Hypertrophic cardiomyopathy associated with left ventricular aneurysm and normal coronary arteries: Case study indicating genetic tendencies of cardiomyopathy

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A 50-year-old man presented with hypertrophic obstructive cardiomyopathy (HOC) associated with a left ventricular aneurysm and normal coronary arteries. His history revealed no evidence of myocardial infarction or atypical angina. Physical examination disclosed HOC but did not suggest the presence of an aneurysm. Although the patient was treated medically, heart failure ensued, and he died suddenly while working his farm. Subsequent investigation of the patient's family revealed that three of his five children were also affected by cardiomyopathy, which was especially pronounced in the eldest, a 22-year-old man.

The possible hemodynamic relationship between HOC and left ventricular aneurysm is discussed, along with probable indications. The role of left ventricular aneurysm is also presented in relation to the natural history of the disease.

Although patients with hypertrophic cardiomyopathy often complain of chest pain and exhibit electrocardiographic patterns of infarction,[1,2]

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large published series have paid little attention to the association of myocardial infarction and hypertrophic cardiomyopathy.[1-3]

Coronary artery disease has been linked with hypertrophic cardiomyopathy,[4] and necropsy studies have shown areas of myocardial fibrosis.[5] Myocardial infarction also may occur with hypertrophic cardiomyopathy in the absence of coronary artery disease, distorting the clinical features and influencing the natural history of hypertrophic cardiomyopathy.[6]

We report a case of hypertrophic cardiomyopathy associated with a left ventricular aneurysm and normal coronary arteries; to the best of our knowledge, such an association has not been previously reported. The unusual clinical features of hypertrophic cardiomyopathy seen in this case were probably imposed by the associated aneurysm.

Case Report

The patient was a 50-year-old man, who had been diagnosed as having "cardiac disease" in childhood. Except for occasional spontaneous, short-term precordial pain and infrequent dizziness, he had been well all of his life. A few days prior to admission, he suffered an episode of dizziness but denied having true angina, dyspnea, or syncope. There was no history of hypertension or myocardial infarction. The patient was a moderate smoker.

The blood pressure was 110/80 mm Hg, and the venous pulse was located 2 cm above the sternal angle. The carotid pulse was normal; the heart rate was 80 B/min. The apex beat was palpable in the fifth intercostal space, 2 cm lateral to the midclavicular line, and was normal in character. No areas of dyskinesia were palpable. A third heart sound was present, and a Grade 1/6 systolic murmur was audible at the left sternal border. The lungs were clear, and all other findings were normal.

A chest X-ray film indicated clear lung fields and moderate enlargement of the left ventricle.

The electrocardiogram showed atrial fibrillation and lateral myocardial infarction (Fig. 1).

Echocardiography revealed hypertrophy of the septum and posterior wall (Fig. 2). The left ventricular cavity was moderately dilated, and the mitral valve exhibited systolic anterior movement.

Results of the following laboratory tests were within normal limits: urinalysis, blood count, cholesterol, triglycerides, glucose, urea, GOT, GPT, LDH, alkaline phosphatase, bilirubin, calcium, phosphorus, and proteins.

On the basis of the clinical history, physical examination, and echocardiogram, the patient was diagnosed as having hypertrophic obstructive cardiomyopathy (HOC) and was discharged on oral propranolol, 160 mg daily. Within a few weeks, he developed dyspnea, which necessitated his readmission to the hospital several months later. At readmission, his blood pressure was 110/70 mm Hg, the venous pulse was located 5 cm

