Hypertrophic cardiomyopathy in identical twins

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SUMMARY Hypertrophic cardiomyopathy was diagnosed in identical twin boys in early childhood. One underwent myomectomy at the age of 12 years because of progressive severe exertional dyspnoea accompanied by considerable obstruction of the left ventricular outflow tract shown on both echocardiography and cardiac catheterisation. Seven years later, at the age of 19, he remains incapacitated to a moderate degree. By contrast, the other twin has led a relatively normal life to date and no left ventricular outflow obstruction has been shown.

Since the recognition of hypertrophic cardiomyopathy in the 1950s,¹⁻⁵ there have been many studies of all aspects of the condition including clinical presentation, haemodynamic function, aetiology, and natural course. In more than half the patients a familial incidence was recognised, the trait being autosomal dominant. We report hypertrophic cardiomyopathy in identical twins with a striking difference in clinical severity.

Case reports

THE FIRST TWIN

The first twin was noted to have a cardiac murmur during routine school medical examination when he was five years old. He was symptom free and the clinical diagnosis was ventricular septal defect. He was first referred to the cardiac clinic when he was 11 because of increasing exertional dyspnoea accompanied by chest pain in the previous year.

On clinical examination there was no cardiomegaly but a loud ejection systolic murmur was audible over the entire precordium and maximal at the aortic area. There was evidence of left ventricular hypertrophy on the electrocardiogram and there was inversion of the T wave in the anteroseptal leads consistent with septal hypertrophy. Echocardiography showed asymmetrical septal hypertrophy with systolic anterior movement of the anterior cusp of the mitral valve. At cardiac catheterisation, there was no detectable intracardiac shunt but there was a systolic gradient of 80 mm Hg across the outflow tract of the left ventricle. The diagnosis of hypertrophic

cardiomyopathy was established and treatment with propranolol was started. Because his breathlessness became worse a repeat investigation was carried out next year and the gradient had increased to 120 mm Hg. Operation was recommended and subaortic myomectomy was carried out. At operation, the aortic valve was normal but there was a tight subaortic stenosis extending 2.5 cm below the valve. On inspection the anterior leaflet of the mitral valve was normal. Myomectomy was carried out to a depth of 7 mm and a width of 10 mm to enlarge the outflow diameter to 22 mm. The gradient was reduced to 15 mm Hg. He was examined each year and he remained considerably incapacitated with persistent left ventricular hypertrophy on the electrocardiogram. Cross sectional echocardiography in 1988 once again showed considerable septal hypertrophy (fig 1).

The short axis sweep from apex to aortic root showed disproportionate thickening of the septum compared with the posterior wall. The gradient both at Doppler examination and repeat catheterisation was 35 mm Hg. Further operation was deferred but treatment with propranolol was changed to verapamil.

THE SECOND TWIN

The second twin was referred to us at the age of 11 years because of an indeterminate episode of chest pain and mild exertional dyspnoea over the preceding year. Clinical examination showed no cardiomegaly and no cardiac murmurs were audible. Chest x ray showed no cardiac enlargement and there was no evidence of ventricular hypertrophy on the electrocardiogram; a Q wave was present, however, in limb lead II and in V6. Echocardiography showed concentric thickening of the left ventricle but the aortic and mitral valves appeared normal. Forty eight

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Fig 1 Cross sectional echocardiographic views in diastole from patient 1. (a) Long axis and (b) short axis at tips of mitral valves. RV, right ventricle; IVS, ventricular septum; LV, left ventricle; LA, left atrium; AO, aorta.

Fig 2 Cross sectional echocardiographic views in diastole from patient 2. (a) Long axis and (b) short axis. See legend to Fig 1 for abbreviations.

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hour Holter monitoring showed infrequent short bursts of paroxysmal supraventricular tachycardia. A diagnosis of hypertrophic cardiomyopathy was not conclusive at this time but verapamil was introduced to control the short bursts of supraventricular tachycardia. Cardiac catheterisation and angiography were carried out in 1985 when the patient was 15 years old and this showed normal left ventricular function, no aortic regurgitation, and no gradient across the left ventricular outflow tract. The most recent echocardiographic assessment carried out in 1988 showed thickening of both the interventricular septum and the posterior wall of the left ventricle but with only slight systolic anterior movement of the mitral valve (fig 2).

