

## A CASE OF CARDIAC AMYLOIDOSIS DIAGNOSED BY TWO-DIMENSIONAL ECHOCARDIOGRAPHY AND <sup>99m</sup>Tc-PYROPHOSPHATE SCINTIGRAPHY

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### Abstract

A case of AL (amyloid fibril protein related to immunoglobulin light chain) cardiac amyloidosis is described. The patient was admitted to our hospital because of syncope. Two-dimensional echocardiography (2-D echo) revealed diffuse severe thickening of biventricular walls, and highly reflectile echoes ("granular sparkling" appearance) of the myocardium. <sup>99m</sup>Tc-PYP myocardial imaging demonstrated diffusely intense uptake throughout the whole heart.

The definitive diagnosis was finally made by right ventricular endomyocardial biopsy and immunohistocytological technique. In the evaluation of amyloidosis, usefulness of noninvasive diagnostic methods including <sup>99m</sup>Tc-PYP and 2-D echo were stressed and we also assessed the utility of MRI.

### Introduction

Clinically significant cardiac amyloidosis accounts for 5% to 10% of noncoronary cardiomyopathy<sup>1)</sup>, and its prognosis is poor. Nevertheless diagnosis of cardiac amyloidosis is commonly difficult antemortem for some reasons, including lack of awareness of prevalence of the entity and nonspecific symptoms and signs. Recently, echocardiography and technetium-99m pyrophosphate (<sup>99m</sup>Tc-PYP) scintigraphy proved useful adjuncts in the noninvasive diagnosis of cardiac amy-

loidosis<sup>2)-5)</sup>.

We experienced a case of AL (amyloid fibril protein related to immunoglobulin light chain) cardiac amyloidosis with plasma cell dyscrasia (PCD) which was strongly suspected by means of echocardiography and <sup>99m</sup>Tc-PYP scintigraphy, and endomyocardial biopsy lead to a definitive diagnosis. We also observed some findings from a X-ray computed tomography (CT) and a magnetic resonance imaging (MRI), so we are presenting the case report together with a discussion.

### Case Report

A 51-year-old Japanese male was hospitalized because of syncopal episodes and edema of legs that appeared seven months prior to admission.

On physical examination, heart rate was regular at 91 beats/min and blood pressure was 90/60 mmHg in supine position, although upright it dropped to 80 mmHg in systole. Faint moist rales were audible at the base of the bilateral lungs, and no murmur and a loud 4th sound was heard.

The liver was palpable 3 cm below the right costal margin, and there was marked pitting edema in the lower extremities.

Laboratory data were summarized in Table 1.

A chest roentgenogram showed slight cardiac enlargement with cardiothoracic ratio of 53%.

An electrocardiogram (ECG) revealed first-degree atrioventricular block, low QRS voltage in

**Table 1** Laboratory findings

Blood chemistry test	
Immunoglobulin ;	
IgG 900, IgA 927, IgM 90 (mg/100ml)	
Immunoelectrophoresis ;	
IgA- $\lambda$ type monoclonal immunoglobulin :	
positive	
Bone marrow examination	
Nucleated cell	57,300/mm <sup>3</sup>
Granulocytic erythroid ratio	2 : 1
Atypical plasma cell	13% (with no cluster formation)

limb leads and right ventricular hypertrophy (Fig. 1).

Two-dimensional echocardiography (2-D echo) in the parasternal position demonstrated left ventricular hypertrophy, small size of ventricular cavity and akinesis of interventricular septum (Fig. 2). The myocardium of interventricular septum and left ventricular posterior wall showed high density echoes which had a subjectively "granular and sparkling" pattern. The right ventricular hypertrophy was also seen in the apical four-chamber view (Fig. 2-c).

<sup>99m</sup>Tc-PYP scintigraphy revealed diffuse and intense uptake throughout the myocardium (Fig 3). Thallium-201 (<sup>201</sup>Tl) myocardial perfusion imaging showed biventricular hypertrophy, but neither low uptake nor defect was delineated.

