Investigation of unexplained left ventricular hypertrophy

The genes responsible for unexplained ventricular hypertrophy are slowly being recognised. Abnormal fibrillary proteins including desmin, heavy chain myosin, tropomyosin, and troponin are responsible for the phenotype we call hypertrophic cardiomyopathy. A very similar cardiac morphology can be produced by storage disorders with glycogen or galactose but systemic abnormalities are present to point to the diagnosis. The study reported below, however, shows that among 270 patients with echocardiographic left ventricular hypertrophy without any systemic disorder seven had plasma and lymphocyte activity of α-galactosidase enzyme far below the normal range. Cardiac biopsy and study of the gene confirmed heterozygous Fabry's disease. Subclinical manifestation of Fabry's disease therefore has to be considered in the differential diagnosis of unexplained left ventricular hypertrophy but this involves either cardiac biopsy with electron microscopy or assay of plasma concentrations of an enzyme that is not likely to figure in the tests offered by most laboratories.

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An atypical variant of Fabry's disease in men with left ventricular hypertrophy

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Background—Fabry's disease is an X-linked recessive disorder that results from a deficiency of α-galactosidase. Left ventricular hypertrophy is one of the common manifestations in men with classic hemizygous disease. Recently, several cases of an atypical variant of hemizygous Fabry's disease, with manifestations limited to the heart, have been reported. Therefore, we assessed the incidence of hemizygosis for Fabry's disease among male patients with left ventricular hypertrophy.

Methods—We measured plasma α-galactosidase activity in 230 consecutive male patients with left ventricular hypertrophy. Clinical manifestations were assessed, endomyocardial biopsies were performed, and the patients were screened for mutations in the α-galactosidase gene.

Results—Seven of the 230 patients with left ventricular hypertrophy (3 percent) had low plasma α-galactosidase activity (4 to 14 percent of the mean value in normal controls). These seven unrelated patients, ranging in age from 55 to 72 years, did not have angiorteromas, acroparesthesias, hypohidrosis, or corneal opacities, which are typical manifestations of Fabry's disease. Endomyocardial biopsy was performed in five patients and revealed marked sarcoplasmatic vacuolization in all five. Samples from four patients were examined by electron microscopy and revealed typical lysosomal inclusions with a concentric lamellar configuration in all four. Two patients had novel missense mutations in exon 1 and exon 6. The remaining five had no mutations in the coding region of the α-galactosidase gene, but the amounts of the α-galactosidase messenger RNA were markedly lower than normal.

Conclusions—Seven unrelated patients with atypical variants of hemizygous Fabry's disease were found among 230 men with left ventricular hypertrophy. Fabry's disease should be considered a cause of unexplained left ventricular hypertrophy.