Sclerosis of the Chordae Tendineae of the Mitral Valve

By Leon Sokoloff, M.D., Samuel K. Elster, Captain, MC, AUS, and Norman Righthand, M.D.

Thickening and sclerosis of the chordae tendineae of the mitral valve are seen fairly frequently in hearts that are not ordinarily considered to be rheumatic. In this report a systematic study of these lesions is presented. Factors involved in their pathogenesis and their significance in the development of the chronic rheumatic deformity are discussed.

In numerous investigations concerning the sclerotic lesions of the valves of the heart, detailed descriptions of the rings and leaflets of the aortic and mitral valves have been made.1-14 These various sclerotic changes have been interpreted as rheumatic, inflammatory, degenerative, or congenital. Although the chordae tendineae of the mitral valve are frequently thickened or otherwise deformed, they have apparently not been the object of systematic study. More than thirty years ago Felsenreich and von Wiesner1 noted that a remarkably large number of isolated chordae were thickened or had low-grade fusion. The histologic appearance of such chordae suggested the extension of an inflammatory process from the leaflet. Previous writers had included these thickenings with the hyperplastic, noninflammatory changes of the mitral leaflet that take place with wear and tear. Deposition of lipid in the chordae, or at their insertions into the mitral leaflet, in persons beyond the third decade of life is common.7, 9-11 Loss of cellularity and microscopic calcification occur at these sites as another manifestation of the aging of the connective tissue of the cardiac “skeleton.”10, 11 The likelihood that mechanical factors influence the development of these changes has been considered by several observers.5, 11 Böhming and Krückberg12 considered the sclerotic changes in the chordae and those of the insertional portion of the leaflet to be the result of various types of systemic infections, a response to foreign proteins “in the broadest sense.”

In the present investigation the dimensions and histologic appearance of the chordae tendineae have been studied in human hearts that were considered grossly to be nonrheumatic. The extent and pattern of distribution of the sclerotic changes were thus determined and correlated with many factors of possible significance in the pathogenesis of the lesions.

Methods and Material

The study was made on 200 hearts examined at necropsy in Bellevue Hospital, New York. These included a large proportion from children, women, and Negroes. Many of the hearts from these were obtained through the courtesy of Drs. Milton Helpern, Robert Fisher, and Henry Weinberg of the Medical Examiner’s Department of the City of New York. All hearts with distinct rheumatic lesions such as fusion of the chordae tendineae and all those from subjects with a history of rheumatic fever were excluded. The hearts were otherwise unselected.

The mitral valves were excised in the region of the annulus and at the origin of the chordae from the papillary muscles. They were fixed in a flattened position in 10 per cent formalin. Precise measurement of the diameter (width) of the chorda was made from photographic enlargements of both leaflets. The surfaces of the leaflets were wiped dry, the valve placed in the negative holder of a photographic en-
larger (Federal § 440), and the image projected onto photosensitive enlarging paper of medium contrast. The magnification used was three diameters. The leaflets were placed ventricular face down in the holder so that this surface was brought into prominence in the photographic image. It was decided that the length and width of the chordae inserting into the ventricular aspect of the leaflets (chordae of the second order [Tandler¹²]) were more amenable to measurement than were those of the chordae inserting into the free margin (chordae of the first order). Letters were used to designate the chordae on either side of the apex of the free margin of the anterior leaflet; the chordae on the anterior (left) side of this leaflet were labeled with a capital letter (A, B, C, and so on), while those on the posterior (right) side were marked with a lower-case letter (a, b, c, and so on). The width (diameter) was measured with calipers and was accurate to 0.1 millimeter. In the majority of instances the main trunk of the chordae was of fairly uniform diameter and offered no difficulty in measurement since major branching of the chordae took place shortly beyond the origin or close to the insertion. When major branching took place at a more intermediate position, the diameters of the branches rather than the main trunks were determined. The length of each chorda was measured between the origin and a line drawn on the photographs along the apex of the arcade between the insertions (fig. 1). Similar observations were made for comparative purposes on fifty bovine mitral valves.