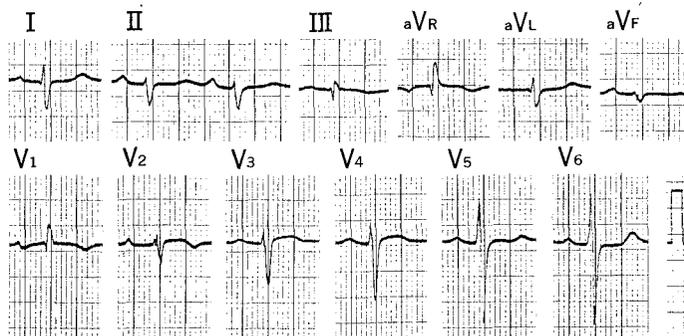
ECG gated radionuclide ventriculography revealed left ventricular ejection fraction (EF) of 50%. On nongated X-ray CT, myocardial density of the interventricular septum was 37 Hounsfield

Units (H.U.). We evaluated this heart by means of ECG gated MRI which was performed with a HITACHI G-10 system with a field strength of 0.15 Tesla (Fig. 4). The imaging sequence was Spine Echo with echo delay time (TE) of 32 msec and repetition time (TR) of 100 msec.

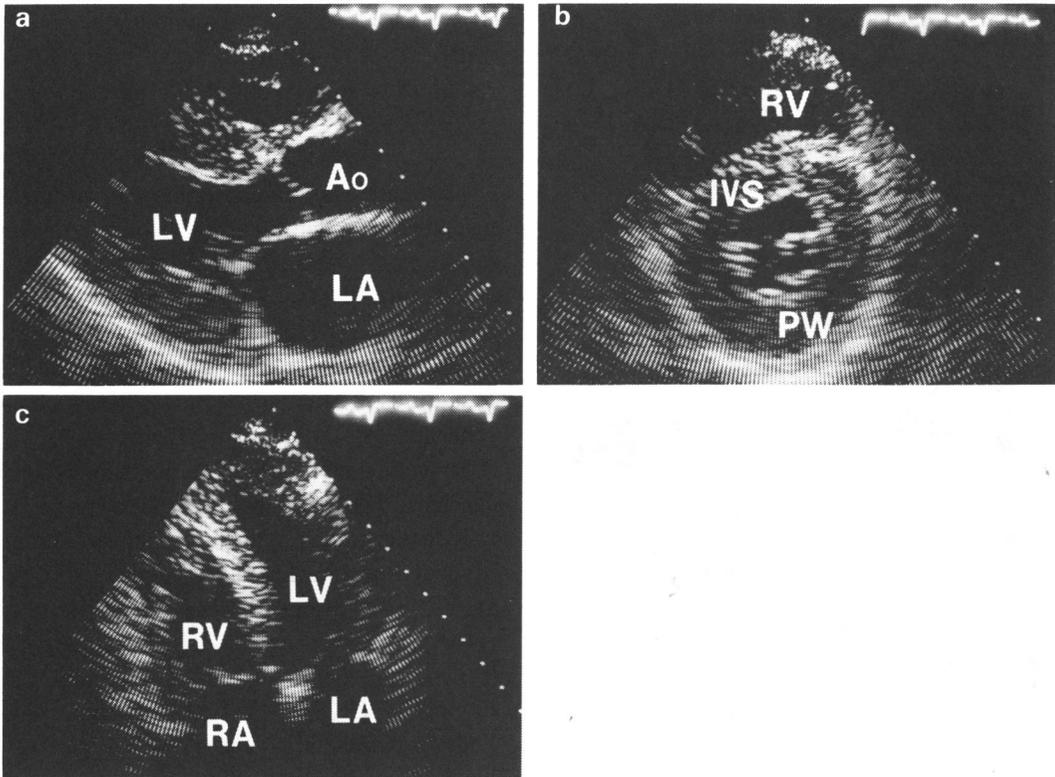
MRI also displayed hypertrophy of right and left ventricular free walls, interventricular septum, and dilated right atrium clearly. From these findings, cardiac amyloidosis was strongly suspected.

