

## A patient with cardiac amyloidosis presenting a rapid increase in technetium-99m-hydroxymethylene diphosphonate accumulation

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We assessed the changes in cardiac condition in a patient with cardiac amyloidosis, by means of dual nuclei single photon emission computed tomographic (SPECT) images with technetium-99m-hydroxymethylene diphosphonate ( $^{99m}\text{Tc}$ -HMDP) and thallium-201 ( $^{201}\text{Tl}$ ). Dual SPECT showed a marked increase in myocardial  $^{99m}\text{Tc}$ -HMDP accumulation along with deterioration of symptoms and signs, while  $^{201}\text{Tl}$  scintigraphy remained almost unchanged.

**Key words:** cardiac amyloidosis, scintigraphy,  $^{99m}\text{Tc}$ -HMDP,  $^{201}\text{Tl}$

### INTRODUCTION

THE CARDIAC manifestations in primary amyloidosis vary depending on the area and the severity of amyloid deposition into the heart.<sup>1</sup> Echocardiography is usually used to diagnose cardiac amyloidosis noninvasively,<sup>2,3</sup> but in patients with advanced cardiac amyloidosis there is no significant echocardiographic change during the follow-up study.<sup>4</sup> Recently scintigraphy with technetium-99m-labeled phosphates has been used for the diagnosis of cardiac amyloidosis.<sup>5-7</sup> However, there are few reports on the progression of cardiac amyloidosis detected by technetium-99m-labeled phosphates scintigraphy.

In this report, we present a patient with primary amyloidosis involving the heart. Myocardial accumulation of technetium-99m-hydroxymethylene diphosphonate ( $^{99m}\text{Tc}$ -HMDP) increased as symptoms and signs deteriorated during a 3 month follow-up, while thallium-201 ( $^{201}\text{Tl}$ ) scintigraphic and echocardiographic findings remained unchanged in this period.

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### CASE REPORT

A 69-year-old man was admitted to our hospital because of dyspnea. One year before admission, he noticed edema in the lower extremities. Then shortness of breath on exertion appeared and rapidly deteriorated. On admission he was in New York Heart Association functional stage III. Biopsy specimens from the duodenal mucosa revealed abundant amyloid deposits, and Congo red staining after treatment of amyloid deposits with potassium permanganate suggested the amyloidosis related to AL protein. There were no relatives known to be affected with amyloidosis. He had not experienced myocardial infarction. Physical examination revealed a blood pressure of 80/60 mmHg and a heart rate of 85 beats/minute.

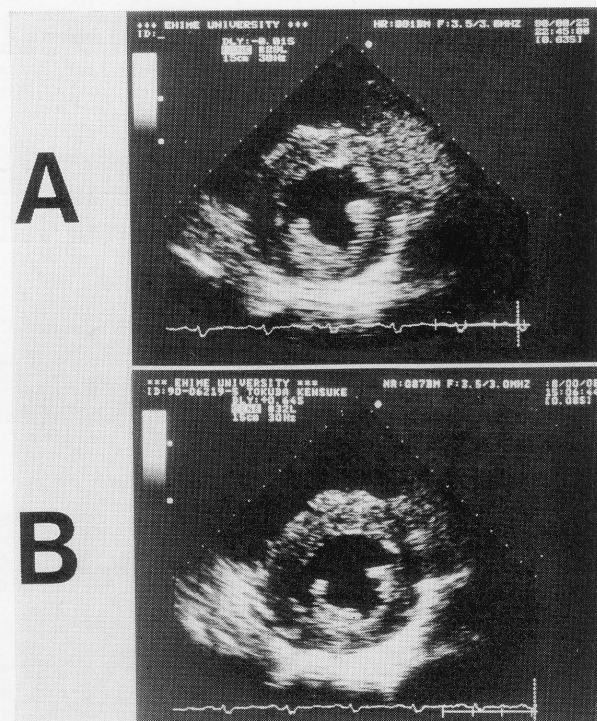
The chest X-ray film showed enlargement of the heart (cardiothoracic ratio 63%) and bilateral pleural effusion. A routine electrocardiogram showed right bundle branch block, poor R progression in precordial leads, and low QRS-voltages. The echocardiogram showed left ventricular hypertrophy (interventricular septal thickness, 18 mm; posterior wall thickness, 12 mm) with highly refractile myocardial echoes, so-called granular sparkling appearance. The left ventricular wall motion was reduced (fractional shortening 18%). Echocardiographic findings remained unchanged during 3 months' hospitalization (Fig. 1).

