CLINICOPATHOLOGIC CORRELATIONS

Coronary Atherosclerosis in Subjects with Mitral Stenosis

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SUMMARY The coronary arteries were examined in 60 specimens from patients with mitral stenosis. In three, localized obstruction was nonatherosclerotic in nature (in one, arterial dysplasia; in two, embolic). In 18 of the remaining 57 cases (31.5%), significantly obstructive atherosclerosis in one or more segments of the coronary arterial system was found. This represented 46% of the males and 27% of the females.

The clinical expressions of mitral stenosis are usually explicable by the altered hemodynamics of this condition. Nevertheless, the presence of mitral stenosis does not preclude the presence of an etiologically unrelated condition in the form of coronary atherosclerosis.

With this view in mind, a study was undertaken to determine the incidence and severity of coronary atherosclerosis as observed at autopsy in a series of specimens from patients with mitral stenosis.

Materials and Methods

The material for this study was obtained from 60 specimens of heart filed in the Cardiovascular Registry of the Miller Division of United Hospitals. About one-half of these were obtained from the University of Minnesota Hospitals and the balance from other sources. In each, mitral stenosis was or had been present, usually of severe degree. In 24 of the cases, mitral valvular replacement had been done, and in most of these death had occurred in the early postoperative period. Cases with mitral regurgitation of any degree or with tricuspid or aortic valvular disease were not included in this study.

Cross sections of the coronary arteries in the epicardium were made with a sharp knife at 3 mm intervals from the ostia of origin to the terminal branches. In cases of doubt regarding degree of narrowing or the nature of disease, sections were examined histologically. In three of the 60 cases histologic examination revealed significant obstruction but by a cause other than atherosclerosis. These three cases will be described in a subsequent section dealing with nonatherosclerotic disease. In each of the remaining 57 cases, there was either no significant disease or there was atherosclerosis of the coronary arteries as determined by gross characteristics alone or by histologic confirmation. Grading of atherosclerosis was done on the basis of percentage reduction of lumen using the same criteria for grading as White and associates.

As controls, values obtained for men by White and associates and for women by Ackerman and associates were used. These investigators had determined the average grade of maximal coronary atherosclerosis in consecutive autopsies by decade of men and women, respectively.

The individual coronary arterial segments used for evaluation were the same as used by White and associates and by Ackerman and associates. These were six in number and are herein called the study segments. They were (1) left coronary main, (2) anterior descending, (3) left circumflex, (4) right, (5) marginal branch of right and (6) posterior descending coronary arteries. The anterior descending, left circumflex and right coronary arteries were subdivided into proximal and distal halves. For the right coronary artery, the terms anterior and intermediate segments were used as defined by Vlodaver and Edwards in identifying the proximal and distal segments, respectively. The posterior descending artery was considered as a segment separate from the right coronary artery. In addition, the marginal branch of the left circumflex artery and the first diagonal branch of the anterior descending artery were examined but not included in the averages of the study segments. In each case, the maximal grade of atherosclerosis was determined for each of the six study segments. For those arteries that were subdivided into proximal and distal segments, only one value was used. This was the greatest degree of atherosclerosis regardless of subdivision of the vessel in which it was found. These values were added and divided by six to give an average of maximal sclerosis for the case. The average grades of maximal sclerosis for each case in each sex-decade group were added and the sum divided by the number of cases in that sex-decade group to yield the average maximal sclerosis for that sex-decade group.

Results

Age and Sex

There were 47 females and 13 males among a total of 60 cases, the ratio of females to males being 3.6:1. For females and for males, the most common decade at the time of death was the sixth.
Nonatheromatous Disease

Among the 60 cases there were six cases with obstructive disease involving only one artery. Histologic examination of the obstructive lesions in these cases showed that in three the lesions were atheromatous in nature. One of the latter was characterized by dysplasia of the media with intimal thickening (fig. 1a), while in two it appeared that the obstruction had been caused by embolism. In one of the latter, the lumen was narrowed by calcific material, while in the other the lumen was obstructed by organized thrombotic material (fig. 1b) and not associated with atherosclerosis. In the case with arterial dysplasia, similar lesions were found in the branches of the aortic arch.

Atheromatous Disease

The remaining three of the six cases with single vessel disease showed the obstructive lesion to be atheromatous in nature. In these, usually there was one lesion of major proportion, while there were other foci of atherosclerosis which did not cause significant obstruction. Two of the three with single vessel atherosclerosis were females (aged 42 and 60 years) and the third was a 62-year-old male. These cases are included in the analysis with the remaining cases, yielding 57 subjects with mitral stenosis exclusive of the three with nonatheromatous coronary disease.

