HYPERTROPHIC CARDIOMYOPATHY IN CHILDREN WITH END-STAGE RENAL DISEASE AND HYPERTENSION

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Summary

Cardiac function was evaluated by echocardiography (echo) in ten paediatric patients, 2.5 to 15 years of age, maintained on chronic dialysis. All had moderate to severe hypertension despite intensive antihypertensive medication.

Four of ten patients showed, on echo, asymmetric septal hypertrophy (ASH) typical of hypertrophic cardiomyopathy (HCM). Two also had signs suggestive of outflow obstruction. Primary cardiomyopathy was excluded by a family survey of first-degree relatives. The incidence of HCM in our series is impressive (40%). The pathogenesis of this cardiac lesion in uraemia is unknown; long-standing severe hypertension may play a role. Early recognition of this form of cardiomyopathy has important clinical considerations. Echo should become a routine examination in the diagnosis, follow-up, and treatment of children with end-stage renal disease.

Introduction

We wish to report a high incidence of hypertrophic cardiomyopathy (HCM) diagnosed by echocardiography (echo) in a small series of children with end-stage renal disease and hypertension, maintained on chronic dialysis replacement therapy.

Patients and methods

Ten children, 2.5 to 15 years of age, were studied; six females and four males. Nine patients received haemodialysis, 12–15 hours per week; one patient was maintained on CAPD. The average duration of dialysis was 16 months (range 2–50 months). The children had rather severe hypertension and all received antihypertensive medications, generally a combination of hydralazine and propanolol. In three children blood pressure could only be controlled after bilateral nephrectomy.
During the period of the study, three children underwent renal transplantation and three children died.

M-mode and 2-dimensional echoes were performed with routine techniques using a commercially available ultrasonoscope. The 2-dimensional examinations were recorded on a videotape and 2-dimensional pictures were taken with a polaroid camera.

Asymmetric septal hypertrophy (ASH) was considered when the interventricular septum (IVS) to posterior left ventricular wall (PLVW) thickness ratio was greater than 1.3. For statistical evaluation of the differences between mean values the Mann-Whitney rank test was used.

**Results**

All ten patients had echocardiographic abnormalities, generally those of congestive cardiomyopathy with concentric left ventricular hypertrophy and enlarged right and left ventricles. Three children had signs of mild pericardial effusion.

![Figure 1. M-mode echocardiogram of patient AR, a 5½-year old girl, on haemodialysis since October 1979. Chronic renal failure probably due to haemolytic uraemic syndrome. Severe hypertension subsided after bilateral nephrectomy (May 1980). Cadaver renal transplantation (February 1981) thus far successful. The echo (February 1981) shows a combination of congestive cardiomyopathy (enlarged RV and LV) and HCM (ASH) with a small pericardial effusion. 2-D echo (not shown) demonstrated disarray of IVS. No clinical or echocardiographic evidence of heart disease in first degree relatives](image-url)
Figure 2. M-mode echocardiogram of SM, an 11½-year old girl on haemodialysis since February 1980. Basic renal disease: membrano-proliferative glomerulonephritis with malignant hypertension. Blood pressure controlled after bilateral nephrectomy (November 1980). The echo (February 1981) shows severe hypertrophy of cardiac muscles with HCM (ASH and SAM) and mild signs of volume overload. 2-D echo (not shown) demonstrated muscle fibre disarray of the IVS. No clinical or echocardiographic evidence of heart disease in first degree relatives.

Four children showed ASH, two with an enlarged left atrium. In addition, two children showed on echo systolic anterior movement of the anterior mitral leaflet (SAM). The echoes of two children, together with a short case summary, are presented in Figures 1 and 2.

The four children with echocardiographic features of HCM were 5½, 11, 12½ and 15½ years of age. In these four children hypertension was not controlled. As a group, these youngsters had a significant higher average predialysis systolic blood pressure than the remaining six patients (153 ± 6.5(SD) mmHg vs 124 ± 13mmHg; p<0.05). The diastolic blood pressure was not significantly different (99 ± 13mmHg vs 87 ± 12.9mmHg; p:NS). No other differences were apparent between the two groups, not in the mean duration of dialysis nor in the degree of residual renal function or in the blood concentrations of calcium (8.3 ± 0.6 vs 8.2 ± 1.5mg/dl; p:NS) and phosphorus (4.4 ± 1.7 vs 5.1 ± 1.1mg/dl; p:NS).

Discussion

Hypertrophic cardiomyopathy (HCM) is characterised by several echocardiographic abnormalities: asymmetric septal hypertrophy (ASH), septal disarray, systolic
anterior movement of the anterior mitral leaflet (SAM), mid-systolic partial closure of the aortic valve, and calcification of the mitral ring [1].

HCM has generally been described as a primary, familial, cardiac disorder of unknown aetiology. Lately, however, HCM has increasingly been reported in a secondary form, particularly in association with increased systolic work load [2,3]. The primary and secondary forms of HCM may well represent entirely different disease processes with similar (non-specific) echocardiographic characteristics.

