Idiopathic Hypertrophic Cardiomyopathy in Identical Twins

Morphological Heterogeneity of the Left Ventricle


We report a pair of identical twins with HC with varying extent of left ventricular hypertrophy and some degree of left ventricular outflow tract obstruction. The diagnosis of identical twins was based on the same sex, blood typings, HLA typings and hybridization patterns to four hypervariable DNA probes. Identical twins are derived from a single zygote and are genetically homogeneous human beings.

Hypertrophic cardiomyopathy is a myocardial disease characterized by a hypertrophic, nondilated LV of unknown etiology. In most patients, this clinical entity occurs familial with an autosomal dominant pattern of inheritance. Within the same family of HC, however, the morphologic appearance of LV hypertrophy in affected relatives may be markedly dissimilar. Identical twins are derived from a single zygote and are genetically homogeneous human beings. We present a pair of identical twins with HC in whom different extents of LV hypertrophy and outflow tract obstruction were noted.

CASE REPORTS

CASE 1

A 35-year-old man, the first twin, was first referred to our hospital following discovery of a heart murmur during routine health examination. He was asymptomatic, and the family history was unremarkable. On admission, the blood pressure was 120/90 mm Hg and the pulse was regular at 72 beats per minute. Cardiac examination revealed a forceful apical impulse and a grade 3/6 systolic ejection murmur best heard along the left sternal border and at the apex. The electrocardiogram showed tall R waves with mild T wave inversions in leads V1 and V6, consistent with LV hypertrophy and strain. A peak systolic pressure gradient of 67 mm Hg across the LV outflow tract was noted at cardiac catheterization, and biplane ventriculography revealed a markedly thickened ventricular septum. A diagnosis of idiopathic hypertrophic subaortic stenosis was made and orally administered verapamil was prescribed.

CASE 2

A 35-year-old man, the second twin, was born 10 min earlier than his brother. He also had no symptoms, and was admitted for the family survey of HC. His facial appearance and body build were quite similar to those of patient 1. The blood pressure was 120/90 mm Hg and pulse rate was regular at 78 beats per minute. A grade 2/6 systolic ejection murmur was best heard along the left lower sternal border. The chest roentgenogram showed a borderline enlarged heart size. The electrocardiogram revealed tall R waves and giant negative T waves in leads V1 and V6. There was no pressure gradient across the LV outflow tract at cardiac catheterization. Biplane ventriculography showed thickening of the midventricular septum that bulged into the LV cavity during systole. A diagnosis of HC was established, and therapy with orally administered verapamil was begun.

Neither patient had had echocardiographic examinations until five years later when they were 40 years of age and were still asymptomatic. The M-mode echo of patient 1 showed asymmetrical septal hypertrophy, systolic anterior motion of the mitral valve and mid-systolic closure of the aortic valve. The thicknesses of the ventricular septum and the posterior wall were 19 and 13 mm, respectively. Two-dimensional echo on the short axis view at the mitral valve level revealed LV hypertrophy involving both the anterior and posterior parts of the ventricular septum as well as the anterolateral free wall (Fig 1, A). A continuous-wave Doppler study demonstrated a peak systolic pressure gradient of 50 mm Hg across the LV outflow tract. In the twin brother, patient 2, however, neither systolic anterior motion of the mitral valve nor mid-systolic closure of the aortic valve was noted on the M-mode echo. The hypertrophy of the LV of patient 2 was limited to the anterior ventricular septum (18 mm) and the anterolateral free wall (18 mm). The thickness of the posterior septum and the posterior free wall were normal (Fig 2, A). The space of the LV outflow tract was relatively large, and no pressure gradient across the LV outflow tract was noted with a Doppler echocardiographic study. The morphologic heterogeneity of the LV in the twin brothers was further confirmed by MRI. The MRI on the short axis view at the mitral valve level revealed diffuse hypertrophy of the ventricular septum in patient 1 and normal thickness of the posterior ventricular septum in patient 2 (Fig 1, B and 2, B). In addition, in the coronal section of patient 1, the ventricular myocardiad was found to be protruding into the LV outflow tract just below the aortic valve level, which was not found in the same section of patient 2 (Fig 1, C and 2, C).