Dual single photon emission computed tomographic (SPECT) images of  $^{99m}\text{Tc}$ -HMDP and  $^{201}\text{Tl}$  were examined on admission and then 3 months later. Three hours after the administration of 740 MBq of  $^{99m}\text{Tc}$ -HMDP, 111 MBq of  $^{201}\text{Tl}$  was administered, and the scintillation camera (GE Starcam 400 AC/T), equipped with a low-energy general purpose collimator, was rotated for 35 seconds in each projection of 32 slices over  $360^\circ$  circulation orbits. Energy discrimination was provided by a 20% window centered on the 140-keV photopeak of  $^{99m}\text{Tc}$ -HMDP and 72-keV photopeak of  $^{201}\text{Tl}$ . Images of 1.33 magnification were recorded at a digital resolution of  $64 \times 64$  matrices with a dedicated computed system.  $^{201}\text{Tl}$  scintigraphy on admission revealed defects in the posterior region as shown in Fig. 2-A, but  $^{99m}\text{Tc}$ -HMDP scintigraphy showed the intense accumulation in posterior and septal regions seen in Fig. 2-B. Dyspnea on exertion progressively deteriorated in spite of treatment with a cardiac inotropic agent and increases in doses of diuretics. After 3 months' hospitalization, dual SPECT showed a marked increase in the accumulation of  $^{99m}\text{Tc}$ -HMDP in the septal region and a new accumulation in the lateral region, while  $^{201}\text{Tl}$  scintigraphy remained almost unchanged (Fig. 3). Just after three months imaging, he suddenly died. His autopsy revealed amyloid deposition in the accumulated area of  $^{99m}\text{Tc}$ -HMDP.

## DISCUSSION

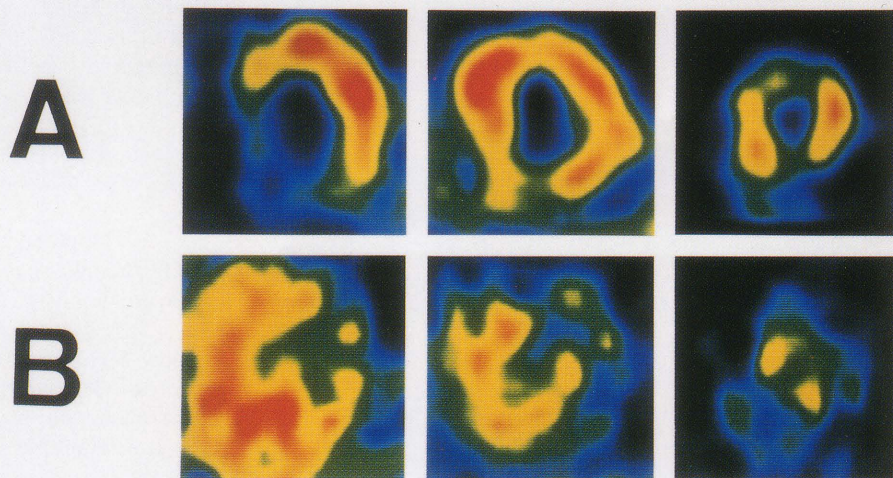
We report a patient with cardiac amyloidosis whose cardiac involvement was assessed by SPECT with  $^{99m}\text{Tc}$ -HMDP and  $^{201}\text{Tl}$ . Since the first report of the cardiac accumulation of  $^{99m}\text{Tc}$ -diphosphonate in patients with cardiac amyloidosis by Kula et al.,<sup>5</sup> scintigraphy with  $^{99m}\text{Tc}$ -labeled phosphates has been used as a noninvasive procedure for the diagnosis of cardiac amyloidosis. However, there are some reports indicating that this technique is not useful because of low incidence of positive scan.<sup>8,9</sup> The exact mechanism of myocardial accumulation of  $^{99m}\text{Tc}$ -labeled phosphates in amyloidosis still remains unclear. It possibly relates to the increased calcium concentration in tissues infiltrated with amyloid, as shown by the study in which there was a strong relation between tissue uptake of  $^{99m}\text{Tc}$ -labeled phosphate and calcium accumulation.<sup>5,10</sup>

$^{99m}\text{Tc}$ -HMDP showed a significantly higher uptake in infarct myocardium than  $^{99m}\text{Tc}$ -methylene diphosphonate and approximate equality with  $^{99m}\text{Tc}$ -pyrophosphate.<sup>11</sup> We used  $^{99m}\text{Tc}$ -HMDP to evaluate the severity of cardiac involvement. On admission,  $^{99m}\text{Tc}$ -HMDP scintigraphy showed an uneven positive accumulation, while  $^{201}\text{Tl}$  scintigraphy showed a