Biopsy of rectal mucosa showed amyloid deposits when examined by polarization microscopy after Congo Red staining. Cardiac catheterization and angiography demonstrated left ventricular filling pressure of 18 mmHg with no dip-and-plateau configuration, diffuse left ventricular hypokinesis with EF of 41%. Coronary arteriographic study revealed squeezing of 75% in the distal portion of the left anterior descending artery. The right ventricular endomyocardial biopsy revealed diffuse marked myocardial infiltration with amyloid deposits (Fig. 5-a). The amyloid kept its affinity for Congo Red after exposure to potassium permanganate, and didn't react with anti-AA antisera in immunoperoxidase method. Electron microscopic examination of the myocardium evidenced amyloid fibrils in the interstitium (Fig. 5-b).

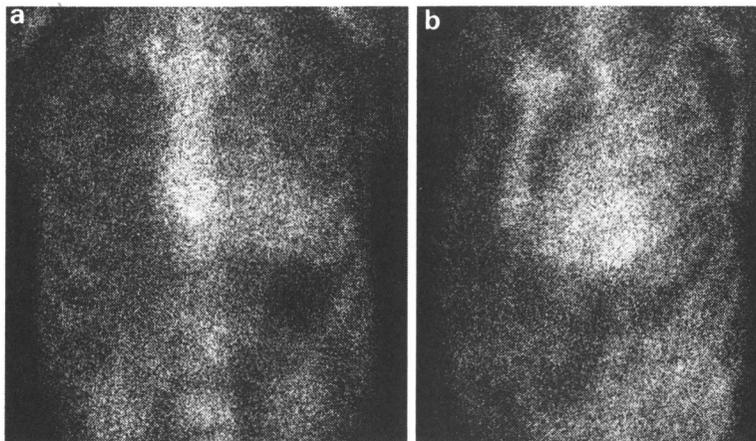
Though Holter-monitor studies demonstrated no arrhythmia to account for the syncope, electrophysiologic study revealed sinus node dysfunction with prolongation of sinus node recovery



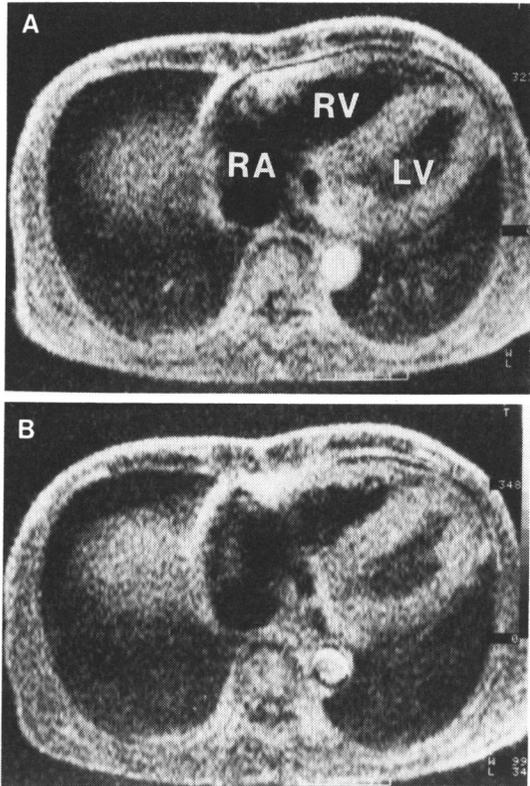
**Fig. 1** ECG showing first-degree atrioventricular block, low QRS voltage in limb leads and right ventricular hypertrophy.



**Fig. 2** 2-D echo. a, b; long-axis and short-axis view of the left ventricle demonstrating symmetrical hypertrophy with highly reflectile echoes in the myocardium. c; apical four-chamber view showing markedly thickened biventricular wall. Ao; aorta, LA; left atrium, LV; left ventricle, RA; right atrium, RV; right ventricle, IVS; interventricular septum, PW; posterior wall.



**Fig. 3**  $^{99m}\text{Tc}$ -PYP scintigraphy indicating intense, diffuse cardiac uptake. a; anterior, b; 60° left anterior oblique views.



**Fig. 4** Gated MRI: Transverse MR image indicating uniform increase of myocardial wall thickness and right atrial enlargement. A; end-diastole, B; end-systole.

time-2600 msec and first-degree infra-His-block (H-V interval of 75 msec). Therefore, with the bone marrow examination a diagnosis of AL cardiac amyloidosis accompanied with PCD was made<sup>6)</sup>, and fully automatic pacemaker (DDD pacing system) was implanted for the purpose of protection of syncope probably due to Sick Sinus Syndrome. The patient was discharged on only diuretics because of hypersensitivity of digitalis and dimethyl sulfoxide.