Gross sections of the thickest chorda of the anterior leaflet were made for histologic study in each case. A strip of paper attached to the ventricular aspect with a 50 per cent solution of gum acacia was used to orient each specimen in the paraffin block. This permitted exact localization of sclerotic alterations. Sections were stained with hematoxylin and eosin, and, when the sclerosis was marked, with Weigert-Van Gieson stains. The thickness of the central (fibrosa) layer and the external (subendocardial) layer was measured with an eyepiece micrometer. Sections of the mitral leaflet were made when the chordae were sclerotic. Sections of myocardium were available except from the hearts of 15 infants or young individuals and 5 adults obtained from the medical examiner's office. In none of these 20 hearts was there appreciable sclerosis.

The following data were recorded when available: weight of the heart; age, sex, race, and arterial blood pressure of the subject; an estimate of the degree of generalized arteriosclerosis; circumference of the ring of the mitral valve; the presence of calcification in the annulus of the aortic and mitral valves, myocardial infarction, pericarditis, and syphilitic aortitis.

The width of a chorda tendineae approximates its diameter only when the chorda is almost round on cross section. In 13 of the adults and 7 of the infants and children, the widest chordae were markedly flattened and measurements of these chordae have been excluded from the calculations.

**Results**

Casual inspection of the valves revealed a relative thickening of certain chordae tendineae of the anterior leaflet of the mitral valve in every heart. The histologic sections of the thickest chorda disclosed that most of its substance was made up of relatively acellular collagen. This material was usually directed, in a normal fashion, parallel to the long axis of the chorda. In the hearts from subjects in the third decade of life or older, a subendocardial layer of collagen frequently encircled this central core, at least in part. When this circular layer was thick, it constituted the bulk of the cross section and could even be distinguished grossly. Such enlarged and altered chordae were readily identified as abnormal (fig. 2). Obviously, there has been an accretion of tissue. A certain degree of subendocardial thickening can be interpreted as analogous to the stratification that occurs in the leaflets of the mitral valve with aging.¹⁰ Chordae that showed only slight subendocardial thickening without gross enlargement were classified as normal for the adult. Those with a thick subendocardial ring were listed as sclerotic chordae tendineae. Separate categories were made for infants, 1 year of age or less, and children, below 16 years. As stated
Fig. 1.—(Left) A working-type photograph of the ventricular aspect of the mitral valve; anterior leaflet above and posterior leaflet below. This is one of the normal adult specimens. Because this is a negative image, the relative positions of the lettered series are inverted; that is, in the actual specimen, chordae designated with capital letters appear on the right and those with lower-case letters on the left. (X1/3.)

Fig. 2.—(Upper right) Mitral valve with slerotic A and a chordae tendineae of the anterior leaflet. From an 82 year old white man. The a chorda is 2.2 mm. wide and 26.7 mm. long. The average diameter of the chordae of the posterior leaflet is 0.32 mm. while the average length is 21.3 mm.

Fig. 3.—(Lower right) Mitral valve with mild rheumatic deformity. There is gross sclerosis of the second order chordae of the anterior leaflet and the adjacent right posterior leaflet chordae. The remaining posterior leaflet chordae are delicate.
TABLE 1.—Diameters of Thickest Second Order
Chorda Tendinea of Anterior Leaflet
(in millimeters)

<table>
<thead>
<tr>
<th></th>
<th>Normal (Adult)</th>
<th>Infants</th>
<th>Children</th>
<th>Sclerotic (Adult)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average</td>
<td>0.86</td>
<td>0.37</td>
<td>0.50</td>
<td>2.15</td>
</tr>
<tr>
<td>Range</td>
<td>0.4-1.5</td>
<td>0.2-0.5</td>
<td>0.4-0.7</td>
<td>1.2-3.8</td>
</tr>
<tr>
<td>Standard deviation</td>
<td>±0.20</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Number of cases</td>
<td>149*</td>
<td>10 (7)</td>
<td>17 (13)</td>
<td>11</td>
</tr>
</tbody>
</table>

* Thirteen cases in which the widest chorda tendinea was flattened are not included in this table.
† The figures in the parentheses represent the number of hearts with chordae that were not flattened and were therefore suitable for the above calculations. The figures not in parentheses include both types of chordae.

