MedicalXpress

Genetic test offers clues about cardiac hypertrophy in children

April 9 2008

A mechanic uses diagnostic tests to determine why your engine is making strange sounds before lifting a wrench to fix the problem. Pediatric cardiologists would love to take a similar approach with patients experiencing cardiac hypertrophy—a thickening of the heart muscle. Rational treatment requires understanding the underlying causes of disease. But doctors know little about the causes of cardiac hypertrophy in children, so no diagnostic tests have yet been developed.

A new study—which appears online April 9 in the *New England Journal of Medicine*—might change that. Working with a team of researchers, Harvard Medical School Professors Christine Seidman and Jonathan Seidman discovered that some children with unexplained cardiac hypertrophy harbor mutations in the same 10 genes responsible for the condition in many adults.

“Labs have done work on the genetic underpinnings of cardiac hypertrophy in adults, but few thought that the research applied to children,” says Christine Seidman, who is also a member of the HMS-Partners HealthCare Center for Genetics and Genomics and an investigator with the Howard Hughes Medical Institute. Her lab is located at Brigham and Women’s Hospital. “For years, doctors assumed the two conditions were clinically distinct.”

According to Christine Seidman, 3 to 4 percent of adults have cardiac hypertrophy. Data from the Framingham Heart Study suggest that mutations in 10 genes—identified by the Seidmans and others—account

for 1/5 or 1/6 of those cases. Most of the genes implicated encode "sarcomere" proteins, which make up the heart's contractile apparatus. They literally help the muscle tighten and relax to pump blood.

"Cardiac hypertrophy increases your risk of all types of negative cardiovascular outcomes, including heart failure and sudden death," says Jonathan Seidman. "Although the condition is rare in children, the prognosis is even worse. Kids with cardiac hypertrophy are often candidates for heart transplantation."

The Seidmans worked with Amy Roberts, assistant professor of pediatrics at Children's Hospital Boston, and Jeffrey Towbin, a professor of pediatric cardiology at Baylor College of Medicine, to find children with cardiac hypertrophy. They extracted DNA from 84 individuals diagnosed with the condition before age 15. Just 33 of those children had family histories of cardiac hypertrophy.

Using a novel chip technology developed by molecular geneticist Heidi Rehm and others at the Harvard-Partners Center for Genetics and Genomics Laboratory for Molecular Medicine, they sequenced the 10 suspect genes. The chip allowed them to read tens of thousands of nucleotides—or letters of the DNA "alphabet"—for a fraction the cost of traditional technology.

The team identified mutations in 25 of the 51 children without family histories and in 21 of the 33 children with family histories.

"I think it's remarkable that we found mutations in nearly 50 percent of the kids who didn't have family histories," says Christine Seidman.

The team took a closer look at the genes of these patients' parents. Eleven pairs of parents agreed to participate in the study. In 7 cases, one parent harbored the same mutation as his or her child. Though these

adults assumed their hearts were fine, echocardiograms revealed thickening of the muscle in some cases.

“We still don’t know why the children presented symptoms so much earlier than their parents,” says Jonathan Seidman. “We suspect that other genes must influence the disease presentation.”

Further genetic testing of children and their parents could shed light on this and help doctors choose appropriate treatments.

“This study demonstrates that kids who present with sporadic cardiac hypertrophy deserve the same genetic test as adults,” says Christine Seidman.

Source: Harvard Medical School