Case Reports

Three Cases of Idiopathic Cardiomegaly in the Aged, with Special References to the Morphological Specificity and to the Conduction System

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Summary

Three cases of idiopathic cardiomegaly in the aged (64, 82 and 73 years old) were presented. All of them were male and had the common finding of cardiac enlargement of unknown etiology, terminating in refractory heart failure. They showed hypertrophy and degeneration of the myocardium with a peculiar accumulation of focal myocardial fibrosis and endocardial fibroelastosis in the posterior wall of the left ventricle. Overdosage of norepinephrine (Case 1), positive serologic test for syphilis (Case 2) and associated mitral insufficiency (Case 3) might give some modifications to the original myocardial disease. A study of the conduction system revealed degenerative changes similar to the myocardium, which caused the left bundle branch block in Case 2.

Additional Indexing Words:
Primary myocardial disease Mypardiopathy Myocardial fibrosis Left bundle branch block Conduction system

Recently under the headings of primary myocardial disease, idiopathic cardiomegaly, idiopathic myocardiopathy, idiopathic cardiomyopathy and so on, heart diseases of obscure origin have been extensively studied and reviewed in Western countries1)-8) and in Japan.9)-17) There has been, however, no decisive classification or nomenclature of them, because of lack in etiologic informations. The purposes of this paper are to describe the clinical and pathological findings of 3 cases with idiopathic cardiomegaly in the aged and to demonstrate the mutual similarities and differences among them, suggesting a new concept on the myocardial changes. The conduction system in one of them with complete left bundle branch block was histologically studied, and peculiar changes were noted.

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CASE REPORTS

Case 1 was a 64-year-old man, who was admitted to the Yoiku-in Hospital with a chief complaint of shortness of breath in August, 1966, after a half year's uneventful life under ambulant control with maintenance doses of digitalis and diuretics. The patient had neither history of heavy drinking nor hypertension, and had experienced recurrent episodes of congestive heart failure in recent 5 years. In 1964, he was admitted to this hospital for dyspnea and dependent edema. Normal blood pressure (114/88 mm.Hg) and atrial fibrillation were noted and he was fairly recovered under digitalis treatment. In December, 1965, a transseptal left heart catheterization was performed for the evaluation of his cardiac status. But the septal puncture was followed by an episode of tachycardia, hypotension with cold sweat, which was successfully treated by a drip infusion of a total of 370 mg. of norepinephrine for 4 days. Physical examination on admission revealed neither anemia nor jaundice at the conjunctivae, and showed moderate pretibial edema. The pulse was 80/min. and irregular, and the blood pressure was 118/78 mm.Hg. The apex beat was felt weak but shifted towards the left anterior axillary line, with neither abnormal cardiac sounds nor murmurs. The liver was palpable 1 fingerbreadth under the right costal margin. The chest X-ray films revealed marked bilateral cardiac enlargement (Fig. 1). The electrocardiograms showed atrial fibrillation, left axis deviation and left ventricular hypertrophy with intraventricular conduction block (Fig. 2). Ruling

Fig. 1 (Left). Chest X-ray film of Case 1, showing cardiac enlargement.

Fig. 2 (Right). Electrocardiograms of Case 1, showing atrial fibrillation, left axis deviation, left ventricular hypertrophy with ST-T changes, taken in December, 1964 and in December, 1966.
Fig. 3 (Left upper). The heart of Case 1 (weight 815 Gm.) with a globular shape.

Fig. 4 (Right upper). Dilatation of the left ventricle (Case 1). White arrows indicate thinning of the posterior wall.

Fig. 5 (Left lower). Histological view of myocardium (Case 1), showing atrophy or degeneration of muscle fibers and marked congestion of the small vessels around the fibrotic area (HE × 100).

Fig. 6 (Right lower). Accumulated fibrosis at the posterior wall of the interventricular septum (Case 1). (EvG × 13).
out the common causes of cardiac enlargement, the diagnosis of idiopathic cardiomegaly was made. An attack of severe dyspnea with Cheyne-Stokes' respiration, loss of consciousness and tachycardia with atrial fibrillation accompanied by an acute swelling of the left leg due to thrombophlebitis appeared after 3 months' hospitalization, and he expired on December 24, 1966.

The autopsy findings: The heart was extremely enlarged (weight of 815 Gm.) and showed a globular shape (Fig. 3). The apex was formed by the left ventricle and a tiny focal fibrosis was seen near the apex. No fresh pericarditis was recognized. There were no significant narrowing of the coronary arteries. Dilatation of all 4 chambers was marked but that of the left ventricle was especially prominent (Fig. 4). The size and wall thickness of each chamber were listed in Table II.

