Non-rheumatic Mitral Insufficiency

Grand Rounds

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I. Mitral insufficiency in a functional sense is the most frequent of all valvular lesions. Rheumatic fever, often considered to be virtually the only etiologic agent, probably is a relatively infrequent cause. Damage to the valve leaflets themselves is not absolutely necessary for the production of mitral insufficiency, even of severe degree. It may be the result of damage to papillary muscles, chordae tendinae, or left ventricular myocardium. The entire atrio-ventricular apparatus must be intact and functioning in sequence; otherwise, some degree of insufficiency is inevitable.

II. The left atrio-ventricular apparatus is made up of the mitral ring, leaflets, papillary muscles, and chordae tendinae. But for practical purposes the entire left heart, omitting only the aortic valve, must be included. The mitral valve is an active structure, with important muscular attachments, and is not activated solely by hydraulic forces. The precise sequence of events, and of movement of the leaflets, in the cardiac cycle has not been established. It is not entirely accurate to say that the valve moves downward during systole. The fact is that some portions move downward, some upward (in relation to the apex). The probable sequence probably goes somewhat as follows:

1. The papillary muscles contract and approximate the leading edges of the mitral leaflets.

2. The ventricular wall begins to contract and pressure begins to rise, causing the belly of the anterior leaflet to billow toward the less mobile posterior leaflet.

3. As contraction proceeds,

   a. The mitral ring begins to become smaller and to descend, its lateral commissure tilting toward the apex (with relation to the aortic ring).

   b. The papillary muscles approach and merge, the anterior fitting into a concavity on the posterior.

   c. The anterior leaflet contacts the posterior over most of its length and begins to billow upward into the left atrial lumen.

   d. At the height of systole, stage c goes still further and mitral closure becomes inviolable. The ring tilts downward still further, the anterior cusp billows still higher into the atrium, and the combined contracted masses of the papillary muscles join with the inward-moving left ventricular walls, partly obliterating the lumen of the left ventricle. The remaining area of the left ventricular outflow tract, just beneath the aortic and mitral rings, contains a varying amount of residual blood.

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It is useful to regard the lumen of the left ventricle as divided into two major parts, largely by the anterior cusp of the mitral valve. The most lateral and posterior half is the inflow tract and, at the height of filling, takes up most of the chamber. With the onset of ventricular contraction, the mitral "curtain" swings laterally so far that the entire ventricular cavity now becomes the outflow tract. Any interference with myocardial or papillary muscular action is likely to produce measurable mitral insufficiency.

Is the mitral valve, like the passively operated aortic valve, always insufficient at the instant of closure? The question remains unanswered after about 150 years of conjecture. Perhaps the strongest suggestion that very slight regurgitation, during early isometric contraction, is physiologic comes from Friedman and co-workers,* who found slight regurgitation in one out of 5 normal dogs (using a very sensitive method).

* Friedman, Ben; Dailey, William M.; and Wilson, Russell H.: Studies on mitral valve function. Effect of acute hypervolemia, premature beats and other arrhythmias. Circ. Research 4:33-37, January, 1956.

The most frequent causes of mitral regurgitation in a very literal sense probably are ventricular premature beats or other ventricular arrhythmias. This was the experience reported by Friedman et al; Daley and colleagues (1955) found that atrial fibrillation always produces mitral regurgitation but the association may be the exception rather than the rule. Ventricular premature beats regularly produce mitral regurgitation during cineangiocardiography employing left ventricular catheterization.

This type of mitral regurgitation is harmless except, perhaps, when arrhythmias producing it continue for long periods of time. It may conceivably contribute to the production of failure in patients with uncontrolled ventricular tachycardia but obviously produces no untoward result in the case of premature ventricular beats.

III. Other "non-rheumatic" causes of mitral regurgitation are:

A. Rupture of chordae tendinae

B. Infarction of papillary muscles, with or without rupture, and

C. Perforation of a mitral cusp.

Rheumatic endocarditis may itself cause rupture of chordae and, in its fulminant form, may erode a mitral cusp. In this sense one can argue that the rheumatic process is almost always involved, a contention that is difficult to prove or disprove. Suffice it to say that the rheumatic process is not an absolutely essential ingredient for either clinical situation.

A. Rupture of chordae tendinae

Apart from active rheumatic endocarditis, the following are known to have been associated with chordal rupture:

1. External trauma to the chest.

2. Bacterial endocarditis.

3. Myocardial infarction (usually subendocardial).

External trauma as a probable cause of chordal rupture has been described most authoritatively by Hugh Barber (1944) and by Bailey and Hickam (1944), but there are many other references to it (Normand et al, 1960; Souques and Harvier, 1908). The matter is occasionally of medicolegal importance but does not come up as often in this regard as questions concerning coronary involvement.

Bacterial (or fulminant rheumatic) endocarditis may erode chordae or valve leaflets themselves. Warren's case (1812) is quite intriguing especially since it was published before mitral regurgitation, stethoscopy, or bacterial endocarditis were known. Barlow's case (1845) is also notable for its quaint and elegant clinical description. Repair is sometimes possible (McGoon, 1960). The article by Osmundson et al (1961) is rewarding and authoritative.

