THE SIGNIFICANCE OF PULMONARY VASCULAR LESIONS IN THE SELECTION OF PATIENTS FOR MITRAL VALVE SURGERY*

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AMONG THE PATIENTS with disabling rheumatic heart disease, a considerable number have difficulties arising almost entirely from circulatory obstruction at the mitral valve. In such patients with pure non-regurgitant mitral stenosis the most promising therapeutic approach would seem to be a direct surgical relief of the stenosis. The problem was first thoroughly investigated by Cutler, Levine, and Beck,[1] but their efforts were terminated because of the death of nine out of 11 patients operated upon. With the subsequent advances in surgical technic, control of infection, anesthesia, and pre- and postoperative care, it has seemed reasonable to reopen this problem for investigation. A much lower mortality in selected patients has already been demonstrated by Bailey and his co-workers.[2] Eighteen of their last 21 patients have survived "mitral commissurotomy." Whether their method can be applied to the severely diseased valve and whether the commissural incision will subsequently heal with recurrence of stenosis are matters that have not yet been established. At the present time technical factors such as these are overshadowed by the problem of selecting patients for operation. It is the purpose of this paper to consider the significance of coexisting pulmonary vascular lesions in candidates for mitral valve surgery.

Patients selected for mitral commissurotomy should have significant disability, reduced life expectancy, and the primarily mechanical problem of mitral obstruction. We must exclude from operation those individuals with little disability as well as those desperately ill patients with severe cardiac and pulmonary damage who have little or no chance of surviving the operation. The futility of removing the circulatory obstruction at the mitral valve in patients with severe myocardial damage, associated defects of other valves, or a large element of mitral insufficiency has been emphasized.[3] We believe it is equally futile to operate upon patients with mitral stenosis who have secondary pulmonary changes sufficiently severe to constitute a coexistent circulatory obstruction of greater degree in the pulmonary vascular bed. The possibility that certain occlusive pulmonary vascular lesions might adversely affect operative results was suggested from pathologic evidence.[7] However, the significance of this contraindication has not been given sufficient attention in the

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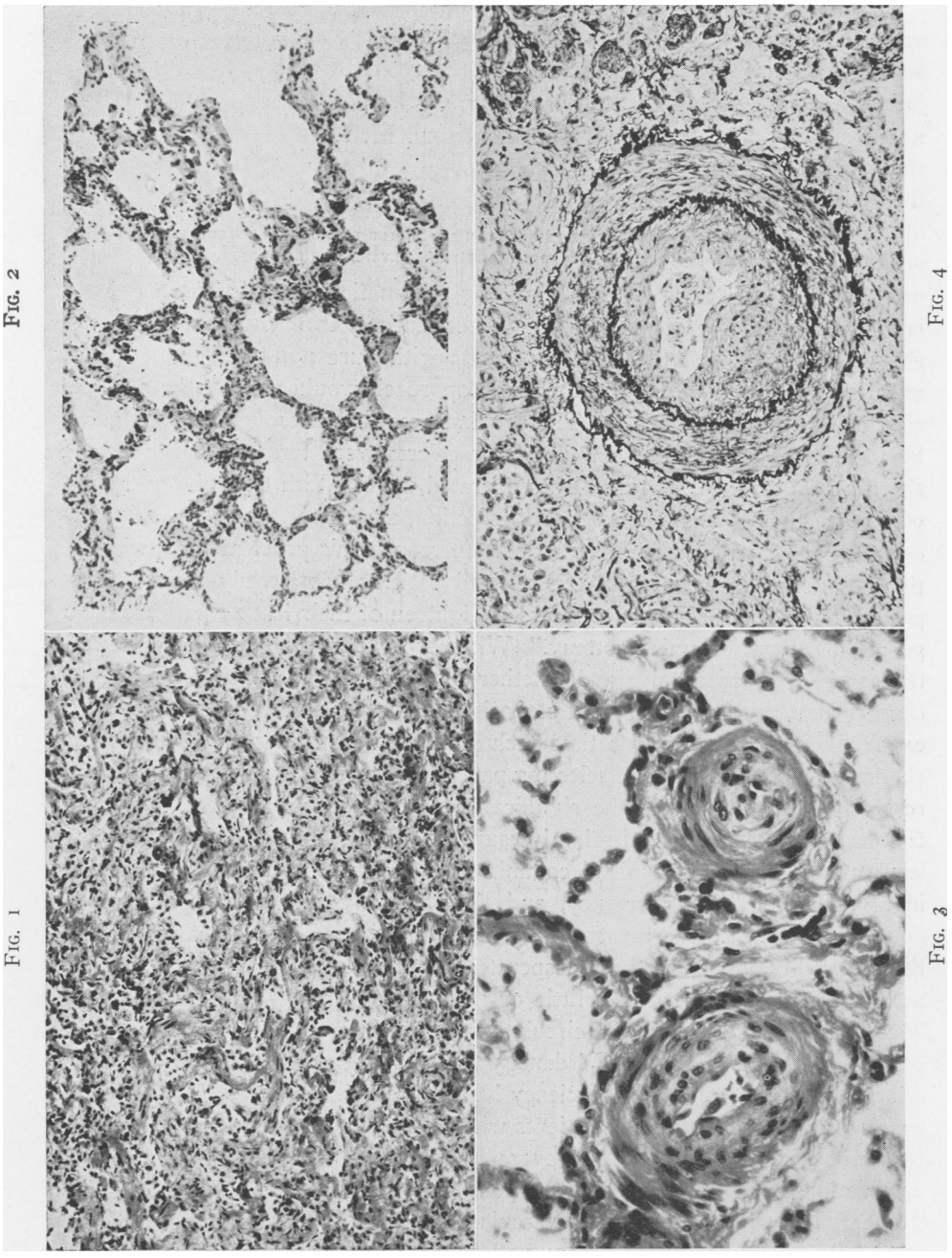

