CONGENITAL CARDIOLOGY SOLUTIONS
(PEDIATRIC CARDIOLOGY AND ADULT CONGENITAL HEART DISEASE)

GENETIC AND VIRAL GENOME ANALYSIS OF CHILDHOOD CARDIOMYOPATHY: THE PCMR/PCSR EXPERIENCE

ACC Poster Contributions
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Background: The underlying etiology of cardiomyopathies in childhood is slowly being elucidated. The most common causes are thought to include genetic disorders (gene mutations in sarcomeric, sarcolemmal, desmosomal, ion channel, nuclear, and metabolic genes) and acquired disease (viral myocarditis, toxicity). We sought to evaluate a carefully phenotyped cohort of children for specific causative factors.

Methods: Blood from 160 probands enrolled in the Pediatric Cardiomyopathy Registry (PCMR) and myocardial specimens from 44 of these subjects was obtained and enrolled in the Pediatric Cardiomyopathy Specimen Repository. DNA was extracted from blood and primers generated for PCR analysis and direct DNA sequencing of the tafazzin gene (TAZ), which is known to cause Barth syndrome in boys. DNA and RNA were extracted from tissue and analyzed by polymerase chain reaction using primers generated to adenovirus, enterovirus, cytomegalovirus, Epstein-Barr virus, and parvovirus B19. Clinical and molecular details were correlated to define etiology.

Results: In 23% (37/160) of subjects screened for mutations in the X-linked gene TAZ, a variant was identified including 7% in males identified to be clinically affected with Barth syndrome. Other variants of uncertain significance were found in both males (25%) and females (22%) with pure hypertrophic cardiomyopathy (HCM, 20%), pure dilated cardiomyopathy (DCM, 24%), pure restrictive cardiomyopathy (30%), and mixed phenotypes (18%) and the absence of Barth syndrome. Myocardial analysis for viral genome was positive only for parvovirus B19 (13.6%, 6 of 44 subjects) and Epstein-Barr virus (4.5%, 2 of 44 subjects).

Conclusions: Viral myocarditis in children currently results most typically from parvovirus B19, as well as from Epstein-Barr virus. Adenovirus, CMV and enterovirus are rarely seen currently. The TAZ gene definitively causes childhood cardiomyopathy in small numbers of children with cardiomyopathy and Barth syndrome (7% of total cohort) but potentially affects a larger cohort of children with HCM and DCM (in up to 22%) without typical Barth syndrome.