CLINICOPATHOLOGIC CORRELATIONS

De Subitaneis Mortibus

VIII. Coronary Arteries and Conduction System in Scleroderma Heart Disease

By THOMAS N. JAMES, M.D.

SUMMARY

In eight cases of scleroderma heart disease studied at necropsy special attention was paid to the cardiac conduction system and the coronary arteries. Six of the eight patients died suddenly, and all had some form of electrical instability of the heart. Distinct morphological abnormalities were present in the sinus node, atrioventricular (A-V) node and His bundle of every case, with sclerotic destruction of the sinus node being particularly striking in four of the hearts. Widespread lesions of the small coronary arteries (less than 1 mm diameter) were present in the ventricular myocardium, the sinus node artery and the A-V node artery. These lesions included mural and intimal fibrosis, endothelial proliferation, medial hyperplasia, fibrinoid necrosis and platelet-fibrin clots. The large coronary arteries were conspicuously normal or minimally diseased except in one case, and in that example there was no myocardial disease attributable to the single large coronary lesion found. It is concluded that arrhythmias and conduction disturbances are an integral component of the clinical picture of scleroderma heart disease, that this is associated with structural abnormalities in the centers of impulse formation and conduction, and that widespread narrowing lesions of the small coronary arteries (but not the major trunks) are important as a basis for fibrotic and degenerative changes throughout the heart. Some components of the fibrosis, particularly in the sinus node, seem disproportionate and suggest that both microvascular and primary collagen abnormalities contribute to the pathogenesis of scleroderma heart disease.

Additional Indexing Words:
Sinus node
Small coronary arteries
A-V node
Electrical instability of the heart
His bundle
Sudden death

THAT PATIENTS WITH SCLERODERMA may have heart disease has been known for about a century.1 However, whether the heart disease was due to scleroderma or to a coincidental but separate disease remained a question until 1943 when Weiss et al.2 convincingly demonstrated that scleroderma heart disease was a distinct clinical entity. There is continuing debate concerning the fundamental pathophysiology of all the varied clinical manifestations of scleroderma, including those in the cardiovascular system. While some have blamed a primary abnormality of collagen formation and metabolism,3,4 others have presented strong arguments that the primary fault is vascular in nature, particularly in small vessels and capillaries.5,6 One may logically suspect that either of these two faults could cause or compound the other.

This study of eight patients with scleroderma heart disease deals in particular with abnormalities found in the coronary arteries and the conduction system at necropsy. Six of the eight died suddenly. There is known to be a significant incidence of disturbances of cardiac rhythm and conduction in scleroderma heart disease.7,12 By carefully examining the sinus node, atrioventricular (A-V) node, His bundle and its branches, as well as their specific nutrient arteries, such a study offers a good opportunity for useful clinicopathological correlation.

Case Reports

General Comments

Table 1 presents the important clinical findings in summary form. All eight patients had the characteristic cutaneous findings of scleroderma on clinical
Table 1

