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Catecholaminergic: Adrenaline or exercise related
Polymorphic: More than one appearance (the beats have multiple shapes on the ECG)
Ventricular: from the lower/pumping chamber of the heart
Tachycardia: rapid heart beat
Catecholaminergic polymorphic ventricular tachycardia (CPVT) is thankfully a rare disorder that causes palpitations, blackouts and sudden death, usually related to exertion or stress. In some situations, there is a family history of other affected members, including tragic sudden death.
Vignette: A fourteen year old female presented with two episodes of loss of consciousness during moderate exercise. She recalled being vaguely aware of a sense of skipping in her chest before losing consciousness. Her friends noticed that she looked pale for a few seconds, and slumped to the ground. She awakened within a few seconds, and felt perfectly well within a few minutes. Her mother and aunt had similar episodes while playing baseball as adolescents, and had given up public singing and baseball as a result. Her great uncle died suddenly at age 22 while playing hockey. Subsequent testing showed normal structure of her heart, and a normal resting ECG without QT prolongation.
Exercise testing resulted in multiple premature ventricular beats (Doctors call them PVCs) coming from several different places of the heart accompanied by a sense of palpitations. When beats became frequent, the patient experienced lightheadedness. Similar findings were noted when her aunt and mother were assessed. Beta blockers were prescribed (medication that inhibits the adrenaline input into the heart), with elimination of PVCs during exercise. She remained free of blackouts for 3 years since her initial testing, when an extended family member had sudden death during exercise. The family requested an implantable defibrillator (ICD), which was implanted after a lengthy discussion with her doctors about the risks and benefits of the device. She is now flourishing in University.
CPVT – The Skinny
The above case illustrates how many patients with CPVT present, and that most patients can have an excellent outcome if the disease is recognized and treated. The disease tends to first present after puberty in early adolescence with palpitations or blackouts. Given the trend of modern smaller families, there may not be any evidence that other family members are affected. Recent evidence has demonstrated mutations on chromosome 1 in the gene that codes for the ryanodine receptor are responsible for CPVT. These are DNA “typos” that lead to misfiring when making the protein that makes up this receptor inside the heart muscle cell. The heart muscle then has trouble appropriately handling calcium inside the cell, which upsets the balance of electrical charges and leads to the abnormal heart beats when the cell is stimulated by

adrenaline. This process is not affected by calcium in the blood or diet, and does not affect the QT interval.

Genetic testing: Genetic testing has the potential to help both individuals and families determine if the disease is present, and assist with treatment decisions. At present, this type of testing is not available in Canada except in specific research settings. Simply checking for the gene is not possible in this condition, like most other genetic causes of arrhythmia. Most new patients will have a new genetic abnormality if it can be detected (called a private mutation), so the process is expensive and time consuming since a gene sequencer has to read every letter of the DNA in the region of the gene to look for the typo. Because this is a relatively new genetic discovery in such a rare disease, little is know about the meaning of specific mutations, how frequently a mutation can be detected, or how often the patients has symptoms if they carry the mutation (called genetic penetrance). As with other conditions, genetic screening raises issues regarding branding (you feel well but your genes tell us you have a disease), life insurance, and the usual range of human responses to family health issues (anger, denial, hypervigilance etc). Nonetheless, there are plenty of situations where the diagnosis is not clear from clinical testing, so that the future clearly will include genetic testing. Cost is a challenge that will continue for the foreseeable future.

Clinical testing: The heart is normal in structure and function in CPVT. Initial testing involves ruling out other causes of PVCs, particularly heart muscle disorders such as dilated cardiomyopathy, ischemic heart disease and arrhythmogenic right ventricular dysplasia (ARVD). An echocardiogram (heart ultrasound) is usually performed, and further assessment of heart function will depend on the situation. Monitoring testing usually includes a resting ECG, and exercise test and often Holter monitoring (1-2 days continuous recording of the ECG). Occasionally, CPVT is suspected in patients with unexplained cardiac arrest. Low does adrenaline infusion in a controlled environment has “unmasked” CPVT in some cases, providing insight into the cause of cardiac arrest.

Treatment: The usual initial treatment is based on the presentation. All patients will receive beta blockers if tolerated, usually started at a low dose and built up over weeks to months. The exercise or Holter test is repeated on the beta blocker to confirm that the PVCs are improved. An ICD is indicated in patients that have suffered a cardiac arrest, or who have recurrent blackouts while taking a beta blocker. In select cases, an ICD may be considered when there is unusual concern regarding the risk, such as a patient with asthma that cannot take a beta blocker. Treatment is always tailored to the individual based on their symptoms and family history.

Ongoing Research in Canada: The best way to understand rare diseases is to share information. Currently, a national network of investigators is being established to collaborate in the area of genetics and arrhythmias. This is currently up and running in 6 centers, with 4 more in the works. The current focus of the network is in the investigation of patients with unexplained cardiac arrest, searching for conditions such as CPVT, Brugada’s Syndrome, Long QT Syndrome and

ARVD. Individual researchers in Canada have varied focuses in the field, funded by local and national funding agencies such as the Heart and Stroke Foundation.

The London Team: Research in London, Ontario includes directing the national registry on testing in unexplained cardiac arrest (Cardiac Arrest Survivors with Preserved Ejection Fraction Registry - CASPER) and focus on Long QT Syndrome. Dr Krahn's research is funded by the Heart and Stroke Foundation of Ontario and Guidant Canada. Dr. Krahn is Professor of Medicine in the Division of Cardiology at University of Western Ontario. His sidekick Bonnie Spindler RN has worked tirelessly in the area of genetics and arrhythmias as his research coordinator for the past 10 years. Additional genetic research assistance has previously come from Dr Robert Hegele at the Robarts Research Institute, and currently from Dr. Michael Gollob at the University of Ottawa. The Arrhythmia Fellows and stress testing staff at London Health Sciences Center have also been immensely helpful.
The Canadian SADS Foundation has always appreciated the support Dr Krahn has extended by submitting articles for publication like this one and speaking at our conferences.