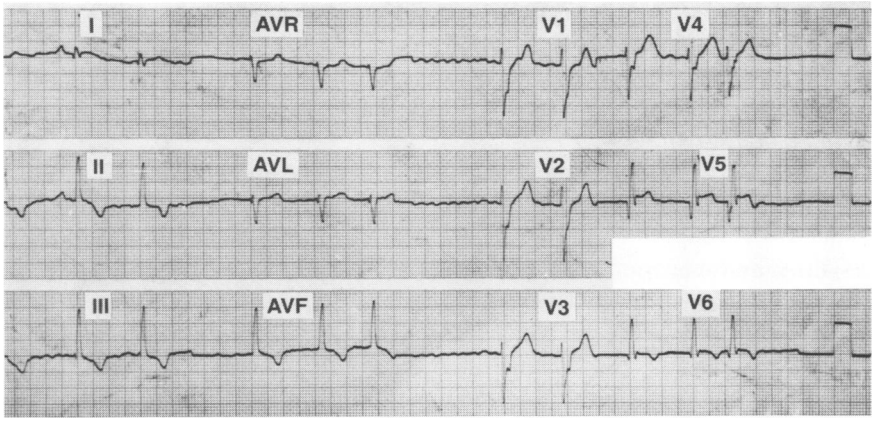

Fig. 1 Echocardiogram showing atrial fibrillation and Q waves in Leads I, aVL, and V_4-V_6, suggesting lateral infarction.

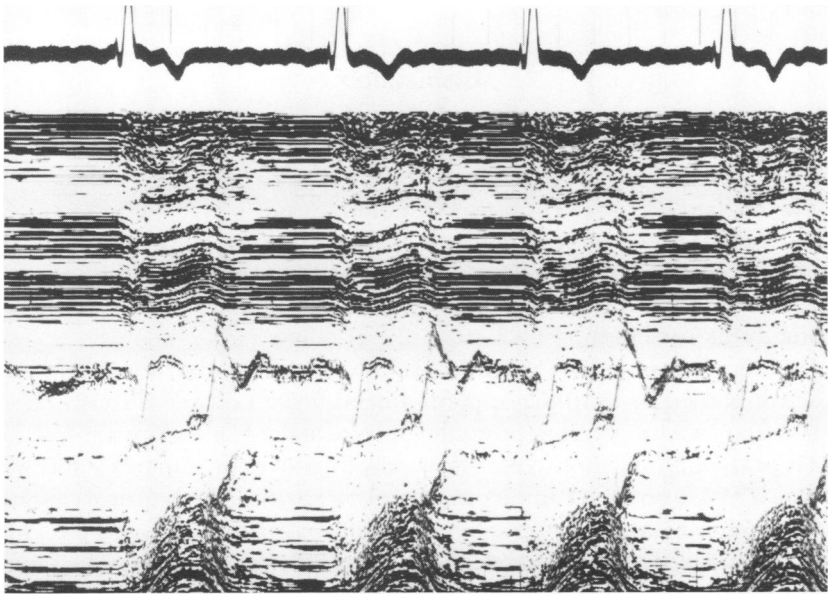

Fig. 2 Echocardiogram showing hypertrophy of the septum and posterior wall, with moderate augmentation (6.2 cm) of the left ventricular diastolic dimension and systolic anterior movement of the mitral valve.

from the sternal angle, and the heart rate was 80 B/min. A third heart sound and a soft systolic murmur were audible. Rales were present in the lung fields, and slight edema of the legs was noted.

The patient underwent complete hemodynamic and angiographic investigation (Table I; Figs. 3 and 4). Hemodynamically, the left ventricular end-diastolic pressure was elevated, and the cardiac output was low; there was no outflow gradient at rest, after isoproterenol infusion, or during

the post extrasystolic beat. Left ventricular angiography showed a dilated ventricle with hypertrophy of the base and posterior papillary muscle. A large area of dyskinesia was observed in the anteroapical and diaphragmatic segments (Fig. 3). Coronary arteriograms were normal (Fig. 4A and 4B).

On the basis of hemodynamic and angiographic findings and the history of heart failure, propranolol was discontinued. The patient was placed on a regimen of digitalis, diuretics, and anticoagulants; he was asymptomatic at the time of hospital discharge. Three months later, he died suddenly while working his farm. No autopsy was performed.

Investigation of the patient's family revealed that three of his five children were also affected by cardiomyopathy (Fig. 5). The eldest, a 22-year-old son, was asymptomatic but had typical clinical, echocardiographic, hemodynamic, and angiographic features of HOC (Figs. 5 and 6; Table II). A 14-year-old son had asymmetric septal hypertrophy, and a 12-year-old son had an atrial gallop, marked right ventricular hypertrophy, and a left anterior hemiblock.

