Severe “Silent” Mitral Regurgitation*
A Potentially Reversible Cause of Refractory Heart Failure

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Hemodynamically critical (“severe”) mitral regurgitation is usually associated with an audible (if not loud) systolic murmur and signs of left ventricular volume overload. However, “silent” severe mitral regurgitation is being increasingly recognized. We review the case histories of nine patients with silent hemodynamically important mitral regurgitation (associated with acute myocardial infarction and chronic valvular, hypertrophic, and ischemic heart disease), six of whom survived mitral valve replacement, of whom five are alive and functioning well more than three years postoperatively. Performance of left ventriculography early in the hospital course of patients with severe unexplained congestive heart failure (with normal or near-normal left ventricular systolic function assessed noninvasively) identifies patients with severe silent mitral regurgitation who may have long-term benefit from mechanical therapy. (Chest 1989; 96:342-46)

Severe mitral regurgitation is diagnosed almost invariably by the presence of a loud apical holosystolic murmur.1-4 Although heart failure with depressed cardiac output may decrease the intensity of the murmur,5,7 it has been thought that the diagnosis of severe mitral regurgitation is not tenable in the absence of a murmur.5 However, severe silent mitral regurgitation has been described with coexisting mitral stenosis,6 endocarditis,7 cardiomyopathy,8 and acute myocardial infarction (AMI).9,10 Although pre-morbid diagnoses have been made and surgery performed in these patients, only one long-term survivor of severe silent mitral regurgitation has previously been reported, to our knowledge.12

We describe nine patients with this syndrome (occurring in three distinct clinical settings: AMI; decompensated valvular and hypertrophic heart disease; and chronic, severe silent mitral regurgitation), six of whom survived mitral valve replacement. A high index of suspicion for hemodynamically important mitral regurgitation in patients with absent or soft heart murmurs, given otherwise unexplained severe and pharmacologically refractory heart failure, led to prompt catheterization and surgery in the survivors.

CASE REPORTS

CASE 1
A 36-year-old woman was transferred to the New York Hospital...
nary rhonchi and a displaced apical impulse in the sixth intercostal space, anterior axillary line. Heart sounds were decreased in intensity; a murmur was not heard. On neurologic examination he was lethargic but arousable. The ECG showed ventricular pacing at 64 beats/min. The following day, a two-dimensional echocardiogram showed near-normal left ventricular function. Right heart catheterization performed on admission demonstrated the following pressures: RA, 19 mm Hg; RV, 50/20 mm Hg; PA, 50/23 mm Hg; and PCW, 35 mm Hg. There was no evidence of an intracardiac shunt. Assessment of left ventricular function by nuclear probe revealed near-normal global systolic function, with an LVEF of 46 percent. Despite insertion of an intra-aortic balloon pump, severe hypotension persisted, with resulting diminished urinary output and renal insufficiency. Left heart catheterization performed the following day showed severe mitral regurgitation. Mitral valve replacement was then emergently performed. Despite use of the intra-aortic balloon pump and norepinephrine and dopamine infusions, the patient remained hypotensive and died shortly after surgery. Postmortem examination revealed severe three-vessel coronary artery disease. The two saphenous vein coronary artery bypass grafts to the left anterior descending coronary artery were free of obstructions. There were both recent and old areas of myocardial necrosis, including the papillary muscles.

Case 3

This 55-year-old woman was admitted with an AMI. Physical examination results revealed normal vital signs. The lungs were clear. As S, gallop, and a soft grade 2/6 systolic murmur were heard at the apex. The patient’s course was complicated by two episodes of paroxysmal supraventricular tachycardia and one episode each of severe hypotension and cardiac arrest. After intubation and resuscitation, bedside right heart catheterization revealed a mean PCW pressure of 20 mm Hg; prominent V waves were not present. The patient subsequently developed diffuse bilateral radiographic pulmonary infiltrates. Cardiac catheterization performed five days after the development of myocardial infarction (three days after the development of pulmonary infiltrates) revealed severe mitral regurgitation. There was inferolateral akinesis. Coronary angiography revealed 50 percent lesions of the proximal circumflex and midright coronary arteries. The patient underwent mitral valve replacement. The postoperative course was complicated by sepsis and recurrent shock, and the patient died two days after surgery.

