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Indium-111 antimyosin monoclonal antibody Fab imaging in patients with cardiomyopathy

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Six patients with cardiomyopathy were imaged following intravenous injection of an indium-111 labeled monoclonal antibody directed against the heavy chain of cardiac myosin. Two patients had hypertrophic non-obstructive cardiomyopathy (HNCM), two patients had dilated cardiomyopathy (DCM), and two patients had specific heart muscle disease. One of 2 patients with HNCM and one of 2 patients with DCM had a positive antimyosin scan. The 2 patients with specific heart muscle disease manifested persistent blood pool activity of the antibody, thereby precluding interpretation of the images. The present report demonstrates that antimyosin antibody imaging may provide evidence of myocardial injury, or necrosis in some patients with cardiomyopathy.

Key words: In-111 antimyosin antibody, cardiomyopathy

INTRODUCTION

KHAW AND COLLEAGUES[1] developed whole murine antibodies to the heavy chain of cardiac myosin in 1976. Following intravenous injection, this radiolabeled antibody demonstrated localization in irreversibly damaged myocytes, where the sarcolemma was disrupted and the intracellular myosin was exposed. Over the ensuing 14 years, modifications of antimyosin resulted in increased specificity, decreased antigenicity, and improved imaging characteristics.[2–10] The current antimyosin antibody is a murine monoclonal Fab fragment linked to a bifunctional chelating agent, diethylenetriamine pentaacetic acid (DTPA), which facilitates radiolabeling with In-111.[11] Within 24 hours of cell death, the membrane becomes so disrupted that intracellular myosin is exposed to the antibody in the extracellular fluid. By means of antigen antibody binding, In-111 monoclonal antimyosin antibody imaging can detect the presence/or absence of myocardial necrosis, thereby providing an index of myocardial viability. The present report describes the qualitative findings derived from antimyosin imaging in 6 patients with cardiomyopathies of diverse etiologies.

Antimyosin murine monoclonal antibody designated as R11D10 (Centocor, Malvern, PA. U.S.A.) is a sterile nonpyrogenic solution containing 0.5 mg of murine monoclonal Fab, modified by conjugation with diethylene triaminepentaaceticacid (DTPA) and provided in sterile vials by Centocor Inc. DTPA-antimyosin antibody Fab was labeled with In-111 chloride (Daiichi Radioisotopes Laboratories Ltd., Tokyo, Japan). Prior to intravenous injection of Fab-DTPA labeled In-111, Fab-DTPA was administered intradermally and the injection site observed for a wheal and flare response over 30 min. If no wheal and flare occurred, the patient was then injected intravenously with 0.5 mg of Fab-DTPA labeled with 74 MBq of In-111. Planar images were acquired at 48 hours after administration of In-111 antimyosin in the anterior, left anterior oblique, steep left anterior oblique, and lateral views. A 39-cm field of-view scintillation camera (ZLC7500, Shimadzu Corp. Ltd., Kyoto, Japan) equipped with a medium-energy collimator was used. Each acquisition lasted for 10 minutes, collecting approximately 500 k counts by means of both photopeaks of In-111 (174 keV and 247 keV).

Visual analysis was performed to assess the presence/or absence of antimyosin uptake in the myocardium by consensus among three observers uninformed of the

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Table 1 Clinical features and results of antimyosin imaging in 6 patients with cardiomyopathy

Case No.	Age	Sex	Diagnosis	Antimyosin uptake	H/L ratio	Location	IVS (mm)	LVPW (mm)	LVDd (mm)	LVDs (mm)	EF (%)	Myocardial biopsy
1	60	M	HNCM	3	1.05	LV	22	12	38	22	80	+
2	15	M	HNCN	0	0.81	—	15	9	45	32	64	+
3	54	M	DCM	Pool	—	—	11	12	68	62	24	+
4	59	M	DCM	3	1.18	LV + RV	10	9	42	37	32	+
5	46	M	Sec CM	Pool	—	—	12	12	60	48	48	–
6	34	F	Sec CM	Pool	—	—(*)	12	12	50	41	40	–