Myocardial (papillary) infarction and necrosis may be associated with chordal avulsion from their attachment to papillary muscles (see next section) and a case from our own experience is probably representative.

CASE REPORT

A 50-year-old [redacted] was seen in [redacted], 1959, because of easy fatigability. Over the past 20 years he has frequently been examined by physicians for various administrative reasons.

In 1956 he had suffered a bout of sharp, sticking pain in the precordial region, lasting about a minute. It did not recur and no medication was required. Physical examination at the time was not noteworthy except for mild obesity. There were no cardiac murmurs. Reexamination a year later again showed no murmurs of any sort; an electrocardiogram at the time ([redacted], 1957) was normal.

He remained well but, on routine examination in [redacted], 1959, a grade I apical systolic murmur was noted. The electrocardiogram was again normal. About this time he noted the onset of undue and unusual fatigue and in [redacted] 1959, he noted recurrence of anterior chest pain. It was not severe, did not radiate, and lasted for hours. Nitroglycerine had no effect. Discovery of a slight lymphocytosis raised the question of infectious mononucleosis and, unfortunately of leukemia, questions which were speedily resolved. Nevertheless, the episode served to increase the patient's agitation considerably.

In [redacted] 1959, after several weeks of mild malaise and sore throat, he developed substernal pain, especially on taking a deep breath. On one occasion he suffered an attack of severe precordial pain, lasting minutes, while in a meeting. Examination at the time disclosed that the apical murmur was now holosystolic, clearly radiated to the axilla, and was of grade IV intensity. There were no diastolic murmurs. Blood pressure was 130/60. Theelectrocardiogram was again normal. Cardiovascular film series showed slight left ventricular prominence.

In [redacted] 1959, after a busy day's schedule, he was too dyspneic at rest to sleep. He was hospitalized and carefully studied for active rheumatic fever and bacterial endocarditis. All tests were negative and he was discharged, much improved, after about 10 days. In [redacted] 1959, he was again studied exhaustively. The murmur was even more prominent, the electrocardiogram unaltered, and the left atrium was seen to pulsate rather violently on fluoroscopy. Antistreptolysin titers and C-reactive protein levels were normal. An LE cell preparation was also normal.

Prolonged rest, moderate weight loss, digitalization, and prophylactic penicillin were recommended. The patient slowly improved symptomatically and ultimately returned to work. In [redacted] 1960, cardiovascular films showed mild biventricular enlargement but the overall size was smaller than it had been a year previously. The murmur and the electrocardiogram were unchanged.

At the present time ([redacted] 1961, two years after the onset of significant symptoms) the patient is asymptomatic and is able to pursue his career with very slight limitation of activity.

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Diagnostically, the only feature on which there is general agreement is the presence of recently acquired, dynamically significant mitral insufficiency. Acute rheumatic fever has never been proved and the various studies would seem to render it unlikely. The possibility that a ruptured chorda tendina may be responsible has been actively under consideration since 1959. The cause of the rupture may have been active endocarditis of some sort or partial infarction of a papillary muscle (with avulsion of a chorda or chordae but not rupture of the papillary muscle itself). There is no reason to suspect physical trauma to the chest. Finally, infarction of a papillary muscle with subsequent replacement of contractile tissue by fibrous elements, without rupture of any kind, may be responsible. Actual rupture of the muscle itself would immediately have produced catastrophic symptoms and probably exitus.

No further therapy is contemplated at present.

B. Infarction of papillary muscles

Arteriosclerotic (coronary) disease causing destruction, but not necessarily rupture, of papillary muscles is an important clinical entity that is inadequately presented in modern medical literature. Many older articles and a few recent ones described it (Allen, 1884; Askey, 1950; Bristowe, 1861; Davidson, 1948;

Gee, 1870; Heveling, 1871; Hope, 1952; Lowry et al, 1941; Merat, 1803; Oeser, 1954; Peacock, 1865; Sanders et al, 1957; Stevenson and Turner, 1935).

Two very good pathologic studies on infarction of papillary muscle are Russian and are not yet available in translation. Netzlin and Samesova* found some evidence of papillary muscle involvement in 20 per cent of patients dying with myocardial infarction. They studied 11 cases with large foci of necrosis (but without rupture) in the papillary muscles very extensively. Nine of them involved posterior and only 2 anterior papillary muscles. Diagnosis was made antemortem in 4 patients on the basis of clinical evidence of sudden massive mitral insufficiency. The murmur is holosystolic, characteristically appears several days after the infarction, and displays an increasing intensity thereafter. They were unable to find specific ECG changes but note that the disorder is more frequent with posterior than with anterior infarcts.

Arkhangelskii** points out that papillary muscles are essential for proper functioning of the AV valves. He studied sections of papillary muscles and found that their subendocardial regions were very frequently involved, a feature which may predispose to avulsion of chordal attachments.

