Assessment of Myocardial Damage in Dilated-Phase Hypertrophic Cardiomyopathy by Using Indium-111-Antimyosin Fab Myocardial Scintigraphy

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For the detection of myocardial cell damage, an ^{111}In-antimyosin Fab study was carried out on seven patients (Group A) in the dilated phase of hypertrophic cardiomyopathy, seven patients (Group B) with dilated cardiomyopathy, and eight control patients (Group C). Imaging was done 48 hr after intravenous injection of 74 MBq of ^{111}In-antimyosin Fab. Myocardial antimyosin uptake was visually graded as 0, +1, +2 or +3. A score of +2 or +3 was considered positive. The heart/lung ratio of antimyosin uptake (antimyosin index) also was determined. Antimyosin uptake was positive in seven (100%), nine (90%) and no (0%) patients in Groups A, B, and C, respectively. The antimyosin index in Groups A and B was 2.46 ± 0.49 and 2.04 ± 0.24, respectively, findings were significantly higher than that in Group C (1.51 ± 0.13) ($p < 0.01$). Positive biopsy findings were noted in only two patients in Group A. Thus, antimyosin uptake was increased in dilated phase hypertrophic cardiomyopathy and dilated cardiomyopathy, which suggests ongoing necrotic changes in these patients.

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Indium-111-labeled monoclonal antimyosin antibodies, which specifically bind to the myosin (*1,2*), have been used in diagnosing active myocyte damage in acute myocardial infarction, acute myocarditis, and acute cardiac rejection (*3–11*). Recently, Obrador et al. (*12*) reported that antimyosin uptake is frequently observed, even in stable chronic dilated cardiomyopathy, which suggests the presence of active myocardial damage in these patients.

Compared to dilated cardiomyopathy, most patients with hypertrophic cardiomyopathy have a good prognosis; however, dilatation of the left ventricular cavity and congestive heart failure occur in some of these patients (*13–15*). Previously, we have reported the association of abnormal thallium perfusion and cardiac enzymes in hypertrophic cardiomyopathy, which progressed to dilated cardiomyopathy [dilated-phase hypertrophic cardiomyopathy (*15,16*)]. These patients had a progressive downhill course similar to idiopathic dilated cardiomyopathy (*17–19*). In this paper, we evaluated the usefulness of determining myocardial uptake of antimyosin antibodies in patients with dilated-phase hypertrophic cardiomyopathy.

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MATERIALS AND METHODS

Patient Selection

Indium-111-antimyosin Fab scintigraphy was carried out in 25 consecutive patients from May to October, 1989. All patients gave informed, written consent. The control group consisted of five men and three women aged 34 to 62 yr (mean 44 ± 12). There were five patients with ischemic heart disease (three with effort angina pectoris and two with previous myocardial infarction) and three with suspicion of dilated cardiomyopathy. Table 1 shows the profiles of the seven patients with dilated-phase hypertrophic cardiomyopathy (Patients 1–7; mean age, 49 ± 8 yr) and the ten with dilated cardiomyopathy (Patients 8–17; mean age 52 ± 11 yr). Echocardiography, thallium scan, and cardiac catheterization were done on all patients. Left ventricular diastolic dimension was evaluated by using echocardiography. Left ventricular ejection fraction and regional wall motion were analyzed by using contrast left ventriculography. The presence of thallium perfusion defects also was evaluated. Right ventricular endomyocardial biopsy (1–2 specimens taken) were done except on control patients. Serum lactic dehydrogenase (LDH) and creatine phosphokinase (CPK) were analyzed in all patients. The normal limits of serum LDH is 100–225 IU/l, while those of serum CPK is 40–160 IU/l (male) and 30–105 IU/l (female), respectively.

Scintigraphic Protocol

Subjects received an intradermal injection of 0.1-ml of labeled antimyosin. If no wheal was observed in 30 min, they were injected with 0.5 mg of R11D10-Fab-DTPA labeled with 2 mCi of ^{111}In (Centocor, USA).