TABLE 2.—Average Diameters of Second Order
Chorda Tendinea of Posterior Leaflet
(in Millimeters)

<table>
<thead>
<tr>
<th></th>
<th>Normal Chorda (Adult)</th>
<th>Sclerotic Chorda (Adult)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average</td>
<td>0.35</td>
<td>0.35</td>
</tr>
<tr>
<td>Range</td>
<td>0.19-0.56</td>
<td>0.29-0.42</td>
</tr>
<tr>
<td>Standard deviation</td>
<td>±0.07</td>
<td>—</td>
</tr>
<tr>
<td>Number of cases</td>
<td>149</td>
<td>11</td>
</tr>
</tbody>
</table>

TABLE 3.—Lengths of Second Order Chordae Tendinea (in Millimeters)

<table>
<thead>
<tr>
<th></th>
<th>Average Posterior Leaflet</th>
<th>Anterior Leaflet</th>
<th>Ratio: Length of Thickest Anterior to Average Posterior</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>C</td>
<td>B</td>
<td>A</td>
</tr>
<tr>
<td>Average of normal chordae (adult)</td>
<td>18.0</td>
<td>18.0</td>
<td>19.0</td>
</tr>
<tr>
<td>Range</td>
<td>10.1-29.0</td>
<td>9.0-33.3</td>
<td>10.0-28.7</td>
</tr>
<tr>
<td>Standard deviation</td>
<td>±3.3</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Number of cases</td>
<td>149</td>
<td>134</td>
<td>147</td>
</tr>
<tr>
<td>Average of sclerotic chordae (adult)</td>
<td>17.3</td>
<td>16.7</td>
<td>17.5</td>
</tr>
<tr>
<td>Range</td>
<td>12.2-22.4</td>
<td>12.3-21.0</td>
<td>11.7-24.0</td>
</tr>
<tr>
<td>Number of cases</td>
<td>11</td>
<td>10</td>
<td>11</td>
</tr>
</tbody>
</table>

### Dimensions of the Chordae Tendinea (Tables 1–3)

In the normal group, there was in every heart a relative thickening of certain of the chordae of the anterior leaflet compared with those of the posterior. The diameter of the thickest of these followed a normal-type distribution curve (fig. 4). The scatter of variation between the posterior leaflet chordae is much smaller. The relative thickening of an anterior leaflet chorda may be expressed as the

![Figure 4](http://circ.ahajournals.org/figs/152638/fig4.jpg)
ratio of its diameter to the average of the diameters of the posterior leaflet chordae. In the normal group this average value was 2.5. In most instances the thickest chordae were those most central of the anterior leaflet (A, B, a). This relationship obtained also in infants and children. In 50 bovine hearts the average diameter of the thickest chorda tendinea of the anterior leaflet was 1.6 ± 0.34 mm. and the general average of the individual average diameters of the posterior leaflet chordae tendineae was 0.7 ± 0.03 mm., a ratio of 2.3.

In the 11 sclerotic hearts the diameter of the chordae was in general very greatly increased. Usually only one or two of the chordae were involved and in this group also the site of predi-

**Fig. 5.—Cross section of the thickest second order chorda tendinea of the anterior mitral leaflet of a 6-month-old infant. Nuclei of fibroblasts are discernible in the central core, and their main axis in some instances is in the plane of the section.** (Hematoxylin and eosin stain. ×80.)

lection for the thickening was the a, A, or B position. In addition, in the group with flattened chordae, thickening due to similar histologic alteration was found in two isolated posterior leaflet chordae and in one anterior leaflet chorda; these are excluded from the present calculations.

In the sclerotic group the thickening did not involve the chordae of the posterior leaflet; the average diameters of the latter were the same in the sclerotic and normal hearts.

In most instances the sclerosis involved the entire length of the chorda. Occasionally there was fusiform swelling of only the trunk of the chorda or a tapered thickening at the insertion into the leaflet.

