PROGRESSION FROM HYPERTROPHIC OBSTRUCTIVE CARDIOMYOPATHY TO TYPICAL DILATED CARDIOMYOPATHY-LIKE FEATURES IN THE END STAGE

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An autopsied patient who had shown typical dilated cardiomyopathy (DCM)-like feature in the end stage of familial obstructive hypertrophic cardiomyopathy (HCM) is presented. The patient, a 38-year-old male, had 2 sisters with HCM. Six years before death, the echocardiogram revealed asymmetric septal hypertrophy (ASH) with systolic anterior motion (SAM). The ventricular septum (VS) to left ventricular posterior wall (LVPW) ratio was 19 mm/10 mm and LVEDd was 47 mm. Subsequently, the signs and symptoms of congestive heart failure became progressively worse and DCM-like findings appeared insidiously. Two months before death, the echocardiogram revealed LV dilatation (LVEDd = 55 mm) with diffuse poor contraction, no ASH (VS/LVPW = 7 mm/9 mm) and no SAM.

At autopsy, the heart weighed 480 g and showed dilated LV hypertrophy with normal wall thickness (VS/LVPW = 9 mm/13 mm). Massive fibrosis (30% in the VS), diffuse disarray (18% in the VS) and severe narrowing of the intramural small arteries and arterioles were found in the middle and outer thirds of the VS and the anterior LV wall. The extramural coronary arteries were not stenosed.

The insidious progression from HCM to typical DCM-like feature related to the chronic progression of necrosis and massive fibrosis, due to severe stenosis of the intramural coronary artery. The data indicate that patients diagnosed clinically as DCM may be HCM, especially in those with family history of HCM.

Key Words:
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In most patients with hypertrophic cardiomyopathy (HCM), dilatation of the left ventricular (LV) cavity and disappearance of asymmetric septal hypertrophy (ASH) do not occur in the clinical course, even in the end stage in patients with congestive heart failure. Therefore, HCM and dilated cardiomyopathy (DCM) are considered to be different diseases. However, Maron et
Fig. 1. Echocardiographic findings.
Echocardiogram at the age of 32 years (1977) showed marked asymmetric septal hypertrophy (ASH), systolic anterior motion (SAM: arrows of the lower panel) and no dilatation of the left ventricular (LV) cavity. The degree of ASH decreased and the LV dimension increased slightly at the age of 34 years (1979). Echocardiogram at the age of 38 years (1983) revealed disappearance of ASH, paradoxical movement of the ventricular septum (VS) and dilatation of the LV cavity. PW = left ventricular posterior wall; MV = mitral valve.

A Japanese man aged 38 years at the time of death had had dyspnea on effort, of 18 years duration. His two sisters had HCM, with or without obstruction. Six years before his death, the echocardiogram revealed marked ASH, systolic anterior motion (SAM) and no dilatation of the LV (left ventricular enddiastolic dimension = DVEDd: 47 mm) (Fig. 1). The wall thickness was 19 mm in the ventricular septum (VS) and 10 mm in the left ventricular posterior wall (LVPW). LV hypertrophy was noted on the ECG (Fig. 2) and chest X-ray (CTR = 62%). Thereafter, the signs and symptoms of congestive heart failure including dyspnea, palpitation, edema, congestion of the lungs and pleural effusion in the chest X-ray, worsened, although the patient had been treated with digitalis and diuretics. Four years before death, the echocardiogram showed mild ASH (VS/LVPW = 13 mm/8 mm), disappearance of SAM, and mild dilatation of the LV cavity (LVEDd: 51 mm) with poor motion (Fig. 1). Intact coronary arteries, diffuse poor contraction of the LV, increase of LV enddiastolic pressure (23 mmHg) and no systolic pressure gradient in the LV were evident at the time of cardiac catheterization. Hypertrophied myocytes with diffuse disarray and fibrosis were noted in the endomyocardial biopsy from the right ventricular septum.

Two months before death, multiple thromboembolism suddenly appeared in the cerebral and renal arteries. The echocardiogram revealed moderate dilatation of the LV cavity (LVEDd: 55 mm), disappearance of ASH (VS/LVPW = 7 mm/9 mm), paradoxical movement of the VS, poor contraction of the LVPW and no SAM (Fig. 1). The patient died of cerebral infarction and acute renal failure. He had had no chest pain, syncopal attack or hypertension.