Planar scintigraphic images were obtained 48 hr after antimyosin injection. Imaging was undertaken in the anterior and left anterior oblique (45° and 70°) projections with a gamma camera (GE 400 AC/T) with a high-resolution medium-energy collimator and a 20% window centered on the 247- and 173-keV

TABLE 1
Patient Profile

Patient no.	Age/Sex	Onset	Antimyosin score	Antimyosin index	Thallium defect	LVDd (mm)	LVEF (%)	Wall motion	LDH (IU/l)	CPK (IU/l)
1	37/F	4 yr	+2	2.01	−	48	61	normal	→	↑ 469
2	57/M	5 yr	+2	1.95	+	60	43	GH	→	↑ 184
3	50/F	7 yr	+3	2.83	+	56	32	GH	→	↑ 212
4	53/M	10 yr	+3	2.36	+	58	39	GH	↑ 275	→
5	59/M	7 yr	+2	2.00	−	47	53	normal	↑ 265	↑ 259
6	37/M	3 yr	+3	3.02	+	54	49	reduced	→	→
7	48/M	2 yr	+3	3.03	+	60	48	reduced	→	→
8	47/F	7 yr	+2	2.25	+	70	32	GH	↑ 255	↑ 287
9	22/M	5 yr	+2	2.11	+	68	31	GH	→	→
10	51/M	8 yr	+1	1.63	+	80	27	GH	→	→
11	66/M	4 yr	+2	2.11	−	77	35	GH	→	→
12	64/M	1 yr	+2	1.79	−	65	21	GH	→	→
13	54/F	3 yr	+2	2.37	+	78	20	GH	→	→
14	59/F	14 yr	+2	2.13	+	70	17	GH	→	→
15	52/M	9 yr	+2	1.80	+	82	27	GH	→	→
16	53/M	9 yr	+2	2.00	+	85	21	GH	→	→
17	52/M	5 yr	+2	2.23	+	73	40	GH	→	→

Patients 1–7 had dilated-phase hypertrophic cardiomyopathy; Patients 8–17 idiopathic dilated cardiomyopathy.
+ = defect or hypoperfusion; onset = onset of disease; LVDd = left ventricular diastolic dimension; LVEF = left ventricular ejection fraction; GH = generalized hypokinesis; reduced = reduced wall motion; CPK, LDH = serum creatine phosphokinase, lactic dehydrogenase; ↑ = elevation; and → = within normal limits

peaks. A minimum of 500K counts were collected in 10 min. Analog and digital images collected in a 64 × 64 matrix were stored for subsequent antimyosin index analysis.

Two days later, planar scintigraphic images were obtained with 2 mCi of ^{201}Tl-chloride administration. Anterior and left anterior oblique (40° and 70°) projections were obtained with a gamma camera (GE 400 AC/T) with a high-resolution low-energy collimator and a 20% window centered on the 75-keV peak. A minimum of 500K counts was collected in 10 min. These data were compared with those of the antimyosin studies. The effects of crosstalk on both images were calculated. Standard samples of the two radiopharmaceuticals containing the same activity were placed without mixing in the center of the camera. The crosstalk values were 8% for ^{201}Tl to ^{111}In and 10% for ^{111}In to ^{201}Tl. The effects of crosstalk on both images were not visually observed.

Interpretation of Antimyosin Findings

This was performed by two experienced observers who did not know the results of the biopsy or clinical and laboratory data. All data were first inspected visually to determine if there was antimyosin uptake in the myocardium. The results were graded as follows: 0, no uptake; +1, mild or faint uptake; +2, clear but moderate uptake; and +3, intense myocardial uptake (Fig. 1). An antimyosin score of +2 or +3 was considered to represent positive uptake.