The lengths of the chordae tendineae of the anterior leaflet varied greatly, usually to a much greater degree than did those of the posterior leaflet. Their relative length in each heart has been expressed as a ratio of the length of the anterior leaflet chorda to the average of the lengths of the chordae of the posterior leaflet. In general, the second order chordae of the anterior leaflet were only slightly longer (1.14) than those of the posterior leaflet. In the sclerotic anterior leaflet chordae the relative length was 1.18. This difference is insignificant and demonstrates that the process of sclerosis was not accompanied by shortening.

**Histologic Structure.** The collagenous core of the normal chorda was continuous with the dense fibrosa layer of the leaflet. In infancy and early adult life it was largely acellular, but the collagen was clearly fibrillar. At this time the fibrils were wavy and therefore courses for a distance in the plane of the cross section although mostly they were directed in the plane of the axis of the chorda (fig. 5). With aging the collagen became less fibrillar, and formed more compact, less cellular bundles. The subendocardial circular layer was rarely prominent in subjects younger than 30 years of age. When it first became prominent it was loosely arranged, and paler than the central core and more cellular. In older subjects in the later decades of life it, too, became hyalinized although the circular arrangement clearly persisted.

In the flattened chorda the collagen was arranged either as a single flattened dense band or as two partially fused, round bundles contained within a single endocardial sheath (fig. 6). The former pattern was more frequent than the latter. The main trunk of a chorda typically had a single core before it gave off its branches.

The sclerotic chordae were composed principally of hyalinized collagen arranged in concentric circles. In the mildest form, this circular layer surrounded a moderately well-preserved central core of axially arranged fibers, while in more advanced lesions the central core became atrophic (fig. 7). In several cases, two or three such axial bundles were found. With Weigert-van Gieson stains, frayed elastic tissue fibrils were seen at the periphery of these axial bun-
The subendocardial layer was stippled with calcific granules in one specimen. The leaflet was thickened also at the insertion of the chorda; when the chorda was sclerotic, this thickening was produced by hyaline collagen and irregular areas of looser, pale, basophilic fibrous tissue. In only two instances was there considerable thickening of the remainder of the leaflet as well. In only one example did the leaflet or valve ring contain blood vessels; these were of the thick-walled type seen commonly in hearts with healed rheumatic valvulitis. The sections of myocardium revealed no Aschoff bodies or paravascular scars. Frozen sections of several of the sclerotic chordae stained with sudan 4 revealed very little lipid. Except for fibroblasts and a few mononuclear cells, there was no cellular reaction. The original core of the chorda was usually centrally placed in the area of thickening.

Influence of Age, Race, and Sex. Sclerotic chordae were found only in the hearts of white men from 37 to 82 years of age. If flattened chordae are excluded, there were no sclerotic

FIG. 7—Section of a sclerotic anterior leaflet chorda from a 62 year old white man. The circular subendocardial layer is greatly increased in thickness and there is atrophy of the central core. (Weigert-van Gieson stains. X35.)

ones in 65 individuals less than 35 years of age. No progressive increase of incidence with age was noted among the hearts of the 11 subjects with sclerotic chordae who were older than 37 years of age (fig. 8). Nevertheless, age would appear to be an important factor in the pathogenesis of this lesion since it was not found in

FIG. 8.—The relation between the diameter of the thickest chorda tendinea of the anterior leaflet and the age of the subject.
subjects who had not reached the fourth decade of life.

There were 122 white and 38 Negro adults in the series. Nine per cent of the former and none of the latter had sclerotic chordae. At first glance this would seem to be a significant difference. Yet Negroes constituted 69 per cent of the adults below 36 years of age and only 12 per cent of those above, and the absence of sclerosis in this group may be due to the younger age. It cannot be denied, however, that the reverse may be true, namely, that the absence of sclerosis in the younger group may theoretically be attributable to the high proportion of Negroes.

There were 112 adult males and 49 females. Nine and eight-tenths per cent of the men but none of the women had sclerotic chordae. Fifty-nine per cent of the young adults were women, whereas in the older group the women comprised only 25 per cent. The sex difference may therefore be attributed in part to age factors. The series is too small to allow a definitive statement in this regard. We have noted sclerotic chordae tendineae in the heart of a woman not included in this series.

