Symposium on Amyloidosis Among the Japanese*

Moderator
Kiku NAKAO, M.D.
Chief Director of the Jichi Medical School

(1) Cardiac Amyloidosis

Shigeaki HINOHARA, M.D.
St. Luke's International Hospital, Tokyo

Amyloidosis had long been understood to be a very rare illness among the Japanese, however, its reported cases have gradually accumulated as increasing attention has been given in recent years.

It is the purpose of this paper to report on the incidence of primary amyloidosis and senile cardiac amyloidosis experienced at our institution and also to report on clinical and pathological findings of the cardiovascular system of amyloidosis, of which data were collected from seventy institutions throughout Japan. Cardiac amyloidosis was terminologically defined to mean cases of systemic amyloidosis, in which the heart was one of the most important localization of amyloid degeneration and also cases of senile cardiac amyloidosis among the aged, in which it is predominantly localized to the heart.

Incidence of primary amyloidosis at our institution:
During the past eighteen years, we have experienced seven cases of primary amyloidosis, five of which were autopsied at our institution. Its incidence is 2.9% among the total 1,719 autopsied cases, which, however, amounts to 3.72% among the 1,345 autopsied cases of over fifteen years old, the highest incidence reported in an institution throughout Japan.

Pathological findings of the heart in systemic amyloidosis:
The survey of deposits of amyloid was done in the hearts of 61 cases. In primary amyloidosis, the pathological involvement of amyloid was observed in the heart as high as 98% of the total cases, which was higher than in any other organs.

In secondary amyloidosis and myeloid-typed amyloidosis, the involvement of the
heart comes to next to any of the organs such as kidney, liver, or other endocrinological organs. Among primary amyloidosis, the average weight of the heart with severe, moderate and mild cardiac involvement were $456.2 \pm 22.0 \text{ g}$, $428.6 \pm 36.3 \text{ g}$ and $334.6 \pm 27.0 \text{ g}$ respectively. It can be said that the heart weighs heavier as its pathological involvement increases. The heaviest one weighed 700 g, which was the case without hypertension.

Clinical features of primary amyloidosis in the circulatory system:

The highest incidence of clinical findings or symptoms of circulatory system on admission to each institution was edema, which was followed by shortness of breath, palpitation, oppressive feeling of the chest or spells of dizziness, and in 54% of the cases, cardiac failure was already recognized on admission.

Diagnostic problem:

Among 63 cases of primary amyloidosis experienced in Japan, 30% of them have been correctly diagnosed, 95% of which were done by the result of microscopic finding of the biopsy. The diagnostic reliability of positive or questionably positive Congo Red test was no more than 56%.

Electrocardiographic features:

Electrocardiograms of 63 cases of primary amyloidosis were examined, of which abnormalities are summarized in Table 1 and 2, and compared with the results in U.S. reported by Buja2). The most common feature is appearance of low QRS voltage in the limb leads (77.4%), left axis deviation of QRS (27.4%) and a QS configuration and/or small R wave in $V_1$ to $V_3$ (41.9%) (Table 1). Other electrocardiographic findings (Table 2) consisted of partial A–V block (30.5%), A–V block (6.8%), A–V nodal rhythm (3.4%), atrial fibrillation (15.3%), RBBB (6.8%), LBBB (3.4%), and paroxysmal atrial tachycardia (3.4%). The combination of LAD of QRS voltage in limb leads, a QS configuration and/or small R in $V_1$ to $V_3$ occurring in the electro-

Table 1. ECG Findings of Cardiac Amyloidosis.

<table>
<thead>
<tr>
<th>Authors</th>
<th>Low Voltage</th>
<th>Axis Deviation</th>
<th>MI Patterns</th>
<th>Small or Absent R($V_1$–$V_3$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buja et al</td>
<td>117/233</td>
<td>50/84</td>
<td>6/84</td>
<td>12/124</td>
</tr>
<tr>
<td>(U.S.A.)</td>
<td>50%</td>
<td>59%</td>
<td>7%</td>
<td>10%</td>
</tr>
<tr>
<td>Hinohara</td>
<td>48/62</td>
<td>17/62</td>
<td>13/62</td>
<td>4/62</td>
</tr>
<tr>
<td>(Japan)</td>
<td>77.4%</td>
<td>27.4%</td>
<td>20.9%</td>
<td>4.8%</td>
</tr>
</tbody>
</table>

Table 2. ECG Findings of Cardiac Amyloidosis.

