Histopathological correlates of sinoatrial disease

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SUMMARY  Six hearts from patients suffering from rhythm disorders consistent with the diagnosis of sinoatrial disease were histologically examined. Four of the patients had shown a tachycardia-bradycardia syndrome, and the remaining two patients episodes of sinus arrest or sinoatrial block with a slow junctional escape rhythm. The rhythm disorders had occurred in the setting of chronic sinoatrial disease (3 cases), acute myocardial infarction (2 cases), and diphtheritic myocarditis (1 case).

The abnormalities which were more consistently observed consisted of (1) total or subtotal destruction of the sinus node (6 cases); (2) total or subtotal destruction of the areas of nodal atrial continuity (5 cases); (3) inflammatory or degenerative changes of the nerves and ganglia surrounding the node (6 cases); (4) pathological changes in the atrial wall (5 cases). Chronic or acute lesions involving the AV node, the bundle of His, and its branches or their distal subdivisions were also found in all 6 hearts.

The relationship between the observed pathological changes and the physiological disorders are discussed.

The clinical profile (Short, 1954; Birchfield et al., 1957; Ferrer, 1968; Rosen et al., 1971; Rubenstein et al., 1972; Kaplan et al., 1973; Kulbertus et al., 1973; Gunther et al., 1976) and electrophysiological behaviour (Mandel et al., 1972; Narula et al., 1972; Strauss et al., 1973) of patients with sinoatrial disease have received much attention in recent years. It is well established that the various components of the syndrome may occur not only chronically but also more acutely, as in myocardial infarction or toxic myocarditis. We have examined histologically the sinoatrial region and conducting system in 6 hearts from patients with sinoatrial rhythm disorders; 3 were chronic cases, 2 had a myocardial infarction, and 1 a diphtheritic myocarditis. The histological findings are reported and an attempt has been made to correlate the observed alterations with the physiological disorders.

Techniques

In each case, the sinoatrial node, nodal atrial junction, atrial myocardium, sinus node artery, and nervous structures were studied. In addition, the specific tissue of the atrioventricular junction was also carefully examined.

SINOATRIAL REGION

The region of the sinoatrial node was obtained in the following manner. A cut was first made from the orifice of the inferior vena cava to the upper part of the right atrial appendage. The second cut passed behind the right atrial appendage and was directed towards the orifice of the superior vena cava; finally, a third cut went from the superior to the inferior vena cava, thus separating a block which was fixed in formalin and embedded in paraffin. 10μ sections were prepared parallel to the long axis of the sinus node. Each fortytih section was stained with haematoxylin and eosin, Azan-Heidenhain's solution, or Masson's trichrome. Furthermore, in each case, 20 to 40 sections were stained by orcein or Congo Red in order to study the pathological changes in elastic fibres and to identify amyloid deposits. Bodian's staining was used to study the nervous structures.

The following morphological criteria were used.

Sinoatrial node

Severe fibrosis was diagnosed when only a few scattered nodal cells remained, embedded in a mass of collagen tissue.

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1The data reported in this paper were included and briefly described in the proceedings of a Symposium on Reentrant Arrhythmias held in Liège in 1976 (Demoulin, J. Cl. and Kulbertus, H. E. Pathological correlates of atrial arrhythmias in reentrant arrhythmias, mechanisms and treatment. H. E. Kulbertus, Ed. MTP Lancaster, p. 99, 1977).
were graded according to Bailey's classification (Bailey et al., 1968): grade I, atrial myocardium grossly normal, or minimal changes only; grade II, moderate to severe fibrosis with preservation of muscle mass and architecture; grade III, extensive fibrosis with loss of muscle and architecture.

Ganglia and nerves
Chronic alterations of the nervous structures were identified from the description by Rossi (1969). The ganglia were thought to be abnormal when their cells showed vacuolar degeneration or atrophy and when there were changes in the pericellular processes or capsular cells. Haemorrhagic and inflammatory infiltrations of the nerves were also carefully looked for.

AV junctions
The AV node, the common His bundle, the left and right bundle-branches and their arborisations, were studied using the technique described by Lenegre (1955).

Results
Six hearts from patients with documented sinoatrial disease were studied. In 4 of the cases, the disease manifested itself by a tachycardia-bradycardia syndrome, and in the remaining 2 instances, there were episodes of sinus arrest or sinoatrial block, with slow junctional escape rhythm.

The significant clinical features and the gross necropsy findings are summarised in Table 1. Table 2 describes the histopathological changes observed in the sinoatrial region. The lesions seen within the AV node, common His bundle, and bundle-branches are listed in Table 3.

The abnormalities which were more consistently encountered were total or subtotal destruction of the sinus node (6 cases), total or subtotal destruction of the areas of nodal atrial continuity (5 cases), inflammatory or degenerative changes in the nerves and ganglia surrounding the node (6 cases), and grade III pathological changes in the atrial myocardium (5 cases). Chronic or acute lesions involving the AV node (Tawara), the bundle of His, its branches, or their distal subdivisions were also found in all 6 hearts.

