Recently identified genetic heart disorder often deadly for young patients

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A study that included young patients with a recently recognized rare type of cardiomyopathy (a disorder of the heart muscle) linked to a genetic mutation finds that progression of this disease may be rapid and often results in early death, according to a study in the March 25 issue of *JAMA*.

Mutations in the lysosome-associated membrane protein gene (LAMP2; known as Danon disease) produce a cardiomyopathy in young patients that clinically is similar to severe hypertrophic cardiomyopathy (HCM; a condition in which the heart muscle becomes thick, making it harder for blood to leave the heart, forcing the heart to work harder to pump blood). However, the natural course of Danon disease has been unclear, according to background information in the article.

Barry J. Maron, M.D., of the Minneapolis Heart Institute Foundation, Minneapolis, and colleagues assessed the natural history associated with LAMP2 cardiomyopathy and the outcomes of diagnostic and management strategies. The study included seven patients (6 boys) who were ages 7-17 years at the time of diagnosis with LAMP2 mutations. Clinical diagnosis in 6 patients occurred as a result of a heart murmur, family screening and findings on routine electrocardiogram (ECG) or by symptoms (chest pain or fainting) and, in 1 patient, by atrial fibrillation (abnormal heart rhythm).

During the subsequent average time of 8.6 years after diagnosis, each of the 7 patients experienced serious adverse clinical consequences by 14 to

24 years of age (average, 21 years). Four patients died of acute or progressive heart failure, and 1 patient underwent heart transplantation. Clinical deterioration was often rapid, with the time interval from clinical stability with little or no symptoms to end-stage heart failure as brief as 6 months. Two other patients experienced sudden unexpected major arrhythmic events, with one patient dying suddenly (age 14 years) from ventricular fibrillation (very rapid, uncoordinated contractions of the ventricles) that was not responding to implantable cardioverter-defibrillator (ICD) therapy.

All seven patients developed left ventricular systolic (contraction of the left ventricle) dysfunction. All patients had received ICDs, which ultimately failed to terminate lethal ventricular tachyarrhythmias (an excessively rapid heartbeat accompanied by an irregular heartbeat) in five patients. The most recent echocardiographic studies obtained of the patients demonstrated marked left ventricular hypertrophy (enlargement) in each. Postmortem examination of 2 hearts showed massive cardiac hypertrophy.

"The clinical course of these 7 patients with LAMP2 mutations provides important insights regarding molecular diagnosis as well as the natural history, pathophysiology, and clinical implications of this recently recognized genetic cardiomyopathy. LAMP2 mutations cause a particularly profound and accelerated cardiac disease process characterized by clinical deterioration and early death, perhaps representing one of the most lethal cardiomyopathies in young and usually male patients. Such an outcome occurred in the patients in our study despite application of the most contemporary treatment strategies, including the ICD …" the authors write.

"The early experience with the distinctive natural history and prognosis of patients with LAMP2 mutations establishes the importance of molecular diagnosis and underscores the utility of genetic testing."

More information: JAMA. 2009;301[12]:1253-1259.

Source: JAMA and Archives Journals (news : web)