Necropsy Finding in a Patient with Apical Hypertrophic Cardiomyopathy

Seiichi Sumino, M.D., Tsuneaki Sugimoto, M.D., Tadashi Koide, M.D., and Satoru Murao, M.D.

SUMMARY

Whether apical hypertrophic cardiomyopathy is a variant of classic hypertrophic cardiomyopathy or a separate entity is controversial. This is a case report of an apical hypertrophic cardiomyopathy. The patient was a 67-year-old man associated with giant negative T waves in electrocardiogram and asymmetric apical hypertrophy on echocardiogram. He died of liver cirrhosis and liver cell carcinoma. At necropsy the heart showed apical hypertrophy grossly and extensive disarray of myocardial fibers near the apex of the left ventricle histologically. The necropsy findings were indistinguishable from those of classic hypertrophic cardiomyopathy. This suggests that apical hypertrophic cardiomyopathy is a variant of hypertrophic cardiomyopathy.

Additional Indexing Words:
Giant negative T wave Asymmetric apical hypertrophy Myocardial disarray

It is still controversial whether apical hypertrophic cardiomyopathy (AHCM), as originally described in Japan,1,2 is a variant of classic hypertrophic cardiomyopathy (HCM) or a separate entity. Particularly since little is known about the histologic changes of the myocardium, except for the biopsy findings in several patients.2,3 Although a study including necropsy in 2 cases has been reported by Maron and his associates,4 the clinical and angiographic findings in their cases were apparently different from those of typical Japanese cases. The present article deals with the necropsy findings of a case of a Japanese with AHCM.
CASE REPORT

A 67-year-old Japanese business man was admitted to the University of Tokyo Hospital on February 18, 1976, because of easy fatigability, pretibial edema and electrocardiographic abnormalities. His past and family histories were noncontributory, except for pulmonary tuberculosis and left upper lobectomy complicated by serum hepatitis at age 52. No electrocardiographic abnormality was found at the time. In 1974 when he had recurrent episodes of exertional precordial oppression an electrocardiographic abnormality suggesting "myocardial ischemia" was found by his family doctor. The electrocardiographic change persisted thereafter. Blood pressure was normal throughout his clinical course. Easy fatigability and pretibial edema developed later, and he was referred to one of us.

On admission, he was 163 cm in height and 53 Kg in weight. He was afebrile, heart rate was 72/min and regular and blood pressure was 130/70 mmHg. The jugular vein was not distended. There were no spider angiomas. Left upper thorax was thin and deformed. On auscultation, fixed splitting of S2, an early diastolic click and grade 3/6 ejection systolic murmur were heard along the left sternal border. There were no rales. A firm liver was palpable 2 cm below the costal arc. Pretibial edema was not present at the time of admission. Urinalysis was normal. On hematology, hemoglobin was 12.4 Gm/dl, RBC 362×10^4/cmm, hematocrit 37.7% and WBC 3600/cmm with normal differentials and platelets 7.6×10^4/cmm. On serum chemistry, total protein was 7.0 Gm/dl of which 20.6% was gamma globulin, cholesterol 157 mg/dl, BUN 13 mg/dl, uric acid 7.3 mg/dl, creatinine 0.81 mg/dl, amylase 274 U, Na 142 mEq/L, K 4.0 mEq/L, Cl 106 mEq/L, Ca 8.8 mg/dl, GOT 61 U, GPT 21 U, LDH 250 U, alkaline phosphatase 5.6 U, gamma-GTP 20 U, LAP 141 U and choline esterase 0.63 U. ICG retention was 26.5% and alpha-fetoprotein was 80 ng/ml. On serological examinations, TPHA and bentonite tests were positive, but CRP and HBs antigen were negative. Erythrocyte sedimentation rate was 8 mm/h. Chest X-ray revealed a thoracic deformity secondary to pulmonary lobectomy and leftward shift of the mediastinum. The cardiac shadow was apparently normal. Electrocardiogram revealed incomplete right bundle branch block, left high voltage of the QRS complex and ST-T changes. T waves were inverted in leads II, III, aVF and V3 through V6 and exceeded 1 mV in leads V4 and V5. An episode of paroxysmal atrial fibrillation was confirmed during admission, at which time the patient had precordial oppression (Fig. 1a). Exercise stress testing was negative. On echocardiography, the apical region of the interventricular septum was thickened to 20 mm and the posterior wall to
Fig. 1a (upper). Electrocardiogram showing high QRS voltage, ST depression and the giant negative T waves (more than 1.2 mV in V4) in the left precordial leads. Paroxysmal atrial fibrillation was confirmed when the patient had precordial oppression. 1b (lower). M-mode echocardiogram. The thickness of the interventricular septum/posterior wall was 12 mm/12 mm in the mid ventricle portion and 20 mm/18 mm near the apex.