FIG. 1

FIG. 2

FIG. 3

FIG. 4

See legends on opposite page.

surgical literature to date, nor has the clinical problem of recognizing such patients been discussed.

Parker and Weiss[4] in 1936 pointed out the existence and significance of vascular lesions in the lungs which they believed to be proportional to the severity and duration of mitral obstruction. Three other series of patients have been reported calling attention to these changes.[5-7] These authors describe a lesion of the capillary basement membrane as one of the changes present in the lungs of patients with mitral stenosis. This lesion was not found in the lungs of a group of patients with congenital heart disease studied by one of us.[8] Of particular interest is the fact that this group included nine patients with combined mitral stenosis and atrioseptal defect (Lutembacher's Syndrome). These results suggest that the capillary basement membrane lesion is specific for pure mitral stenosis. It does not occur in other types of congestive failure, acyanotic congenital heart disease, pulmonary embolism, or infection. While most patients with mitral stenosis have pulmonary vascular changes,[4-7] advanced lesions are found at autopsy in only about one third. From these various observations made on pathologic study of the lungs of patients with mitral stenosis, the following sequence of events might be postulated to explain the pathogenesis of the vascular lesions: The pulmonary capillary bed lacks significant pericapillary tissue support. Hence, the increased pressure referred back from the left auricle in mitral obstruction results in a pericapillary transudate. Failure to absorb this high protein fluid from the pericapillary space results in organization and fibrosis, with thickening of the capillary basement membrane which increases at the expense of the capillary channel. Extension of the process into the septae results in diminished expansibility and loss of pulmonary reserve. This combination of events results in an increased resistance to the flow of blood through the lungs. The resulting pulmonary hypertension is associated with obliterating pathologic changes in the pulmonary arterial tree that add to this resistance. This can lead to pulmonary artery dilatation and pulmonic valve incompetence, throwing even greater burden on the right side of the heart.

It is thought that in the advanced stage these pulmonary vascular lesions result in a second circulatory obstruction in the pulmonic circuit which is in

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FIG. 1.—Non-functioning area from the right lower lobe showing end results of chronic passive congestion. Masson's trichrome light green 80x.