Influence of Blood Pressure, Weight of Heart, Arteriosclerosis, and Other Lesions. Blood pressure readings were available in 116 of the 160 adults; 106 had normal chordae while in 10 there were sclerotic chordae. The subjects whose blood pressure readings were available were grouped into three classes: those with low blood pressure (less than 100/70)—4; those with normal blood pressure (100/70 to 148/88) —75; those with high blood pressure (150/90 and higher)—37. The incidence of the thickening of chordae of the normal type was almost identical in the hypertensive and normotensive groups. Two of the 10 patients with sclerotic lesions (20 per cent) had hypertension; 34 per cent of the persons with nonsclerotic chordae had elevated blood pressures. Arterial hypertension was thus not a significant factor in the development of this lesion.

The weight of the heart in the adults bore no relation to the diameter of the thickest chorda tendinea of the anterior leaflet or to the development of the sclerosis (fig. 9). The latter was seen in hearts weighing from 170 to 620 grams. The heart weighed more than 490 grams in only 2 subjects with sclerotic chordae. In general the length of the chordae of the second order was greater in hypertrophied hearts than in small ones, but there was much individual variation. The circumference of the mitral ring could not be correlated with the presence of the lesion.

The degree of generalized arteriosclerosis was graded as none, mild, moderate, or severe. There were 17 young adults without appreciable arteriosclerosis. Sclerosis of the chordae tendineae was not present in any of these nor in the other young adults who had some arteriosclerosis. Among the older group 7.6 per cent of those with mild, 5.6 per cent of those with moderate, and 10.8 per cent of those with severe arteriosclerosis had marked lesions of the chordae. Similarly there was no striking correlation with the incidence of myocardial infarction or calcification of the rings of the mitral or aortic valves.

In 2 of the 11 subjects with sclerosis there was an associated syphilitic aortitis without insufficiency of the aortic valve. Pericarditis was absent in all eleven. In 2 subjects the principal anatomic diagnosis was pulmonary tuberculosis; in four there was a carcinoma of the upper gastrointestinal tract; in the remaining the diagnoses included generalized arteriosclerosis, and duodenal ulcer with perforation.

Discussion

The results demonstrate that relative thickening of some of the chordae tendineae of the second order of the anterior mitral leaflet occurs with regularity in the human heart. Two types may be distinguished: (1) thickening as a normal structural pattern, or (2) an acquired sclerotic thickening.

That the first type of thickening of the chordae in this region is inherent in the construction of the valve is indicated by the regularity of its occurrence in human beings of all ages, even in newborn infants, and in animals (e.g., bovine) in which acquired rheumatic or arteriosclerotic heart disease is not known to occur. It usually is of mild degree but the diameter of these chordae may be two to three times or
more than that of the chordae of the posterior leaflet. In most instances the entire chorda is thickened. Little is known of the fetal development of the chordae tendineae. Cordier and Roux have described them in several early embryos. In a 9.5-mm. embryo the anlage of second order chordae may be seen on the anterior ("internal") leaflet. In the 13.5-mm. embryo, as the bulbus arteriosus divides and the interventricular septum is completed, the chordae of the anterior leaflet undergo resorption. This leaves a chorda-free hiatus and the thickened chordae are on either side of this gap. This position would suggest that mechanical factors, stemming from the character of the blood flow in this region, influence the thickness of these chordae. As aging takes place, the collagen of the chorda becomes more compact and hyaline. Feitelberg and Kaunitz in x-ray diffraction studies of the chordae tendineae of the human heart noted increasing orientation of the collagen molecules in the axis of the chordae after childhood. The histologic appearance of the central core of collagen suggests an axial arrangement of the fibrils. In infancy and childhood these fibrils are wavy and run, in part, therefore, in the plane of the cross section as well.