HNCM = hypertrophic non-obstructive cardiomyopathy, Sec CM = secondary cardiomyopathy, DCM = dilated cardiomyopathy, Pool = cardiac pooling image, IVS = thickness of interventricular septum, LVPW = thickness of left ventricular posterior wall, LVDd = left ventricular diastolic dimension, LVDs = left ventricular systolic dimension, (*) = increased antimyosin uptake in the breast, H/L ratio = heart/lung ratio.

clinical information. A five point scale was applied: 0, normal; +1, possible uptake; +2, definite, but not intense uptake (less than the sternal uptake); +3, definite, clear and intense uptake (at least equal to the sternal uptake); +4, very intense uptake (greater than or equal to hepatic uptake). With respect to the heart/lung ratio, the anterior image after 48 hr was used to adjust a region of interest in the myocardium and in a region of interest in the lung. Average counts per pixel in the myocardium were divided by average counts per pixel in the lung to get the heart/lung ratio.

CASE REPORT

Six patients with cardiomyopathies were selected for the present study. Two patients had hypertrophic non-obstructive cardiomyopathy, two had idiopathic dilated cardiomyopathy, and two were diagnosed as having specific heart muscle diseases: polymyositis involving the myocardium and the other with peripartum heart disease, respectively (Table 1). In 5 of the 6 patients, diagnosis was confirmed by normal coronary arteries on a coronal angiogram. The myocardial biopsy was performed on 4 of these patients (Table 1). Contrast ventriculography showed decreased LVEF less than 50% in 4 of them. Antimyosin scan showed diffuse myocardial uptake in two cases and residual blood pool activity in 3 cases (Table 1). In one case there was an increase in antimyosin uptake in the breast (Case 6).

Case 1

An asymptomatic man was found to have an abnormality in his electrocardiogram during a screening examination 25 years ago. Based on further evaluation he was diagnosed as having hypertrophic cardiomyopathy. In June, 1989 he was admitted to Kurume University Hospital for more exact evaluation with respect to the abnormal ECG. The ECG showed a sinus rhythm, with a heart rate of 72 BPM, the electric axis being right, PQ interval 0.16 sec, QTc time 0.39 sec, QRS time 0.08 sec, and the QS pattern