FIG. 2.—Showing thickening of alveolar septal walls with pericapillary fibrosis and nearly complete obliteration of vascular channels in an area from the right middle lobe. Micrometer measurements of the thickness of septal walls in this field averaged 42μ or twice normal. Hematoxylin and Eosin 50x.

FIG. 3.—Obliterating endarteritis in a 230μ vessel and hyperplastic arteriosclerosis in a 108μ vessel. The adjacent parenchyma appears normal. This field was selected from the apical portion of the right upper lobe. Hematoxylin and Eosin 250x.

FIG. 4.—Intimal atherosclerosis in a 1 mm. vessel in the apical portion of the right lower lobe. The elastic membranes are preserved and the subendothelial connective tissue proliferation results in marked reduction of the lumen. Verhoeff-van Gieson elastic tissue 100x.

large part irreversible. The importance of this was demonstrated recently in a patient with long standing mitral obstruction who died following a technically successful commissurotomy. This case is reported as an example of a patient with mitral stenosis whose far advanced pulmonary vascular lesions caused her death despite the surgical relief of her mitral obstruction.

Case Report.—E. W., a 36-year-old white female with rheumatic heart disease was admitted to the University of Pennsylvania Hospital for mitral valve surgery. At age 11 she had her first attack of rheumatic fever. At age 22 she was found to have auricular fibrillation, and the murmur typical of mitral stenosis. At age 23 she became dyspneic and had her first bout of hemoptysis. Nine years later she had developed persistent hepatomegaly and re-accumulating ascites with dyspnea, but without orthopnea or basal râles. At the time of her present admission, she was a bedridden, cardiac invalid.

Physical examination revealed a pale, dyspneic woman, with marked venous distention. She was not orthopneic and the lungs were clear of basal râles. The cardiac rhythm was totally irregular, with a rate of 80 per minute and no pulse deficit. At the apex, the first sound was accentuated, and a grade two systolic murmur was present. In diastole there was a "mitral opening snap" followed by a grade three rumbling diastolic murmur. At the base, the second sound was accentuated and a soft diastolic murmur was present in the pulmonic area. The liver edge was firm, non-pulsating and extended 5 cm. below the costal margin. After the removal of 1300 cc. of ascitic fluid, a moderately enlarged spleen was palpable. There was no edema of the sacral or pretibial areas. Clubbing and cyanosis were not present.

Special Studies. Roentgen ray examination revealed marked cardiac enlargement, particularly of the right ventricular and left auricular chambers. The pulmonary artery was prominent and showed increased pulsations. There was no evidence of pulmonary congestion.

An electrocardiogram showed auricular fibrillation, with a ventricular pattern suggesting right ventricular hypertrophy and digitalis effects.

On cardiac catheterization, the mean pulmonary arterial pressure was found to be greater than 100 mm. of mercury. It was possible by oxygen determination and pressure readings to rule out significant complicating tricuspid stenosis, septal defect, or pericardial constriction.

Pulmonary function studies showed that the arterial oxygen saturation was 93 per cent, that the residual capacity was increased in the face of normal gas distribution, and that the vital capacity was 60 per cent of normal. These are the results usually obtained with pulmonary congestion and edema and yet basal râles were not evident clinically. Spirographic tracings suggested the existence of relatively rigid and inelastic lungs.

A bromsulphalein test showed 16 per cent retention. All other liver function studies were negative, including serum albumin and globulin, prothrombin time, cephalin flocculation, and colloidal gold test.

Hospital Course and Operative Findings. Preoperatively she was maintained on digitalis, mercurial diuretics, low salt diet and bedrest in an unsuccessful attempt to relieve the ascites, hepatomegaly, and elevated venous pressure. An antero-lateral mitral commissurotomy[2] was performed, with the feeling that this represented her only chance of relief. A striking finding at operation was that of an enormous pulmonary artery with a pressure that, by palpation, seemed almost equal to that of the much smaller aorta. After commissurotomy the pressure in the pulmonary artery did not change appreciably to palpation.

