Asymmetrical Hypertrophic Cardiomyopathy Simulating Mitral Stenosis

By RALPH SHABETAI, M.D., M.R.C.P., (Edin), and SIDNEY DAVIDSON, M.D.

SUMMARY
Hypertrophic cardiomyopathy usually involves the left ventricle more severely than the right, and when asymmetrical may produce the syndrome of idiopathic subaortic stenosis. Less commonly, clinical manifestations of inflow-tract obstruction predominate and produce a syndrome that may be mistaken for mitral stenosis, principally because of an apical diastolic rumbling murmur. The probability of this diagnostic error and the risk of a consequent unnecessary operation can be reduced by appreciating the significance of the clues to left ventricular disease revealed by the electrocardiogram and the chest roentgenogram. Furthermore, proper timing of the heart sounds differentiates the protodiastolic filling sound of cardiomyopathy from the opening snap of mitral stenosis. The correct diagnosis is established following ventriculographic and hemodynamic studies.

Additional Indexing Words:
Mitral valvotomy
Cardiomyopathy with inflow-tract obstruction
Left ventriculogram

IN 1958, TEARE, with considerable difference, reported eight cases of asymmetrical hypertrophy of the heart. Soon thereafter, a vast literature appeared stressing the importance of left ventricular outflow obstruction in hypertrophic cardiomyopathy. In his description, however, Teare included a case of fishmouth distortion and narrowing of an intrinsically normal mitral valve, but did not mention outflow obstruction. His patient had atrial fibrillation, an apical rumbling diastolic murmur and thrill, and a soft aortic diastolic murmur. The chest roentgenogram showed the heart to be of "mitral shape," but the electrocardiogram demonstrated "left ventricular preponderance" and abnormal Q waves. The patient died 1 day after mitral valvotomy. The importance of this observation has been obscured by the interest subsequently aroused by the description of idiopathic hypertrophic subaortic stenosis and the controversy regarding the mechanism responsible for outflow-tract gradients. Although Goodwin and his co-workers in their earlier studies of hypertrophic obstructive cardiomyopathy stressed the importance of outflow-tract obstruction, they also alluded to inflow-tract obstruction and emphasized that diminished diastolic compliance of the left ventricular myocardium is an important component of the pathophysiology of this condition. In their later reports these investigators reemphasized that diastolic filling is limited by the inordinately high left ventricular diastolic pressure and by septal hypertrophy, and they stated that "we now believe that resistance to..."
ventricular filling consequent upon hypertrophy and rigidity is the most important feature of the disease” and “may well be of greater significance than outflow tract gradients.” Apical rumbling and blowing diastolic murmurs have frequently been reported in obstructive cardiomyopathy with outflow-tract obstruction, while Braunwald and associates reported finding a diastolic murmur in only one of 64 such patients studied.

Echocardiograms of patients with hypertrophic obstructive cardiomyopathy have demonstrated that in early diastole the velocity of posterior motion of the anterior leaflet of the mitral valve is reduced in a manner comparable to that found in mild or moderate mitral stenosis. Analysis of the slope of descent of the left atrial V wave has furnished additional evidence that left ventricular filling in hypertrophic obstructive cardiomyopathy is slower than normal. Factors which may be responsible for impaired left ventricular filling include hypertrophy and increased wall thickness per se, altered diastolic compliance of the myofibril, and impedance posed by the septum or by the anterior leaflet of the mitral valve.

The purpose of this paper is to report three cases of hypertrophic cardiomyopathy with obstruction confined to the inflow tract of the left ventricle. We are reporting them, not as clinical curios, but because the syndrome may mimic mitral stenosis, with potentially disastrous consequences.