At autopsy, the heart weighed 480g and showed dilated hypertrophy in the LV, right
Fig. 2. Electrocardiographic findings.
ECG at the age of 32 years (upper) showed left ventricular hypertrophy (LVH), left axis deviation and large P wave. Left axis deviation and large P wave disappeared in ECG at the age of 34 years (middle). ECG at the age of 38 years (lower), 2 months before death, reveals LVH and atrial fibrillation.

Fig. 3. Macroscopic findings of the autopsied heart and distributions of fibrosis and disarray.
left: longitudinal section of the heart showing considerable dilatation of both the right (RV) and left ventricular (LV) cavities.
right: transverse section of the LV at the level of the mitral leaflets, showing the extents of fibrosis (dark areas) and disarray (dotted areas).
The extent of fibrosis was traced at the magnification of x10 in the 4μ-thick preparation stained with Masson-Trichrome and the extent of disarray was traced at the magnification of x40 in the 25μ-thick preparation stained with hematoxylin eosin. Quantitative analysis was done using image analyzer (Olympus VIP-21). Transmural massive fibrosis and diffuse disarray are seen in the ventricular septum (VS) and the anterior LV wall. Note that the most of the fibrosis is present in the middle and outer thirds of the LV wall. In the VS, fibrosis was accounted for 30% and disarray for 18%.
ventricle and left atrium (Fig. 3). The wall thickness was 9 mm in the VS and 13 mm in the LVPW and the LV diameter was 42 mm. These data coincided with the echocardiographic findings in the end systole two months before death. The extent of fibrosis and disarray is shown in

Fig. 4. Microscopic findings.
A: small artery with stenosis due to intimal thickening in the ventricular septum (VS) (elastica Van Gieson x100)
B: arterioles with stenosis in the VS (elastica Van Gieson x200)
C: myocardial fascicular disarray in 25 μ thick section (hematoxylin eosin x40)

Fig. 3. Massive transmural fibrosis (30% in the VS), diffuse disarray (18% in the VS) and narrowing of the intramural small arteries and arterioles (Fig. 4) were localized in the VS and the anterior LV wall, mostly in the middle and outer thirds of the LV wall. Mural thrombi were present in the

left atrium, whereas coagulation necrosis was not evident and the extramural coronary arteries were not stenosed.

The clinical and macroscopic pathological findings at the end stage were typical of those seen in DCM. However, the familial history, the echocardiographic findings observed for 6 years and the presence of diffuse disarray of 18% in the VS4-6 indicated that this man had HCM with obstruction. Massive and transmural fibrosis is unusual in HCM and DCM. We reported that an increase of transmural muscle layers in the VS was the pathogenesis of ASH. The incisive disappearance of ASH and dilatation of the LV with progressive congestive heart failure were related to the decrease of transmural muscle layers following necrosis of myocytes, and the chronic progression of fibrosis in the VS and anterior LV wall.

Systemic thromboembolism, probably thrombi from the left atrium, was first noted 2 months before death. The hypertrophy of the VS was not marked, even 6 years before death, compared to findings in usual cases of HCM4-6. The patient had no syncopal attack or chest pain and extramural coronary arteries were not stenosed. These findings indicated that thromboembolism, a brief period of hypoxia or hypotension and hypertrophy in the VS are untenable for the pathogenesis of chronic progressive massive fibrosis. Also, spasms of major coronary arteries were excluded, because massive fibrosis was mostly present in the middle and outer thirds of the LV wall. The most plausible cause of the massive fibrosis in the VS and anterior LV wall was multiple ischemia in these regions, following narrowing of the intramural small coronary arteries which is sometimes seen in the patients with HCM. Vasospasm of intramural coronary arteries was also considered. The distribution of massive fibrosis in this case coincided with that of disarray seen in the usual HCM4-6. Therefore, it is likely that the tissue areas with disarray contained the stenosed coronary arteries and the myocytes were replaced by massive fibrosis. In light of these findings, patients diagnosed clinically as having DCM may be have HCM with diffuse transmural fibrosis, especially those with family members who have HCM.

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REFERENCES

7. FUJIWARA H, HOSHINO T, YAMANA K, FUJIWARA T, FURUTA M, HAMASHIMA Y, KAWAI C: Number and size of myocytes and amount of interstitial space in the ventricular septum and in the left ventricular free wall in hypertrophic cardiomyopathy. Am J Cardiol 52: 818, 1983

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