18 mm. The upper interventricular septum and the left ventricular posterior wall were not hypertrophied (12 mm). Left ventricular wall movement, including the apex was normal (Fig. 1b). Right heart catheterization revealed a normal cardiac index (3.0 L/min/m²) and normal pressures. Liver scin-
Fig. 2a (upper). Reconstruction of outflow tract of the left ventricle in the longitudinal section at necropsy. The heart showed an apical hypertrophic pattern which resulted in the left ventricular cavity narrowing in the apical portion. 2b (middle). There were hypertrophied myocardium, disorganized architecture and "whirl" formation of the myocardial fibers in association with interstitial fibrosis at the interventricular septum near the apex (hematoxylin-eosin stain ×90). 2c (bottom). A large thick abnormally branched myofibre from the same area (scanning electron microscope ×380).
tigraphy revealed hepatosplenomegaly and visualization of the bone marrow. A fine nodular liver was seen on laparoscopy.

The patient was discharged on March 22, 1976 with a clinical diagnosis of liver cirrhosis and hypertrophic cardiomyopathy. His subsequent course was apparently stable until December, 1977, when he was readmitted because of epigastralgia and abdominal fullness. On the second admission anemia (hemoglobin 6.3 Gm/dl), ascites and leg edema were prominent. His GOT was 276 U, GPT 72 U, bilirubin 2.39 mg/dl and alpha-fetoprotein 1,740 ng/ml. Ascites was hemorrhagic. There was an abnormal accumulation of $^{67}$Ga in the liver. Cardiologic findings were essentially the same as on the first admission. Hepatic coma developed in April, 1978 and the patient died on April 8, following massive hematemesis. The final clinical diagnosis was liver cirrhosis, liver cell carcinoma and hypertrophic cardiomyopathy.

**Pathology**

At necropsy the position of the heart was normal despite left upper lobectomy. Heart weight was 340 Gm and was normal relative to his height. The left ventricular cavity was banana-shaped because of the catenoid-shaped interventricular septum and was narrowed apically because of thick papillary muscles and trabeculae (Fig. 2a). The thickness of the interventricular septum and free wall was normal (compact muscle layer 11–13 mm). However, the thickness of the apical region was equal to or more than that of the base or mid ventricle, differing from the controls (Table I).

<table>
<thead>
<tr>
<th>tissue location</th>
<th>percent area of myocardial disarray*</th>
<th>wall thickness (mm)**</th>
<th>wall thickness (mm)**</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IVS A and LW</td>
<td>PW</td>
<td>present case</td>
</tr>
<tr>
<td>basal</td>
<td>7% 5% 0</td>
<td>11 11 11</td>
<td>14.8±2.5 13.6±1.7 12.7±2.1</td>
</tr>
<tr>
<td>mid ventricular</td>
<td>12% 21% 6%</td>
<td>13 13 11</td>
<td>13.3±1.9 12.4±2.3 11.4±1.6</td>
</tr>
<tr>
<td>apex</td>
<td>27% 18% 22%</td>
<td>12 13 12</td>
<td>11.2±2.3 11.8±2.1 11.6±1.8</td>
</tr>
<tr>
<td>wall thickness ratio</td>
<td></td>
<td></td>
<td>1.10 1.18 1.10</td>
</tr>
<tr>
<td>apex/base</td>
<td>0.92 1.00 1.09</td>
<td>0.84 0.95 0.91</td>
<td></td>
</tr>
</tbody>
</table>