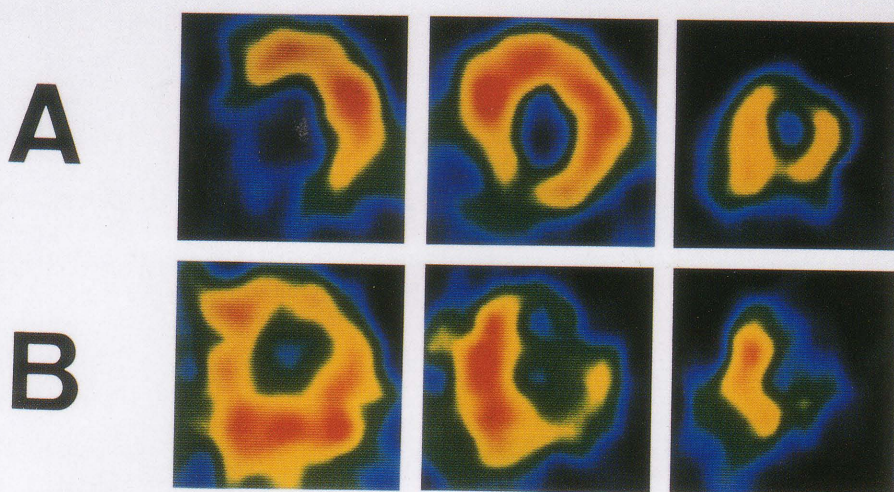


**Fig. 1** Two-dimensional echocardiograms of the patient, (A) on admission and (B) after 3 months of the admission. Both echocardiograms almost unchanged.

regional defect. The region of accumulation of  $^{99m}\text{Tc}$ -HMDP almost exactly corresponded to the defect seen in the  $^{201}\text{Tl}$  image, and 3 months after the initial scintigraphic study, the accumulation of  $^{99m}\text{Tc}$ -HMDP markedly increased. Hongo et al.<sup>6</sup> reported that myocardial accumulation of  $^{99m}\text{Tc}$ -pyrophosphate was detected in cardiac amyloidosis, while no cardiac perfusion defect of  $^{201}\text{Tl}$  was observed. They<sup>7</sup> also reported in cases with familial amyloidosis that no significant changes in the area and the degree of  $^{99m}\text{Tc}$ -pyrophosphate accumulation in cardiac amyloidosis were observed at least in a 3-year follow-up period. Takezaki et al.<sup>12</sup> reported that  $^{99m}\text{Tc}$ -pyrophosphate accumulation and  $^{201}\text{Tl}$  defect were observed in cardiac amyloidosis, and the accumulation of  $^{99m}\text{Tc}$ -pyrophosphate was observed in the same regions as the perfusion defect seen with  $^{201}\text{Tl}$ , which is similar to our case. They suggested that  $^{201}\text{Tl}$  defect might reflect the myocyte damage due to amyloid deposits in connective tissue of the myocardium. Three months after the initial SPECT, the extension and increase in  $^{99m}\text{Tc}$ -HMDP accumulation were observed, while the  $^{201}\text{Tl}$  defect remained unchanged. We supposed that amyloid deposits increase, as indicated by the increase in  $^{99m}\text{Tc}$ -HMDP accumulation, followed by myocardial cells degeneration, resulting in the subsequent appearance of the  $^{201}\text{Tl}$  defect.



**Fig. 2** Short axis image of thallium-201 ( $^{201}\text{Tl}$ ) myocardial SPECT on admission showed a defect in septal and posterior wall regions (A) and a accumulation of technetium-99m hydroxymethylene diphosphonate ( $^{99\text{m}}\text{Tc-HMDP}$ ) was observed (B) in these regions where  $^{201}\text{Tl}$  defect existed.



**Fig. 3** After 3 months of the admission, short axis image of  $^{201}\text{Tl}$  (A) remained unchanged, but that of  $^{99\text{m}}\text{Tc-HMDP}$  (B) showed a marked increase of uptake compared to that on admission.

Hongo et al.<sup>13</sup> reported that the incidence and the degree of abnormalities in echocardiography in patients with amyloidosis were correlated with the duration of the illness. In our case, unlike the scintigraphic data, echocardiographic findings were unchanged during the 3-month follow-up period. Thus echocardiography might not be useful for defecting the progression of advanced cardiac amyloidosis in a short term.<sup>4</sup>

The combination of <sup>201</sup>Tl and <sup>99m</sup>Tc-HMDP SPECT is of value in assessing the degree and distribution of the infiltrative process of amyloidosis in cardiac tissue. Serial examinations would permit the estimation of the progression of the disease, and they might aid in evaluating the efficacy of the treatment regimen for amyloidosis.

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