A Histopathological Study on the Hypertrophy of the Atrioventricular Conduction System

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A microscopical study of the AV conduction system using a serial sectioning method, was performed on 81 autopsied hearts with blocks anywhere in the AV conduction system, 44 with miscellaneous arrhythmias, and 65 control hearts without arrhythmia. Pre-blockade hypertrophy in the AV conduction system was seen in 38%, 38%, 50–58% corresponded respectively to 3° AV block, 1–2° AV block and bundle branch block (including left hemiblock). Post-blockade hypertrophy was also observed in 58%, 38% and 42–25% of the above mentioned types of blocks respectively. Hypertrophy anywhere in the AV conduction system was seen in 77%, 42%, 78%, 39%, 30% and 74% of the cases with blocks, sick sinus syndrome, pre-excitation syndrome, other arrhythmias, normal hearts and hypertrophied hearts without arrhythmia, respectively. Hypertrophy of the proximal AV conduction system to the bundle of His was specific for arrhythmia group, whereas hypertrophy of the bundle branches occurred in either hypertrophy without arrhythmia or in bundle branch block. Hypertrophy of the Purkinje cells was remarkable in sudden cardiac death by clinically-proved ventricular fibrillation. Incidence of sclerosis of the AV node artery was high in the arrhythmia group, especially the highest (90%) in the sudden death group.

Though there have been a few histopathological studies on the atrioventricular (AV) conduction system, their intention was limited only to the AV block and its morphological development. We have studied microscopically the AV conduction system using the serial sectioning method for AV block, bundle branch block and its derivatives, pre-excitation syndrome, sick sinus syndrome, sudden cardiac death, etc.1–7 From these studies, we recognize the evidence that the conduction system could show hypertrophy under certain selected conditions. The aim of this paper is to clarify the significance of the hypertrophy of the AV conduction system in cases with various arrhythmias.

MATERIALS AND METHODS

Twenty-nine autopsied hearts with 3° AV block, 16 with 1–2° AV block, 12 with a combination of right bundle branch block and abnormal axis deviation, 12 with bundle branch block, 12 with abnormal axis deviation, 12 with the sick sinus syndrome, 9 with the pre-excitation syndrome and 23 with miscellaneous arrhythmias other than the above mentioned categories were subjected for this study. As for the control, 46
### TABLE I INCIDENCE OF HYPERTROPHY IN THE AV CONDUCTION SYSTEM

<table>
<thead>
<tr>
<th>With blocks:</th>
<th>Pre-blockade hypertrophy</th>
<th>Post-blockade hypertrophy</th>
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</thead>
<tbody>
<tr>
<td>3° AV block</td>
<td>38%</td>
<td>58%</td>
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<tr>
<td>1–2° AV block</td>
<td>38</td>
<td>38</td>
</tr>
<tr>
<td>RBBB + Abnormal left axis deviation</td>
<td>50</td>
<td>42</td>
</tr>
<tr>
<td>Bundle branch block</td>
<td>58</td>
<td>25</td>
</tr>
<tr>
<td>Hypertrophy</td>
<td></td>
<td></td>
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<tr>
<td>With arrhythmias:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sick sinus syndrome</td>
<td>42%</td>
<td></td>
</tr>
<tr>
<td>Pre-excitation syndrome</td>
<td>78</td>
<td></td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>39</td>
<td></td>
</tr>
<tr>
<td>Without arrhythmias:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal heart</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>Hypertrophied heart</td>
<td>70</td>
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</tr>
</tbody>
</table>

Age-matched normal hearts and 19 hypertrophied hearts without arrhythmias were studied in the same manner. The autopsied hearts were examined macroscopically after formalin-fixation for coronary sclerosis, grade of dilatation and hypertrophy and abnormalities of valvular apparatus. The AV conduction system from the coronary sinus to the trabecula septomarginalis was serially sectioned by 7 micro according to Lev's method. The sinus node and its approaches, internodal tracts and intraventricular Purkinje cell net works were semiserially sectioned. Each 10th slice was picked up for alternative staining with hematoxylin-eosin and Weigertvan Gieson’s methods for microscopic study. Diagnosis of the hypertrophy of the cells in the AV conduction system was made as follows: for the AV node cells, larger ones than normal atrial cells; for the bundle of His, larger ones than ventricular cells; for the bundle branches, 1.5 times larger ones than ventricular cells, and for Purkinje cells, 3 times larger ones than ventricular cells, were presumed to be hypertrophied.

**RESULTS**

Table I shows incidence of the hypertrophy in the AV conduction system in various categories of arrhythmias and control cases. The overall incidence of the hypertrophy anywhere in the AV conduction system in cases with the blocks, was 77%. It was almost the same level as 78% in those with the pre-excitation syndrome, and 70% in those with the hypertrophied hearts with no arrhythmia. The incidence of hypertrophy was low as 42% in cases with the sick sinus syndrome, 39% in the miscellaneous arrhythmias and 30% in the normal control. The hypertrophy in cases with the blocks showed a particular character which consisted of pre-blockade and post-blockade hypertrophy.