* Percent area of myocardial disarray was measured by Maron's method.4) ** The wall thickness was measured on the longitudinal section of the heart and did not include trabeculations, papillary muscles and the crista supraventricularis. *** The controls were 20 consecutive Japanese male cadavers over 60 years of age, without cardiovascular disease, and with the heart weight within 10% of the present case. IVS=interventricular septum; A and LW=anterior and lateral wall of the left ventricle; PW=posterior wall of the left ventricle.
no evidence of left ventricular outflow tract obstruction. The other cardiac chambers were slightly dilated. Cardiac valves, great vessels and the pericardium were normal. No significant stenosis was present in the extramural coronary arteries.

Microscopically, disarray and whirling of thick (more than 35 μm in diameter) myocardial fibers and patchy interstitial fibrosis were extensive near the apex, in both the interventricular septum and the left ventricular free wall (Fig. 2b). Occasional muscle fibers had bizarre-shaped nuclei. Myofibrillar dissolution was not seen. Similar lesions were seen also in the upper interventricular septum, but were less extensive when measured by Maron’s method5) (Table I). Many bizarre-shaped and hypertrophied muscle cells were identified in the septal tissue by scanning electron microscopy after isolation with EDTA treatment (Fig. 2c). Other pathologic findings included a huge hepatic cell carcinoma in a cirrhotic liver and ruptured esophageal varices.

DISCUSSION

AHCM2) or asymmetric apical hypertrophy,1) as originally described in Japan, is a clinical syndrome in which left ventricular hypertrophy is restricted mainly to the apical region and the apical left ventricular cavity is narrowed. This form of the left ventricular cavity is characteristically of spade-like appearance on RAO angiogram.2) The syndrome is associated with a tendency toward deep inversion of left precordial T waves, which frequently exceed 1 mV (giant negative T wave) on electrocardiogram.1) Whether this syndrome is a variant of classic HCM or a separate entity is still controversial. The syndrome is seen mostly in elderly men3),6) and a dominant mode of inheritance is unlikely.6) While these features suggest some difference between AHCM and HCM, little is known about the myocardial histology. Although Maron and his associates4) reported 2 necropsy cases with AHCM which had histologic findings indistinguishable from those of classic HCM except for the location of the lesion, these cases were young siblings from a family with other cases of typical HCM. In addition, they had neither giant negative T waves nor spade-like left ventricular cavities, and thus were atypical of AHCM. Results of biopsy study in several typical cases of AHCM have also been reported,2),3) but these were conflicting and inconclusive. The present case was a typical case of AHCM clinically. The clinical suspicion was apparently supported by the gross anatomical findings. On the other hand, the histologic findings of the myocardium shared some characteristic features with classic HCM. Myocardial disarray and fibrosis were extensive near the apex and thick and bizarre-shaped myocardial cells were present in the septal
tissue. Although myocardial disarray is seen normally in the apical region,\textsuperscript{7,8} the area is usually limited and less extensive than in the present case. The necropsy findings were thus similar to those reported by Maron and his associates\textsuperscript{4} for the less typical cases of AHCM and were indistinguishable from those of classic HCM, except for the location of the lesion. Probably AHCM is a variant of HCM, in which the localization of the lesion is confined mainly to the apex.

**Acknowledgments**

We are grateful to Prof. Y. Urano of the Department of Pathology, University of Tokyo, for the necropsy and suggestions and to Prof. K. Kawamura of the Third Department of Internal Medicine, Osaka Medical School, for the scanning electron micrograph.

**References**