Discussion
Very few reports relating the histopathological anomalies associated with the syndrome of sinoatrial rhythm disturbances have been published (Hudson, 1960; James and Birk, 1966; Rossi, 1969; Acar et al., 1970; Rasmussen, 1971; Rosen et al., 1971b;
Kaplan et al., 1973; Kulbertus et al., 1973; Warem- bourg et al., 1974). Two recent reports have appeared during the preparation of this paper. Thery et al. (1977) described their findings in a group of patients of whom 6 had a bradycardia-tachycardia syndrome, 12 had evidence of sinoatrial block, and 1 had permanent atrial standstill. Evans and Shaw (1977) also described the pathological data from 8 patients diagnosed during life as having chronic sinoatrial disorder. The results of these different studies were consistent: lesions of the sinus node and of the atrial wall were commonly found in sinoatrial disease.

The present investigation corroborates those findings and stresses two additional features. First, the structural bridges which connect the node to the common atrial myocardium seem to be frequently damaged in this clinical syndrome. Secondly, the nervous structures surrounding the node are also often the site of pathological changes.

It seems generally agreed that the syndrome under discussion comprises: (1) bradyarrhythmias with episodes of sinus bradycardia, sinus arrest or pauses, and/or sinoatrial block, (2) a reluctance of junctional escape pacemakers to emerge, and (3) in about two-thirds of cases, episodes of supraventricular, mainly atrial, tachyarrhythmias. Each of these three manifestations may be related to the anatomical abnormalities.

The bradycardic episodes may reflect reduced sinus node automaticity or impaired conduction from the centre of the node to its periphery or from the node to the atrial myocardium. These disorders can surely be accounted for by the severe changes observed within the node itself, by the disruptive lesions located along the areas of nodal atrial continuity and, finally, by the pathological involvement of the perinodal nervous structures. Similar pathological features are sometimes seen though rarely, in individuals maintaining a normal sinus rhythm (Demoulin and Kulbertus, 1977). At present, the minimum number of functioning nodal cells needed to ensure the formation of a proper sinus impulse remains unknown. Furthermore, it seems well established that the distribution of pacemaker cells is not limited to the area of the node itself and that pacemaker cells can also be found around the node, more particularly towards the region of the crista terminalis. This might explain the persistence of a satisfactory sinus rhythm in some patients in spite of very severe intranodal fibrosis (Demoulin and Kulbertus, 1977; Thery et al., 1977). This might also be the reason for apparently normal or very short sinoatrial conduction times recorded in patients with sinus node dysfunction (Strauss et al., 1976).

The fact that a satisfactory junctional escape pacemaker may not always emerge might be accounted for by at least two different mechanisms. First, the AV junction is quite commonly the site...
Histopathological correlates of sinoatrial disease

Fig. 3 Case 4. Haemorrhagic infiltration (arrow) is seen to interrupt a region of continuity between the sinus node (san) and the common atrial myocardium (cam). (Azan × 100.)

Table 1 Summary of clinical details and necropsy findings

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Age (y)</th>
<th>Sex</th>
<th>Clinical data</th>
<th>Rhythm and conduction disturbances</th>
<th>Necropsy findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>63</td>
<td>M</td>
<td>Myocardial infarction</td>
<td>PSVT; SA with SEJR; transient 1st and 2nd degree AV block; RBBB</td>
<td>Enlargement of ventricular cavities; old anterolateral infarct; thrombosis of CxA, obstruction of CxA and stenosis of LADA</td>
</tr>
<tr>
<td>2</td>
<td>28</td>
<td>M</td>
<td>Diphtheritic myocarditis; congestive heart failure</td>
<td>PAT; PAF; PAF1; SB and pauses; transient 3rd degree AV block; LPHB with RBBB; SB; SA with SEJR; PAF; PAT, ventricular bigeminy</td>
<td>Large area and apical scar extending inferiorly and surrounded by fresh necrotic tissue; LADA obstructed; CxA and RCA stenosed</td>
</tr>
<tr>
<td>3</td>
<td>72</td>
<td>M</td>
<td>Coronary heart disease; ventricular arrhythmias</td>
<td>SB; SA with SEJR; PAF; PAT, ventricular bigeminy</td>
<td>Ostium primum ASD; sarcoïd granulomata in myocardium and mediastinal lymph nodes</td>
</tr>
<tr>
<td>4</td>
<td>75</td>
<td>F</td>
<td>Blood loss from gastro-intestinal disease</td>
<td>PST; SB and SA</td>
<td>Subacute inferior, apical, and postero-basal infarction; thrombosis of RCA</td>
</tr>
<tr>
<td>5</td>
<td>66</td>
<td>F</td>
<td>Hypothyroidism; acute inferior infarction; Adams-Stokes attacks; cardiogenic shock</td>
<td>SB; SA with SEJR; transient 3rd degree AV block</td>
<td>Primary amyloidosis</td>
</tr>
<tr>
<td>6</td>
<td>67</td>
<td>M</td>
<td>Congestive cardiomyopathy; syncopal attacks</td>
<td>PST; PAT; SA with SEJR; RBBB</td>
<td></td>
</tr>
</tbody>
</table>

