Functional Mitral Stenosis in Patients with Massive Mitral Annular Calcification

Luis E. Osterberger, M.D., Sidney Goldstein, M.D., Fareed Khaja, M.D., and Jeffrey B. Lakier, M.D.

SUMMARY Mitral insufficiency with mitral annular calcification occurring predominantly in elderly females has been described. We studied six patients with mitral diastolic obstruction associated with mitral annular calcification without stenosis of the mitral leaflets. Three were males and three were females, ages 43–77 years. All had significant diastolic gradients across the mitral valve (mean gradient 16 mm Hg) recorded at catheterization. Two patients had aortic and three had mitral valve replacement. No patient had retraction of the mitral leaflets, diffuse thickening or fusion of the commissures at surgery or pathologic examination. Three patients had severe mitral insufficiency, one associated with voluminous prolapsing mitral leaflets and one as a result of ruptured chordae tendineae. The left ventricle was dilated in three patients, two with mitral regurgitation and one with mixed aortic valve disease.

Active mitral annular motion is a normal event and is necessary for normal valvular function; severe calcification of the ring interferes with its normal diastolic relaxation and this alone may explain the holodiastolic mitral gradient found in these patients.

MITRAL ANNULAR CALCIFICATION is a well-recognized pathologic, radiologic and echocardiographic finding that occurs predominantly in elderly females.1,2 The clinical and hemodynamic consequences of this entity are not completely known, although mild-to-moderate mitral regurgitation has been described with mitral annular calcification.3 Recently a diastolic pressure difference across the mitral valve in patients with mitral annular calcification was reported by Hammer et al.4 and by Hakki and Iskandrian.5 These patients had relatively normal mitral valve leaflets associated with a noncompliant left ventricle and outflow tract obstruction. The authors proposed that the gradient is a result of the combination of mitral annular calcification and a small, noncompliant left ventricle.

In this report, we present six patients with severe mitral annular calcification in whom a large pressure difference was recorded across the mitral valve at the time of cardiac catheterization. We propose that in these patients, the mitral annular calcification itself causes the observed pressure difference.

Material and Methods

The six subjects of this study were selected from patients who underwent right- and left-heart catheterization (Judkins or Sones technique) for evaluation of valvular disease. All six patients had fluoroscopic and radiographic evidence of severe mitral annular calcification.

Complete hemodynamic measurements were obtained in each patient. Pressure differences across the mitral valve were determined by simultaneous pressure recordings using fluid-filled catheter systems from the pulmonary wedge position (Swan-Ganz catheter) and left ventricle (fig. 1). Great care was taken to ensure accurate pulmonary wedge and left ventricular pressure pulses that were properly damped. Cardiac output was determined by the thermodilution method. Left ventricular volume and ejection fraction were calculated from a single-plane ventriculogram that was free of ventricular premature beats and obtained in the right anterior oblique position using the area-length method of Sandler and Dodge.6 An M-mode echocardiogram was performed on each patient and mitral annular calcification was diagnosed when previously described features were present.7,8 We used the electrocardiographic criteria of Romhilt and Estes9 to diagnose left ventricular hypertrophy.

Results

Clinical findings in the six patients are presented in table 1. There are three males and three females, mean age 68 years. All patients had symptoms of chronic congestive heart failure. Three patients had symptoms compatible with angina pectoris. Four patients had hypertension and one was on chronic hemodialysis for chronic renal failure. Five patients had left ventricular enlargement by physical examination. A holosystolic murmur of mitral regurgitation was detected in patients 2, 3 and 5. Two of these had severe mitral regurgitation and both had a third heart sound and short mid-diastolic murmur at the apex. Patient 4 had a grade III/VI systolic ejection murmur that increased with the Valsalva maneuver, suggesting hypertrophic obstructive cardiomyopathy. Patients 1 and 6 had a combination of aortic stenosis and aortic insufficiency, associated in one with a murmur of mild mitral regurgitation. An opening snap or holodiastolic rumble was absent in all patients.

All but one patient were in sinus rhythm and all had electrocardiographic evidence of left ventricular hypertrophy (table 1). M-mode echocardiography (table 1) revealed features of mitral annular calcification in three patients and holosystolic mitral valve prolapse in two. The mitral valve was not satisfactorily visualized in one patient due to technical difficulties, but features of mitral stenosis were absent

From the Division of Cardiovascular Medicine, Henry Ford Hospital, Detroit, Michigan.