Clinical Data on Eight Patients with Scleroderma Heart Disease

<table>
<thead>
<tr>
<th>Patients</th>
<th>Congestive failure</th>
<th>Pericarditis</th>
<th>Arrhythmia</th>
<th>Heart block</th>
<th>Sudden death</th>
<th>Skin</th>
<th>Arthritis</th>
<th>Lungs</th>
<th>GI tract</th>
<th>Kidneys</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. WF 65</td>
<td>Severe, chronic</td>
<td>Chronic</td>
<td>Atr. fibrill. PAT &amp; block</td>
<td>Varying A-V block</td>
<td>Yes</td>
<td>Typical</td>
<td>Fingers</td>
<td>—</td>
<td>Dysphagia severe</td>
<td>—</td>
</tr>
<tr>
<td>2. WM 13</td>
<td>Severe, chronic</td>
<td>Chronic &amp; acute</td>
<td>Sinus bradycardia</td>
<td>RBBB</td>
<td>Yes</td>
<td>Typical</td>
<td>Fingers</td>
<td>Pulmonary fibrosis</td>
<td>Dysphagia severe</td>
<td>Renal failure</td>
</tr>
<tr>
<td>3. WM 33</td>
<td>Severe, chronic</td>
<td>Chronic &amp; acute</td>
<td>Tachycardia (type ?)</td>
<td>Uncertain</td>
<td>No</td>
<td>Typical</td>
<td>Polyarthr.</td>
<td>Pulmonary fibrosis, pneumonia</td>
<td>Dysphagia severe</td>
<td>Renal failure</td>
</tr>
<tr>
<td>4. BF 66</td>
<td>Terminally</td>
<td>Chronic &amp; acute</td>
<td>Atr. fibrill.</td>
<td>RBBB L. ax. dev.</td>
<td>Yes</td>
<td>Typical</td>
<td>Polyarthr.</td>
<td>—</td>
<td>Dysphagia severe</td>
<td>—</td>
</tr>
<tr>
<td>5. WF 35</td>
<td>Severe, chronic</td>
<td>None</td>
<td>PAT &amp; block</td>
<td>Second degree</td>
<td>No</td>
<td>Typical</td>
<td>Polyarthr.</td>
<td>Pneumonia</td>
<td>Esoph. ulcer</td>
<td>Renal insuffic.</td>
</tr>
<tr>
<td>6. WF 54</td>
<td>Severe, chronic</td>
<td>None</td>
<td>PAT &amp; block</td>
<td>First &amp; second degree, RBBB and LBBB</td>
<td>Yes</td>
<td>Typical</td>
<td>Fingers</td>
<td>Pulmonary hypertens. &amp; fibrosis</td>
<td>Dysphagia</td>
<td>—</td>
</tr>
<tr>
<td>7. WF 47</td>
<td>Minor</td>
<td>None</td>
<td>Sinus bradycardia</td>
<td>Probable (abrupt rate changes 80 -&gt; 40)</td>
<td>Yes</td>
<td>Typical</td>
<td>Fingers</td>
<td>Pulmonary fibrosis</td>
<td>Duodenal ulcer</td>
<td>Renal failure</td>
</tr>
<tr>
<td>8. BF 52</td>
<td>Chronic, severe</td>
<td>Chronic &amp; acute</td>
<td>Atrial premature</td>
<td>PR 0.22 L. ax. dev.</td>
<td>Yes</td>
<td>Typical</td>
<td>Fingers</td>
<td>Pulmonary fibrosis</td>
<td>Dysphagia</td>
<td>Renal insuffic.</td>
</tr>
</tbody>
</table>
Table 2

