G29 Postmortem Diagnosis of Genetic Arrhythmia Syndromes

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After attending this presentation, attendees will understand current methods of postmortem diagnosis of genetic arrhythmia syndromes.

Genetic arrhythmia syndromes, which are almost certainly underdiagnosed by medical examiners, have been theorized to cause some deaths from Sudden Infant Death Syndrome and have been implicated in the development of fatal arrhythmias during exercise. A presentation by an M.E. about cases where genetic analysis supported an etiology for fatal arrhythmia may encourage others to increase their index of suspicion for these disorders and to support efforts to develop cost-effective screening methods.

Genetic disorders predisposing to sudden death from arrhythmia in the absence of cardiac anatomic abnormalities account for an unknown number of deaths presenting to the medical examiner. Two cases illustrate the importance of clinical history in such deaths and the methods by which postmortem diagnosis of these conditions can be accomplished.

A 15-year-old girl collapsed in front of witnesses while swimming and died despite immediate medical attention. Autopsy revealed no injuries, anomalies or acute disease process, and electrolyte analysis and toxicology were non-contributory. Medical history was significant for two fainting episodes in the past year under conditions of emotional stress. Review of antemortem EKG's showed mild prolongation of the Q-T interval and increased Q-T with increased heart rate. Molecular studies of frozen myocardium have shown a mutation in a cardiac ryanodine receptor gene associated with catecholaminergic polymorphic ventricular tachycardia. Also present was a polymorphism in the KCNE1 potassium subunit gene; mutations in that gene have been associated with Long Q-T Syndrome. The death has been classified as due to cardiac arrhythmia; further molecular studies are ongoing.

A 43-year-old woman was found dead where she had been shoveling snow. A complete autopsy revealed no cause of death. The information that her previously healthy sister had collapsed and died on hearing of her death prompted molecular analysis of a liver specimen archived for toxicology. A mutation was present in a cardiac potassium channel gene known to be associated with congenital Long Q-T Syndrome.

Genetic sequencing for mutations associated with sudden death from fatal arrhythmia is expensive, time-consuming and not widely available. Review of the circumstances of death, family history and medical records following a negative autopsy facilitates selection of the rare case appropriate for molecular testing. Frozen myocardium is currently the best specimen for analysis, and should be retained in suspected cases.

Simplification of screening for known mutations or abnormal gene products would enhance the ability of the medical examiner to determine that a genetic arrhythmia syndrome caused a death. These conditions are heritable and can often be managed by pharmacotherapy, avoidance of arrhythmia inducing substances and medications, and/or defibrillator placement. Surviving family members may therefore benefit from counseling and electrophysiologic screening. These interventions have the potential to save lives.

Long Q-T Syndrome, Molecular Diagnosis, Arrhythmia

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