American and British literature points out the gross difference between necrosis and scarring of papillary muscles, on the one hand, and rupture of a papillary muscle, on the other. The latter produces the "bellows" murmur and is almost always rapidly fatal (minutes to hours). Simple involvement of papillary muscles, however, may produce mitral insufficiency and varying degrees of disability but is not necessarily fatal. It is a serious factor in prognosis, however, and must be taken into account along with the history of underlying coronary disease.

CASE REPORT 2

A 68-year-old [redacted] man was brought to the emergency room on [redacted], 1959, because of extreme weakness, fever, and irrational conduct for about 2 days. The full history, as obtained over a period of some weeks from all available sources, contained the following features:

In 1929, he sustained a shotgun wound to the left forearm which had to be amputated as a result. He recovered and was well until about 1939 when some form of heart disease was thought to have developed. No details were given.

In 1949, he was seized with upper abdominal pain which was especially severe in the right upper quadrant. Cholecystectomy was carried out without incident. He remained in poor health after the operation but gave no specific complaints but seems to have had some dyspnea on exertion and several bouts of what may have been paroxysmal nocturnal dyspnea in the decade before exitus.

In [redacted], 1959, he developed dull pain in the left anterior chest, nausea, fever, and severe dyspnea. He was admitted to another hospital on [redacted]-59. On examination he had severe tachycardia and rales at the bases of his lungs. There was a grade III systolic murmur over the lower precordium. An electrocardiogram ([redacted]-59) showed sinus tachycardia, incomplete left bundle branch block, and symmetrically inverted T-waves in LL 2 and 3, and in AVF. The changes had appeared since [redacted] 1957. Chest film was negative. Leukocyte count (8-4-59) was 13,000 with 81 per cent neutrophilic cells and marked shift to the left. The patient was mildly febrile for 12 days and was discharged, undiagnosed but improved, 2 weeks after admission.

He did very poorly outside the hospital. He became progressively weaker and developed severe shaking chills in mid-[redacted]. He also lost about 30 pounds in [redacted].

*[Infarction of papillary muscles. Clinical and pathological observations]. Klinicheskaya Meditsina 29:51-57, 1951.

**[On the changes of the papillary muscles of the heart in myocardial infarction]. Arkhiv Patologii 21:48-54, 1959.

Physical examination ([redacted]59) showed a temperature of 101 degrees, pulse rate 120, and blood pressure 108/70. The patient was poorly oriented and extremely sluggish. There were numerous petechiae over the right forearm and hand. The heart was slightly enlarged and there was a grade IV holosystolic murmur at the apex, obscuring both sounds and radiating well into the axilla. P_2 was accentuated. Both the liver and the spleen were easily palpable and tender.

Electrocardiograms (3) were of poor quality but showed uniformly low voltage and flat T-waves in the limb leads. There was an intraventricular conduction defect of indeterminate type. Chest films showed moderate left ventricular enlargement and later [redacted]-59) showed increase in the size of the heart, plus scattered wispy areas of parenchymal density.

There was severe anemia (7-9 grams of hemoglobin) and marked increase in neutrophils in the peripheral blood. The urine contained many red and white cells and showed 4 plus tests for albumin. The BUN was 62 on entry but declined later. Circulation time (arm-to-tongue) was 20 seconds and venous pressure was normal. Blood cultures yielded coagulase positive staphylococcus.

Despite vigorous treatment with various antibiotics and other agents, the patient's course was inexorably unfavorable. Dyspnea gradually became more marked and on [redacted] signs suggestive of cerebrovascular accident appeared. He died on [redacted], twenty days after admission.

At autopsy, there were multiple petechiae over the arms and legs. The gallbladder was absent and the spleen was slightly enlarged. The kidneys had multiple petechiae on their surfaces. The heart weighed 520 grams; there was a moderate outpocketing from the posterolateral wall of the left ventricle the wall of which was well calcified. Both ventricles were considerably dilated. The papillary muscles of the left ventricle were represented by thin fibrous bands to which normal chordae tendinae were attached. Both papillary tabs were markedly displaced upward, resulting in considerable distortion and tilting of the mitral ring. The anterior mitral cusp had a friable vegetation on its atrial surface near its margin. Neither cusp was thickened or ulcerated. The aortic valve and the valves of the right side were normal. The left coronary artery was occluded by calcium and atheroma just proximal to the origin of the anterior descending branch. The right coronary artery was patent.

C. Perforation of a mitral cusp

This event, like rupture of a papillary muscle, is likely to produce failure and death quite rapidly. The processes most likely to cause it have already been discussed.

IV. Conclusions

Any disturbance of the delicate functional sequence in the application of muscular and hydraulic forces on the left side of the heart is capable of producing mitral regurgitation. Involvement of the valve leaflets is not essential.

The role of arteriosclerotic (coronary) heart disease in the production of functionally significant mitral regurgitation is abundantly established. The contribution made by this type of acquired mitral regurgitation to the clinical picture of coronary disease is important and needs reemphasis.