Fig. 1A shows pre-blockade hypertrophy of the right bundle branch proximal to the blocked portion, and Fig. 1B illustrates post-blockade hypertrophy of the left bundle branch distal to the block. Hypertrophy in the AV conduction system was observed to be approximately 60% in the larger portion, either proximal (pre-blockade) or distal (post-blockade), developing to severe interruption, and 30 to 40% in the lesser portion, if the median point of the AV conduction system was presumed to set at the base of the bundle branches. The incidence of hypertrophy of this type was 30 to 40% in cases with incomplete blocks.

Fig. 1C shows hypertrophied AV node in a case with the pre-excitation syndrome with a node-ventricular and 2 Mahaim’s accessory bundles which were pathologically proved.

Fig. 1D shows hypertrophied left bundle branch in a hypertrophied heart, due to hypertension without arrhythmia, and Fig. 1E shows markedly hypertrophied Purkinje cells surrounded by fibrous tissue in a case with the Romano-Ward’s syndrome.

Incidence of hypertrophy of the AV conduction system in cases with 3° AV block, with hypertrophied and normal hearts without arrhythmia, is shown in Fig. 2 by location and age group. There was a difference of mode of the hypertrophy between the 3° AV block and hypertrophied hearts: more hypertrophy at the bundle of His in the former and more at the left bundle branch in the latter. No particular

tendency according to age was noticed. Sclerosis of the AV node artery was increasing with age in the cases with 3\textdegree AV block.

Incidence of the hypertrophy in the incomplete AV block and bifascicular block which included right bundle branch block and right or left axis deviation, showed the same tendency to that of the 3\textdegree AV block as shown in Fig. 3.

The hypertrophy in cases with the bundle branch block and abnormal axis deviation was also an imitation of that in the AV and bifascicular block, as shown in Fig. 4.

The sick sinus syndrome and the AV dissociation showed no particular hypertrophy different from the normal control. In contrast, the preexcitation syndrome showed hypertrophy in the AV node and the bundle of His, and the QT prolongation group including Romano-Ward’s
syndrome showed hypertrophy in the Purkinje cell network, as shown in Fig. 5.

Fig. 6 shows cases with sudden cardiac death. Extensive hypertrophy in the AV conduction system especially remarkable at the Purkinje cells, except the bundle branches, was characteristically seen in the organic cardiac disease group with recurrent ventricular fibrillation. In this group, marked sclerosis of the AV node artery shown at Fig. 1 F, was seen most often, as indicated at the left end of Fig. 6.

On the other hand, no hypertrophy even less than the normal control, was noticed in the Pokkuri disease.

From the nature of pathological lesions, Fig. 7 shows almost equivalent potency of degeneration, inflammation and ischemia, as major pathologic processes in the conduction system to induce the hypertrophy.

**COMMENT**

Hypertrophy of the working myocardium has been studied in detail, and the mechanism for its development was fairly understandable such as a reaction against increased wall stress due to volume and/or pressure overloading. The conduction system has no reason for hypertrophy against such mechanical overloading, whereas, it may receive much influence from autonomic nervous stimulation through rich nerve endings, and hypertrophy may be induced after repetitive stimulation. The hypertrophy of the AV conduction system seems to be not specific for either blocks or other arrhythmias, and it is even associated to cardiac hypertrophy without arrhythmia. This is explained from the assumption that the promoting factors for hypertrophy of both working musele and the AV conduction system are at least partially common, for ex-
ample, excessive catecholamine release may stimulate both the working myocardium and the conduction system to hypertrophy. This assumption is also advocated by the evidence that, whatever the etiologies are, almost equivalent hypertrophy is followed after conduction blocks.

Sclerosis of the AV node artery associated to hypertrophy of the AV conduction system and sudden cardiac death is also explained by excessive nervous stimulation which is common to produce the hypertrophy of the conduction system for rich nerve endings around the node artery.

There is an interesting difference in the hypertrophy of the AV conduction system between hypertrophy-conditioned and block-conditioned ones. The former hypertrophy does not include the bundle of His and the latter one is rather remarkable at the bundle of His. This phenomenon might suggest the hypertrophy of the AV conduction system due to a compensatory mechanism as a feedback biological reaction after the blocks, and the same logics are applicable to explanation for pre- and post-blockade hypertrophy.

It should be worth to mention that the hypertrophy of the Purkinje cells in cases with QT prolongation might be a common denominator for sudden cardiac death, whatever the etiologies of the cardiac lesions are. Some increase of catecholamin release or hypersensitivity to it of the cells in the conduction system seems from the histopathologic study to be a major promoting factor for the hypertrophy in the AV conduction system.

REFERENCE