To calculate the antimyosin uptake index, the 48-hr digital unprocessed anterior projection was used, with the region of interest adjusted in the myocardium and the lungs. Lung regions were drawn as extensively as possible, but the sternum, bone structures of the shoulder, and the liver were avoided. Average counts/pixel in the myocardium were divided by average counts/pixel in the lung to obtain the final antimyosin uptake index (*9, 10*). The relationships between antimyosin uptake and myocardial perfusion were assessed visually for the same projection images of ^{111}In-antimyosin and ^{201}Tl-chloride.

Data among groups were expressed as mean ± one standard deviation (m ± s.d.). One-way analysis of variance and Student's t-test were used to analyze differences between pairs of groups.

RESULTS

As shown in Figure 2, the antimyosin index correlated with the antimyosin score ($r = 0.88$ $p < 0.01$). The anti-

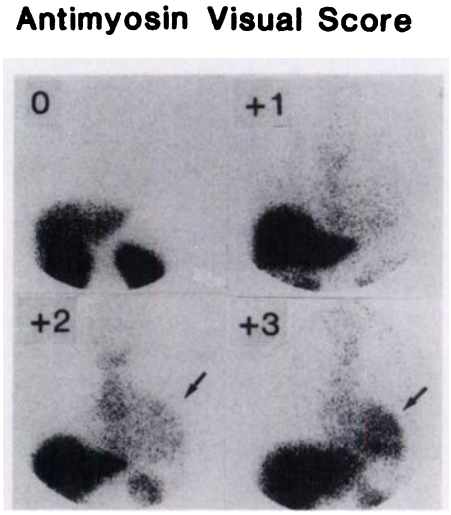

FIGURE 1. Visual interpretation of antimyosin scan in an anterior planar image. 0: no uptake, +1: mild uptake, +2: moderate uptake, and +3: intense uptake.

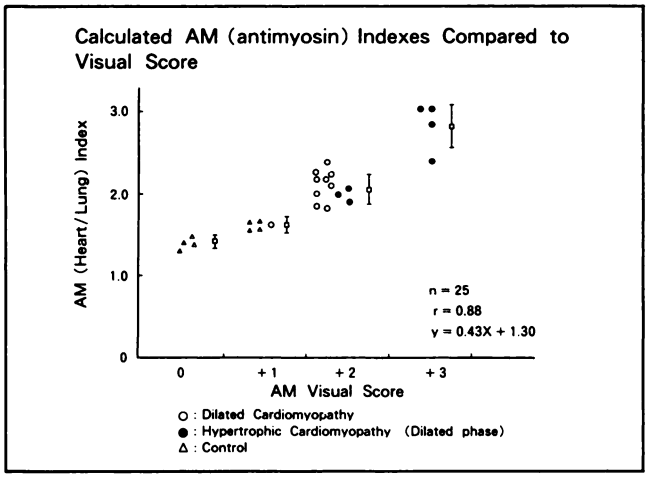

FIGURE 2. Comparison of calculated antimyosin indices to visual analysis. Antimyosin index was determined as follows: isotope activity in the cardiac region is divided by the activity in different pulmonary areas of interest to obtain a heart-to-lung ratio.

myosin index was 1.46 ± 0.04, 1.64 ± 0.10, 2.06 ± 0.10, and 2.81 ± 0.27 for antimyosin scores of 0 (n = 4), +1 (n = 5), +2 (n = 12), and +3 (n = 4), respectively.

Mean antimyosin indices in patients with dilated-phase hypertrophic cardiomyopathy, those with dilated cardiomyopathy, and in control patients were 2.46 ± 0.49, 2.04 ± 0.24 and 1.51 ± 0.13, respectively (Fig. 3). The difference between the cardiomyopathy groups and the control group was significant ($p < 0.01$).

As shown in Table 1, all patients with dilated-phase hypertrophic cardiomyopathy had diffuse positive antimyosin uptake. Five had focal thallium perfusion defects, five had abnormal ejection fraction (less than 50%) and abnormal left ventricular wall motion, and five had elevation of serum creatine phosphokinase and/or lactic dehydrogenase.

