H34 Undiagnosed Metabolic Cardiomyopathy as a Cause of Pediatric Sudden, Unexpected Death: Case Report and Review of the Literature

Lauren M. Woertz, 2121 W Harrison Street, Chicago, IL 60612; Steven M. White, MD, PhD, County Cook OME, 2121 W Harrison Street, Unit D7, Chicago, IL 60612; and Audrey Deeken-Draisey, MD, Northwestern Memorial Hospital, 208 W Washington Street, Unit 1206, Chicago, IL 60606*

After attending this presentation, attendees will understand the potential for undiagnosed cardiomyopathy resulting from Inborn Errors of Metabolism (IEM) as a cause of sudden, unexpected death in children and will recognize the gross and histologic findings suggestive of cardiomyopathy resulting from a metabolic disorder.

This presentation will impact the forensic science community by enhancing the recognition of pediatric cardiomyopathies occurring due to metabolic disorders as a cause of sudden cardiac death in children. The forensic community will understand the diagnostic methodologies required for the postmortem detection of metabolic disorders. This presentation also highlights the fact that potentially lethal IEM may not be detected by routine neonatal screening.

Pediatric cardiomyopathies are a relatively rare and varied group of disorders that differ widely in their causes and outcomes. They are also an important cause of morbidity and mortality in this population, and children with cardiomyopathy are at risk for sudden cardiac death.[1] While the etiology for the development of cardiomyopathy is varied, IEM have been shown to cause a substantial proportion of pediatric cardiomyopathies.[2] The detection methods for identification of IEM have improved, although there remains a significant risk for complications if the cardiomyopathies remain undiagnosed and untreated.

Inborn errors of metabolism in pediatric patients have recently been shown to account for 26% of hypertrophic cardiomyopathies and 16% of dilated cardiomyopathies.[3] IEM occur in approximately 1 in 4,000 newborns and comprises over 1,000 unique diagnoses. Forty types of IEM have been documented to cause cardiomyopathy, including fatty acid oxidation defects, organic acidemias, glycogen storages diseases, amino acidopathies, and peroxisomal, mitochondrial, and lysosomal storages disorders. Only about 5% of IEM cases are associated with cardiomyopathies and rarely is the heart the only affected organ.[4] Most pediatric cardiomyopathies are diagnosed early in life due to the development of symptoms; however, they may go undiagnosed, first presenting at autopsy. In addition to determining the cause of death, establishing a diagnosis of cardiomyopathy due to IEM may have important implications for surviving family members and may influence family planning in cases of hereditary IEM.

This presentation pertains to the case of a 21-month-old Caucasian female with no significant past medical history. The child experienced two days of flu-like symptoms including a cough, congestion, and fever prior to developing labored breathing and becoming unresponsive in the arms of a caregiver. She died a mere 22 minutes later in the hospital. There was no family history of heart disease or sudden infant death. The child had normal development, met appropriate milestones, and the newborn laboratory screen performed at birth was normal. Postmortem toxicology and microbiology tests were non-contributory. At autopsy, the heart was dilated with a globoid shape, and the formalin-fixed specimen weighed 123 grams (expected 33-89 grams). Histologic examination of the heart revealed vacuolated cardiac myocytes in a patchy distribution. An Oil Red O stain performed on a frozen section of formalin-fixed tissue revealed intracellular lipid accumulation within the vacuoles; Periodic Acid-Schiff (PAS) stains with/without diastase were negative. Histologic examination of the liver revealed steatosis in a centrivenular pattern. The gross and histologic findings of the heart were consistent with dilated cardiomyopathy due to a probable metabolic disorder of unknown etiology. Intracellular lipid accumulation can be seen in both lipid-storage disorders and mitochondrial disorders. Whole genome sequencing is currently pending to further classify the specific metabolic disorder that contributed to the decedent's death.

*Presenting Author

Reference(s):

1. Bharucha T., Lee K., Daubeney P., et al. Sudden death in childhood cardiomyopathy. *Journal of the American College of Cardiology*. 2015; 65(21): 2302-2310.
2. Towbin J.A., Lowe A.M., Colan S.D., et al. Incidence, Causes, and Outcomes of Dilated Cardiomyopathy in Children. *Journal of the American Medical Association*. 2006; 296(15): 1867-1876.
3. Kindel S., Miller E., Gupta R., et al. Pediatric cardiomyopathy: importance of genetic and metabolic evaluation. *Journal of Cardiac Failure*. 2012; 18(5): 396-403.
4. Cox G. Diagnostic approaches to pediatric cardiomyopathy of metabolic genetic etiologies and their relation to therapy. *Progress in Pediatric Cardiology*. 2007; 24 (1): 15-25.

Metabolic Disorder, Cardiomyopathy, Pediatric Sudden Death