Four months later, he died suddenly from loss of consciousness. Necropsy revealed bilateral hydrothorax and massive ascites. The heart was greyish and weighted 500 g and showed general hypertrophy (Fig 5-c). Microscopic examination revealed abundant amyloid deposits in almost all of the organs, and especially prominent in the heart. Extensive amyloid deposits were also seen

in sinoatrial node. As craniotomy was not permitted by his family, precise cause of death remained a subject of speculation.

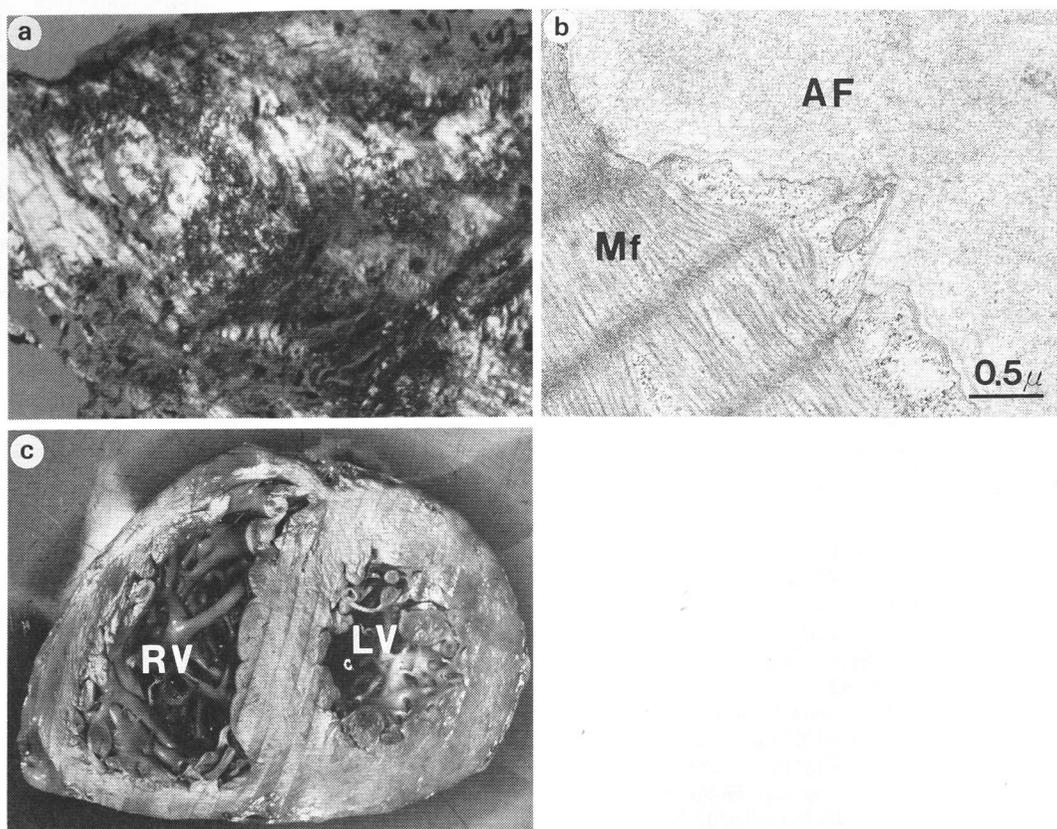
### Discussion

This case was diagnosed as AL cardiac amyloidosis by endomyocardial biopsy and immunoperoxidase method with anti-AA antisera coincided with potassium permanganate reaction method<sup>7)8)</sup>. In this particular case, the first step of its diagnosis of cardiac amyloidosis owned much to noninvasive diagnostic modalities, such as 2-D echo and <sup>99m</sup>Tc-PYP scintigraphy.

First, the echocardiographic manifestation of cardiac amyloidosis are biventricular hypertrophy with a "granular sparkling" appearance of the myocardium<sup>2)3)</sup>. From the echocardiographic standpoint, various disease which causes ventricular hypertrophy should be considered in differential diagnosis, as hypertrophic cardiomyopathy (HCM)<sup>9)10)</sup>, systemic hypertension, Fabry's disease<sup>11)</sup>, glycogen storage disease<sup>12)~15)</sup>. So, 2-D echo has limitation of making a diagnosis of cardiac amyloidosis.