These cases of primary myocardial disease were characterized by exertional dyspnea, a loud apical first sound, a low-pitched apical diastolic murmur, and an initial clinical diagnosis of mitral stenosis. All of them were referred to the University of Kentucky Medical Center for mitral valvotomy. Since in many centers patients with mitral stenosis undergo cardiac surgery without cardiac catheterization, we feel that it is important to

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**Figure 1**

Case 1 (M.R.). (A) Posteroanterior and (B) lateral chest radiograms showing left atrial enlargement, enlarged pulmonary conus, and prominent upper-lobe veins. These findings were considered to be in agreement with the clinical diagnosis of mitral stenosis.
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Figure 2
Case 1 (M.R.). The P wave is wide and notched and has a wide posterior vector. The AQRS is approximately 75°. T is biphasic in V1 and V2, and inverted in V6. S is of large amplitude in V1-3 and QRS is notched in V6. In spite of the changes suggesting left ventricular disease the record was interpreted as compatible with the clinical diagnosis of mitral stenosis.

draw attention to this syndrome which may simulate mitral valvular obstruction but is not amenable to operative treatment.

Report of Cases

Case 1 (M.R.)
The patient, a 44-year-old woman, complained of palpitations and mild exertional dyspnea. During the year before admission progressive exertional dyspnea, orthopnea, nocturnal dyspnea, and hemoptysis developed. She was referred to a university hospital where mitral valvotomy without prior catheterization was recommended. The patient refused operation but continued to experience severe exertional incapacity. She was admitted to the medical center on November 23, 1966, for mitral valvotomy.

Physical findings included elevated venous pressure and jerky arterial pulses of small amplitude. A right parasternal lift was palpable, and the apical first heart sound was loud and was followed by a short apical systolic murmur. A third sound preceded a loud apical diastolic rumbling murmur. A high-pitched murmur of semilunar insufficiency was heard. Cardiac fluoroscopy revealed no valvular calcification. Chest roentgenograms showed that the left atrium and both ventricles were enlarged (fig. 1). The ECG showed several abnormalities. The P wave was wide and displayed a large late posterior vector. The mean QRS axis in the frontal plane was approximately 75°. The QRS complexes displayed deep S waves in leads V1 and V2 and a late rightward force. The T waves were inverted in leads V5 and V6 (fig. 2). A clinical diagnosis of rheumatic heart disease with dominant mitral stenosis was made. Surgical intervention again was advised and for this reason cardiac catheterization was performed. Cardiac catheterization (table 1) revealed no diastolic pressure difference between the left atrium and the left ventricle. The ventricular septum and the posterior papillary muscle were greatly hypertrophied. Left atrial injection through a transseptal catheter demonstrated poor opacification of the appendage, wide patency of the mitral valve, and asymmetrical hypertrophy of the left ventricle (fig. 3A). The aortogram revealed minimal aortic insufficiency. The left ventricular diastolic pressure was elevated and the cardiac output was reduced. Left ventricular systolic pressure was equal to that in the ascending aorta.

Six months later, the patient was readmitted with axillary vein thrombosis and pulmonary embolism. In the ensuing months pulmonary embolism recurred frequently and progressive cardiac failure developed. The apical systolic murmur became louder and longer suggesting that mitral incompetence had worsened. The
Table 1

Summary of Data on Cardiac Catheterization

<table>
<thead>
<tr>
<th></th>
<th>Case 1 (M.R.)</th>
<th>Case 2 (P.P.)</th>
<th>Case 3 (S.M.)</th>
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<tr>
<td>Pressure (mm Hg)</td>
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<td>20</td>
<td>31</td>
<td>25</td>
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<tr>
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<td>47/15</td>
<td>67/41</td>
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</tr>
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<td>104/20</td>
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<tr>
<td>LV septum thick</td>
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<tr>
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<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
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<td>+/-+++</td>
<td>++++/+++++</td>
<td>0</td>
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Abbreviations: PC = pulmonary capillary; PA = pulmonary artery; RV and RA = right ventricle and atrium; LV and LA = left ventricle and atrium.

Figure 3

Case 1 (M.R.). Left ventriculogram, October 10, 1968. (A) Anterior posterior projection. (B) Lateral projection. (A) The lower arrow points to the hypertrophic interventricular septum, and the upper arrows point to the unusually clear mitral "wash in" which is a further sign of septal hypertrophy. (B) The arrow points to diastolic coning of the outflow area caused by the hypertrophic rigid septum.
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cardiac signs were otherwise unchanged. Echocardiography showed rapid and extensive motion of the anterior leaflet of the mitral valve (fig. 4A) inconsistent with mitral stenosis, but compatible with mitral incompetence.