Discussion

In the presence of an associated form of heart disease, the typical clinical features of hypertrophic obstructive cardiomyopathy (HOC) may become distorted,[7-11] as in the case presented here.

Our initial diagnosis of HOC was based on physical signs, episodes of dizziness, echocardiography, and electrocardiography. Although the case presented several unusual features, the left ventricular aneurysm remained unsuspected.

In typical cases of HOC, atrial fibrillation appears at a late stage[3,12] and is accompanied by dyspnea or pronounced heart failure;[12,13] our patient, however, was initially asymptomatic despite atrial fibrillation.

Hypertrophic cardiomyopathy usually improves or remains stable with propranolol, and heart failure rarely occurs within such a short time as was seen here.[2] In light of the hemodynamic and angiographic data (Table I; Figs. 3 and 4), it is possible that propranolol actually produced heart failure. This would explain the patient's prompt recovery with digitalis and diuretics after the withdrawal of propranolol.

Despite the associated aneurysm, physical signs were similar to those reported by Maron et al,[6] who observed seven cases of HOC and myocardial infarction with normal arteries.

Echocardiography is a valuable means of diagnosing HOC.[14] At first glance, our patient's echocardiogram appeared typical, but unusual signs became apparent with further observation. In contrast to typical HOC, where left ventricular dimensions are normal or even reduced,[14,15] our patient's left ventricular dimensions were greater than normal (Fig. 2).

The mitral echogram showed that the diastolic closure rate (DCR), which reflects the left ventricular filling rate[16] and is therefore diminished

TABLE I. Hemodynamic Data

Cardiac output	2.8 L/min
Cardiac index	1.79 L/min/m^2
Total systemic resistance	2114 dynes/sec/cm^{-5}
Total pulmonary resistance	742 dynes/sec/cm^{-5}
Pulmonary arteriolar resistance	114 dynes/sec/cm^{-5}
Pulmonary wedge pressure	22 mm Hg (mean)
Left ventricular pressure	106/22 mm Hg
Aortic pressure	106/70 mm Hg
Right atrial pressure	8 mm Hg (mean)
Right ventricular pressure	36/3 mm Hg
Pulmonary arterial pressure	36/18 mm Hg

Provocation maneuvers (isoproterenol infusion and postectopic response) of the left ventricular gradient were negative.

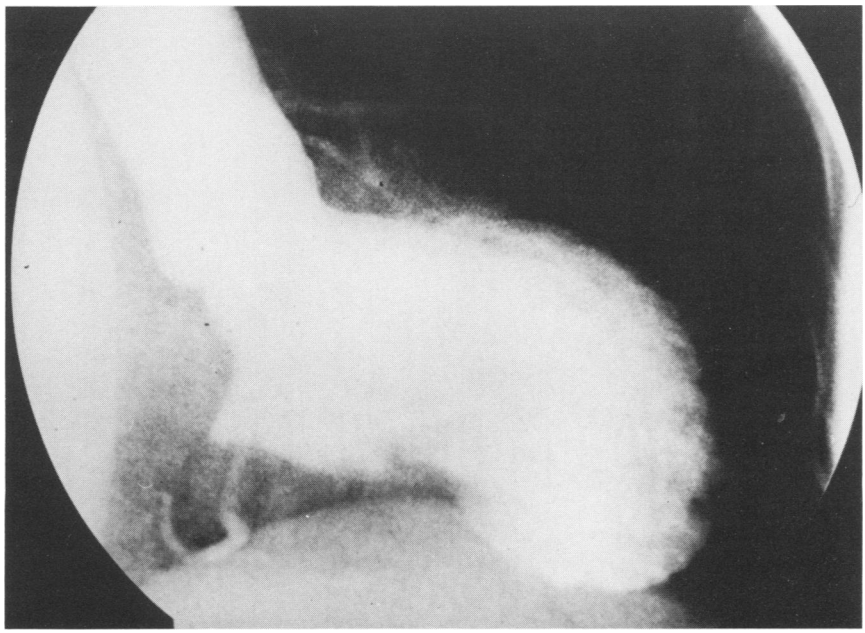

Fig. 3 Left ventricular angiogram (RAO, systolic frame), showing a large area of dyskinesia involving the anteroapical and diaphragmatic segments.

