

Cincinnati Children's Discovers Novel Genetic Cause of Cardiomyopathy

Clinical History and Presentation

In 2003, a 6-week-old infant was hospitalized with congestive heart failure in her native Trinidad and Tobago. Once stabilized, she was brought to the Heart Institute at Cincinnati Children's Hospital Medical Center for heart failure management and cardiac transplant evaluation by Robert Spicer, MD, medical director of Cardiac Transplantation in the Heart Institute.

Though the patient presented with signs and symptoms of congestive heart failure, her team of doctors would later discover she had a mitochondrial disorder, leading to the discovery of a new gene mutation.

Our Approach

The patient's initial battery of studies at Cincinnati Children's included ECGs, echocardiograms and a cardiac catheterization with angiography. The patient was diagnosed with cardiomyopathy secondary to left ventricular non-compaction, a type of idiopathic cardiomyopathy.

After a week-long hospitalization for testing and the initiation of new heart medications, Heart Institute specialists were able to stabilize the patient so that transplantation was not felt to be indicated. She returned to Trinidad and Tobago, where Dr. Spicer continued to follow the patient by email and telephone calls to her physicians.

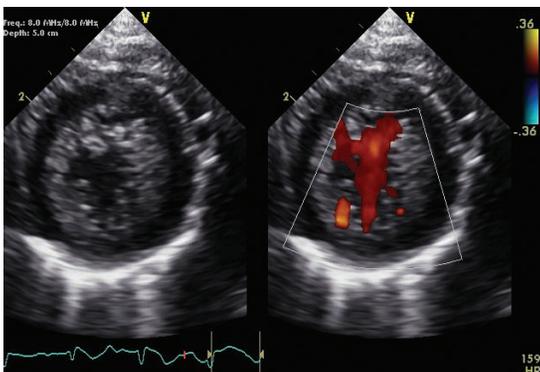
Follow Up by Multidisciplinary Team

After two years free from symptoms of congestive heart failure, the patient returned for multidisciplinary follow-up with specialists from neurology, genetics and cardiology, arranged by Cincinnati Children's Clinical Concierge service.

An echocardiogram revealed hypertrophic, non-compacted ventricular myocardium with improved, now low-normal left ventricular systolic function. In addition, she presented with delayed developmental milestones and generalized skeletal weakness, including the inability to stand up on her own.

Heart Institute geneticist Stephanie Ware, MD, PhD, evaluated the patient and recognized the symptoms as features commonly seen in mitochondrial disorders.

Under Dr. Ware's direction, the patient underwent metabolic screening tests as well as skin and muscle biopsies. Identifying the underlying etiology of mitochondrial disorders is challenging because there are many possible genetic causes with overlapping symptoms. Dr. Ware stayed in close contact with the testing laboratory in an effort to identify a precise genetic diagnosis in this patient with a suspected mitochondrial disorder.



These echocardiographic images demonstrate the characteristic hypertrophied and spongiform appearance of left ventricular non-compaction.

Cardiomyopathy Leadership

Jeffrey Towbin, MD
Co-Director
Pediatric Cardiologist

Stephanie Ware, MD, PhD
Co-Director
Clinical Geneticist

Cincinnati Children's is ranked in the top 10 for Heart Care and Heart Surgery and is one of only 10 pediatric hospitals in the United States included on the Honor Roll in U.S. News & World Report's 2009 edition of America's Best Children's Hospitals.

Results: A Novel Discovery

As a result of her persistence and open communication with the lab, Dr. Ware was able to confirm the patient had a mitochondrial disorder caused by a novel mutation in the mitochondrial genes ATPase 6 and 8. Identification of the etiology confirmed the best course of treatment for the patient, which included a vitamin cocktail to help improve mitochondrial function.

Identifying the underlying cause of the patient's mitochondrial disorder allowed for genetic testing of family members. The patient's mother was found to carry the gene mutations, and based on mitochondrial inheritance, was counseled that she had a very high recurrence risk for future pregnancies. The patient's maternal aunt was found to not carry the gene mutations and therefore does not share the same risk.

Since identification of this novel cause of mitochondrial disease in our patient, four other patients presenting with hypertrophic cardiomyopathy in infancy have been found to carry the same ATPase 6 and 8 mutation.

The patient, now age 6, sees her Heart Institute team of doctors twice a year. She continues to make slow progress in walking and jumping and does not currently have escalating heart problems. She remains on only one heart medication, Enalapril.

Impact on Care

Children with mitochondrial disorders can become gravely ill from minor illnesses and have an increased risk of developing vision and hearing loss as well as other complications. Finding a precise diagnosis allows the establishment of baseline evaluations for comprehensive care as well as anticipation and prevention of future problems.

Identification of etiology is important for clinical management and significantly impacts the prognosis and outcome of children with pediatric cardiomyopathy. Effort should be made to determine the cause of pediatric cardiomyopathy, including consideration of mitochondrial etiologies in infants presenting with cardiomyopathy.

Drs. Ware, Spicer and Erin Miller, MS, CGC, genetic counselor with the Heart Institute, published their findings in the May 2009 issue of the Journal of Medical Genetics.

Cardiomyopathy Clinic Referrals

To refer a patient to the Cardiomyopathy Clinic at the Cincinnati Children's Heart Institute, visit us online at www.cincinnatichildrens.org/cardiomyopathy or call Physician Priority Link at 1-888-636-7997 and ask for the attending cardiologist on call.