Postmortem Findings in Eight Patients with Scleroderma Heart Disease

<table>
<thead>
<tr>
<th>Patients</th>
<th>Major cor. arteries</th>
<th>Sinus node</th>
<th>A-V node</th>
<th>His bundle</th>
<th>Vent. myoc.</th>
<th>Small cor. arteries</th>
<th>Skin</th>
<th>Esophagus</th>
<th>Lungs</th>
<th>Kidneys</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. WF 65</td>
<td>Normal</td>
<td>Scirrhous</td>
<td>Narrow AVNA (75%)</td>
<td>Mild fibrosis</td>
<td>Focal fibrosis</td>
<td>Focal narrowing</td>
<td>Typical</td>
<td>Typical</td>
<td>Edema</td>
<td>Glomerulosclerosis and art. narrowing</td>
</tr>
<tr>
<td>2. WM 13</td>
<td>Normal</td>
<td>Focal fibr. Pericarditis</td>
<td>Narrow AVNA (85%)</td>
<td>Focal fibrosis</td>
<td>Marked fibrosis</td>
<td>Extensive narrowing &amp; capill. thromb.</td>
<td>Typical</td>
<td>Typical</td>
<td>Edema &amp; fibrosis</td>
<td>Acute &amp; chronic art. narrowing</td>
</tr>
<tr>
<td>3. WM 53</td>
<td>Minor athero-sclerosis</td>
<td>Focal degener. Pericarditis</td>
<td>Focal degener.</td>
<td>Focal fibrosis</td>
<td>Focal narrowing</td>
<td>Typical</td>
<td>Typical</td>
<td>Fibrosis &amp; edema</td>
<td>Glomerulosclerosis and arteries</td>
<td></td>
</tr>
<tr>
<td>4. BF 66</td>
<td>Minor athero-sclerosis</td>
<td>Scirrhous Pericarditis</td>
<td>Focal fibrosis marked</td>
<td>Fibrosis; art. narrow.; LBB</td>
<td>Focal fibrosis</td>
<td>Focal narrowing</td>
<td>Typical</td>
<td>Typical</td>
<td>Edema</td>
<td>—</td>
</tr>
<tr>
<td>5. WF 35</td>
<td>Narrowed LAD (80%)</td>
<td>Moderate fibrosis</td>
<td>Multiple narrow AVNA &amp; focal degener.</td>
<td>Moderate fibrosis</td>
<td>Focal fibrosis</td>
<td>Focal narrowing</td>
<td>Typical</td>
<td>Ulcer &amp; fibrosis</td>
<td>Edema</td>
<td>Glomerulosclerosis and art. narrowing &amp; fibrinoid necrosis</td>
</tr>
<tr>
<td>6. WF 54</td>
<td>Minor athero-sclerosis</td>
<td>Moderate fibrosis</td>
<td>Focal fibrosis &amp; hemorr.</td>
<td>Degener. LBB &amp; RBB</td>
<td>Focal fibrosis</td>
<td>Fibrinoid &amp; chronic focal narrowing, severe</td>
<td>Typical</td>
<td>Typical</td>
<td>Arteriolar sclerosis, Edema</td>
<td>—</td>
</tr>
<tr>
<td>7. WF 47</td>
<td>Normal</td>
<td>Scirrhous SNA occl.</td>
<td>Moderate fibrosis</td>
<td>Degener. &amp; sclerosis LBB</td>
<td>Focal fibrosis</td>
<td>Focal narrowing</td>
<td>Typical</td>
<td>—</td>
<td>Fibrosis &amp; edema</td>
<td>Glomerulosclerosis &amp; art. narrowing</td>
</tr>
<tr>
<td>8. BF 52</td>
<td>Normal</td>
<td>Scirrhous SNA narrow Pericarditis</td>
<td>Marked fibrosis</td>
<td>Degener. &amp; sclerosis LBB</td>
<td>Focal fibrosis</td>
<td>Focal narrowing</td>
<td>Typical</td>
<td>Typical</td>
<td>Fibrosis &amp; edema</td>
<td>Glomerulosclerosis &amp; art. narrowing</td>
</tr>
</tbody>
</table>
examination. In six of the eight patients arrhythmias or conduction disturbances were major clinical problems and were documented electrocardiographically; a seventh patient had probable paroxysmal heart block based on numerous episodes in the nurse’s pulse record; the eighth patient had tachycardia of an undetermined nature with terminal congestive heart failure but no ECG at that time.

Table 2 is a summary of abnormalities present at necropsy. In every heart the regions of the sinus node, A-V node, and His bundle with proximal branches were cut into serial blocks of tissue about 2 mm thick. From each block several screening slides were prepared with the Goldner trichrome strain, and then serial sections were made where initial histological findings or clinical suspicion warranted. The methods of these examinations have been reported previously. To determine the state of the blood supply to the special centers of impulse formation and conduction in the heart, careful dissection was made of the major coronary trunks and their patency or occlusion was noted with particular reference to the site of origin of the sinus node artery and the A-V node artery. Histological sections of the two latter arteries completed the assessment of this special blood supply.

Certain general findings in all eight cases at necropsy included diffuse focal fibrosis in the ventricular myocardium and focal narrowing of multiple small coronary arteries (less than 1 mm in external diameter). In most instances the narrowing of small coronary arteries was a histological mixture of endothelial proliferation and medial hyperplasia or fibrosis, but some exceptions are noted in individual cases. All had some degree of congestive heart failure and thereby some pulmonary edema. None had significant disease of cardiac valves or large coronary arteries except case 5 as noted. Seven of the eight had histological abnormalities of the esophagus considered characteristic of scleroderma. Cutaneous histopathology was typical of scleroderma in every case.