Postoperatively, absence of the "mitral opening snap" and of the mitral diastolic murmur suggested satisfactory relief of the valvular obstruction. However, systemic hypotension developed and the venous pressure rose in the absence of significant postoperative pulmonary complications or physical signs of pulmonary congestion (*i.e.*, basal

râles). With this clinical picture it seemed likely that she had an obstruction in her pulmonary vascular bed accounting for the absence of râles, failure of filling of the left side of the heart, and diminished cardiac output. The systemic hypotension and elevated venous pressure continued until the time of her death 3 days later.

AUTOPSY FINDINGS

Except for ascites, and chronic passive congestion of the liver and spleen, the principal findings were limited to the heart and lungs.

Heart—Gross. The heart was twice normal in size and weighed 640 Gm. This enlargement was predominantly right-sided. On opening the surgical incision in the left auricular appendage, the interauricular septum was found to be intact and there was a typical "fishmouth" deformity of the mitral valve. The original opening measured only 8 mm. in diameter. The commissurotomy incision appeared satisfactory, being anterolateral, 1.3 cm. in length, and showing no evidence of healing. The valve was sufficiently pliable so that the incision apparently had relieved the stenosis. There was minimal rheumatic involvement of the aortic valve. The cut surface of the myocardium appeared normal and the coronary vessels were patent. The right ventricular wall measured 1.0 cm. in thickness, and the left 1.5 cm. The main pulmonary artery showed atherosclerotic change and measured 9.5 cm. in circumference 2.0 cm. distal to the valve. This was nearly twice the circumference of the aorta at the same level.

Heart—Microscopic. There were numerous foci of scarring in the myocardium. However, there was no evidence of active rheumatic myocarditis.

Lungs—Gross. On cut surface, the sclerotic smaller branches of the pulmonary artery stood out sharply and there was evidence of "brown induration" with superimposed terminal congestion.

Lungs—Microscopic. (1) Method: Several blocks of tissue were taken from each lobe, and were fixed in 10 per cent Formalin. Sections from these blocks were stained with hematoxylin and eosin, a combination of Van Gieson's and Verhoeff's elastic tissue method on the same section, and Masson's trichrome light green. The vascular changes encountered were so striking that it seemed superfluous to make the calculation of wall to lumen ratios recommended by Kernohan, *et al.*[9] An ocular screw micrometer was used to measure the external diameter and medial coats of vessels and to determine to what degree the capillary basement membrane lesion of Parker and Weiss was present.

(2) Findings: The alveolar septal lesion described by Parker and Weiss[4] varied in severity but was uniformly present in the lower two thirds of each lung. In these areas fibrosis was marked and the normal architectural pattern was destroyed (see Fig. 1). Above this level there was a gradual change to a coarse latticed structure with marked thickening of the alveolar septae due to collagen deposition. This amorphous material compressed or obliterated alveolar capillary channels and separated them from air filled spaces. Such an area is included in Figure 2.

In addition to the pericapillary lesions, severe and constant obliterating vascular lesions were encountered throughout all lobes of the lungs. The arterioles showed a laminated sclerosis of the type commonly seen in the systemic arteries in hypertension. The lumina of these vessels were often reduced to capillary size. Obliterating endarteritis was consistently found in the small arteries. Figure 3 shows both of these lesions in a section taken from the apical portion of the right upper lobe. Grossly this part of the lung appeared normal. Marked reduction in lumen is seen in a 1 mm. vessel in Figure 4. In all of the arteries greater than 1 mm. in external diameter which were examined microscopically, severe atherosclerotic changes were found. Changes in the medial coat of vessels were not impressive in the Verhoeff/van Geison preparations. The type of arteritis described by Von Glahn and Pappenheimer in cases of active rheumatic infection was not found.[10] There was no evidence of extensive thrombosis with reorganization. The pulmonary veins appeared normal but were of large size.

DISCUSSION

Despite a technically successful commissurotomy this patient died with severe hypotension and remarkable engorgement of the peripheral veins and liver. We believe that she died in spite of relieving the mitral stenosis, because there was a coexistent obstruction of a greater degree in the pulmonary circulation. The vascular changes in the lungs found on pathologic examination seemed to explain her inability to fill adequately the left side of the heart.