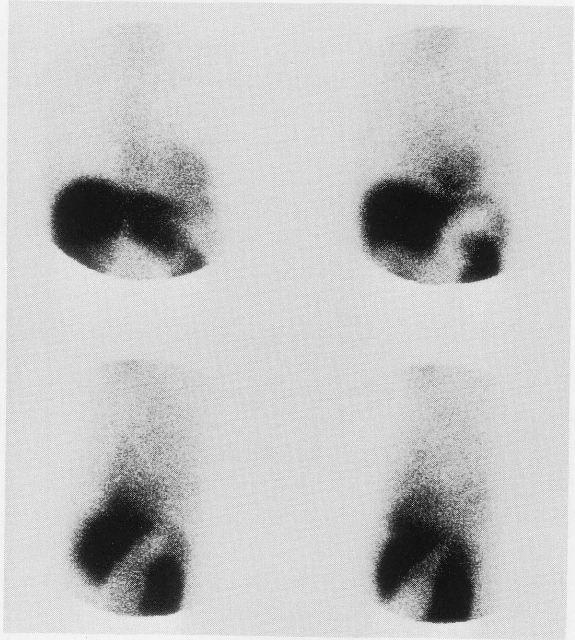
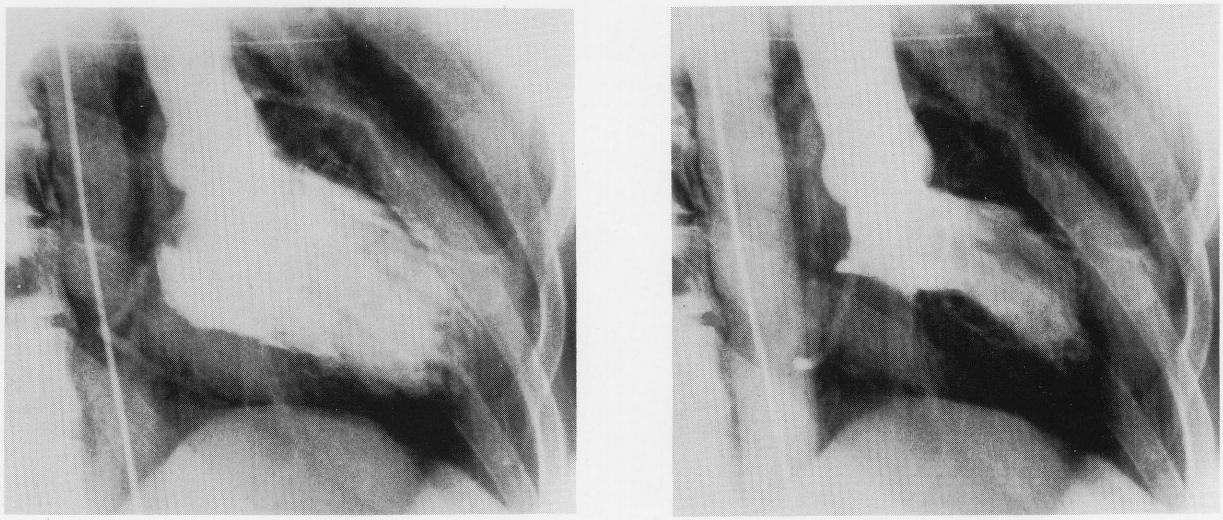


Fig. 1 In-111 antimyosin scan in patient with hypertrophic non-obstructive cardiomyopathy (No. 1) was positive in all lesion of myocardium (grade +3). In particular, the uptake increased in septum and apex. (Left upper: anterior projection, Right upper: left anterior oblique 45 degree projection, Left lower: left anterior oblique 70 degree projection, Right lower: lateral projection.)

in V_{5-6}. The data for the echocardiogram on admission are shown in Table 1. IVS/PWT was 1.83. Asymmetric septal hypertrophy was identified by the echocardiography. The patient demonstrated a positive antimyosin scan. Very intense uptake of this radiopharmaceutical was noted in the septum and LV apex (Fig. 1). Left ventriculography (LVG) (Fig. 2) revealed anterobasal and antero-lateral hypokinesis. The apical portion was severely hypokinetic in LVG. The myocardial biopsy resulted in hypertrophic cardiomyopathy.

Case 4

On 1982, he had cough and did not recover in 5 or 6



A B

Fig. 2 Left ventriculography (diastole: A, systole: B) was demonstrated.

months. In 1983, he had edema of the face and legs. He was treated with medication for congestive heart failure. In 1989, his heart failure worsened, and he developed abdominal edema. Working up to that time led to the development of idiopathic dilated cardiomyopathy. The electrocardiogram showed a sinus rhythm, minus 10 degree axis, P wave being 0.08 sec, high voltage of P wave seen in II, III, and V_1, PQ interval 0.20 sec, low QRS voltage , the decreased R wave in V_1–V_5, and QS pattern in V_6. The echocardiogram data are shown in Table 1. The patient had a positive antimyosin scan, with diffuse uptake of this agent as shown in Figure 3. The myocardial biopsy was interpreted as idiopathic dilated cardiomyopathy. LVG (Fig. 4) did not show marked dilatation of the left ventricle. The echocardiography demonstrated marked dilatation of the right ventricle and atrium with grade III tricuspid regurgitation despite no significant dilatation of the left ventricle. The present case was diagnosed as DCM predominantly involved in the right ventricle and atrium. In July, 1992 he died of congestive heart failure.

Both patients with specific heart muscle diseases (Case 5 and 6) demonstrated significant blood pool activity, thereby precluding evaluation of myocardial uptake, but one case had antimyosin uptake in the breast (Fig. 5).