Case 1

A white woman of 65 had clinical manifestations of scleroderma for five years, beginning with dysphagia. Three years before death congestive heart failure appeared and gradually grew worse. For two years she had a variety of atrial arrhythmias which included atrial fibrillation and paroxysmal atrial tachycardia with varying block (fig. 1). Along with the esophageal complaints she also had Raynaud’s phenomenon which eventually progressed to gangrene of some fingers. Her death was sudden and postulated to be a fatal arrhythmia, although this was not documented.

Necropsy findings in this and the subsequent cases are summarized in table 2. In this patient the esophageal disease was marked. Scirrhous fibrosis virtually replaced the sinus node, leaving only a few surviving cells (fig. 2). Intimal proliferation narrowed the main A-V node artery about 75% and there was focal hemorrhage within the A-V node.

Case 2

A white boy of 13 had been ill for one year with Raynaud’s phenomenon beginning with poor healing of minor injuries in his fingers. He had severe dysphagia throughout his illness. For several months congestive heart failure had gradually increased and in the last week of life there was a loud pericardial friction rub. During that week he developed right bundle branch block and left axis deviation, with intermittent sinus tachycardia (120/min) and sinus bradycardia (less than 50/min). The day of death his pulse varied from 140 to 80/min, with several periods of 40 and 46/min. The terminal event was abrupt “cardiac arrest,” with resuscitative efforts failing.

At necropsy there was severe chronic and acute pericarditis, but the two more striking cardiac abnor-
Figure 2

Scirrhous destruction of the sinus node from case 1 (below) is compared at the same magnification to the normal appearance of the sinus node from another human heart of about the same age. All the tissue surrounding the central artery (seen to the right) is sinus node and the paucity of nodal cells in case 1 is apparent. Goldner trichrome stain here and in all other photomicrographs except as indicated.

malities were the extent of focal fibrosis plus focal narrowing of small arteries in the ventricular myocardium (fig. 3), and the marked narrowing of the main A-V node artery (fig. 4).

Case 3

A white man of 53 had polyarthritis for fifteen years, and dysphagia with mild congestive heart failure for two years. The last year of life he developed progressive renal insufficiency, increasing difficulty with Raynaud's phenomenon, clinical evidence of pulmonary fibrosis, and increasing congestive failure. Terminally he had gangrene of the fingers and toes, ulcers of the right hand and both ankles, bronchopneumonia and gastrointestinal hemorrhage. An ECG two years prior to death was unremarkable and no subsequent ones were made, although an increasing tachycardia was noted the last few weeks of life.

At necropsy there was generalized vasculitis,
Focal fibrosis and widespread narrowing of small coronary arteries are seen in the ventricular myocardium of case 2. Thrombotic occlusions of two small vessels (arrows) are seen on the right. Magnification is the same in both panels.

Pneumonia and pericarditis. Focal degeneration in the sinus node was associated with recent thrombosis within the adjacent trabecular recesses of the right atrium. Focal narrowing of small arteries in the A-V node and His bundle as well as the entire ventricular myocardium was associated with commensurate degrees of focal fibrosis and degeneration in those sites.

Case 4

A black woman of 66 had mild arterial hypertension for a decade, and for one year had Raynaud’s phenomenon with polyarthritis. Eight months before death she had an unexplained syncopal episode. As her skin became worse she also developed progressively worsening dysphagia. Except for one bout of recorded atrial fibrillation at the onset of her Raynaud’s phenomenon, she remained in sinus rhythm at several other examinations. The last day of life she again developed atrial fibrillation at which time there was also a new right bundle branch block in addition to the older left axis deviation (fig. 5). She was unexpectedly found dead at midnight.

At necropsy there were generalized changes of scleroderma, particularly in the skin and esophagus.

In the A-V node of case 2 the main artery was narrowed (arrow, left panel) and there was focal degeneration (right panel). The central fibrous body (CFB) is seen at the lower right of the left panel.

