Thorax 1982;**37**:711–712

Short report

Cardiac amyloidosis with asymmetrical septal hypertrophy and deterioration after nifedipine

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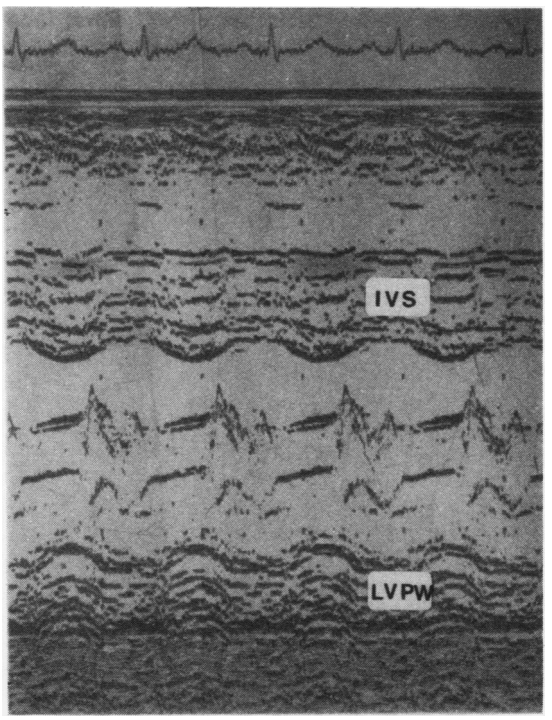
M-mode echocardiography has a key role in the diagnosis of hypertrophic cardiomyopathy. A thickened, immobile septum and asymmetric septal hypertrophy are two major features of the disease discernible by echocardiography. The latter, however, is not specific to hypertrophic cardiomyopathy and may be found in many other conditions, such as pressure overload states of the right and left ventricles, ischaemic heart disease, congenital heart disease, and endocrine disorders, and even in normal children and athletes.[1,2] Asymmetric septal hypertrophy due to amyloid deposition has only lately been reported.[3]

Case history

A 57-year-old man was admitted with a 10-month history of increasing dyspnoea. He was in sinus rhythm, with a normal carotid pulse, and had left ventricular hypertrophy. Auscultation showed an apical fourth heart sound and a soft ejection murmur maximal at the fourth left interspace, unchanged with posture or the Valsalva manoeuvre. An electrocardiogram showed left atrial and left ventricular hypertrophy. A chest radiograph showed normal heart size and evidence of pulmonary venous hypertension. An M-mode echocardiogram showed an immobile, hypertrophied septum, appreciable asymmetrical septal hypertrophy with no associated systolic anterior motion of the mitral valve or aortic valve preclosure, and abnormal systolic and diastolic left ventricular function—features in keeping with non-obstructive hypertrophic cardiomyopathy. The echocardiogram was digitised with a Numonics graphics analyser (for derived indices see fig).

Cardiac catheterisation showed angiographic evidence of left ventricular hypertrophy but no outflow tract obstruction. The coronary arteries appeared normal. A myocardial biopsy was attempted but abandoned after an acute vasovagal episode when the bioptome was passed through the aortic valve orifice. A rectal biopsy specimen showed no amyloid infiltration. The patient's breathlessness increased despite diuretic, digoxin, and isosorbide treatment. As nifedipine had been reported to improve systolic and diastolic left ventricular function in a patient with non-obstructive hypertrophic cardiomyopathy,[4] we decided to try it in our patient. All treatment apart from frusemide 80 mg/day and digoxin 0·5 mg/day was stopped five days before repeat cardiac catheterisation. Haemodynamic measurements were recorded and simultaneous M-mode echocardiograms taken before and 20 minutes after a 10-mg sublingual dose of nifedipine. Cardiac output was determined in duplicate by the dye dilution technique. Within 20 minutes nifedipine precipitated



Echocardiogram of left ventricle and mitral valve of the patient with cardiac amyloidosis, showing the considerably hypertrophied and immobile interventricular septum and the severe asymmetric septal hypertrophy. The left ventricular end-diastolic dimension is within normal limits but the fractional shortening of the left ventricle is reduced. No systolic anterior motion of the mitral valve is seen. Echocardiographic data (digitisation performed with Numonics graphics analyser): left ventricular internal dimension—end-diastolic 4·6 cm, end-systolic 3·6 cm; fractional shortening of left ventricle—21%; interventricular septal thickness (IVS_t)—1·8 cm; left ventricular posterior wall thickness ($LVPW_t$)—1·0 cm; IVS_t: $LVPW_t$—1·8:1·0; ejection fraction—48%; normalised peak velocity of circumferential fibre shortening—1·68 /s; peak filling rate—5·4 cm/s; rapid filling period 84 ms; relaxation time index—42 ms.