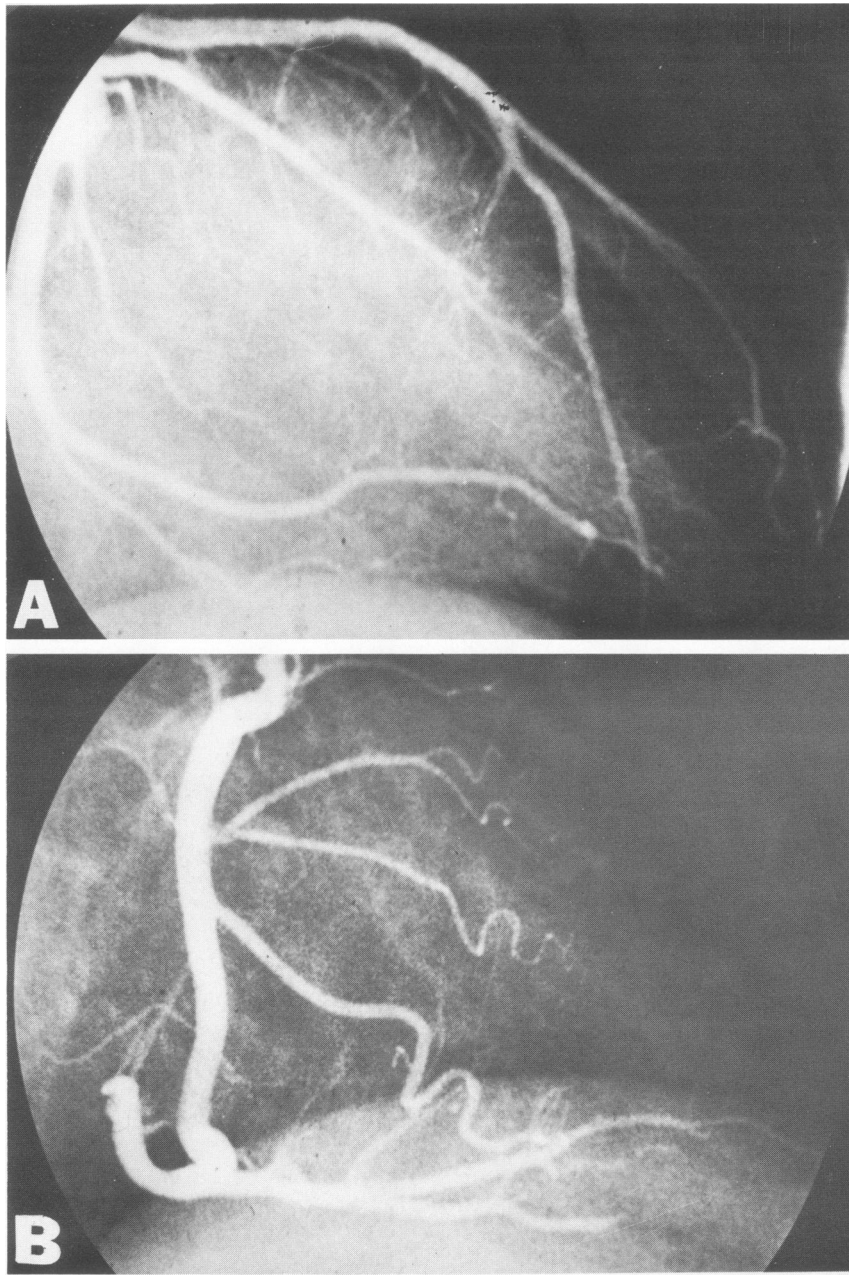

Fig. 4 (A) Principal branches of the left coronary artery (RAO orientation). (B) Right coronary artery (RAO orientation).