The diagnosis of hypertrophic cardiomyopathy was established but the patient remains well and at work.

Testing with Jeffries's hypervariable DNA probe confirmed that the DNA fingerprints were identical and that the twins were monozygotic. The mother of the twins was examined and although clinical examination was unremarkable, echocardiographic and Doppler studies showed thickening of the interventricular septum, but there was neither systolic anterior movement of the mitral valve nor left ventricular outflow obstruction.

Discussion

Hypertrophic cardiomyopathy is known to be a familial condition. Greaves *et al* studied 193 first degree relatives of 50 patients with the condition by clinical examination, electrocardiography, and cross sectional echocardiography.⁶ In 28 of the 50 families studied a familial occurrence was recorded; in 15 the pattern was consistent with an autosomal dominant trait. Maron and Mulvihill in a review of the genetics of hypertrophic cardiomyopathy concluded that between 50 and 90% of reported cases were familial,⁷ and the condition was recorded in three generations of a large Norwegian family.⁸ There is, however, no mention in published reports of the occurrence of hypertrophic cardiomyopathy in twins.

Both our patients were monozygotic twins (confirmed on testing with the Jeffries's hypervariable DNA probe) and presented in childhood. In the first, the condition was rapidly progressive and the boy required myectomy at an early age. The other twin by comparison has lived a normal life throughout 10 years' supervision. The morphology of hypertrophic cardiomyopathy can be heterogeneous⁹ and the patterns and extent of left ventricular hypertrophy can vary greatly.¹⁰ These features can influence the course and clinical features of the condition as they did in our twins. Although both the

diastolic and systolic function of the left ventricle are impaired in hypertrophic cardiomyopathy, the disordered haemodynamic function affecting both diastolic filling and distensibility of the left ventricle seems to be the principal factor leading to progression of the disease and the onset of symptoms such as exertional dyspnoea, angina, variable types of arrhythmias and, in severe cases, transient syncope episodes.¹⁰ The most serious arrhythmias reported are supraventricular and ventricular tachycardia, aberrant atrioventricular nodal pathways, and complete heart block. The disturbance most predictive of sudden death is ventricular tachycardia. The annual mortality is 2–3%,^{11,12} tending to affect predominantly younger patients, particularly when there is a family history of the condition. In the first twin left ventricular hypertrophy with strain was present on the electrocardiogram but 24 hour ambulatory electrocardiographic monitoring showed no serious arrhythmias and only infrequent ventricular extrasystoles despite the severity of his condition. His twin brother, however, had several episodes of supraventricular tachycardia on Holter monitoring. The difference in clinical presentation in these twins is most striking and unusual.

Serial echocardiographic and Doppler studies are most important in the long term management of these patients. The sheet-anchor in the management is medication with either β blockers, calcium channel blockers, or in some cases both.^{13,14} Verapamil improved left ventricular diastolic function by improving rapid diastolic filling—thereby increasing exercise tolerance and leading to symptomatic improvement.¹⁵ Amiodarone has also been shown to be effective¹⁶ but side effects tend to become increasingly common the longer the duration of treatment.¹⁷ The role of cardiac surgery in hypertrophic cardiomyopathy is still somewhat controversial.^{18,19} Surgical treatment is undoubtedly indicated when the outflow gradient exceeds 50 mm Hg, and there is substantial evidence that operation can improve symptoms and the quality of life. There is no conclusive evidence to date, however, that it does in fact prolong life. Subaortic myectomy in our first twin undoubtedly produced considerable clinical benefit with lessening of the left ventricular outflow gradient. To date, surgical treatment has not been necessary in his twin brother. A more recent innovation is that of transarterial laser myoplasty,²⁰ but again its precise role in the overall management of the condition has yet to be defined. Its principal advantage seems to be that the procedure can be repeated if necessary.