Case 4

A 66-year-old man was referred for evaluation of severe chronic congestive heart failure (New York Heart Association functional class 4). He had sustained a large diaphragmatic myocardial infarction in 1982 and subsequently undergone quadruple saphenous vein coronary artery bypass graft surgery. There was mild mitral regurgitation noted at the preoperative catheterization. Following surgery, the patient had moderately severe pulmonary vascular congestion which was refractory to digoxin, furosemide (Lasix), and arterial vasodilators. A radionuclide cineangiogram performed at that time showed a global LVEF of 25 percent. The patient subsequently received amrinone for six months before this admission. On admission, the blood pressure was 90/60 mm Hg. The respiratory rate was 24 breaths/min, and the pulse rate was 110 beats/min. The jugular venous pressure was mildly elevated; carotid pulses were normal; there was a left parasternal lift; the lungs were clear. A grade 2/6 apical systolic murmur was heard, which was absent on subsequent examinations. The patient underwent right heart catheterization, which revealed the following pressures: RA, 7 mm Hg; RV, 50/14 mm Hg; PA, 50/24 mm Hg; PCW, 30 mm Hg; and V-wave, 40 mm Hg. The patient was treated with IV sodium nitroprusside and underwent cardiac catheterization, which revealed a LVEF of 25 percent with akinesis of the inferior wall and apex. There was severe mitral regurgitation. Digital subtraction supravascular aortography demonstrated patency of three of the four previously implanted saphenous vein bypass grafts. The patient underwent mitral valve replacement. Although the postoperative course was complicated with prolonged intubation, respiratory failure, and sepsis, the patient was discharged and is alive more than five years following surgery, with improved functional capacity despite reduction in medical therapy. Left ventricular function by echocardiography has shown persistent moderate global hypokinesia.

Case 5

A 69-year-old woman was transferred to the New York Hospital because of hypotension. The patient had a history of systemic hypertension and diabetes mellitus, and had recently sustained a myocardial infarction with recurrent acute pulmonary edema. The patient was admitted to another hospital with dyspnea and rapid atrial fibrillation. Physical examination results there revealed a grade 2/6 systolic murmur and a 2/6 diastolic murmur at the apex. Echocardiography revealed a large left atrium with mitral stenosis and mild depression of left ventricular systolic function. Right heart catheterization revealed the following pressures: PA, 50/24 mm Hg; PCW, 24 mm Hg; and V-wave, 35 mm Hg. Radionuclide cineangiogram showed near-normal LVEF and right ventricular ejection fractions (RVEF). The patient had recurrent episodes of pulmonary edema culminating in cardiogenic shock, treated with IV norepinephrine and intubation. She was then transferred to the New York Hospital, where she underwent placement of an intra-aortic balloon pump. The systemic arterial pressure rose. Cardiac catheterization was performed one day after admission and revealed severe mitral regurgitation, moderate aortic regurgitation, and inferoseptal hypokinesia of the left ventricle, with a global LVEF of 39 percent. Coronary angiography revealed angiographically important luminal obstructions of the left main and right coronary arteries. That evening, the patient underwent emergency aortic and mitral valve replacement, with placement of saphenous vein coronary artery bypass grafts. She was discharged ambulatory but had a mild-low output syndrome that required several admissions with severe heart failure and arrhythmias. She died 12 months after surgery owing to respiratory failure and sepsis.

Case 6

A 67-year-old man with Klinefelter’s syndrome was admitted with increasing dyspnea, fever, and rapid atrial fibrillation. The patient had a previous history of rheumatic fever and bacterial endocarditis. Previous echocardiograms and cardiac catheterization revealed asymmetric septal hypertrophy and moderate (2+/++) mitral regurgitation. On initial physical examination, the systemic arterial pressure was 100/60 mm Hg, heart rate, 130 beats/min, temperature, 39°C (R), and respirations, 40 breaths/min. There were mild elevation of jugular venous pressure and bilateral basilar rales. The apical beat was diffuse. A grade 2/6 systolic murmur and grade 2/6 diastolic murmur were heard at the apex and at the lower left sternal border, respectively. Echocardiography revealed asymmetric hypertrophic cardiomyopathy with systolic anterior motion of the mitral valve, aortic and mitral valvular calcification, and vegetations. There was an enlarged left atrium and a small pericardial effusion. Right heart catheterization revealed the following pressures: PA, 32/18 mm Hg; PCW, 16 mm Hg; V-waves, 35 mm Hg. The patient was treated with digoxin, diuretics, and preload- and afterload-reducing agents. He continued to have unheralded episodes of acute pulmonary edema and subsequently developed renal insufficiency. Because of suspected active endocarditis and renal failure, cardiac catheterization was not performed, but the patient underwent emergency surgery at which severe mitral regurgitation was found. Mitral valve replacement and septal myectomy were performed. Although the patient had a complicated postoperative course, he has survived for more than three years. Left ventricular function by echocardiography one year after surgery revealed near-normal global systolic function.
CASE 7