The secondary forms of HCM have mainly been reported in adults, in patients with aortic stenosis, in hypertensive patients with persistent high systolic and diastolic blood pressure and in a small number of patients with chronic renal failure (CRF) with or without maintenance dialysis therapy [5]. In the paediatric age group, HCM has been described in infants of diabetic mothers [4].

The majority of CRF patients show a different picture of myocardial damage: concentric hypertrophy and left ventricular dilatation, the hallmarks of congestive cardiomyopathy and/or varying degrees of pericarditis with or without pericardial effusion [6,7].

The reasons for cardiac involvement in CRF are multiple. Foremost are those factors which impose increased systolic work such as anaemia, arteriovenous shunting of blood, persistent volume overload and hypertension. Whether a primary uraemic cardiomyopathy exists is still an enigma. Lately, it has been proposed that PTH is a prominent and perhaps the major uraemic toxin [8]. PTH has been shown to influence the contractility of heart muscle fibres.

All our patients had abnormalities on echo, generally those of congestive cardiomyopathy. However, the high incidence (40%) of HCM in our small series was surprising and impressive. The mean duration of dialysis in these patients was relatively short (16 months). The four patients with HCM differed from the remaining six patients in that they had more severe, uncontrolled hypertension despite intensive dialysis and antihypertensive medication. In one patient (Figure 2) the initial echo showed concentric cardiac hypertrophy whereas six months later a definite change was observed towards a full-blown picture of HCM (Figure 3). During the same period of time, blood pressure was not controlled. This may point to a possible pathogenic relationship between hypertension and HCM.

It is unlikely that hyperparathyroidism played a major role in the pathogenesis of HCM. Renal osteodystrophy was clearly evident in only one patient with HCM. PTH concentrations, available in only two patients, were in the normal range. Blood calcium and phosphorus in the patients with and those without HCM did not differ.

Familial HCM was ruled out by an appropriate family survey of first-degree relatives in the majority of our patients.

The cause of secondary HCM in chronic renal failure is not known. HCM in this case probably constitutes an atypical reaction of the myocardium to increased work load and, in particular, to hypertension. Whether the uraemic state contributes to this unusual reaction of the myocardium is not known.

The recognition of HCM in chronic renal failure patients with hypertension has theoretical and pathogenetic importance as well as clinical significance. Two
Figure 3. M-mode echocardiogram of AA, a 12½-year old girl with chronic renal failure and hypertension due to reflux nephropathy. Haemodialysis (June 1979) was uncomplicated. Sudden, cardiac death after four months of dialysis therapy. The echo (July 1979) shows HCM with signs of outflow obstruction (ASH, extreme SAM)

of the patients with HCM showed signs which suggest the existence of left ventricular outflow obstruction, as indicated by SAM. In these patients medication such as digitalis, and to a lesser degree hydralazine, may be contraindicated. Instead, betablockers, such as propanolol, probably will have a beneficial effect.

Our findings indicate that all children with chronic renal failure need a careful cardiac evaluation during the course of their disease. Echo is an important tool to evaluate, diagnose, and follow ‘uraemic’ cardiomyopathies in the young.

If hypertension is indeed an aetiologic factor our data emphasise once more that rigid blood pressure control in these patients is imperative.

References

1. Maron BJ, Epstein SE. Am J Cardiol 1980; 45: 141
2. Darsee JR. Am Heart J 1981; 101: 124
Open Discussion

SCHÄRER (Chairman) Perhaps you can elaborate your last remark? At what stage of renal failure would you advocate performing echocardiography? How often should it be repeated?

DRUKKER That will depend on your cardiological facilities. Echocardiography is a non-invasive technique which does not involve much work and can be done in a very short period of time. Therefore, I suppose one should do it at least at the onset of chronic renal failure; if there is no hypertension, perhaps every half year to a year when things are stable, and once patients go into a phase of end-stage renal disease I think it should probably be repeated every three months. These are rough guidelines.

DRÜEKE (Paris) I was impressed by the presence of hypertension in all your patients with asymmetrical hypertrophy. In our experience there was no such predominance of asymmetrical septal hypertrophy in adult haemodialysis patients and I wonder whether there is another more specific cause in your patients than hypertension?

DRUKKER This may be true but asymmetrical septal hypertrophy has certainly been described in patients with primary hypertension with or without dialysis replacement therapy. In the cardiac literature one finds more and more reports of secondary HCM.

Perloff, a cardiologist, reports in the American Heart Journal of February this year, that the genetic, familial form of hypertrophic cardiomyopathy has something to do with catecholamines and the affinity of catecholamines for the developing muscle fibres of the heart. Now there seems to be more and more evidence that in dialysis patients there is involvement of the autonomic nervous system with changes in catecholamine metabolism. It is speculation that changes in catecholamine metabolism could be a cause, but I would guess that in the paediatric age group secondary HCM is probably related to severe hypertension.