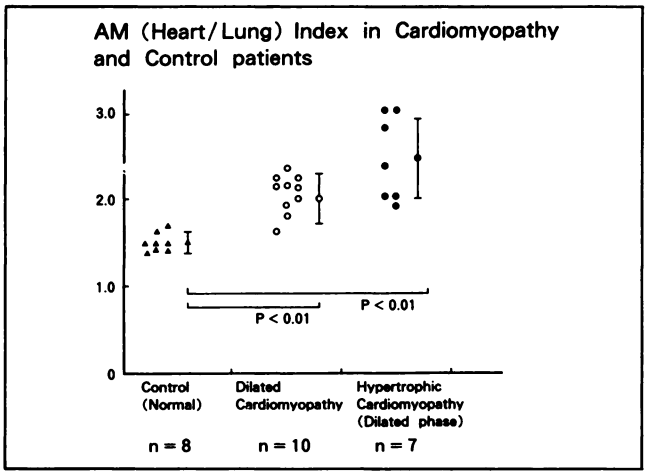

FIGURE 3. Calculated antimyosin indices in idiopathic dilated cardiomyopathy, dilated-phase hypertrophic cardiomyopathy, and controls.

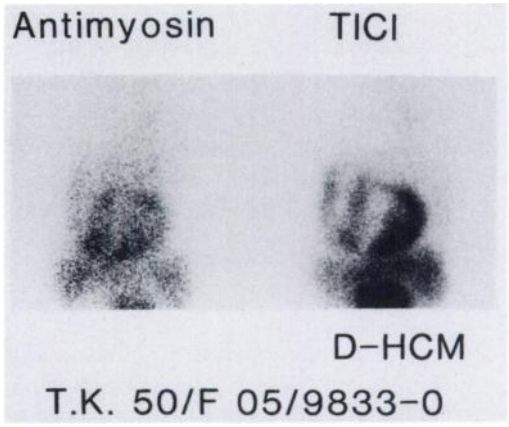

FIGURE 4. Indium-111-antimyosin Fab and ^{201}Tl-chloride myocardial planar images in a patient with dilated-phase hypertrophic cardiomyopathy (Patient 3). Note the diffuse and intense myocardial antimyosin uptake, while anteroseptal perfusion defect was observed by thallium scan.

Right ventricular biopsy findings in all patients revealed myocardial hypertrophy and disarray in addition to myocardial fibrosis. Only two patients (Patients 3 and 4) had positive findings such as myocyte degeneration with lymphocyte infiltration. Figure 4 shows the left anterior oblique images of ^{111}In-antimyosin and thallium in a representative case of dilated-phase hypertrophic cardiomyopathy (Patient 3). Intense antimyosin uptake was observed in the whole left ventricular wall, with a thallium perfusion defect at the anteroseptal wall.

Of 10 patients with dilated cardiomyopathy, 9 had diffuse and moderate positive antimyosin uptake. Eight had focal thallium hypoperfusion or defect with left ventricular dilatation. All had low ejection fraction (mean 27% ± 5%) and generalized left ventricular hypokinesis. Right ventricular biopsy findings revealed myocardial hypertrophy and fibrosis in all patients. None of these patients had evidence of myocarditis.

Figure 5 shows a representative case with dilated cardi-

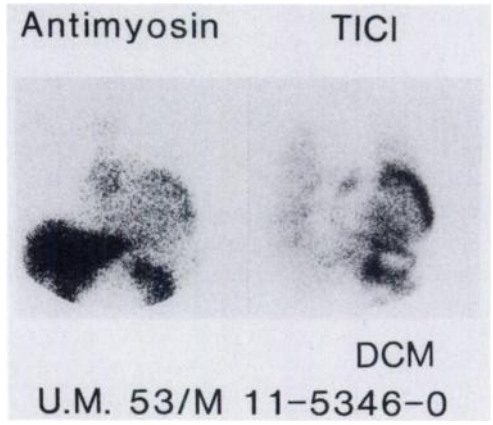

FIGURE 5. Indium-111-antimyosin Fab and ^{201}Tl-chloride myocardial planar images in a patient with idiopathic dilated cardiomyopathy (Case 16). Note the diffuse and mild antimyosin uptake. Antimyosin and thallium uptake overlapped.

omyopathy (Patient 16). Moderate and diffuse antimyosin uptake was observed in the entire left ventricular wall, with a thallium perfusion defect at the inferoposterior wall in anterior images.