<table>
<thead>
<tr>
<th>Authors</th>
<th>Total</th>
<th>RBBB</th>
<th>LBBB</th>
<th>Partial A–V Block</th>
<th>Complete A–V Block</th>
<th>A–V Nodal Block</th>
<th>At. Fib.</th>
<th>PAT with 2:1 Block</th>
<th>PAT with 3:1 Block</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buja et al</td>
<td>57/98</td>
<td>14/42</td>
<td>10/42</td>
<td>37/142</td>
<td>13/149</td>
<td>10/147</td>
<td>28/147</td>
<td>2/142</td>
<td>2/142</td>
</tr>
<tr>
<td>(U.S.A.)</td>
<td>58%</td>
<td>18%</td>
<td>6%</td>
<td>26%</td>
<td>9%</td>
<td>7%</td>
<td>19%</td>
<td>1%</td>
<td>1%</td>
</tr>
<tr>
<td>Hinohara</td>
<td>32/59</td>
<td>4/59</td>
<td>2/59</td>
<td>18/59</td>
<td>4/59</td>
<td>1/59</td>
<td>9/59</td>
<td>1/59</td>
<td>1/59</td>
</tr>
<tr>
<td>(Japan)</td>
<td>54.2%</td>
<td>6.8%</td>
<td>3.4%</td>
<td>30.5%</td>
<td>6.8%</td>
<td>1.7%</td>
<td>1.7%</td>
<td>1.7%</td>
<td>1.7%</td>
</tr>
</tbody>
</table>
cardiogram of an elderly patient usually in congestive heart failure, without a past history of heart disease, should bring to mind the possibility of cardiac amyloidosis.

The death of the patients with primary amyloidosis:
Most of the patients with primary amyloidosis died of heart failure. The age of death for man and woman in these series was 55.5 years and 56.2 years old respectively, and 61.9% of the total cases died of heart failure, in one thirds of which immediate cause of death seemed to be the cardiac still, including death due to digitalis intoxication.

Amyloidosis and blood pressure:
In our series of primary amyloidosis, hypertension was observed only exception-ally in spite of the fact that there observed renal involvement in most of the cases, at the time of admission to each institution.

At the time of admission elevated systolic blood pressure of over 160 mmHg was found in only 15% (8 among 52 cases) and elevated diastolic blood pressure of over 110 mmHg was found in 5.8% (3 among 52 cases). In most cases of a long term observation, blood pressure gradually decreased as the involvement of amyloid progressed. The orthostatic hypotension was observed in 13% of cases with primary amyloidosis. As to familial type of amyloidosis, orthostatic hypotension was observed in much higher percentage such as 80% among the 13 cases, which may be attributed to the amyloid involvement of the sympathetic ganglion.

Senile cardiac amyloidosis among the Japanese:
It has recently been recognized in western countries that heart failure or ab-normal conduction or arrhythmia of the aged hearts may be attributed to amyloid involvement of the heart. In Japan investigations on this subject were done by Hosokawa3) and Ikee4).

We investigated aged heart of over 70 years old of 41 cases died of various diseases and were autopsied at our hospital. Amyloid deposits were observed in 26.8% by Congo Red staining of cardiac tissues. However, its average weight was no more than 333 g and was definitely of less weight than that of the average cardiac weight of the cases with primary amyloidosis. In most of the cases its amyloid deposits were of a minor grade. However it can not be denied that such a minor pathological change may have something to do with the cause of unexpected death of the aged. In Table 3 is shown the incidence of senile cardiac amyloidosis

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>50-</td>
<td>0 %</td>
<td>- %</td>
<td>- %</td>
<td>- %</td>
<td>- %</td>
<td>- %</td>
</tr>
<tr>
<td>60-</td>
<td>0.1</td>
<td>0</td>
<td>22.2</td>
<td>49-59% (13.6%)</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>70-</td>
<td>1.5</td>
<td>3.0</td>
<td>27.8</td>
<td>31.2</td>
<td>21.1</td>
<td></td>
</tr>
<tr>
<td>80-</td>
<td>6.3</td>
<td>7.0</td>
<td>32.5</td>
<td>43.2</td>
<td>26.3</td>
<td></td>
</tr>
<tr>
<td>90-</td>
<td>18.6</td>
<td>50.0</td>
<td>57.5</td>
<td>80.0</td>
<td>66.6</td>
<td></td>
</tr>
</tbody>
</table>
of each decade of our series in comparison with that of other authors in Japan and abroad\textsuperscript{5,6}.

Discussion and conclusion:

The author made statistical survey, clinical and pathological observation of cardiac amyloidosis among cases with systemic amyloidosis, particularly of primary amyloidosis which have been reported in Japan during the past ten years.

Incidence of senile cardiac amyloidosis among the Japanese observed at our institution was also reported and was compared with those of other authors.

The author considers that incidence of cardiac amyloidosis in Japan will be increasing as attention of physicians to this disease increases when they treat patients with heart failure, dysrhythmia, progressive hypotension and abnormal electrocardiographic features, such as low voltage of QRS in limb leads, QS pattern in V\textsubscript{1}–V\textsubscript{4} and axis deviations of QRS.

Reference


(2) Not submitted