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Case reports

Hypertrophic cardiomyopathy simulating an infiltrative myocardial disease

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SUMMARY Congestive heart failure developed in a patient with low electrocardiographic QRS voltages, diffuse thickening of the septum and free cardiac wall, and a reduction in left ventricular internal diameter, which suggested an infiltrative heart muscle disease. Histological examination at necropsy showed hypertrophic cardiomyopathy with symmetrical left ventricular hypertrophy. Myocardial disarray of type 1A disorganisation was extensive and equally distributed in the ventricular septum and the left anterior and left posterior ventricular free walls. Severe fibrosis (40%) was also present and may have been a possible cause of the electrocardiographic abnormalities as well as of the lack of ventricular dilatation.

Hypertrophic cardiomyopathy, particularly at an advanced stage, manifests physical signs[1 2] and electrocardiographic[3] and echocardiographic[4] changes, which aid in the clinical diagnosis. Congestive heart failure may complicate advanced hypertrophic cardiomyopathy and make the diagnosis more difficult.

We report a patient with congestive heart failure in whom electrocardiographic and echocardiographic changes suggested an infiltrative heart muscle disease and histological examination at necropsy showed typical features of hypertrophic cardiomyopathy with symmetrical left ventricular hypertrophy.

Case report

A 70 year old man was admitted because of congestive heart failure. For the previous two months he had complained of fatigue and dyspnoea, which were progressive and accompanied by oedema in the lower limbs and ascites. His clinical and family histories were unremarkable: in particular he denied any previous history of systemic hypertension or heart murmurs or instance of sudden death in first degree relatives.

Previous chest radiographs and electrocardiograms were unavailable. On physical examination he was in great distress with anasarca and jugular venous congestion. His heart rate was regular at 110 beats/min. The heart sounds were muffled and a gallop rhythm was present. No cardiac murmurs were heard. Blood pressure was 100/80 mm Hg. Chest radiographs showed mild cardiomegaly, pulmonary congestion, and a bilateral pleural effusion. Renal function tests and examination of the ocular fundus were normal, and possible cardiac damage secondary to chronic high blood pressure was excluded.

An electrocardiogram (Fig. 1a) showed low QRS voltages, first degree atrioventricular block (PR interval 0·26 ms), and poor progression of the R wave in the right precordial leads. Cross sectional echocardiography (Fig. 1b) showed diffuse severe thickening of the interventricular septum as well as of the left and right ventricular free walls. The left ventricular end diastolic dimension was reduced (37 mm); the right ventricular maximum dimension assessed in the four chamber apical projection was 27 mm. Mild left ventricular hypokinesia was present. Left and right atrial sizes were within normal limits. The inferior vena cava and hepatic veins were dilated. An M mode echocardiogram showed anterior motion of the mitral valve leaflet and a reduced E-F slope; systolic motion was normal. Tricuspid, aortic, and pulmonary valve movement was normal. The thickness of the interventricular septum and the posterior wall was 23 mm at the level of the mitral valve tip and papillary muscles.

Because of the congestive heart failure, treatment with digoxin 0·125 mg/day, diuretics (frusemide 25