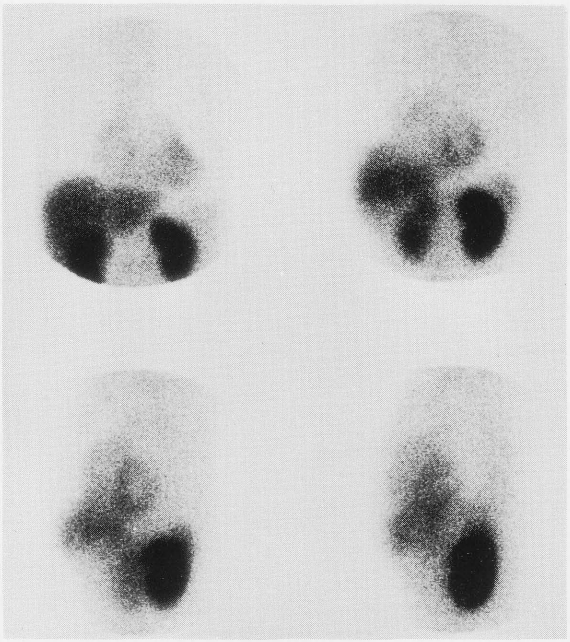


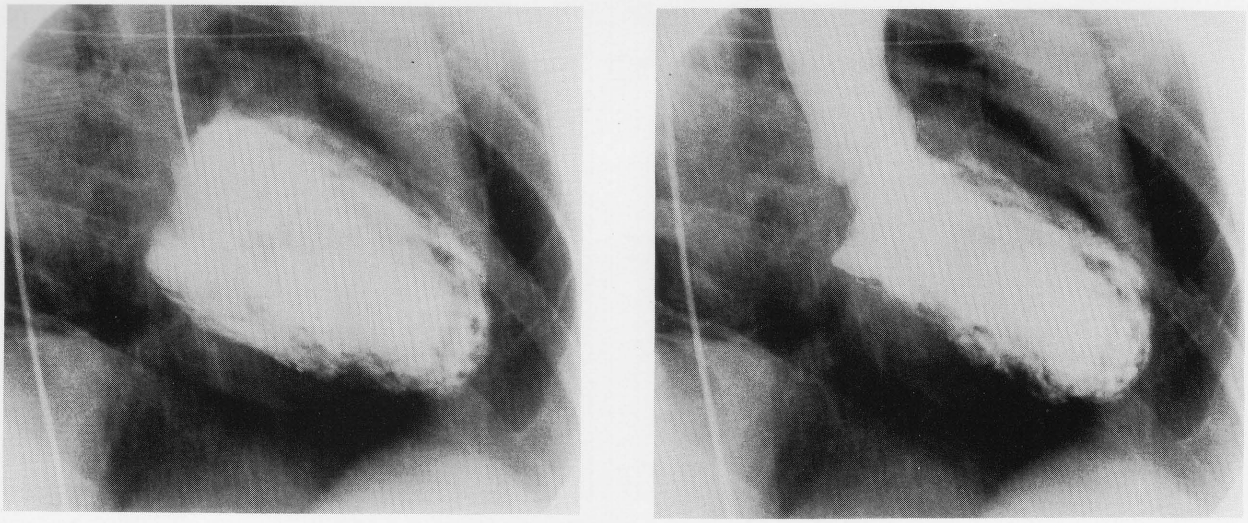
Fig. 3 In-111 antimyosin scan in patient with dilated cardiomyopathy (No. 4) was positive in all lesion of myocardium (grade +3). The faint uptake was detected in right ventricle. (Left upper: anterior projection, Right upper: left anterior oblique 45 degree projection, Left lower: left anterior oblique 70 degree projection, Right lower: lateral projection.)

DISCUSSION

The clinical/experimental application of antimyosin imaging in patients with acute myocardial infarction[2,12–15] and myocarditis[16–19] has been well described. In the present case report, patients with cardiomyopathy not associated with active, clinically apparent CAD/myocarditis underwent In-111 antimyosin imaging. Myocardial injury or necrosis in some patients with cardiomyopathy was detected by the antimyosin scan.

