P-37

First Report of Autosomal Recessive Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT1), Caused by Homozygous Mutation in the RYR2 Gene

Ta-Shma A., Shauer A., Perles Z., Elitzur Y., Ta-Shma A., Elpeleg O., Luria D.
Hadassah, Hebrew University Medical Center, Jerusalem, Israel

Introduction: Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT) is a rare tachyarrhythmia typically presenting with bidirectional ventricular tachycardia, appearing during physical or emotional stress. Mutations in the Ryanodine receptor gene, RYR2, are known to cause an autosomal dominant type of the disease (CPVT1). As part of our effort to elucidate the molecular basis of cardiac anomalies in consanguineous families, we studied the genetic basis of CPVT in a consanguineous family with healthy parents and two siblings who presented with cardiac arrest and had a diagnosis of CPVT.
Methods: We obtained thorough family history and complete patients' phenotype including: ECG, stress tests, echocardiography. We did comprehensive genotyping with the use of Whole Exome Sequencing analysis and verification was done with Sanger sequencing.
Results: A nineteen years old asymptomatic male presented with cardiac arrest during physical stress. While visiting him in the intensive care unit, his thirteen years old sister experienced major emotional stress, and suffered from cardiac arrest as well. Thorough family workup including ECG, stress test and echocardiography, revealed asymptomatic parents and siblings, one of which was found to have multifocal premature ventricular contractions (PVCs) during stress test. Echocardiography for all family members revealed normal cardiac anatomy. The three affected members underwent implantable cardiac defibrillator (ICD) implantation and received metoprolol therapy. During nine years of follow up, the female had an episode of multiple ventricular fibrillation and shocks. The Metoprolol dose was increased and no further episodes occurred.
Whole Exome Sequencing identified homozygous Gly3118Arg missense mutation in the RYR2 gene. The mutation segregated with the phenotype in the family: The affected members were homozygous for the mutation whereas the non-affected parents and siblings were heterozygous. The mutation is located in the cytosolic component of the RYR2 protein.
Conclusion: This is a first report of autosomal recessive CPVT1 caused by homozygous RYR2 mutation.