Address for correspondence: Luis E. Osterberger, M.D., 2799 West Grand Boulevard, Detroit, Michigan 48202.

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of calcium in the area of the mitral annulus in all patients. These deposits involved at least two-thirds of the circumference and limited motion during the cardiac cycle.

Hemodynamic, angiographic, surgical and pathologic findings are shown in table 2. The mean pressure differences between the pulmonary artery wedge pressure and the left ventricular diastolic pressure, after correcting for time delay of the pulmonary wedge pressure, ranged from 6–34 mm Hg (average of 16.1 mm Hg). Although an early diastolic gradient across the mitral valve has been recorded in patients with isolated severe mitral regurgitation, holodiastolic pressure differences have not been observed. All of our patients had a holodiastolic pressure difference (fig. 1), which indicates that this gradient was not secondary to the mitral regurgitation.¹⁴,¹⁸ Two patients had severe aortic stenosis with pressure differences across the aortic valve of more than 70 mm Hg. Three patients had large left ventricular end-diastolic and end-systolic volume indexes and three had normal left ventricular volumes.

Severe mitral regurgitation seen in three patients during angiography was associated with pronounced mitral valve prolapse in one. Left ventricular cavity obliteration was seen in the one patient with hypertrophic obstructive cardiomyopathy. Significant coronary artery disease was found in two patients with mitral regurgitation.

All patients except patient 4 underwent surgery; Three had mitral valve and two aortic valve replacement. Heavy calcification was seen or palpated in the mitral valve annulus in all five patients undergoing surgery. Mitral commissural fusion was absent and the leaflets and chordae tendineae were normal in

Table 1. Clinical, Electrocardiographic and Echocardiographic Findings

<table>
<thead>
<tr>
<th>Pt</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Angina</th>
<th>NYHA functional class</th>
<th>Clinical diagnosis</th>
<th>ECG</th>
<th>Echocardiogram</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>75</td>
<td>M</td>
<td>-</td>
<td>III</td>
<td>Severe calcific aortic stenosis and insufficiency</td>
<td>NSR 1° AV block, LVH</td>
<td>LA = 40 mm, LVEDD = 68 mm, poor LV contractility, Ca++, AS and AI, mitral annular Ca++</td>
</tr>
<tr>
<td>2</td>
<td>64</td>
<td>M</td>
<td>-</td>
<td>III</td>
<td>Severe mitral insufficiency secondary to ruptured chordae tendineae</td>
<td>NSR, LVH</td>
<td>LA = 50 mm, LVEDD = 55 mm (1 year before catheterization), MV prolapse, pulmonary hypertension</td>
</tr>
<tr>
<td>3</td>
<td>43</td>
<td>M</td>
<td>-</td>
<td>IV</td>
<td>Severe mitral insufficiency; chronic renal failure</td>
<td>NSR, LVH, LAD</td>
<td>LA = 52 mm, LVEDD = 59 mm, mitral annular Ca++, hyperdynamic LV</td>
</tr>
<tr>
<td>4</td>
<td>77</td>
<td>F</td>
<td>+</td>
<td>II</td>
<td>Hypertrophic obstructive cardiomyopathy</td>
<td>NSR, LVH, IVCD</td>
<td>LA = 51 mm, hypertrophic obstructive cardiomyopathy, mitral annular Ca++</td>
</tr>
<tr>
<td>5</td>
<td>71</td>
<td>F</td>
<td>+</td>
<td>II</td>
<td>Severe mitral insufficiency</td>
<td>AF</td>
<td>LA = 48 mm, LVEDD = 63 mm, pansystolic prolapse of the mitral valve</td>
</tr>
<tr>
<td>6</td>
<td>76</td>
<td>F</td>
<td>+</td>
<td>II</td>
<td>Severe calcific aortic stenosis and insufficiency; mild mitral insufficiency</td>
<td>NSR, LVH, strain</td>
<td>LA = 53 mm, LVEDD = 57 mm, decreased septal wall motion</td>
</tr>
</tbody>
</table>