This ECG from case 4 illustrates predominantly atrial fibrillation although complexes resembling P waves are seen in leads 2 and 3. There is wide variability in QRS configuration, but the most prevalent pattern found in longer strips of each lead is indicated with black dots. Paper speed is 50 mm/sec.
The sinus node was virtually destroyed by scirrhus fibrosis (fig. 6), which included the local ganglia and nerves. Old focal fibrosis was present in the A-V node. In the His bundle there was marked fibrosis plus recent degeneration at the origin of the left bundle branch (fig. 7).

Case 5

A 35-year-old white woman had Raynaud’s phenomenon and polyarthritis for four years. The last year of life she developed increasing congestive heart failure and several paroxysms of atrial tachycardia with block. Although normotensive at her terminal admission, on the tenth day her blood pressure unexpectedly rose to 240/120 mm Hg. Her heart failure continued to worsen and she died with pulmonary edema and convulsions.

At necropsy there was an old sclerotic narrowing of the proximal left anterior descending artery for 80% of its lumen, but no evidence of ischemia or infarction in

Figure 6

Sclerotic destruction of the sinus node in case 4 is seen here at two magnifications. The normal sinus node can be compared from figure 2. Except for a small segment of adjacent atrial myocardium in the lower right of the top panel, all the tissue shown is sinus node.
the region that artery supplied. The other major coronary arteries were normal. Moderate fibrosis was present in the sinus node and His bundle. There was marked narrowing of the A-V node artery and of several of its branches with focal degeneration of the A-V node. The brain was not examined. There was fibrinoid necrosis of small renal arteries.

Case 6

A 54-year-old white woman had multiple gastrointestinal complaints and Raynaud’s phenomenon for eleven years. The last year of life she developed congestive heart failure and a variety of atrial arrhythmias which included paroxysmal atrial tachycardia and atrial flutter with block (fig. 8). She also had first and second degree heart block at normal rates and electrocardiographic evidence of both right and left bundle branch block. While convalescing from a right femoral embolectomy, on the second postoperative day she suddenly developed ventricular tachycardia and then fibrillation which did not respond to resuscitative efforts.

Figure 7

The His bundle of case 6 had from moderate (top panel) to marked (bottom panel) fibrosis, with recent degeneration of the origin of the left bundle branch (LBB) at one point and fibrotic interruption of both branches at another. Section in panel below is about 1 mm anterior to the one in panel above. A small sclerotic artery is seen near the top of the His bundle cross section in the lower panel.

Figure 8

In this ECG of case 6 there is atrial flutter with 2:1 A-V block, and delayed activation of the right ventricle with absent normal left septal activation (QR in V1 and RS without a Q in V6).

Figure 9

Photomicrographs of two different sections of the His bundle from case 6 are shown, with the above being about 1 mm posterior to the one below. In both there is degeneration at the origin of the left bundle branch (LBB and L) which is more recent in the panel above and fibrotic in the panel below. In the lower panel there is hemorrhage and early degeneration at the origin of the right bundle branch as well (R).
The day was 182/106. Terminally the blood pressure rose to 255/115 for several hours at which time the heart rate varied abruptly between 80 and 40 per minute and she suddenly died.

At necropsy there was a recent left cerebral hemorrhage and an active duodenal ulcer. The sinus node artery was occluded by a bizarre medial hyperplasia (fig. 11) and there was scirrhous fibrotic destruction of the sinus node. Focal fibrosis was present in the A-V node and His bundle, with special involvement of the left bundle branch.

Case 7
A 47-year-old white woman had vague gastrointestinal complaints for thirteen years. For five years she had polyarthritis, Raynaud’s phenomenon and clinical evidence of pulmonary fibrosis. Palpitations began five years before death. Increasing congestive failure was present for the last four years. Over the thirteen years her PR interval gradually increased from 0.15 seconds to 0.22 seconds. The last year of life she had multiple premature atrial beats and marked left axis deviation in the ECG. One day she was brought to the emergency room because of moderate dyspnea and suddenly died.

There was moderate fibrosis and focal hemorrhage in the sinus node, A-V node and His bundle with focal degeneration at the origins of both the left and right bundle branches (fig. 9). In those structures and throughout the ventricular myocardium there were focal hemorrhage and multiple narrowings of small coronary arteries. The small coronary lesions included mural fibrosis, intimal proliferation and widespread fibrinoid necrosis (fig. 10), with occasional platelet-fibrin occlusions.