This 62-year-old woman was admitted with the sudden onset of pulmonary edema and respiratory failure. A Starr-Edward aortic valve prosthesis had been implanted 19 years earlier for severe aortic regurgitation of rheumatic etiology. Three years before admission, mild exercise intolerance was noted. Serial M-mode echocardiography done 15 months before admission revealed normal left ventricular size and function, slight left atrial dilatation, and a thickened mitral valve, with decreased EF slope but normal posterior leaflet motion. On admission, the patient was intubated and underwent mechanical ventilation, diuresis, and treatment with nitrates.

Examination results on admission revealed acute respiratory distress and diffuse pulmonary raales. The left ventricular impulse was diffuse but not displaced; crisp prosthetic clicks were heard, and a grade 1/6 systolic ejection murmur at the base radiating to the carotids was noted. The cardiac examination remained unchanged subsequently. Right heart catheterization, performed after clinical stabilization, showed normal pressures: RA, 2 mm Hg; RV, 28/2 mm Hg; PA, 25/12 mm Hg; and PCW, 10 mm Hg. The ECG showed a sinus rhythm at 90 beats/min and a left bundle branch block. Serial cardiac enzyme determinations showed a small myocardial infarction, with peak CK of 500 IU, MB positive. Echocardiography (M-mode and two-dimensional) showed previously noted findings; the prosthetic aortic valve appeared to function adequately. Radionuclide ventriculography showed slight depression of global left ventricular function (40 percent) without regional abnormality; right ventricular function was normal. Cardiac catheterization was undertaken to exclude valvular dysfunction and to ascertain the cause of the pulmonary edema. Coronary arteriography was normal. Retrograde catheterization of the left ventricle demonstrated no significant transaortic gradient. Direct left ventriculography demonstrated severe (4 + 4 +) mitral regurgitation and normal global left ventricular performance. The patient underwent uncomplicated mitral valve replacement. Pathologic examination demonstrated a deformed rheumatic valve. She has remained asymptomatic three years after surgery, with normal global systolic function as assessed by two-dimensional echocardiography.

CASE 8

This 74-year-old woman was admitted with syncope and ventricular fibrillation. In the emergency room, electrical countershock restored sinus rhythm. The postconversion ECG revealed sinus tachycardia at 120 beats/min, a new right bundle branch block and ST segment elevation in the anterolateral leads. Past history was notable for a successful aortic valve replacement eight years earlier with a Starr-Edward aortic valve for symptomatic severe calcific aortic stenosis. The patient was asymptomatic until several hours before admission, when she noted dyspnea and mild chest discomfort. After defibrillation, the patient was comatose with evidence of brain stem function. The blood pressure was 140/90 mm Hg; heart rate, 90 beats/min; the patient was intubated and mechanically ventilated. Lung examination showed bibasilar rales. The carotid upstroke was brisk and the jugular venous pressure normal. The left ventricular impulse was sustained but not displaced. The prosthetic sounds were normal. A grade 1/6 basal systolic ejection murmur was noted. Right heart catheterization and temporary transvenous pacemaker insertion were performed on admission; right heart pressures were: RA, 6 mm Hg; RV, 24/6 mm Hg; PA, 24/16 mm Hg; and PCW, 18 mm Hg. There was no evidence of an intracardiac shunt. Over the next 6 h, severe pulmonary venous hypertension and several episodes of severe systemic hypertension occurred. Inotropic therapy, intravenous aortic balloon counterpulsation, and vasodilator therapy were instituted, with stabilization of arterial blood pressure. Pulmonary venous hypertension persisted (PCW pressure, 30 to 40 mm Hg), with ventricularization of the pulmonary artery pulse tracing. The peak CK was 5,500. Radionuclide left ventriculography revealed severely depressed global left ventricular function (26 percent) with septal and apical dyskinesia. Cardiac catheterization was performed three days after admission to define the etiology of the refractory heart failure. Selective coronary arteriography revealed a total thrombotic occlusion of the proximal left anterior descending coronary artery and 70 percent occlusion of the posterior descending branch of the right coronary artery. There was no significant transaortic gradient across the prosthetic valve. Left ventriculography showed severe (4 + 4 +) mitral regurgitation and severely depressed global left ventricular function (24 percent) with anterolateral and apical dyskinesia. The patient recovered neurologic function, but renal failure required peritoneal dialysis. The patient survived mitral valve replacement, performed two weeks after admission, and despite a prolonged hospitalization was discharged and has remained alive three years postoperatively. Echocardiography performed postoperatively revealed persistent moderate left ventricular systolic dysfunction.