Cardiac catheterization was repeated on July 9, 1968 (table 1). The changes that had taken place in 20 months were due to the development of severe mitral incompetence, as documented by left ventriculography, echocardiography, and the appearance of tall V waves with rapid Y descent in the pulmonary wedge tracing.

Isoproterenol infusion (4 µg/min) did not provoke a systolic pressure difference between the cavity of the left ventricle and the aorta.

Case 2 (P.P.)

This 32-year-old woman was referred on October 25, 1965, for mitral valvotomy. Complete left bundle-branch block was discovered in a routine ECG made in October 1964. She was well until March 1965 when she began to experience exertional dyspnea.

On examination, the venous pressure was normal but showed a dominant a wave. The blood pressure was 120/70 mm Hg and the heart rate was 76/min. The apex beat was in the midclavicular line, and a left parasternal lift was palpable. The intensity of the first heart sound at the apex was increased, and the second heart sound was paradoxically split. A third heart sound and an apical diastolic rumbling murmur with loud presystolic accentuation were auscultated at the apex. Roentgenographic studies revealed slight cardiomegaly and left atrial enlargement. The ECG showed complete left bundle-branch block.

Cardiac catheterization was carried out on October 27, 1965 (table 1). The left ventricular end-diastolic pressure was elevated, and the degree of pulmonary hypertension was commensurate. The opacified left ventricle showed hypertrophy of the septum and an anterior, tonguelike protrusion. The right ventricular diastolic pressure was abnormal and displayed the configuration of an early diastolic dip followed by a high plateau. There was practically no difference between the pulmonary wedge and left

Figure 4

Echocardiograms from left to right: case 1 (M.R.), case 2 (P.P.), and case 3 (S.M.). (A) (M.R.) Closure is rapid and characteristic of severe mitral incompetence. (MVE = mitral valve echo, SE = septal echo.) (B) (P.P.) Slowing of the diastolic movement toward closure. The septal echo is not represented. (C) (S.M.) Early diastolic closure is slowed and the leaflet remains in the mid open position through the latter two thirds of diastole.

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ventricular pressures at end-diastole, but this difference averaged from 10 to 5 mm Hg during the first half of diastole.

Clinical reevaluation was undertaken on September 17, 1969. She reported an episode of pulmonary embolism. Upon recovery, she was leading a moderately active and asymptomatic life. The only change on clinical, electrocardiographic, and roentgenographic examination of the heart was an increase in the apical systolic murmur. The echocardiogram (fig. 4B) showed an ample range of motion of the anterior leaflet of the mitral valve, but some slowing of its movement toward closure.

Case 3 (S.M.)

This 48-year-old woman was admitted in February 1967 for treatment and evaluation of aphasia and right hemiparesis of 8-days' duration. The blood pressure was 110/70 and the pulse rate was 120/min and irregular. The apex beat was normally located, but she had a left ventricular heave. The apical first heart sound was abnormally loud, and she had a third heart sound and a soft rumbling apical diastolic murmur (fig. 5). The chest roentgenogram showed moderate cardiac enlargement and prominence of the left atrial appendage. The ECG recorded atrial fibrillation and small Q waves in leads II, III, aVF, V5, and V6. Nine weeks later, she underwent cardiac catheterization (table 1). At the beginning of diastole there was a pulmonary wedge to left ventricular diastolic pressure gradient of 10 mm Hg. However, the gradient diminished during diastole, such that in a long cardiac cycle the pressures were equal from mid-diastole onward. A diagnosis of mitral stenosis was made, but operation was not advised because the obstruction was judged to be mild and the ECG suggested coronary artery disease.

After discharge, exertional symptoms increased to the point that she was no longer able to accomplish her household duties. This led to a review of her left ventriculogram and ECGs and a revised diagnosis of primary myocardial disease. The vectorcardiogram suggested left ventricular hypertrophy. The echocardiogram (fig. 4C) was abnormal in that the slope of closure of the anterior leaflet of the mitral valve was interrupted by a long plateau.