Abbreviations: NSR = normal sinus rhythm; AV = atrioventricular; LVH = left ventricular hypertrophy; LAD = left-axis deviation; IVCD = intraventricular conduction delay; AF = atrial fibrillation; AS = aortic stenosis; AI = aortic insufficiency; LA = left atrium; LVEDD = left ventricular end-diastolic dimension; LV = left ventricle.
<table>
<thead>
<tr>
<th></th>
<th>Hemodynamics</th>
<th>Angiography</th>
<th>Mitral valve pathology</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pt (mm Hg)</td>
<td>LV EDVI (ml/m²)</td>
<td>LV ESVI (ml/m²)</td>
</tr>
<tr>
<td>1</td>
<td>60/26 (40)</td>
<td>153</td>
<td>120</td>
</tr>
<tr>
<td></td>
<td>v = 41 (27)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>77/30 (40)</td>
<td>154</td>
<td>56</td>
</tr>
<tr>
<td></td>
<td>v = 56 (40)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>84/32 (52)</td>
<td>82</td>
<td>37</td>
</tr>
<tr>
<td></td>
<td>v = 60 (40)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>35/13 (28)</td>
<td>60</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>v = 10 (7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>33/14 (22)</td>
<td>124</td>
<td>49</td>
</tr>
<tr>
<td></td>
<td>v = 14 (10)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>70/20 (37)</td>
<td>55</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td>v = 34 (20)</td>
<td></td>
<td></td>
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</tbody>
</table>

Values in parentheses are mean pressures.

Abbreviations: PAP = pulmonary artery pressure; PWP = pulmonary wedge pressure; v = v wave; LVP = left ventricular pressure; MVG = mitral valve gradient; AOP = aortic pressure; CI = cardiac index; LVEDVI = left ventricular end-diastolic volume index; LVESVI = left ventricular end-systolic volume index; EF = ejection fraction; MAC = mitral annular calcification; AVR = aortic valve replacement; MVR = mitral valve replacement; CABG = coronary artery bypass graft.
patients 1, 3 and 6. Patient 5 had ruptured chordae tendineae with normal leaflets and patient 2 had a voluminous myxomatous valve. Patient 1 died after aortic valve replacement. At necropsy, the mitral valve leaflets were of normal thickness with small areas of fibrosis and without commissural or chordal fusion. The amount of calcium in the mitral annulus made it a very thick and stiff structure, protruding like a “shelf” into the inflow tract of the left ventricle and under the mitral leaflets (fig. 2).

Discussion

Calcification of the annulus fibrosus of the mitral valve is a frequent finding in elderly patients. The predominance of females with this finding has been stressed by many authors. Although mitral annular calcification has been described in patients with mitral valve prolapse, its etiological correlation has not been established. The hemodynamic abnormality most commonly associated with mitral annular calcification is mitral insufficiency. Mitral stenosis in the absence of rheumatic involvement has been attributed in some instances to mitral annular calcification, but not until recently has the pressure gradient across the mitral valve been described in this syndrome.

The diastolic pressure difference across the mitral valve found in patients with severe mitral annular calcification has been explained on the basis of a severely calcified mitral annulus alone. The mitral valve annulus has been thought of as a rigid structure that does not contribute to the opening or closing of the mitral orifice. In dogs, the mitral ring has been shown to change in size throughout the cardiac cycle. Tsakiris has shown that coincident with the P wave of the ECG there is a rapid reduction in the size of the mitral annulus that continues throughout atrial and ventricular contractions, and is followed during left ventricular isovolumic relaxation by a rapid increase in annular size, reaching its maximum in late diastole. Measured changes in the area of the mitral orifice in dogs ranged from 10–54% of its largest diameter during diastole. Annular narrowing in the canine occurs eccentrically and is maximal in the posterolateral region of the ring, the same area in which maximal calcification was noticed in our patients.

We believe the annular calcification observed in our patients leads to rigidity of the mitral annulus, which in turn prevents normal function of the ring during systole and diastole. The absence or reduction of normal annular dilatation during diastole results in functional mitral stenosis and its failure to contract at end-diastole helps produce mitral regurgitation.

Hammer et al. hypothesized that a small, thick-walled, noncompliant left ventricle with a restricted inflow tract is an important contributing cause of the mitral diastolic pressure difference. Hakki and Iskandrian supported this hypothesis, but our findings do not substantiate it. Two of our patients with severe mitral regurgitation (patients 1 and 5), as well as patient 1, who had aortic stenosis and aortic insufficiency, had dilated left ventricular cavities. Of the remaining three patients, one had a normal left ventricular volume and only two of them had small, hypertrophied, restricted left ventricles. We believe, however, that massive mitral annular calcification causing rigidity of the annulus with consequent loss of
normal annular function explains the holodiastolic pressure difference across the mitral valve encountered in these patients. In some patients with mitral annular calcification, this associated hemo-
dynamic abnormality may contribute to the symp-
toms of left ventricular decompensation.

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