G97 Sudden Death in a 6-Year-Old Due to a RyR2 Mutation Associated With Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT)

Jess Baker, BA, 124 Bloomingdale Pike, Apt E49, Kingsport, TN 37660; Teresa A. Campbell, MD*, DeBusk College of Osteopathic, Medicine Lincoln Mem University, 6965 Cumberland Gap Parkway, Harrogate, TN 37752; Karen Cline-Parhamovich, DO, OCME, William L. Jenkins Forensic Center, PO Box 70425, Johnson City, TN 37614-1707; Dawn R. Lajoie, MD, William L. Jenkings Forensic Center, Johnson City, TN 37601; Charles E. Ganote, MD, East Tennessee State University, James H Quillen Col of Medicine, Dept. Of Path, PO Box 70568, Johnson City, TN 37614; and Mark Dunn, Forensic Pathology, Box 70425, Johnson City, TN 37614*

After attending this presentation, attendees will have an understanding of the clinical features and pathophysiology of a RyR2 mutation associated with Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT).

This presentation will impact the forensic science community by raising awareness that sudden unexplained death may be caused by an undiagnosed cardiac channelopathy and that funding for genetic testing is needed in medical examiner jurisdictions with budgetary constraints.

A 6-year-old boy with no antecedent complaints of illness was found in cardiopulmonary arrest on the bathroom floor at school. Subsequent advanced resuscitative measures failed. Further investigation revealed no family history of sudden unexplained deaths or known cardiac abnormalities. The decedent had a negative past medical history with no history of dizziness, syncopal episodes, or palpitations, and by all accounts had been a normal, active 6-year-old boy. At autopsy, external examination was unremarkable with no evidence of injury. Internal examination revealed no anatomic cause of death. The heart was anatomically normal with biventricular dilation. Histologically, thin, stretched myocytes with groups of wavy fibers consistent with the dilation seen grossly were present. The conduction system was unremarkable. Acute contraction band necrosis of immediately subendocardial cardiomyocytes as well as deep within the papillary muscles was present microscopically. Complete histological examination of all organs as well as toxicological, biochemical, and microbiological studies revealed no cause of death. No funding to obtain genetic testing for cardiac channelopathies was available; however, the parents expressed a willingness to procure financing for these studies with hopes of determining a definitive cause of death. Genetic testing for cardiac channelopathies was obtained and a RyR2 Ser2246Leu Class I mutation was detected which is associated with CPVT. The RyR2 gene encodes the ryanodine receptor 2 protein which forms channels controlling release of calcium ions from the sarcoplasmic reticulum into the cytoplasm which activates cardiomyocyte contraction. Over 70 mutations of the RyR2 gene causing CPVT have been found. Individuals with CPVT may develop polymorphic ventricular tachycardia during exercise or intense emotion which may self-correct or degenerate into ventricular fibrillation with subsequent death. Age of onset is typically from 7 to 9 years, but initial manifestation of CPVT has been known to occur in adults as well. RyR2-related CPVT is inherited in an autosomal-dominant manner which prompted genetic testing of a sibling and the parents. This presentation discusses the clinical features and pathophysiology of a RyR2 mutation associated with CPVT, indications for genetic testing in sudden unexplained death, and the fiscal challenges in obtaining such testing.

RyR2 Mutation, Channelopathy, Sudden Death

 ** Presenting Author*