CASE 9

This 62-year-old woman was admitted to the New York Hospital in 1984 with severe dyspnea. There was a history of rheumatic fever, and in 1970 a Starr-Edward aortic valve prosthesis was inserted at another hospital for severe aortic stenosis. Although the patient had relief of dyspnea, one year later she was readmitted with angina pectoris. Coronary angiography demonstrated an important stenosis at the ostium of the left main coronary artery, which was attributed to prior surgical trauma. A single vessel coronary artery bypass was done, using a graft from the left subclavian artery to the left anterior descending coronary artery. The patient had symptomatic relief from this operation and did well until 1984. Physical examination results on admission revealed a systemic arterial pressure of 130/70 mm Hg and a pulse rate of 80 beats/min. Jugular venous pressure was normal. There was a delayed upstroke of the carotid arterial impulse, and a transmitted murmur was auscultated. Her lungs were clear. There was a heaving apical impulse, laterally and inferiorly displaced, crisp prosthetic valve sounds, and a grade 3/6 systolic ejection murmur in the precordial area radiating up to the carotids. There was a grade 2/6 diastolic rumble at the apex; an opening snap was not auscultated. There was a hemolytic anemia with a hematocrit of 28 percent and LDH of 1,200 IU. The ECG showed left ventricular hypertrophy with secondary ST-T changes. Echocardiography revealed a calcified mitral valve with a diminished excursion and diminished EF slope and neutral motion of the posterior leaflet consistent with moderate mitral stenosis. The left atrium was 5 cm, and left ventricular size and wall thickness were normal. The posterior wall motion was normal, but the interventricular septum had sustained right ventricular dysplasia. The right ventricle was mildly dilated (2.4 cm). Radionuclide cineangiogram revealed a LVEF at rest of 34 percent with global hypokinesia, which, with exercise, increased to 36 percent without changes in regional wall motion. The patient refused further evaluation, but was subsequently readmitted with dyspnea and chest pain; the hematocrit was 24 percent. Cardiac catheterization was performed one month later with retrograde crossing of the aortic valve. There was a 10- to 20-mm Hg gradient across the prosthetic aortic valve during systole. There was no aortic regurgitation. Left ventriculography showed normal global left ventricular systolic function, with an ejection fraction of 50 percent. There was moderately severe (3 + 4 +) mitral regurgitation. Selective graft and coronary arteriography revealed a borderline critical (50 percent) stenosis at the insertion of the bypass graft into the left anterior descending artery. The patient subsequently underwent reoperation, where deterioration of the cloth lining of the aortic prosthesis was found. There was rheumatic mitral stenosis with moderately severe mitral regurgitation. Björk-Shiley prosthetic valves were placed into the aortic and mitral positions, and a single-vessel coronary artery bypass graft was performed from the aorta to the left anterior descending
coronary artery distal to the insertion of the prior graft. The patient had an uncomplicated postoperative course and was discharged from the hospital. Postoperative two-dimensional echocardiography revealed persistent moderately subnormal global systolic left ventricular function. She is alive three years following surgery.