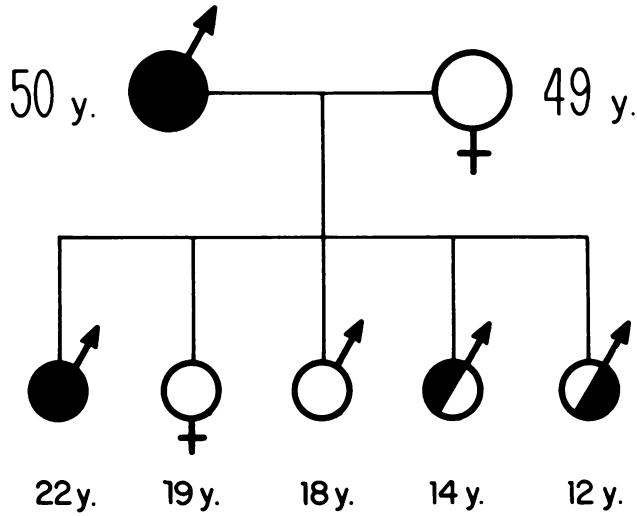

Fig. 5 The patient's family tree. Three children are affected by cardiomyopathy.

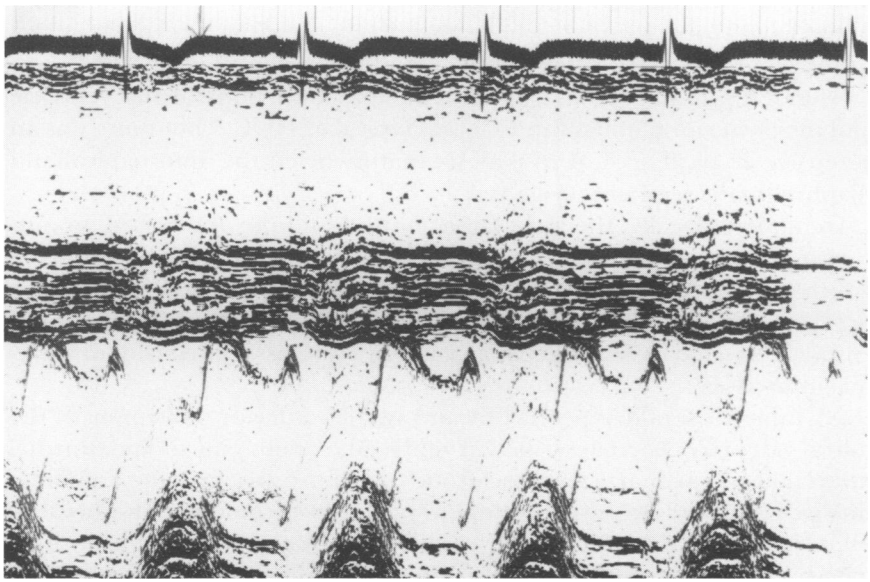

Fig. 6 Echocardiogram of the patient's eldest son, showing asymmetric left ventricular hypertrophy and systolic anterior movement of the mitral valve.

TABLE II. Hemodynamic Data for the Patient's Eldest Son (A 22-Year-Old Man)

Cardiac output	6.8 L/min
Cardiac index	3.6 L/min/m^2
Total systemic resistance	988 dynes/sec/cm^{-5}
Total pulmonary resistance	153 dynes/sec/cm^{-5}
Pulmonary arteriolar resistance	35 dynes/sec/cm^{-5}
Pulmonary wedge pressure	10 mm Hg (mean)
Left ventricular pressure	150/10 mm Hg
Aortic pressure	103/73 mm Hg
Right atrial pressure	2 mm Hg (mean)
Right ventricular pressure	18/14 mm Hg
Pulmonary arterial pressure	18/9 mm Hg
Basal left ventricular outflow gradient	50 mm Hg

in HOC,[15-17] was unexpectedly normal in our patient (Fig. 2). The left ventricular dilatation produced by the aneurysm probably caused an improvement in ventricular filling rate as reflected by the DCR. A similar improvement has been shown echocardiographically in cases of HOC treated with propranolol, where the drug's negative inotropic effect produces ventricular dilatation and a modest acceleration in DCR.[18]

Angiographically, hypertrophy of the basal portions of the ventricle and the posterior papillary muscle was typical of HOC,[19] but there was an extensive atypical area of dyskinesia that involved the anteroapical and diaphragmatic segments (Fig. 3).