The pathogenesis of the sclerotic type of thickening is difficult to evaluate. Its location suggests that mechanical factors may be concerned. As in the normal group, the central chordae of the anterior leaflet are chiefly involved. This suggests that the same factors may be involved in both varieties of thickening. Sclerotic changes in other parts of the cardiovascular system have been attributed to mechanical influence such as the local blood pressure and the fixation or mobility of the part. It is noteworthy that the region of in-
sertion of these central chordae into the ventricular aspect of the anterior leaflet of the mitral valve unlike the region of insertion in the posterior leaflet is very frequently the site of atheromatous deposits. Such plaques may be seen to extend to the contiguous portions of the chordae. This does not imply necessarily that this chordal sclerosis is simply a process of atherosclerosis. Indeed there is no simple correlation between the degree of atherosclerosis of

the leaflet and the sclerosis of the chorda. The importance of the mechanical factor is suggested by the observations that the sclerosis sometimes occurs with the sclerosis of the anterior mitral leaflet that accompanies insufficiency of the aortic valve due to syphilis or to isolated calcific stenosis of the aortic valve.

The fact that the chorda may be more sclerotic than the leaflet, and that the sclerosis may even be focal at a distance from the leaflet, contradicts the thesis that these changes are simply due to extension of an inflammatory (or other) process from the leaflet on to the chorda.

On the other hand, there are certain features of close similarity of this lesion to those of healed rheumatic valvulitis. The pattern of subendocardial fibrosis may be indistinguishable in the two. The existence of several axial bundles of collagen within the thickened mass may correspond to the fusion of the chordae. The striking similarity between the thickened chordae of healed rheumatic inflammation and the sclerotic chordae of the present series may be noted in figures 7 and 10. It cannot, however, be assumed that the existence of more than one axial bundle within the sclerotic chorda necessarily proves that fusion of pre-existent chordae has taken place and that the lesion is, therefore, of rheumatic origin. There may be, as pointed out previously (fig. 6), more than one fibrous core initially within a normal chorda tendinea. Furthermore, a single central core may conceivably become disorganized into two or more bundles during the process of sclerosis. One may speculate that the laying down of collagen in the present instance compensates for the weakening of the central core that attends its atrophy. It may be pointed out that the atrophy of this structure in the rheumatic cases is more likely secondary to the fibrosis, associated with the healing of endocardial and subendocardial inflammation. May not the attenuation of the central core be the result of the sclerosis in the present series as well? Other facts that argue against the rheumatic origin in these cases are the absence of fusion and shortening of the chordae, vascularization of the ring and leaflet (except in one instance), characteristic myocardial scars, pericardial adhesions, history of rheumatic fever, and the failure to find such sclerosis in younger adults. Furthermore, milder degrees of subendocardial sclerosis are seen in a large proportion of the normal adult hearts.

The similarity of the appearance of the sclerotic chordae to those of the healed rheumatic lesion suggests another possibility. In the milder examples of healed rheumatic valvulitis, in which the landmarks are not entirely destroyed, the earliest and most severe damage involves the chordae of the anterior leaflet,
particularly in the region of the right posterior wall attachments (the $a$, $b$, $c$, $d$ positions according to the present scheme of nomenclature) (fig. 3). The previously mentioned considerations would suggest that mechanical factors may possibly accentuate the development of the fibrosis in chronic rheumatic deformity of the chordae of the valve also. Such a concept is consistent with the commonplace observations that fibrosis and stenosis far more frequently complicate acute rheumatic inflammation of the mitral than of the tricuspid valve.

That repeated systemic infections, or other toxic states in which foreign proteins may be present, may play a role cannot be disproved. Nevertheless, severe chronic inflammatory foci were not found more frequently in individuals who had marked sclerosis of their chordae than in those who did not.

SUMMARY

The dimensions and histologic appearance of the second order chordae tendineae of the mitral valve were studied in 200 human hearts that were considered grossly to be free from rheumatic inflammation. Two types of relatively thick chordae were found. The central chordae of the anterior leaflet were thickened in all hearts, in subjects of all ages, and a similar pattern was found in the bovine heart. This suggests that this finding is a normal developmental phenomenon. Another type of thickening was seen in 11 of 160 adult hearts. This was of much greater extent and was associated with laying down of large amounts of subendocardial collagen. Of the many factors possibly involved in the pathogenesis of this sclerosis, only two are suggested to be of importance: (1) the lesion was not seen in subjects younger than 37 years of age, and age, therefore, plays a role; (2) the predilection of central chordae of the anterior leaflet of the mitral to undergo this change suggests that mechanical factors, stemming from the character of the blood flow in this region, also are involved.

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REFERENCES

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