Histological changes in the myocardium consisted of hypertrophy of each muscle fibers, enlargement and pyknosis of the nuclei, eosinophilic and hyalinoid appearance of the cytoplasm with loss of striation and of moth-eaten type vacuolar degeneration.

Fig. 7 (Upper). X-ray films of the chest (Case 2), demonstrating right pleural effusion and cardiac enlargement on admission (left) and cardiomegaly following therapy for 1 month (right).

Fig. 8 (Lower). Electrocardiograms of Case 2, showing atrial fibrillation and left ventricular hypertrophy (a) and later occurrence of complete left bundle branch block (b).
Multiple focal perivascular fibrosis was diffusely scattered in the myocardium. Atrophy or degeneration of muscle fibers and congestion of the small vessels were more marked around the fibrosis (Fig. 5). Special accumulation of the fibrosis was noticed at the posterior wall of the interventricular septum (Fig. 6) and thinning of the wall at the site was even macroscopically observed (Fig. 4). Neither narrowing nor sclerosis existed in small intramyocardial arteries. Pulmonary congestion was associated with some emphysema and generalized congestion in the systemic organs was marked. A thrombophlebitis was found at the left femoral vein, but there was no pulmonary embolism.

Case 2 was an 82-year-old man, who was admitted to the Yoiku-in Hospital with complaints of palpitation and dyspnea in May, 1967. He had a history of venereal disease in adolescence. On admission, the patient was anemic and dyspneic. His pulse showed an arrhythmia absoluta, and the blood pressure was 120/78 mm.Hg. His face was puffy and there was moderate pretibial edema. Right hydrothorax and ascites were disclosed. X-ray films of the chest (Fig. 7) demonstrated right pleural effusion and cardiac enlargement. Electrocardiogram showed atrial fibrillation and left ventricular hypertrophy (Fig. 8a), later associated with complete left bundle branch block (Fig. 8b). Laboratory examination disclosed no abnormality in blood chemistry and liver function tests. Urinalysis was positive for protein but normal

Fig. 9 (Left). Transverse sections of the heart of Case 2, showing the moderate dilation of both ventricles and marked hypertrophy of the left ventricle.

Fig. 10 (Middle). Histological findings of the myocardium (Case 2), showing hypertrophy of muscle fibers and nuclei, focal perivascular fibrosis with cellular infiltration (HE ×100).

Fig. 11 (Right). Relatively fresh fibrosis with dilated vessels of the posterior wall of the left ventricle and a thick endocardial fibroelastosis in Case 2 (EvG ×20).
in microscopic findings. Serologic test for syphilis was positive. Clinical diagnosis was idiopathic cardiomegaly with congestive heart failure and atrial fibrillation. Those cardiac symptoms reacted fairly well to digitalis and diuretics, followed by an uneventful course until October, 1967, when he died of recurrent attack of congestive heart failure.

Autopsy showed an enlarged heart of 470 Gm., with moderate dilatation of both ventricles and marked hypertrophy of the left ventricle (Fig. 9). There were no abnormalities in the valves and in the coronary arteries. Histological findings of the myocardium were marked hypertrophy of the muscle fibers and nuclei with various degeneration, focal perivascular fibrosis with mild cellular infiltration, which consisted mostly of fibrocytes and of few lymphocytes and plasma cells (Fig. 10). Relatively fresh fibrosis with dilated vessels was accumulated at the posterior wall (Fig. 11), with endocardial fibroelastosis.

Case 3 was a 73-year-old man, who entered the Yoiku-in Hospital with a complaint of shortness of breath in January, 1960. Approximately 50 years ago, he had been treated for beriberi heart disease and in 1958, an apical harsh holosystolic murmur was recorded, and was diagnosed as mitral insufficiency. On admission, the blood pressure was 130/100 mm.Hg and the cardiac murmur was compatible with mitral insufficiency. X-ray films of the chest revealed bilateral cardiac enlargement (Fig. 12) and the electrocardiogram showed atrial fibrillation, left ventricular hypertrophy and ST-T changes (Fig. 13). His hospital course was uneventful.

Fig. 12 (Left). Chest X-ray film of Case 3, revealing bilateral cardiac dilatation with pleural effusion.