Hemodynamically, the low cardiac output and the absence of an outflow gradient can probably be explained by the presence of the aneurysm, which dilated the left ventricle and inhibited pump function, thus reducing the ventricular outflow gradient.[19,20] The absence of an outflow gradient was reported by Maron et al[6] in cases of HOC associated with myocardial infarction.

Asymmetric septal hypertrophy and systolic anterior movement of the mitral valve have been described in ventricular aneurysm and myocardial infarction of coronary atherosclerotic origin.[21,22] Because the combination of HOC and a ventricular aneurysm is so exceptional and because HOC is frequently a familial disease,[20] our patient's family was investigated. Three sons exhibited signs of hypertrophic cardiomyopathy; one had a pronounced case of the obstructive variety (Table II; Figs. 5 and 6).

Transmural myocardial infarction with normal coronary arteries is not uncommon (15%) in HOC. Such infarctions are usually silent,[6] and they may progress to aneurysm, as probably occurred in this patient.

The clinical features of our case were similar to those recently reported for combined hypertrophic cardiomyopathy and myocardial infarction[6] in that: (1) true angina was absent; (2) heart failure was present; (3) the EKG showed diffuse T wave inversions, supraventricular arrhythmias, and atrial fibrillation with no evidence of left ventricular hypertrophy; (4) echocardiography revealed ventricular dilatation; (5) the patient succumbed to sudden death; and (6) the disease was genetically transmitted to three of the patient's sons.

In patients with hypertrophic cardiomyopathy, myocardial infarction is difficult to diagnose, because it is usually silent (as was the ventricular aneurysm in our case); nevertheless, the above-mentioned features may aid the clinician in diagnosing infarction in selected patients.

Although the cause of myocardial infarction or aneurysm with normal coronary arteries in patients with hypertrophic cardiomyopathy is unknown, possible etiologic agents may include coronary artery spasm, emboli, small-vessel disease,[23] and coronary myocardial bridging.[24] If severe enough, the latter may result in arrhythmias[25] or ischemia.[26]

Some patients with HOC may develop congestive heart failure, usually without left ventricular dilatation.[6,13,27]

The case presented here illustrates another mechanism for the development of congestive heart failure during the natural course of hypertrophic obstructive cardiomyopathy. It also adds to the number of reported cases combining hypertrophic cardiomyopathy and myocardial infarction with normal coronary arteries.[6]

Acknowledgment

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References

1. Frank J, Braunwald E: Idiopathic hypertrophic subaortic stenosis. Clinical analysis of 126 patients with emphasis on the natural history. Circulation 37:759-788, 1968
2. Shah PM, Adelman AG, Wigle ED, Gobel FL, Burchell HB, Hardarson T, Curiel R, de la Calzada C, Oakley CM, Goodwin JF: The natural (and unnatural) history of hypertrophic obstructive cardiomyopathy. Circ Res 34-35 (Suppl II):179-195, 1974
3. Hardarson DT, de la Calzada CS, Curiel R, Goodwin JF: Prognosis and mortality of hypertrophic obstructive cardiomyopathy. Lancet 2:1462-1467, 1973
4. Walston A, Behar V: Spectrum of coronary artery disease in IHSS. Am J Cardiol 38:12-16, 1976.
5. Roberts WC, Ferrans VI: Pathological aspects of certain cardiomyopathies. Circ Res 34-35 (Suppl II):128-144, 1974