During the present developmental phase of mitral valve surgery, it is probably inevitable that most of the patients with mitral stenosis subjected to operation will be those whose prognosis is otherwise poor. It is important, therefore, to attempt to recognize and to exclude individuals who will not be helped by operation. The patient reported above represents one type of contraindication; namely, the individual with pulmonary vascular obstruction of a degree sufficiently severe to make it relatively useless to relieve the mitral stenosis. The following characteristics shown by this patient deserve emphasis and might allow preoperative recognition of this contraindication in the future:

1. A history of disability of long duration was obtained in a patient with known mitral stenosis.

2. Long-standing signs of venous distention, hepatomegaly, and ascites were present and were not cleared up by medical treatment.

3. Severe dyspnea occurred on effort, but significant orthopnea and basal râles were not present.

4. An unusually large and hyperpulsatile pulmonary artery was observed fluoroscopically and was considered suggestive of hypertension within the pulmonary circulation.

5. A markedly elevated pulmonary artery pressure was found on cardiac catheterization. The mean pressure was over 100 mm. Hg., even though the reading was made after a prolonged period of treatment directed towards relief of cardiac failure. Studies of a series of patients will be necessary before a range of pressure can be determined above which operation is likely to fail. Serial cardiac catheterization has been shown to offer information about changes in pulmonary artery flow as well as the degree and lability of pulmonary hypertension.[11, 12]

6. Pulmonary function studies revealed a diminished arterial oxygen saturation and delay in the oxygen diffusion rate.*

* Pulmonary function studies have been somewhat disappointing thus far in helping to assess these patients preoperatively. It should be possible theoretically to estimate the severity of the alveolar septal lesion by determining the functional state of the alveolocapillary membrane. Unfortunately the alteration in oxygen diffusion rate expected with pericapillary fibrosis occurs in a number of other conditions. Such changes must therefore be interpreted in the light of other findings, such as the presence or absence of râles. Spirographic tracings probably give more information as to the existence of parenchymal and vascular damage.

The above points may help to characterize the individual with severe pulmonary vascular changes. This type of patient must be distinguished from individuals with mitral stenosis complicated by other lesions of congenital or rheumatic origin, such as tricuspid disease, septal defects, or constrictive pericarditis. Although ability to recognize such severely handicapped patients is helpful, we are still faced with the problem of how severe pulmonary changes may be and yet permit the patient to be improved following surgical release of the mitral obstruction. Our tentative feeling is that a patient does not have pulmonary vascular lesions of sufficient severity to contraindicate surgery if (1) he can be freed of failure on medical treatment, (2) the venous pressure and arm to lung circulation time become normal, and (3) the pulmonary artery pressure is not fixed at a markedly elevated level.

At present, no combination of laboratory tests infallibly assesses the degree and extent of obstructing pulmonary vascular changes. It has been demonstrated that quantitative evaluation of vascular change is possible by establishing the resistance to flow and pressure gradient across the pulmonary capillary bed.[13] Direct pressure measurements of this general type could be obtained at the time of operation in patients with mitral stenosis. In the event of a markedly increased pressure gradient between the pulmonary artery and vein, one would anticipate little improvement after operation upon the mitral valve. However, reversibility of vascular and parenchymal damage may be possible to some degree.

CONCLUSION

1. Pulmonary vascular lesions may produce secondary obstruction within the pulmonic circuit in patients with long standing mitral stenosis.

2. The significance of these pulmonary vascular lesions in the selection of patients for mitral valve surgery has been given only scant attention in the surgical literature.

3. A patient with mitral stenosis is described in whom pulmonary vascular lesions were present to a marked degree. These seemed to account for failure of the mechanically adequate mitral commissurotomy to relieve the existing circulatory obstruction.

4. Previous observations and a review of the literature suggest that such patients will not derive benefit from surgical measures aimed at the relief of mitral stenosis.

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