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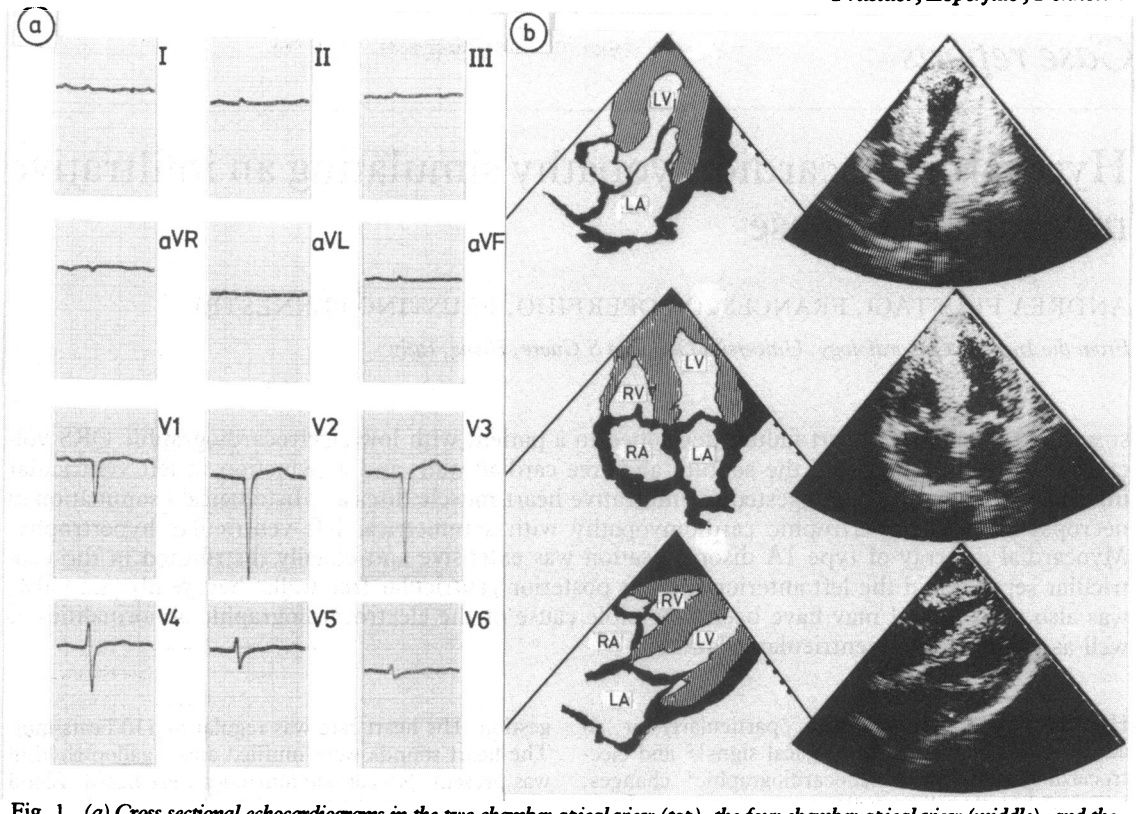

Fig. 1 *(a) Cross sectional echocardiograms in the two chamber apical view (top), the four chamber apical view (middle), and the four chamber subxiphoid view (bottom) showing diffuse thickening of the septum and ventricular free walls and a small left ventricular cavity. (b) Standard electrocardiogram showing first degree atrioventricular block, low QRS voltages in the peripheral leads, and poor progression of R wave in the right precordial leads.*

mg/day and spironolactone 100 mg/day), and salt free albumin 25 g/day was started. Seven days later the patient's clinical condition improved. The ascites and peripheral oedema disappeared and the pleural effusion was no longer visible on radiographs. The electrocardiographic abnormalities were unchanged and the heart rate was reduced to 85 beats/min. A ventricular endomyocardial biopsy was not undertaken as the patient suffered a stroke and died on the tenth day of admission.

NECROPSY FINDINGS

On macroscopic examination the heart was hypertrophied and firm to the touch. The hypertrophy was concentric, the septum and posterior and lateral free walls each measuring 23 mm at mid-ventricular level. The left ventricular cavity was reduced in size, but the right one was normal. The atrioventricular valves were thickened along the free margin. The endocardium showed no abnormality. Apart from minor arteriosclerotic thickening, the coronary arteries were normal. No necrotic or fibrotic areas were seen.

Histological examination

Method—Tissue sections were taken from the septum and the anterior and posterior left ventricular free walls about halfway between the aortic valve and left ventricular apex. In the anteroposterior plane the tissue sections were obtained from the full thickness of the ventricular septum, the anterior left ventricular free wall about 2 cm from the left anterior descending coronary artery, and the posterior left ventricular free wall between the papillary muscles. All tissue specimens were fixed in 10% formalin and embedded in paraffin. Five micrometre thick sections were cut on a base sledge microtome and stained with haematoxylin and eosin, Miller's elastic van Gieson stain,[5] and congo red (for amyloid). The diameter of the myocardial fibres in the area of the nucleus was measured at a magnification of ×460. The interstitium was measured using a grid and point counting system.[6] Cardiac muscle cell disorganisation was quantified using Maron's grading system.[7]

Findings—In the middle layer of the myocardial wall, the septum, and the left anterior and posterior