Fig. 13 (Right). Electrocardiograms of Case 3, showing atrial fibrillation and various ST-T changes.
with good response to digitalis for a year, then he died of an attack of cardiac asthma.

Autopsy findings were as follows: the heart weight was 360 Gm. with moderate dilatation of left ventricle and minimal coronary sclerosis. Dilated mitral ring with its circumference of 10.5 cm. and abnormal connections of chordae tendineae at the

Fig. 14. Dilatation of the left ventricle and mitral ring, and abnormal attachment of chordae tendineae, resulting in the minor prolapse of anterior leaflet (between 2 arrows).

Fig. 15. A-V bundle and interrupted initial portion of left bundle branch by fatty tissue (a: HE ×13), and degeneration and fibrosis of the conduction cells with cellular infiltration in the A-V bundle. Arrows indicate atrophic left bundle branch, which was interrupted a little peripherally (b: HE ×100).
posteromedial commissure were thought responsible to the mitral insufficiency, though the mitral cusps were normal (Fig. 14). Microscopically, there were mild to moderate hypertrophy and marked degeneration of muscle fibers and diffusely scattered fibrosis, which formed a considerable scar at the posterior wall.

**STUDY ON THE CONDUCTION SYSTEM**

A histological study of the conduction system was performed for the left bundle branch block in Case 2. The A-V node, the bundle of His and both bundle branches were serially cut according to Lev's method after embedding into paraffin. Weigert-van Gieson stain, H.E. stain and P.A.S. or toluidine blue stain were applied. Both posterior and anterior radiations of the left bundle branch showed almost complete interruptions due to fatty metamorphosis and fibrosis (Fig. 15 a). The other conduction system including the A-V node, A-V bundle and right bundle branch had some degenerative changes but they were milder in degree than those in the left bundle branch, except slight cell infiltrations (Fig. 15b). Only minor increase of both acid and neutral mucopolysaccharides was proved in the conduction system.

**DISCUSSION**

Clinical and pathological findings of 3 aged cases of idopathic cardiomegaly were summarized in Table I and II. Common denominators found in these cases were old age, male, marked cardiac enlargement, arrhythmias including atrial fibrillation and conduction disturbances, congestive heart failure with pulmonary congestion, absence of known nutritional and metabolic disorders, and absence of alcoholism and hypertension. On the treatment, cardiac failure reacted well to digitalis or diuretics at the first stage, but they became gradually resistant to any treatments. From the morphological view, hypertrophy and degeneration of muscle cells were common, in spite of a considerable difference in the heart weight. A special interest should

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Sex</th>
<th>Diagnosis</th>
<th>Initial Signs</th>
<th>B.P. (mm.Hg)</th>
<th>ECG</th>
<th>Clinical Course</th>
<th>Remarks</th>
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<tbody>
<tr>
<td>1</td>
<td>64</td>
<td>M</td>
<td>I.C. CHF</td>
<td>Dypsnea Edema</td>
<td>114/88</td>
<td>AF LVH</td>
<td>3 y</td>
<td>Norepinephrine 370 mg./4 days, Thrombophlebitis</td>
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<tr>
<td>2</td>
<td>82</td>
<td>M</td>
<td>I.C. CHF</td>
<td>Dypsnea Edema</td>
<td>120/78</td>
<td>AF LBBB</td>
<td>10 m</td>
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<tr>
<td>3</td>
<td>73</td>
<td>M</td>
<td>I.C. CHF M.I.</td>
<td>Dypsnea</td>
<td>130/100</td>
<td>AF LVH</td>
<td>1 y</td>
<td>Beriberi in history, but no rheumatic fever</td>
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**Table I. Clinical Summary**

*Abbreviations:* I.C.: Idiopathic Cardiomegaly, CHF: Congestive Heart Failure, M.I.: Mitral Insufficiency, AF: Atrial Fibrillation, LVH: Left Ventricular Hypertrophy, LBBB: Left Bundle Branch Block, y: years, m: months.
Table II. Measurement of the Heart

<table>
<thead>
<tr>
<th>Case</th>
<th>Heart Weight (Gm.)</th>
<th>Volume (ml.) and Thickness (mm.)</th>
<th>Valvular Ring (mm.) and Thickness (mm.)</th>
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<tr>
<td></td>
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<td>LA</td>
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<tr>
<td></td>
<td>1-4</td>
<td>1-4</td>
<td>2-4</td>
</tr>
</tbody>
</table>


be focused to the tendency of accumulation of focal fibrosis at the posterior wall of the left ventricle in all 3 cases. The most peripheral zone of the coronary arteries in a sense of distance from the orifices is the posterior wall and it could be a locus resistantiae minoris for diffuse myocardial involvement of any kinds by relative anoxia.