Case 8
A 52-year-old black woman had vague gastrointestinal complaints for thirteen years. For five years she had polyarthritis, Raynaud’s phenomenon and clinical evidence of pulmonary fibrosis. Palpitations began five years before death. Increasing congestive failure was present for the last four years. Over the thirteen years her PR interval gradually increased from 0.15 seconds to 0.22 seconds. The last year of life she had multiple premature atrial beats and marked left axis deviation in the ECG. One day she was brought to the emergency room because of moderate dyspnea and suddenly died.

Small coronary arteries of case 6 are shown here with focal fibrosis and hemorrhage in the ventricular myocardium. There is predominantly mural fibrosis in the artery above, and fibrinoid necrosis below.

Figure 10

Two different sections of the sinus node of case 7 illustrate the unusual form of narrowing of the sinus node artery (top) and fibrosis of the node with lesser narrowing in the section of artery shown below.

Figure 11
Figure 12
Disruptive fibrosis of the A-V node of case 8 is seen above, and an adherent platelet clot in the A-V node artery is shown below (arrow).

Figure 13
Sclerotic fibrosis of the sinus node of case 8 is shown above, and marked narrowing of the sinus node artery is seen below (Verhoeff-Van Gieson stain).
There was marked fibrosis in the A-V node (fig. 12), His bundle and at the origin of the left bundle branch. There was also marked narrowing of the sinus node artery, some disseminated intravascular coagulation in its branches and elsewhere, and scirrhous destructive fibrosis of the sinus node (fig. 13).

Discussion

Sudden death is not so dramatic an event when it occurs in a patient with some chronic disease. Among others,18,19 there are two especially memorable examples of sudden death in scleroderma heart disease: that described by Westphal in a young woman in 1876,17 and the striking first case of Weiss et al.2 in which a 27-year-old woman unexpectedly died while eating lunch. There is both clinical and histopathological evidence that the cardiac conduction system must frequently be involved in scleroderma heart disease.2,7-14 This is not to say that all sudden deaths in scleroderma heart disease need be due to electrical instability of the heart, but it is important that in the present eight cases all had significant histopathological abnormalities in their cardiac conduction systems.

Taking the six sudden deaths in this series of eight, five have strong clinicopathological correlative evidence to support a presumptive diagnosis of a lethal terminal electrical instability of the heart. The sixth (case 7) had a cerebral hemorrhage but also such abrupt changes of heart rate that one must consider whether the terminal acute hypertension and stroke caused or were caused by the changes in cardiac rhythm (with their potential consequences). Without belaboring which of these sudden deaths were in fact due to the morphologic abnormalities present in the cardiac centers of impulse formation or conduction, collectively they do suggest that abnormalities in the rhythm of the heart are an integral clinical feature of scleroderma heart disease and that electrical instability of the heart may be responsible for sudden death in such patients.

While it is now generally accepted that scleroderma heart disease is a distinct clinical entity, it is unsettled whether there is a vascular component in its etiology. Some have emphasized that the myocardial disease in scleroderma is not of a vascular nature,8, 18 while others have described various degrees of abnormalities in the small myocardial arteries.10,19 In their original establishment of the entity of scleroderma heart disease, Weiss and his colleagues deliberated the evidence for and against a vascular etiology for the myocardial disease2 without concluding whether it was a major factor. In their persuasive arguments favoring a vascular etiology for scleroderma in general, Norton and Nardo6 do not discuss the myocardium relative to small vessel disease.