In general, the average grade of maximal sclerosis of each sex-decade group was lower than that reported earlier by White and associates and by Ackerman and associates (fig. 2). Nevertheless, 18 of the 57 cases (31.5%) showed severe degrees of coronary atherosclerosis in one or more coronary arteries. Among the 44 female subjects, 12 (27%) showed severe coronary atherosclerosis in one or more foci, while among the 17 males severe atherosclerosis was noted in six (46%).

Among the females, the youngest age in which significant degrees of coronary atherosclerosis were observed was the fifth decade with minimal decline in the sixth and seventh decades. In the males, the youngest age in which significant disease was noted was the sixth decade (fig. 3). This figure, which is out of agreement with general observations, may be a reflection of the small number of males in this series. It is of interest that of the six subjects in the eighth decade (four females, two males), none showed significant coronary atherosclerosis.

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**FIGURE 1.** Two examples of nonatherosclerotic obstructive coronary disease in mitral stenosis. a) Left main coronary artery showing medial dysplasia. The media shows extensive elastosis. The intima is thickened by fibrous tissue which causes luminal narrowing. Elastic tissue stain; X 21. b) Lumen of a coronary artery obstructed by organized thrombotic material which is considered to have been embolic in origin. H & E; X 24.

**FIGURE 2.** Comparison of average maximal grade of coronary sclerosis in mitral stenosis (dotted lines) with controls of White and associates in the male and of Ackerman and associates in the female.
Among the 18 cases with severe atherosclerosis, the number of cases by number of coronary arteries so involved was as follows: one vessel, three cases; two vessels, eight cases; three vessels, six cases; and four vessels, one case.

From the 18 cases with severe atherosclerosis, a tabulation was made of the relative frequency of involvement by severe disease of the various segments of the coronary arterial tree (fig. 4). This showed that among such cases the proximal half of the anterior descending artery was involved in two-thirds of the cases, while both the anterior and inter-medial segments of the right coronary artery were involved less frequently (44%).

Comment

From angiographic studies on 26 living men with mitral stenosis, Befeler and associates6 found evidence of significant coronary atherosclerosis in five (18%), while eight showed mild atheromatous disease and 13 had normal arteries. Gardner and White,6 in 1949, found evidence of coronary disease in ten of 314 clinical cases of mitral stenosis (five of the ten came to autopsy and significant coronary atherosclerosis was confirmed).

Our pathologic studies showed a higher incidence of significant coronary atherosclerosis than might be implied from the foregoing. In all males in our series the incidence was 46% and in all females 27%. For males, our figures are less than the incidence of significant atherosclerosis as observed in consecutive cases by White and associates. Using the figures of White and associates for consecutive autopsies on males from the fifth through the eighth decades, 62% of cases showed severe atherosclerosis at one or more points in the coronary system. This compares with a figure of 44% in our series.

We averaged the figures for females in the study of Ackerman and associates for the decades that corresponded in their studies and in ours. From this, it may be gained that 26% of females in Ackerman's series showed significant atherosclerosis at one or more points in the coronary system. This compares with a figure of 35% for the comparably aged females in our series.

The differences in incidence of significant atherosclerosis in our series as compared with those in the studies cited may be explained in part by the relatively small number of cases. In any event, it is to be recognized that for a given case with mitral stenosis, the existence of the valvular disease does not preclude the coexistence of significant coronary atherosclerosis.

This may have a bearing on the interpretation of chest pain in the patient with mitral stenosis. While in the majority of cases this symptom may be brought on by the pulmonary hypertension associated with mitral stenosis, in others it may be true angina pectoris of coronary origin.

Regardless of the relatively high incidence of significant coronary atherosclerosis at one or several points in the coronary system in mitral stenosis, it is of interest that the average grade of maximal sclerosis per sex-decade in our series was, in general, lower than in the consecutive cases cited. This difference may reflect the phenomenon that in subjects with mitral stenosis the number of vessels involved by coronary disease is less extensive than in the general population.

In our series of 18 patients with significant coronary atherosclerosis, only one or two vessels were involved in 11 cases (61%). In a series of patients with angina, Guthrie and associates6 found that 21% showed significant disease restricted to only one or two vessels, the majority (79%) showing three or more vessels involved.

References
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