From an etiological consideration, a part of the myocardial lesions in Case 1 would be related to overdosage of norepinephrine 1 year prior to his death. Szakacs18) and Shenk and Moss19) described the cardiac lesions of sustained norepinephrine infusions in man, rabbits, cats, and dogs, which consisted of focal degeneration, necrosis and fibrosis of muscle fibers with subendocardial hemorrhage. But the evidence that he had a sign of congestive heart failure before the norepinephrine treatment, was compatible with the preexisting myocardial disease.

In Case 2, positive serologic test for syphilis should be carefully considered for an etiological factor. Syphilitic myocarditis was first reported by Warthin20) in 1914, but this diagnosis could not be made in the absence of gummas.21) The myocardial lesions of our case were different from the gumma but the localized perivascular edema and focal infiltrations of lymphocytes and plasma cells suggested a possibility of participation of hypersensitive or allergic reaction which might be related to syphilis. Therefore, it was rational that myocardial hypertrophy was primary, which could be modified by syphilis.

In Case 3, mitral insufficiency might be a cause of cardiomegaly. But
the morphological features (normal cusps, mitral ring dilatation, and minute change of chordae tendineae) could not explain the genesis of cardiac enlargement. Therefore, it was highly possible that the mitral insufficiency was secondary to the primary degenerative myocardial disease. After these considerations, the authors' conclusion was that the diagnosis of 3 cases was idiopathic cardiomegaly with some modifications by norepinephrine, syphilis and mitral insufficiency, respectively.

Since the first description of the idiopathic cardiomegaly by Josserand and Gallavardin (1901), many cases have been reported everywhere in the world. But even in the present day, no definite conclusion has been reached to explain its etiology. For example, Mattingly\(^1\),\(^2\) and Segal\(^3\) classified primary myocardial disease in 2 groups: one by known specific etiologies and the other by unknown (idiopathic) etiology. In Japan, Ueda and Okada\(^11\) classified them and showed criteria and definition of 'idiopathic cardiomegaly of adult type'. On the other hand, Fowler\(^4\)\(^-\)\(^6\) strictly used the term of "primary", only in cases of "idiopathic myocardial disease."

Histologically, it was said that there were hypertrophy of myocardial fibers and myocardial fibrosis, with or without localized endocardial thrombosis or fibroelastosis.\(^10\) All the 3 cases fulfilled completely these criteria. Recently, one of the authors proposed a new classification of the idiopathic myocardiopathy from a pure pathological standpoint, that is, (1) degeneration, (2) hypertrophy, (3) fibrosis and (4) combined type were classified by the predominant histological feature of the myocardium.\(^13\),\(^14\) Types of the myocardial lesions in our 3 cases were 'hypertrophy' in Case 1 and 2 and 'degeneration' in Case 3, though each main lesion was associated with a considerable secondary fibrosis. From macroscopic findings, Case 1 and 2 showed marked increase in the heart weight and thick ventricular wall as well as marked dilatation, and Case 3 showed a predominant dilatation with a mild hypertrophy (Table II). This fair correspondence between gross and microscopic findings in the myocardium suggests a hypothesis that myocardial hypertrophy reacting to the luminal dilatation makes hypertrophy and its absence makes dilatation without hypertrophy. If the main myocardial lesion is diffuse myocardial degeneration, the reactive hypertrophy could not occur, and if the myocardium recovers reactivity to excessive dilatation, secondary hypertrophy becomes possible. Therefore, the subdivisions of the idiopathic myocardiopathy or cardiomegaly might not indicate essential difference between each type but difference of grade of initial damage or recovery course from pathologic states.

None of our 3 cases had clear pathogenetic factors for their myocardial lesions. Myocardial degeneration and its sequelae were always present and
their distribution had a regular pattern, and no inflammatory signs, no previous hypertension and no coronary sclerosis with insidious onset of cardiac symptoms postulate unknown kind of metabolic disorder in the myocardium as a primary lesion.

The pathological changes of the conduction system in Case 2 suggested the common pathogenetic factor is working in the conduction system as in the myocardium, because neither degeneration of the central fibrous body nor ischemic changes were responsible for the production of left bundle branch block, which were the main lesions among the 8 cases of complete left bundle branch block.22)

REFERENCES