Secondly, <sup>99m</sup>Tc-PYP scintigraphy also useful device in the setting of suspected cardiac amyloidosis. Recently, many reports showed that cardiac amyloidosis produced a positive myocardial <sup>99m</sup>Tc-PYP scintigraphy<sup>4)5)</sup> and the degree of uptake was correlated with increased wall thickness<sup>16)</sup>. The exact mechanism of <sup>99m</sup>Tc-PYP uptake in amyloid heart is unclear but it is postulated the uptake to be due to the affinity for the calcium associated with the p-component of amyloid<sup>17)</sup>. This patient showed intense uptake of <sup>99m</sup>Tc-PYP in the whole heart. But some other disease (myocarditis, pericardial inflammation etc.) also indicates this phenomenon<sup>18)19)</sup>, so this uptake is not specific for cardiac amyloidosis. Therefore, combination of 2-D echo and <sup>99m</sup>Tc-PYP might be resolution in making a diagnosis of cardiac amyloidosis.

To evaluate the histopathological characteristics of cardiac amyloidosis, X-ray CT was performed. Sekiya et al reported that the density of the myocardium with amyloid infiltration was



**Fig. 5** a; Myocardial-biopsy specimen showing characteristic birefringence by polarization microscopy after Congo Red staining. b; Electron micrograph of myocardium showing amyloid fibrils (AF) in the interstitium. Mf; myofibril, c; Transverse section of the autopsied heart.

significantly lower ( $30.6 \pm 3.4$  H.U.) than the of HCM (ranged from  $38.8 \pm 5.7$  to  $45.9 \pm 4.4$  H.U.) and normal myocardium (ranged from  $41.9 \pm 4.3$  to  $44.8 \pm 4.4$  H.U.) on X-ray CT<sup>17</sup>). Although amyloid infiltration may be assumed to have an influence on the density of myocardium, this case didn't indicate distinct lower density (37 H.U.). Therefore we couldn't tell this amyloid infiltrative heart from HCM or normal heart on CT.

We referred to the MRI which is expected to the usefulness in the diagnosis of cardiovascular system<sup>21)22)</sup>. As MRI demonstrated thickened ventricles and dilated right atrium clearly in this case, it was of value in regard to the recognition of the cardiac morphology along with 2-D echo, <sup>201</sup>Tl myocardial scintigraphy and X-ray. Moreover, quantitative assessment of histopathological

characteristics is constructed by measuring the chemical parameter such as  $T_1$  and  $T_2$  relaxation times. Waters et al have indicated that variance of spin echo A intensity within the cardiac cycle was different from normal myocardium but not for HCM<sup>23)</sup>. Even though  $T_1$  and  $T_2$  values were not measured in this case, MRI will be promising modality which detects the histopathological changes of cardiac amyloidosis if relaxation times are altered.

#### Acknowledgement

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断層心エコーおよび<sup>99m</sup>Tc-ピロリン酸心筋シンチグラムにて  
診断し得た心アミロイドーシスの1例

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雨宮	邦子	・中村	憲司	・木全	心一
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非侵襲的検査法にて診断し得た AL タイプの心アミロイドーシスの1例を報告する。患者は51歳の男性で失神発作を主訴に当科へ入院した。1度房室ブロック、心拡大より心病変が疑われた。断層心エコー(2-D echo)では両心室壁はびまん性の肥厚を認め、いわゆる“granular sparkling 像”を呈していた。また、<sup>99m</sup>Tc-ピロリン酸心筋シンチグラム(<sup>99m</sup>Tc-PYP)では、心筋全体に著明な集積像が認められた。以上2検査の結果より心アミロイドーシスが強く疑われ、確定診断は右室心内膜生検法にてなされた。心アミロイドーシスの診断過程において2-D echo と<sup>99m</sup>Tc-PYP の相補的診断にて、生検前に心アミロイドーシスと診断し得、また CT scan, 心電図同期 MRI の心筋病変に対する有用性が期待された。