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References

- 1 Brock R. Functional obstruction of the left ventricle (acquired aortic subvalvar stenosis). *Guy's Hospital Rep* 1957;106:221-38.
- 2 Teare D. Asymmetrical hypertrophy of the heart in young adults. *Br Heart J* 1958;20:1-8.
- 3 Bercu BA, Diettert GA, Danforth WH, Pand EE Jr, Ahlvin RC, Belliveau RR. Pseudoaortic stenosis produced by ventricular hypertrophy. *Am J Med* 1958;25:814-8.
- 4 Goodwin JF, Hollman A, Cleland WP, Teare D. Obstructive cardiomyopathy simulating aortic stenosis. *Br Heart J* 1960;22:403-14.
- 5 Morrow AG, Braunwald E. Functional aortic stenosis; a malformation characterised by resistance to left ventricular outflow without anatomic obstruction. *Circulation* 1959;20:181-9.
- 6 Greaves SC, Roche AHG, Neutze JM, Whitlock RML, Veale AMO. Inheritance of hypertrophic cardiomyopathy: a cross sectional and M mode echocardiographic study of 50 families. *Br Heart J* 1987;58:259-66.
- 7 Maron BJ, Mulvihill JJ. The genetics of hypertrophic cardiomyopathy. *Ann Intern Med* 1986;105:610-2.
- 8 Haugland H, Ohm O-J, Boman H, Thorsby E. Hypertrophic cardiomyopathy in three generations of a large Norwegian family: a clinical, echocardiographic, and genetic study. *Br Heart J* 1986;55:168-75.
- 9 Ciro E, Nichol PF, Maron BJ. Heterogenous morphologic expression of genetically transmitted hypertrophic cardiomyopathy. Two dimensional echocardiographic analysis. *Circulation* 1983;67:1227-33.
- 10 Maron BJ, Bonow RO, Cannon RO, Leon MB, Epstein SE. Medical progress. Hypertrophic cardiomyopathy. Interrelations of clinical manifestations, pathophysiology, and therapy. *N Engl J Med* 1987;316:780-9.
- 11 Shah PM, Adelman AG, Wigle ED, et al. The natural (and unnatural) history of hypertrophic obstructive cardiomyopathy. *Circ Res* 1973;34 and 35(suppl 2):1179-95.
- 12 Maron BJ, Savage DD, Wolfson JK, Epstein SE. Prognostic significance of 24 hour ambulatory electrocardiographic monitoring in patients with hypertrophic cardiomyopathy: a prospective study. *Am J Cardiol* 1981;48:252-7.
- 13 Harrison DC, Braunwald E, Glick G, Mason DT, Chidsey CA, Ross J Jr. Effects of beta adrenergic blockade on the circulation, with particular reference to observations in patients with hypertrophic subaortic stenosis. *Circulation* 1964;29:84-98.
- 14 Brigden W. Hypertrophic cardiomyopathy. *Br Heart J* 1987;58:299-302.
- 15 Bonow RU, Dulsizian V, Rosing DR, Maron BJ, Bacharach SL, Green MV. Verapamil induced improvement in left ventricular diastolic filling and increased exercise tolerance in patients with hypertrophic cardiomyopathy: short and long term effects. *Circulation* 1985;72:853-64.
- 16 McKenna WJ, Harris L, Rowland E, et al. Amiodarone for long term management of patients with hypertrophic cardiomyopathy. *Am J Cardiol* 1984;54:802-10.
- 17 Paulus WJ, Nellens P, Heyndrickx GR, Andries E. Effects of long term treatment with amiodarone on exercise haemodynamics and left ventricular relaxation in patients with hypertrophic cardiomyopathy. *Circulation* 1986;74:544-54.
- 18 Morrow AG, Reitz BA, Epstein SE, et al. Operative treatment in hypertrophic subaortic stenosis: techniques, and the results of pre and post operative assessments in 83 patients. *Circulation* 1975;52:82-102.
- 19 Bircks W, Schulte HD. Surgical treatment of hypertrophic obstructive cardiomyopathy with special reference to complications and to atypical hypertrophic obstructive cardiomyopathy. *Eur Heart J* 1983;4 (suppl F):187-90.
- 20 Serruys PW, den Boer A. What will be the requirements for acute interventional procedures in Europe? *Eur Heart J* 1987;8 (suppl F):55-9.