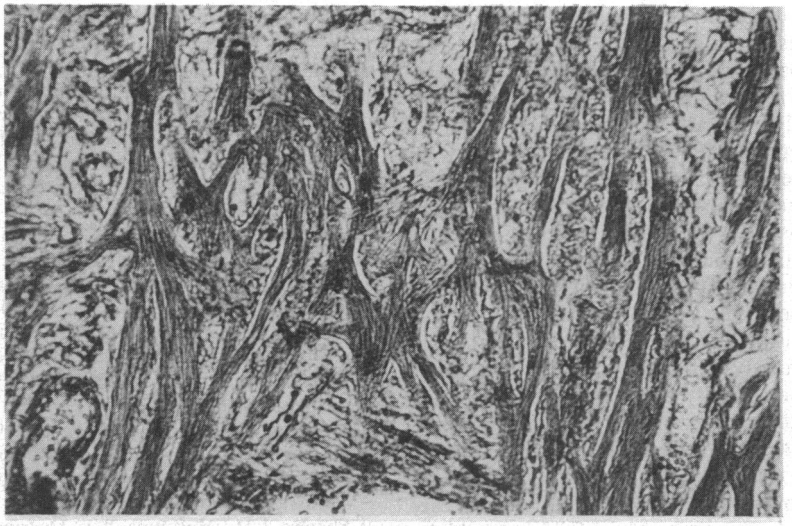

Fig. 2 *Photomicrograph showing severe hypertrophy with type IA disorganisation of myocardial fibres and extensive fibrosis interrupting the cardiocytes. (Haematoxylin and eosin ×100.)*

ventricular free walls the myocardial fibres were severely hypertrophied (measuring 60 μm in diameter) and in total disarray. In particular, adjacent cardiac muscle cells cut longitudinally were aligned perpendicularly or obliquely to each other (Fig. 2) in accordance with the type 1A disorganisation of Maron's classification.[7] Quantitative analysis of the distribution of myocardial cell malalignment in the three regions of the left ventricle showed that the mean area of disorganised muscle cells per section was 45% in the left ventricular septum, 44% in the left anterior ventricular free wall, and 44·5% in the left posterior ventricular free wall. The nuclei were bizarre in shape, and several were surrounded by a clear zone, the so called perinuclear halo. The interstitium was severely widened, occupying more than 40% of the areas assessed morphometrically; the interstitium projected between the myocardial fibres and interrupted the cardiocytes (Fig. 2). The special staining for amyloid showed a negative result. The histological hypertrophic cardiomyopathy index was 80%, which is well within the limit of diagnostic reliability for hypertrophic cardiomyopathy.[8]

Discussion

The histological features in our patient were typical of hypertrophic cardiomyopathy. The diagnosis was supported by the presence of severe hypertrophy with disarray of myocardial fibres, bizarre shaped nuclei, extensive fibrosis, and a perinuclear halo, which together produced a diagnostic hypertrophic cardiomyopathy index of 80%.[8] Because of the diffuse thickening of the left ventricular wall (septal to posterior wall thickness ratio 1·0), this patient had a symmetrical form of hypertrophic cardiomyopathy. Shapiro and McKenna reported the clinical findings in patients with hypertrophic cardiomyopathy and symmetrical left ventricular hypertrophy.[9] To our knowledge, however, the necropsy findings in such patients have not yet been reported.

In our case, a qualitative analysis of cardiac muscle cell alignment showed a type 1A disorganisation according to Maron *et al*'s classification.[7] The extent of myocardial cell malalignment, studied quantitatively by Maron's grading system, was great (mean area of disorganised cells per section 44·5%) and equally distributed in the septum and the left anterior and left posterior ventricular free walls.

Further features of our patient were the unusual clinical presentation and the echocardiographic findings. Cross sectional echocardiography showed severe thickening of the interventricular septum and the left and right ventricular free walls. The left ventricular cavity was considerably reduced in size and left ventricular contractility was slightly decreased. In the absence of systemic hypertension or aortic valve disease these findings are consistent with an infiltrative heart muscle disease or hypertrophic cardiomyopathy. The electrocardiographic changes of low QRS voltages were, however, more suggestive of the first process.[10] Nevertheless, the clinical as well as the necropsy findings failed to show any common cause for these electrocardiographic abnormalities. In particular, the heart was normally sited in the chest, and a pericardial effusion as well as pulmonary

emphysema were absent. A possible explanation for the low voltages in this case of hypertrophic cardiomyopathy may have been the extensive fibrosis which occupied more than 40% of the areas assessed morphometrically. Some authors have reported patients with hypertrophic cardiomyopathy in whom the QRS voltages had fallen over approximately 10 years.[3] We suggest that fibrosis in hypertrophic cardiomyopathy is a progressive time-dependent phenomenon that produces electrical loss if life threatening ventricular arrhythmias do not interrupt its natural course.

Cardiac failure in patients with hypertrophic cardiomyopathy is rarely associated with left ventricular dilatation[11-13] and mostly affects patients who have undergone myotomy-myectomy.[13] In our patient the extensive fibrosis could have prevented the development of cardiac dilatation. Quantitative studies of a large number of patients with hypertrophic cardiomyopathy and congestive heart failure would be required to test this hypothesis.

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