In the control group, no tracer distribution within cardiac regions was usually seen, but a faint signal in the lower left parasternal region was occasionally detected (score 0 to 1).

DISCUSSION

The present study demonstrated a high incidence of antimyosin uptake in patients with dilated-phase hypertrophic cardiomyopathy in addition to those with dilated cardiomyopathy. These findings suggest myocardial cell degeneration in the hypertrophied heart. These patients are likely to develop dilatation of the left ventricle and poor contraction, which may progress to congestive heart failure (*13–16*). Therefore, diagnosis and follow-up of these patients is especially important, and they must be differentiated from those patients with other hypertrophic cardiomyopathies.

Blood-pool activity at 24 hr in antimyosin scans has not been a problem when delineating myocardial infarcts, but it can be a problem when studying diffuse disease such as congestive heart failure (*5,6,9,10*). In our study, patients studied at 24 hr after injection presented with apparent blood-pool activity, but this was not seen on the 48-hr images. Therefore, it is important to differentiate positive antimyosin uptake from cardiac blood-pool activity on the 48-hr images.

Our visual criteria for antimyosin uptake correlated well with the antimyosin index determined by the heart/lung ratio. This semiquantitative index was initially described by Carrio et al. (*9,10*), who showed lung activity mainly due to circulating antibody. They demonstrated that the antimyosin index was highly reproducible and the calculated antimyosin indices in patients after cardiac transplantation were correlated with the results of right ventricular biopsy (*9,10*). Thus, we also adapted these visual and semiquantitative methods for the assessment of antimyosin uptake.

Obrador et al. (*12*) noted a high incidence of antimyosin uptake in patients with dilated cardiomyopathy, and positive results were not due to left ventricular dilatation or to the results of heart failure, since a similar cardiac impairment was present in negative scan patients with congestive heart failure and coronary heart disease. These findings are very important since myocardial uptake of antimyosin in patients with dilated cardiomyopathy probably reflects the presence of active myocyte damage, despite the fact that biopsies revealed myocyte damage in only 1 of the 17 patients (*12*).

A similar discrepancy has been found in myocarditis and cardiac transplantation (*9,10*). In our series, positive antimyosin uptake was demonstrated in 9 of the 10 dilated cardiomyopathy patients and all 7 of the patients with dilated-phase hypertrophic cardiomyopathy. However, positive biopsy findings (*20*) were noted in only two of those with dilated-phase hypertrophic cardiomyopathy. In the present study, it is not clear whether myocardial uptake reflects diffuse cellular damage undetected by microscopy or a false-positive result. Nevertheless, antimyosin indices in these patients clearly differed from those in normal subjects, which strongly suggests active myocardial damage in these patients. Further studies (e.g., clinical and ventriculographic) are needed to evaluate antimyosin uptake in these patients.

Dilated cardiomyopathy may be a common pathway of many diverse end-stage heart diseases (*17–19*). However, the high incidence of positive antimyosin uptake in these patients, compared with that in patients with other types of end-stage heart disease, indicates that dilated cardiomyopathy is a distinct clinical entity. Furthermore, dilated-phase hypertrophic cardiomyopathy also tends to have more intense, diffuse antimyosin uptake than dilated cardiomyopathy. These patients had abnormal thallium perfusion and cardiac enzymes. This suggests the presence of severe ongoing necrotic changes (*13–16*). The prognostic value of antimyosin uptake in these patients is still uncertain because of the limited number of cases examined. In our series, cardiac death occurred in one patient with dilated cardiomyopathy (Patient 17) and in two with dilated-phase hypertrophic cardiomyopathy (Patients 2 and 3) within 6 mo after antimyosin imaging. The continual myocardial antimyosin uptake may explain the steady clinical deterioration in these patients. Although our study was limited to patients with dilated-phase hypertrophic cardiomyopathy, some patients with other hypertrophic cardiomyopathies also may develop congestive heart failure. Therefore, antimyosin imaging should be performed on these patients.

