H55 Deaths Due to Cardiomyopathy of Unknown Etiology in Children and Young Adults

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Learning Overview: After attending this presentation, attendees will better understand the autopsy findings of deaths due to cardiomyopathy of unknown etiology in children and young adults in the Cook County Medical Examiner's Office in Chicago, IL.

Impact on the Forensic Science Community: This presentation will impact the forensic science community by illustrating cases of sudden, unexpected death in which the hearts were abnormal (either grossly or microscopically), but there was no known underlying etiology for the cardiomyopathy.

Cardiomyopathies are a heterogeneous group of diseases of the heart muscle that can lead to heart failure, cardiac arrhythmia, and sudden death. Although there are many etiologies for cardiomyopathies, they typically manifest as an enlarged heart or a heart with normal weight with microscopic pathology (fibrosis, inflammation, etc.). Since cardiomyopathy is not a specific diagnosis, this study has attempted to determine the underlying etiologies in our population. Diseases such as hypertension, obesity, chronic alcoholism, and genetic abnormalities can all cause cardiomyopathies and have similar gross and microscopic findings. This project focused on cases of cardiomyopathies in which no underlying etiology could be found through medical history or autopsy.

The files of the Cook County Medical Examiner's Office in Chicago, IL, were searched for cases of subjects between 1 and 40 years of age with "cardiomyopathy" as a cause of death, from January 2013 to June 2018. Cases were reviewed for age, sex, race, cause and manner of death, medical history, and autopsy findings.

In total, 140 cases were identified: 116 cases (83%) with cardiomyopathy due to hypertensive cardiovascular disease, 1 case with cardiomyopathy due to obesity, 1 case with cardiomyopathy due to chronic alcoholism, 2 cases with cardiomyopathy due to alcoholism and obesity in combination, and 20 cases (14%) with an unknown etiology, which is the group examined for this study.

Regarding the 20 cases with a cardiomyopathy of unknown etiology, 16 were males and 4 females; 15 were African American and 5 Caucasian. Ages ranged between 14 and 40 years old: two decedents were <20 years old, eight ranged between 21-30 years, and ten ranged between 31-40 years. The manner of death was determined to be natural in all cases.

Cardiomegaly was present in 16 out of 20 decedents (80%) with heart weights ranging between 376 grams and 840 grams. Additional gross pathological changes were present in 15 out of 20 cases (75%), consisting mostly of dilated ventricles, hypertrophic ventricles, and myocardial scarring.

All 20 cases showed microscopic pathology consisting of the following changes: fibrosis (17 cases), cardiac myocyte hypertrophy (13 cases), interstitial chronic inflammation (10 cases), and interstitial adipose tissue (5 cases). In 4 out of 20 cases (20%), there were no gross pathological changes, but histology showed one or more of the above-listed abnormalities.

Regarding medical history, 10 out of 20 cases had other associated diseases, with the most common being obesity, asthma, and fatty liver. Obesity was present in 6 out of 20 cases (BMI ranged between 32 kg/m^2 and 35.3kg/m^2). In cases in which obesity was considered as the etiology of cardiomyopathy, BMI ranged between 40kg/m^2 and 46kg/m^2.

Genetic testing is being offered to decedents' families to search for an underlying etiology and counsel families. To date, this study has results from 3 out of 20 cases. So far, no pathogenic mutations have been identified. Genetic variants of uncertain significance have been identified, including missense variants of genes PRKAG2, DOLK, DMD, NEBL, PDLIM3, and DSG2. At this point, it is unclear how these variants may contribute to the development of cardiomyopathies. Therefore, in all the autopsy reports, it was recommended that first-degree (immediate) family members undergo cardiovascular screening and possible genetic evaluation by experienced cardiologists and geneticists to diagnose and prevent sudden death in surviving family members.

This study shows that in children and young adults, there are a significant number of decedents with cardiomyopathy with no known etiology after a complete autopsy and review of medical records. In some cases, the heart may appear grossly normal and show only microscopic evidence of pathology. Screening for cardiovascular disease and possible genetic testing should be performed in immediate family members of a child or young adult dying from a cardiomyopathy of unknown etiology.

Cardiomyopathy of Unknown Etiology, Sudden Death, Genetic Testing