These two brothers were confirmed to be monozygotic (identical) twins based on the same sex (male), blood typing (blood group A and Rh positive), HLA typing (HLA-A1, A2, A3, B1, B2, CW1, CW2) and hybridization patterns to four hypervariable DNA probes (D14S1, α-globin-3'-HVR, insulin-3'-HVR, C-Ha-ras-3'-HVR).

DNA = deoxyribonucleic acid; HC = hypertrophic cardiomyopathy
FIGURE 1. Two-dimensional echocardiogram (A) and MRI results (B, C) of patient 1. The figures illustrate diffuse hypertrophy of the LV at the mitral valve (MV) level on the short axis view (A, B) and protrusion of the ventricular myocardium into LV outflow tract in the coronal section (C). Arrows indicate the posterior septum and arrowheads indicate part of the borders of endocardium and epicardium.

**DISCUSSION**

The morphologic patterns of LV in identical twins with HC are described. Although diffuse LV hypertrophy involving the ventricular septum and the anterolateral free wall was noted in both, detailed analysis using two-dimensional echocardiography revealed some differences in the extent of LV hypertrophy and obstruction of the LV outflow tract. Magnetic resonance imaging, known to provide another means of

FIGURE 2. Two-dimensional echocardiogram (A) and MRI results (B, C) patient 2. In contrast to findings on patient 1, the figures show asymmetrical hypertrophy of the ventricular septum at the mitral valve (MV) level with normal thickness of the posterior septum (arrows) (A, B) and no protrusion of ventricular myocardium into left ventricular outflow tract in the coronal section (C). Arrowheads indicate part of the borders of endocardium and epicardium.
accurately depicting the site and extent of myocardial hypertrophy, further confirmed the morphologic heterogeneity of the LV in the twin brothers. Six pairs of identical twins with HC have been described in the literature. Littler reported the first two pairs of identical twins; the clinical courses were markedly different in one pair, but no morphologic study using echocardiography was performed. Clark et al described a pair of identical twins with asymmetrical septal hypertrophy and identical septal thickness. With a detailed two-dimensional echocardiographic analysis, Cirò et al found the same ventricular morphology in two pairs of identical twins. Recently, Reid et al reported another pair of identical twins showing differences in clinical symptoms, patterns and extent of LV hypertrophy as well as outflow tract obstruction. It is likely that heterogeneity in morphologic expression of the LV is not uncommon in identical twins with HC.

Difference of LV hypertrophy in identical twins with HC cannot be attributed to genetic factors. Identical twins are derived from a single zygote that separates into two embryos during an early developmental stage; their birth provides an unusual opportunity for observing two genetically homogeneous human beings. Since there is no genetic distinction between these twins, observed differences in phenotype can be considered environmental in origin. In the patients reported here, the only observed difference is the presence of outflow tract obstruction in the younger brother, which may further aggravate with time the extent and degree of previous LV hypertrophy. Hypertension, valvular heart disease and other congenital defects of the heart usually are associated with LV hypertrophy, but such was not the case for these twin brothers. Outflow tract obstruction may not be the sole hemodynamic factor that causes heterogeneity in morphologic expression of HC.

Recently, the genetic locus of familial HC in one large Canadian family was mapped to chromosome 14q1 by molecular genetic techniques. Further studies have revealed that familial HC is a genetically heterogeneous disorder; the genetic defect in some families is located on the β cardiac myosin heavy chain gene. Chromosome 18q has also been reported as possible genetic loci for familial HC. Future discovery of more defective genes, as well as better understanding of the molecular pathophysiology, should lead to unraveling the cause and course of this disease.

REFERENCES
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