In conclusion, uptake of monoclonal antimyosin antibodies is increased in dilated-phase hypertrophic cardiomyopathy and in dilated cardiomyopathy, even when right ventricular biopsy findings are negative. This method may be useful for the noninvasive assessment of active myocardial damage in these patients.

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SELF-STUDY TEST

Gastrointestinal Nuclear Medicine

Questions are taken from the *Nuclear Medicine Self-Study Program I*, published by The Society of Nuclear Medicine

DIRECTIONS

The following items consist of lettered headings followed by a list of numbered phrases or statements. For each numbered phrase or statement, select the *one* lettered heading that is most closely associated with it. *Each lettered heading may be selected once, more than once, or not at all.* Answers may be found on page 1352.

For each pair of glycine-1-^{14}C-cholic acid breath tests and fecal fat excretion results shown in Figures 1–4, and items 1–4, select the most appropriate interpretation (options A–E). (Normal fecal fat is < 6.0 g/24 hr)

A. normal subject
B. pancreatic insufficiency
C. ileal resection
D. bacterial overgrowth in small bowel
E. fish tapeworm infestation

1. Figure 1
2. Figure 2
3. Figure 3
4. Figure 4

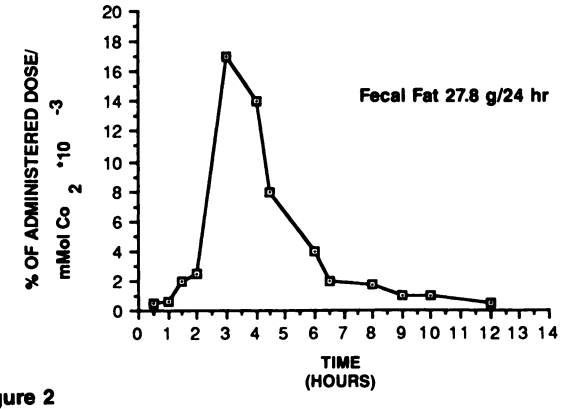

Figure 2

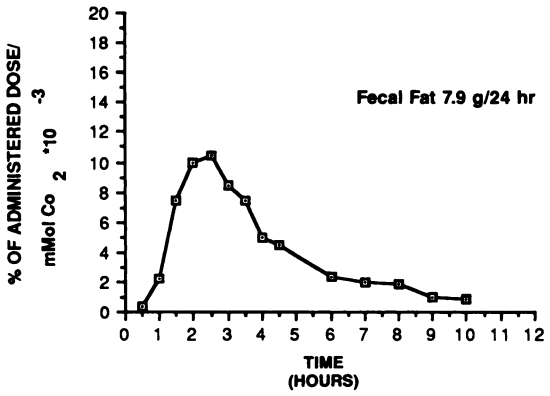

Figure 1

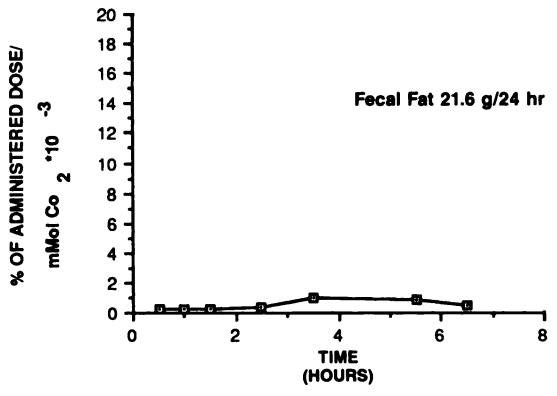

Figure 3

(continued on p. 1352)