DISCUSSION

Although unusual, severe silent mitral regurgitation has been observed in several clinical settings: mitral stenosis, endocarditis, congestive cardiomyopathy, AMI, and, as shown here, with combined valvular and myocardial disease. Mitral regurgitation in the setting of AMI is probably underdiagnosed; a prevalence as high as or exceeding 50 percent has been documented. The soft or silent murmur of severe mitral regurgitation in the setting of AMI has been attributed to diminished flow across the valve from low cardiac output and diminished myocardial contractility. However, silent mitral regurgitation in mitral stenosis and valvular heart disease can occur with a maintained cardiac output. In addition, high left atrial pressures may lead to only a soft, early systolic murmur. Other factors such as cardiac rotation, barrel chest, extrinsic noise from ventilators, and intra-aortic balloon pumps may make the murmur of mitral regurgitation difficult to hear. More important, although a murmur may be auscultated, it may sound "innocent" and belie the hemodynamic severity of mitral regurgitation.

In this report, three patients presented with severe "silent" mitral regurgitation in the setting of prior aortic valve replacement with a ball cage prosthesis. Prosthetic sounds and murmurs may impair the bedside diagnosis of mitral regurgitation. Retrograde left ventriculography can safely be performed in these patients, and valve dysfunction of the nonprosthetic valve may be present in as many as 20 percent of such patients. Although Doppler echocardiography may be of assistance in defining murmurs in such patients, the predictive accuracy of hemodynamic severity (eg, 2+ or 3+) may not be sufficient to forgo ventriculography.

Our series demonstrates that severe "silent" mitral regurgitation may be the cause of pharmacologically refractory congestive heart failure in the critically ill patient with ischemic, myocardial, or valvular heart disease. As noted above, the physical examination may be unreliable in such cases. Prominent V-waves in the PCW pressure tracing, and in particular, PA recordings are helpful in suggesting the possibility of severe mitral regurgitation but their absence has a low predictive value. Moreover, the presence of a large V-wave in the PCW tracing does not assure the presence of hemodynamically important mitral regurgitation.

This series of patients was treated before the widespread clinical availability of Doppler echocardiography, and hence this tool was unavailable for assessment of mitral regurgitation. Nevertheless, the definitive method of diagnosing a potentially reversible mechanical defect of the left ventricle is cardiac catheterization with left ventriculography.

However, given the increased risk of ventriculography in patients with severe mitral regurgitation and borderline hemodynamic status, at present, a noninvasive (radionuclide or echocardiographic) assessment of global left ventricular function and Doppler echocardiography should still be used to triage patients for catheterization. Those patients who have normal or only moderately depressed left ventricular function who are considered otherwise salvageable and candidates for open heart surgery and who are thought to have a mechanical and surgically remediable lesion should undergo left heart catheterization and direct left ventriculography, perhaps using the digital subtraction technique to reduce acute contrast loads and the possibility of hemodynamic deterioration or using non-ionic, contrast agents. In addition, before catheterization elective endotracheal intubation and insertion of an intra-aortic balloon pump should be considered on an individual basis to avoid hemodynamic compromise during catheterization.

Using this approach (sans Doppler), we have had five long-term survivors, one patient (case 5) dying one year following surgery related to intractable left ventricular dysfunction. This latter patient had mitral and aortic regurgitation and required both mitral and aortic valve replacement in addition to coronary artery bypass graft surgery.

Five patients had pharmacologically refractory heart failure and would have died without surgical correction of the mitral regurgitation. The long-term survivors have had clinical and hemodynamic improvement as a result of mitral valve replacement, although there has been persistent left ventricular systolic dysfunction in those who had such abnormalities at initial presentation. Particularly in patients with adequate global systolic left ventricular function, early detection of a possible mechanical defect and corrective surgical therapy should be aggressively pursued.

Recently, Heuser et al reported on the successful use of percutaneous transluminal coronary angioplasty in three patients with severe mitral regurgitation associated with AMI, underscoring the importance of identifying patients with silent mitral regurgitation who may benefit from this nonsurgical mechanical therapy.

The prognosis of patients with pharmacologically refractory heart failure and mechanical defects (including those with severe "silent" mitral regurgitation) appears to be related to global left ventricular function and to recognition early in the hospital course of a
mechanical defect that may be amenable to either valve replacement or to repair (or in certain circumstances coronary angioplasty) before irreversible end-organ damage secondary to hypoperfusion occurs.

REFERENCES