6. Maron BI, Epstein SE, Roberts WC: Hypertrophic cardiomyopathy and transmural myocardial infarction without significant atherosclerosis of the extramural coronary arteries. Am J Cardiol 43:1086-1102, 1979
7. Harrison EF, Sbar SS, Martin H, Pupello DF: Coexisting right and left hypertrophic subaortic stenosis and fixed left ventricular outflow obstruction due to aortic valve stenosis. Am J Cardiol 40:133-136, 1977
8. Hamby RI, Roberts GJ, Meron JM: Hypertension and hypertrophic subaortic stenosis. Am J Med 51:474-479, 1971
9. Somerville J, Becu L: Congenital heart disease associated with hypertrophic cardiomyopathy. Br Heart J 40:1034-1039, 1978
10. Kronzon J, Glassman E: Mitral ring calcification in hypertrophic subaortic stenosis. Am J Cardiol 42:60-66, 1978
11. Spilkin S, Mitha AS, Matisonn RE, Chester E: Complete heart block in a case of idiopathic hypertrophic subaortic stenosis. Circulation 55:418-422, 1977
12. Glancy DL, O'Brien KP, Gold HK, Epstein SE: Atrial fibrillation in patients with idiopathic hypertrophic subaortic stenosis. Br Heart J 32:652-656, 1970
13. Goodwin JF: Prospects and predictions for the cardiomyopathies. Circulation 50:210-219, 1974
14. Henry WL, Clark CE, Epstein SE: Asymmetrical septal hypertrophy (ASH): Echocardiographic identification of the pathognomonic abnormality of idiopathic hypertrophic subaortic stenosis. Circulation 47:225-233, 1973
15. De la Calzada CS, Ziady GM, Georgiou V, Hardarson T: Echocardiographic features of hypertrophic obstructive cardiomyopathy. Proceedings of the British Cardiac Society. Br Heart J 36:396, 1973
16. De Maria A, Miller RR, Amsterdam EA, Markson W, Mason DT: Mitral valve early diastolic closing velocity on echogram: Relation to sequential diastolic flow and ventricular compliance. Am J Cardiol 37:693-700, 1976
17. Stewart S, Mason DT, Braunwald E: Improved rate of left ventricular filling in idiopathic hypertrophic subaortic stenosis and valvular aortic stenosis. Circulation 37:8-13, 1963
18. Saenz de la Calzada C, Ziady GM, Hardarson T, Curiel R, Goodwin JF: Effect of acute administration of propranolol on ventricular function in hypertrophic obstructive cardiomyopathy measured by non-invasive techniques. Br Heart J 38:798-803, 1976
19. Braunwald E, Morrow AG, Cornell WP, Aygen MM, Hilbish TF: Idiopathic hypertrophic subaortic stenosis: Clinical, hemodynamic and angiographic manifestations. Am J Med 29:924-930, 1960
20. Epstein SE, Henry WL, Clark CC, Roberts WC, Maron BJ, Ferrans VJ, Redwood DR, Morrow AG: Asymmetrical septal hypertrophy. Ann Int Med 81:650-680, 1974
21. Greenwald J, Yap JF, Franklin M, Lichtman AM: Echocardiographic mitral systolic motion in left ventricular aneurysm. Br Heart J 37:684-690, 1975
22. Henning H, O'Rourke RA, Crawford MH, Righetti A, Karliner JS: Inferior myocardial infarction as a cause of asymmetrical septal hypertrophy. Am J Cardiol 41:817-822, 1978
23. Arnett EN, Roberts WC: Acute myocardial infarction and angiographically normal coronary arteries. Circulation 53:395, 1976
24. Pichard AD, Meller J, Teichholz LE, Lipnik S, Gorlin R, Herman MV: Septal perforator compression (narrowing) in idiopathic hypertrophic subaortic stenosis. Am J Cardiol 40:310-314, 1977

25. Faruqui AMA, Malloy WC, Felner JM, Schlant RC, Logan WD, Symbas P: Symptomatic myocardial bridging of the coronary artery. Am J Cardiol 41:1305-1310, 1978
26. Noble J, Bourassa MG, Petitclerc R, Dyrda I: Myocardial bridging of the left anterior descending coronary artery: Normal variant or obstruction. Am J Cardiol 37:993-999, 1976
27. Oakley CM: Hypertrophic obstructive cardiomyopathy. Patterns of progression. In Wolsteuholme GEW, O'Connor M (eds): *Ciba Foundation Study Group No. 37: Hypertrophic Obstructive Cardiomyopathy.* Churchill, 1971. Pp 9-29