Some of the confusion about the possible vascular etiology of scleroderma heart disease is attributable to the popular equating of coronary disease exclusively with abnormalities of the larger branches, ignoring the smaller coronary arteries as if they were a part of some other system. In these eight patients there was indeed no abnormality attributable to large coronary disease. Reluctance by many to interpret the significance of narrowing lesions in small coronary arteries is understandable relative to the ventricular myocardium, where occasional small scars are seldom of much clinical or pathological significance. However, when the small coronary artery perfuses a distinctive and crucial small structure such as the sinus node, then focal disease in that artery coupled with morphological changes in the node and clinical evidence of abnormalities of cardiac rhythm combine into convincing evidence for significant small coronary disease. One may analogously consider multiple small scars throughout the ventricular myocardium coupled with multiple narrowings of small ventricular arteries. The various methods and logic for the clinical and pathological interpretation of small coronary disease have been discussed elsewhere.20, 21 For the subject at hand, in these eight patients with scleroderma there can be no doubt of the significance of small coronary disease in the pathogenesis of their cardiac abnormalities.

Having emphasized the role of the abnormal small coronary arteries, it should be added that there are other myocardial abnormalities to account for. In the sinus node of four of the hearts there was disproportionate scirrhous fibrosis virtually replacing the sinus node. This plus the seemingly excessive fibrosis in other portions of the heart speak for some abnormality of collagen formation or deposition beyond that which is readily attributable to focal ischemia alone. In lupus erythematosus the sinus node also has a combination of vascular and nonvascular pathology,22 but there the collagen appears cystic rather than undergoing the obliterator hyperplasia seen in the examples with scleroderma. One other condition in which such complete destruction of the sinus node appears is cardiac amyloidosis,23 but there the original architecture of the node is remarkably well preserved with delicate casts of the former nodal cells which have been replaced by amyloid.

Actually, collagen partitioning and supportive framework are integral components of the normal anatomy of the human sinus node and His bundle in particular.18, 24 In the human fetus the sinus node is comprised of closely packed nodal cells with collagen being very sparse. With normal maturation in
childhood and adolescence an intricate but substantial collagen framework develops throughout the sinus node surrounding its central artery. For such a delicately controlled fibroplastic process to occur in an orderly way there must be some precisely controlled intercellular cognitive mechanism. The scirrhouss destruction of the sinus node in scleroderma heart disease may represent a failure or disruption of that normal process.

Similarly, the human A-V node and His bundle also undergo a distinct postnatal molding and shaping which includes intricately controlled fibroplasia. Whereas the collagen framework of the sinus node is normally rather dense, that in the His bundle is of a finer pattern and that in the adult A-V node is still more sparse. This normal difference in collagen content between the sinus node on the one hand and the A-V junctional tissues on the other may partially explain why fibrosis was so much more conspicuous in the sinus node in the present cases. But it is the combination of sinus node destruction with excess focal fibrotic partitioning in the A-V junction which is the likely basis for the unusual incidence of paroxysmal atrial tachycardia in the present series, the electrophysiologic consequences being failure of normal automaticity concomitant with the provision of multiple anatomic routes for A-V junctional re-entry.

In the clinicopathological spectrum of collagen diseases, involvement of the heart by scleroderma resembles some and significantly differs from others. None of the present cases had valvular abnormalities, which on the contrary are frequently present in rheumatic fever and lupus erythematosus, and this is a particular puzzle if there is a primary fault in collagen formation in scleroderma heart disease. In polyarteritis nodosa both the large and small coronary arteries are abnormal, while in scleroderma the large arteries are spared. A common factor in the cardiac involvement by virtually all collagen diseases is pericarditis, present in five of the eight patients reported here. Pericarditis always affects at least the superficial layers of the sinus node, the depth of damage being dependent in general on the severity of the pericarditis. This in turn is a partial explanation for certain atrial arrhythmias and other forms of sinus node malfunction observed in patients with any type of pericarditis.

On the basis of the eight cases of scleroderma heart disease reported here it may be concluded that structural abnormalities of the sinus node, A-V node, His bundle and its branches are a distinct component of the clinical entity. While abnormalities of the large coronary arteries are conspicuously not the cause of scleroderma heart disease, extensive narrowings of the smaller coronary branches are an indisputable contributing factor; the spectrum of those histopathological changes includes mural and intimal fibrosis, intimal proliferation, fibrinoid necrosis and disseminated intravascular coagulation. Finally, it seems likely that some abnormality of collagen formation is an additional component of the problem in scleroderma heart disease beyond what can be accounted for by focal ischemia, especially as concerns sclerotic destruction of the sinus node.

References

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