PSVT, paroxysmal supraventricular tachycardia; PAF1, paroxysmal atrial flutter; SB, sinus bradycardia; RBBB, right bundle-branch block; LADA, left anterior descending artery; PAT, paroxysmal atrial tachycardia; PST, paroxysmal sinus tachycardia; SA, sinus arrest; LPHB, left posterior hemiblock; CxA, circumflex artery; PAF, paroxysmal atrial fibrillation; SEJR, slow escape junctional rhythm; RCA, right coronary artery.
no. Case Table 2 Summary of pathological findings in SA node region

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Sinus node</th>
<th>Nodal-atrial junctions</th>
<th>Perinodal ganglia and fibres</th>
<th>SA node artery</th>
<th>Atrial wall</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Anterior margin</td>
<td>Inferior margin</td>
<td>Endocardial margin</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Dense fibrosis (body and tail); haemorrhage (body and head)</td>
<td>Fibrosis</td>
<td>Haemor. infiltration</td>
<td>Haemor. infiltration</td>
<td>Infl. and haemor. infiltration</td>
</tr>
<tr>
<td>2</td>
<td>Dense fibrosis (body and tail); infl. infiltration (head)</td>
<td>Fibrosis</td>
<td>Fibrosis</td>
<td>Infl. infiltration</td>
<td>Infl. infiltration</td>
</tr>
<tr>
<td>3</td>
<td>Severe fibrosis</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>Degeneration</td>
</tr>
<tr>
<td>4</td>
<td>Dense fibrosis (body and tail); haemor. infiltration</td>
<td>Replaced by fibrosis</td>
<td>Moderate fibrosis</td>
<td>Interrupted (haemor. infiltration)</td>
<td>Degeneration; haemor. infiltration</td>
</tr>
<tr>
<td>5</td>
<td>Extensive fibrosis; areas of coagulation necrosis and inflammatory infiltration</td>
<td>Interrupted (fibrosis)</td>
<td>Interrupted (fibrosis)</td>
<td>Fibrosis and haemor. infiltration</td>
<td>Infl. infiltration</td>
</tr>
<tr>
<td>6</td>
<td>Amyloid deposits; dense fibrosis</td>
<td>Interrupted (fibrosis)</td>
<td>Subtotal destruction (fibrosis)</td>
<td>Interrupted (fibrosis)</td>
<td>Amyloidosis</td>
</tr>
</tbody>
</table>

Haemor., haemorrhagic; Infl., inflammatory; N, normal.

Table 3 Summary of pathological findings in AV junction

<table>
<thead>
<tr>
<th>Case no.</th>
<th>AV node</th>
<th>Common His bundle</th>
<th>Right bundle-branch</th>
<th>Left bundle-branch</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>—</td>
<td>Dense fibrosis</td>
<td>Almost total fibrosis</td>
<td>Mild fibrosis of initial portion; posterior radiation severely fibroed</td>
</tr>
<tr>
<td>2</td>
<td>Dense fibrosis of node approaches; inflammatory infiltration in node</td>
<td>—</td>
<td>—</td>
<td>Dense fibrosis of posterior fascicle; inflammatory infiltration of anterior radiation</td>
</tr>
<tr>
<td>3</td>
<td>—</td>
<td>—</td>
<td>Mild fibrosis (initial portion)</td>
<td>Dense fibrosis of anterior radiation; mild fibrosis of posterior fascicle</td>
</tr>
<tr>
<td>4</td>
<td>Dense fibrosis; areas of myofibrillar degeneration</td>
<td>Dense fibrosis</td>
<td>Dense fibrosis</td>
<td>Dense fibrosis of posterior radiation</td>
</tr>
<tr>
<td>5</td>
<td>Coagulation necrosis</td>
<td>Dense fibrosis</td>
<td>Coagulation necrosis of 3rd position</td>
<td>Dense fibrosis of midseptal and anterior fibres; coagulation necrosis of posterior radiation</td>
</tr>
<tr>
<td>6</td>
<td>Amyloidosis; dense fibrosis</td>
<td>Amyloidosis and fibrosis</td>
<td>Amyloidosis with fibrosis</td>
<td>Amyloidosis and fibrosis</td>
</tr>
</tbody>
</table>

1977; Thery et al., 1977). However, some patients with hearts showing anatomical changes like those described in this paper may be in sinus rhythm or may present with isolated chronic atrial fibrillation (Demoulin and Kulbertus, 1977; Thery et al., 1977). Thus, the physiological disturbance cannot necessarily be predicted from the anatomical findings; there is no doubt that there is a need for further studies in this field.

References


Histopathological correlates of sinoatrial disease

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