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Haemodynamic and echocardiographic data on patient with cardiac amyloidosis

	Before nifedipine	*After nifedipine*
Heart rate (beats/min)	96	110
Mean pulmonary artery pressure (s/ed) (mm Hg)	70/25 (45)	80/26 (50)
Mean pulmonary capillary wedge pressure (mm Hg)	30	36
Mean right atrial pressure (mm Hg)	5	8
Mean aortic pressure (s/ed) (mm Hg)	95/60 (80)	100/60 (80)
Left ventricular pressure (s/ed) (mm Hg)	95/30	100/36
Cardiac index (l/min/m^2)	2·20	1·75
Systemic vascular resistance (dynes/s cm^{-5})	1,600	1,920
Pulmonary vascular resistance (dynes/s cm^{-5})	320	373
Left ventricular internal dimension (cm)		
end-diastolic	4·8	4·8
end-systolic	4·0	4·2
Fractional shortening of the left ventricle (%)	16	12

severe acute left ventricular failure. The haemodynamic and echocardiographic data are shown in the table. The decrease in cardiac output and fractional shortening of the left ventricle, with an increase in end-systolic left ventricular volume and filling pressure but with an increase in systemic arterial pressure, are consistent with acute left ventricular failure due to a decrease in myocardial contractility—a consequence of the negative inotropic effect of nifedipine.

After his discharge the patient deteriorated and died three months later. Necropsy showed widespread primary amyloidosis. The heart was considerably hypertrophied (heart weight 615 g) as a result of amyloid infiltration, which was greatest in the subendocardial and subepicardial layers of the left ventricle and particularly affected the mid and upper interventricular septum, where the ratio of septal thickness to left ventricular wall thickness was 1·6:1.

Discussion

Hypertrophic cardiomyopathy is recognised with increasing frequency by means of M-mode echocardiography. A major echocardiographic feature of this disease, asymmetric septal hypertrophy, was thought to be specific to it but has subsequently been found in several other conditions, all of which may be differentiated by careful clinical evaluation.[1 2] The characteristic echocardiographic signs of infiltrative heart disease are the features of concentric left ventricular hypertrophy, a reduced ejection fraction in the presence of a normal left ventricular end-diastolic dimension, and pericardial effusions.[5]

Our patient presented with unexplained heart failure. Non-obstructive hypertrophic cardiomyopathy was thought the most likely diagnosis. Necropsy, however, showed primary amyloidosis with appreciable cardiac infiltration that especially affected the upper and mid septum. The echocardiographic features that were consistent with a diagnosis of infiltrative cardiomyopathy were the reduced fractional shortening of the left ventricle and left ventricular posterior wall hypokinesis in the presence of a normal left ventricular end-diastolic dimension. In view of the widespread endocardial deposition of the amyloid infiltrate a successful left ventricular biopsy would have allowed a diagnosis of cardiac amyloidosis to be made, and this investigation should normally be included in the assessment of patients presenting with these features.

In view of the reported beneficial effect of nifedipine on left ventricular relaxation[6] and on left ventricular systolic and diastolic function in a patient with non-obstructive hypertrophic cardiomyopathy,[4] we decided to evaluate the haemodynamic effects of this drug. The adverse result of this trial was consistent with the negative inotropic effect of the drug on left ventricular function that outweighed the beneficial effect of any improvement in left ventricular relaxation or afterload reduction. Indeed, systemic vascular resistance paradoxically increased after the dose of nifedipine. Occasional reports attest to the detrimental effect of nifedipine on left ventricular function[7 8]; but this negative inotropic effect is insignificant with normal left ventricular function and compensatory reflex mechanisms. In patients with critical left ventricular dysfunction this effect becomes haemodynamically important. A beneficial haemodynamic effect should be shown before such patients are treated with nifedipine.

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