Hypertrophic cardiomyopathy

Hypertrophic cardiomyopathy may manifest a variety of clinical features, pathological findings, and natural history. Matsumori and colleagues[20] emphasized that antimyosin antibody might accumulate in viable myocyte with progressive degeneration as well as in necrosis. Our data demonstrated In-111 antimyosin uptake in one of two patients with asymmetric septal hypertrophy (ASH).



A B

Fig. 4 Left ventriculography (diastole: A, systole: B) was demonstrated.

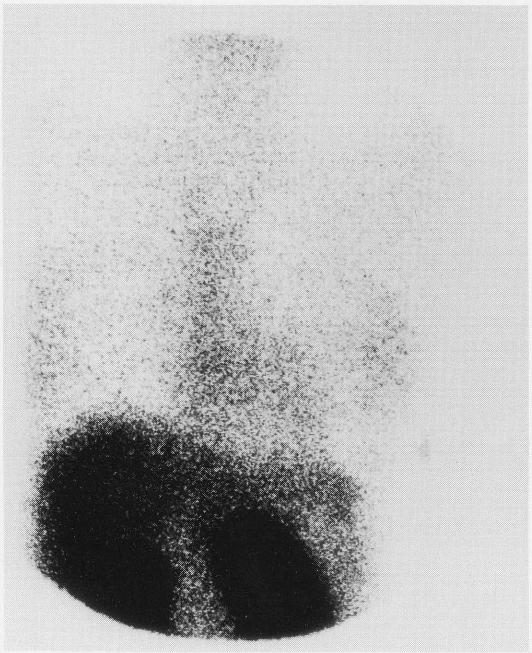


Fig. 5 In In-111 antimyosin scan in patient 6 with secondary cardiomyopathy, the increased and intense uptake was demonstrated in the breast.

Similar reports concerning possible necrosis/fibrosis have been described previously in subjects with ASH.[21] Nakata et al.[22] also reported that of two patients with hypertrophic cardiomyopathy one patient with an extremely hypertrophied septal wall had less antimyosin uptake than in the lateral wall in the other patient. Our data revealed intense antimyosin uptake in one patient with ASH but the other patient had no antimyosin uptake. It was interesting that the LVEF was 80% in one patient, who had antimyosin uptake in the myocardium. This may indicate that the left ventricular function may not simply depend on the evidence of myocardial necrosis detected by scintigraphy. The following is one possible explanation: myocardial necrosis may occur in a small amount of the myocardium and left ventricular function may therefore be preserved. In this sense, myocardial necrosis may be silent in these patients and a further follow-up study may be important.

Dilated cardiomyopathy

Obrador et al.[23] reported that abnormal antimyosin uptake was seen in 12 (70%) of 17 patients with idiopathic cardiomyopathy. Subsequently, Matsumori and colleagues[20] reported that in patients with dilated cardiomyopathy antimyosin uptake relates inversely to left ventricular function. One of the patient with DCM and a positive antimyosin scan had also a marked reduction in the left ventricular ejection fraction at rest (LVEF 32%). In this case, the antimyosin scan suggested the progressive myocardial injury. Antimyoisn positive scan may provide available information in the clinical management of patients with DCM.

Secondary cardiomyopathy

In the present report, the patients with secondary cardiomyopathy did not show signs of antimyosin uptake. Our data indicated that not all patients with secondary cardiomyopathy may show evidence of necrosis.

Limitation

Our report was performed as a phase II clinical trial in Japan. We could therefore not study a large group of patients with cardiomyopathies.

In conclusion, In-111 antimyosin images may be positive in some patients with cardiomyopathy, suggesting progressive myocardial injury or necrosis. This observa-

tion implies a need for further study of a large group of patients with cardiomyopathies to determine potential prognostic/therapeutic significance in such subjects.

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