Cardiac catheterization was repeated 20 months after the first study. The pulmonary artery and pulmonary capillary pressures had increased, the mitral insufficiency had worsened, and the cardiac output had diminished. The difference between pulmonary wedge and left ventricular end-diastolic pressure remained zero following long R-R intervals. The left ventriculogram disclosed triangulation of the outflow tract typical of septal hypertrophy. This appearance was very similar to that of the earlier study, but mitral incompetence had greatly increased. No evidence of outflow-tract obstruction was elicited by infusion of 4 μg/min of isoproterenol.

Discussion

The history was not helpful in diagnosis. Exertional dyspnea, orthopnea, palpitations, and peripheral edema are identical to those of rheumatic mitral valvular stenosis. Likewise, a history of pulmonary or cerebral embolization and of atrial fibrillation is a nonspecific indication of heart disease.

The clinical examination yielded findings that were deceptive and led, in all three patients, to the erroneous diagnosis of mitral stenosis. In all, the apical first heart sound was abnormally loud, and in all a delayed apical
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diastolic murmur with a low-pitched rumbling quality was heard. The murmur was indistinguishable from that of mitral stenosis. Under the circumstances, the third heart sound was mistaken for the opening snap of mitral stenosis, an error that would have been avoided had simultaneous apex cardiograms been obtained. An apical systolic murmur, which is common even in "pure" mitral stenosis, is the rule in mixed mitral valve lesions, and therefore is not helpful in distinguishing primary myocardial disease from rheumatic mitral valve disease. A left ventricular heave without evidence of mitral incompetence, aortic valve disease, or hypertension is an anomalous finding in a patient with the auscultatory findings of mitral stenosis and should strongly suggest the diagnosis of primary myocardial disease.

All three of our patients showed unequivocal roentgenographic evidence of left atrial enlargement. Pulmonary venous congestion with prominence of the upper-lobe vasculature was indistinguishable from that seen in patients with mitral stenosis. All had straightening of the left heart border, but in case 1 (M.R.) the films also suggested left ventricular enlargement, a finding which should have led to clinical distrust of the diagnosis of pure or dominant mitral stenosis. Calcification of the mitral valve was absent in all the patients. Conventional radiologic study of this syndrome yields results that superficially suggest mitral stenosis, but more thorough scrutiny discloses abnormalities which implicate left ventricular enlargement.

Electrocardiography

The ECG can be helpful in differentiating inflow-tract obstruction from mitral stenosis; however, the ECGs recorded from case 1 (M.R.) showed atrial fibrillation or P mitral and a frontal plane QRS axis of 75° and were considered to be consistent with mitral stenosis. However, the deep S waves in the right precordial leads and the T inversions in the left precordial leads should certainly have aroused suspicion of left ventricular hypertrophy. The ECGs in the other two cases were more helpful. That in case 2 (P.P.) registered complete left bundle-branch block, an extraordinarily rare finding in mitral stenosis but a common one in myocardial disease and left ventricular hypertrophy. In case 3 (S.M.), Q waves in leads reflecting the inferior and lateral aspect of the myocardium were useful in establishing the diagnosis of primary myocardial disease. This finding and the vectorcardiogram, which showed signs of left ventricular hypertrophy, would not be expected in ordinary mitral stenosis. Thus, while some features consistent with mitral stenosis may be seen on the electrocardiogram, the tracing may be expected to reveal in addition evidence of left ventricular hypertrophy and myocardial abnormality.

Echocardiography

Echocardiography was helpful in excluding significant mitral stenosis but was disappointing in that, so far, it has not yielded a pattern diagnostic of inflow-tract obstructive cardiomyopathy. Excursion of the anterior leaflet of the mitral valve was normal or supranormal in all the cases, and this observation established that the valves were pliable. In S.M. and P.P. the rate of mitral valve closure was slower than normal. In these cases it is probable that impedance to left ventricular filling caused by reduced diastolic compliance of the left ventricle or extrinsic distortion of the valve as in Teare's case was the cause of slow closure of the anterior leaflet of the mitral valve. Further experience with echocardiography in hypertrophic cardiomyopathy without outflow-tract obstruction may clarify this problem.

Cardiac Catheterization

Hemodynamic studies were helpful, but interpretation was not always straightforward. The data in case 1 (M.R.) provided unequivocal evidence against mitral stenosis because left atrial and left ventricular diastolic pressures equilibrated perfectly at rest and during exercise. The cardiac output was diminished and the left ventricular end-diastolic pressure was elevated. These data were compatible with myocardial disease and incompatible with mitral stenosis but failed to disclose the
reasons for the clinical simulation of mitral stenosis.

The pressure data from cases 2 and 3 (P.P. and S.M.) demonstrated a gradient of 2 to 3 mm Hg across the mitral valve confined to early diastole. Such small pressure differences, although sometimes found in mild mitral stenosis, especially in association with low cardiac output, are not uncommon for patients without mitral stenosis. In case 2 (P.P.) the left ventricular end-diastolic pressure was conspicuously increased. Diminution of cardiac output and elevation of left ventricular diastolic pressure were not documented until the second cardiac catheterization in the third case (S.M.). The left atrial or pulmonary wedge pressure tracings showed large V waves at the time of the second catheterization in both the patients in whom this procedure was repeated. Evidence for outflow-tract obstruction was not disclosed in any of the cases by postextrasystolic beats, exercise, or isoproterenol infusion.

Left ventriculography was of crucial importance. In all three patients the opacified left ventricle appeared grossly abnormal. The myocardium was thick and showed much hypertrophy of the septum and a ragged, concave diaphragmatic surface. Mitral incompetence was demonstrated by reflux of contrast medium into an enlarged left atrium in all three patients. In both patients who underwent second hemodynamic studies 18 and 20 months after their first catheterizations, mitral incompetence had substantially increased.

As in all types of primary myocardial disease, the etiology is obscure. None of the patients had evidence of preceding myocarditis, but viral studies were not undertaken. These cases of asymmetrical left ventricular hypertrophy with inflow-tract obstruction lack the clinical ventriculographic and hemodynamic indicators of outflow-tract obstruction and cannot be considered to be cases of idiopathic subaortic stenosis.

**Clinical Course**

The clinical course suggests that the natural history is one of rapid deterioration, with atrial fibrillation, thromboembolic complications, progressive mitral incompetence, and rapidly advancing cardiac failure. The clinical features changed dramatically in the last 3 years of M.R.’s life. In that span, the signs of mitral stenosis gave way to those of a mixed mitral valve lesion. Atrial fibrillation, axillary vein thrombosis, pulmonary emboli, and intractable cardiac failure followed relentlessly upon each other. In the 2 years that have elapsed since we first examined P.P., she has sustained pulmonary emboli and episodic heart failure. When we first encountered S.M., she displayed the findings of mitral stenosis. Two years later she had signs of mitral incompetence. Her subsequent course has been that of progressive cardiac failure.

**Conclusions**

The mechanisms for the loud apical first heart sound and diastolic rumbling murmur remain in doubt. The P-R interval was not abbreviated in any instance. In individual cases the mechanisms differ. Thus, in S.M. and P.P., echocardiography and small mitral diastolic pressure gradients were compatible with mitral valve distortion, but in M.R. evidence for mitral restriction was absent.

The prognosis is poor and the specific dangers are pulmonary or cerebral embolism, atrial fibrillation, progressive mitral incompetence, and cardiac failure. The diagnosis depends upon recognizing that apical diastolic rumbling murmurs are not necessarily diagnostic of mitral stenosis or left-to-right shunt. They may be audible in left ventricular dysfunction. The ECG may offer valuable pointers to left ventricular disease, and the echocardiogram excludes severe mitral stenosis. The apex cardiogram is valuable in distinguishing early protodiastolic gallop sounds from late opening snaps. Careful roentgenographic evaluation will frequently disclose evidence of left ventricular disease incompatible with the diagnosis of predominant mitral stenosis. Hemodynamic studies exclude severe mitral stenosis and provide functional and structural proof of left ventricular disease.
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References

1. TEARE D: Asymmetrical hypertrophy of the heart in young adults. Brit Heart J 20: 1, 1958
11. MEERSCHWAM: Hypertrophic Obstructive Cardiomyopathy. Baltimore, Williams & Wilkins Co., 1969
18. SURAWICZ B, MERCER C, CHLEBUS H, REEVES JT, SPENCER FC: The role of the phonocardiogram in the evaluation of the severity of mitral stenosis and the detection of associated valve lesions. Circulation 34: 798, 1966
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