Indium-111-Antimyosin Fab Imaging to Demonstrate Myocardial Involvement in Systemic Lupus Erythematosus

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Indium-111-antimyosin Fab imaging has been used to indicate myocardial injury. This report describes antimyosin accumulation in two patients with myocardial involvement in systemic lupus erythematosus. Both patients complained of chest pain, and significant stenoses of extramural coronary arteries were ruled out by angiography. The first patient, a 64-yr-old woman, had immunopathologic findings suggestive of systemic lupus. Indium-111-antimyosin Fab imaging showed myocardial tracer uptake. This prompted endomyocardial biopsy providing evidence of systemic lupus. The patient improved under immunosuppressive therapy. The second patient, a 47-yr-old man, had systemic lupus diagnosed by immunopathologic findings and skin biopsy. He had evidence of pericarditis on electrocardiography and echocardiography. Indium-111-antimyosin Fab imaging demonstrated additional myocardial involvement, which supported the initiation of immunosuppressive therapy. Our results suggest that ^{111}In-antimyosin Fab imaging may provide valuable diagnostic information and influence patient management in systemic lupus erythematosus with suspected myocardial involvement.

Key Words: indium-111-antimyosin; cardiomyopathy; myocarditis; systemic lupus erythematosus; Fab imaging

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Monoclonal antimyosin antibody fragments are a specific marker for myocytes that have lost their membrane integrity (*1*). Indium-111-labeled antimyosin Fab has been used to indicate myocardial injury in experimental (*2–4*) and clinical (*5,6*) myocardial infarction, experimental (*7*) and clinical (*8*) cardiac transplant rejection and in dilated cardiomyopathy (*9,10*). In an animal model for viral myocarditis [mice infected with coxsackie B3 virus (*11*)] and encephalomyocarditis virus (*12*), myocardial radioiodinated antimyosin Fab accumulation was more intense compared to noninfected mice in all phases of infection. Indium-111-antimyosin Fab accumulation was also observed in a study of patients with suspected myocarditis who had a positive endomyocardial biopsy (*8,13*). Moreover, immunoscintigraphy seemed to be more sensitive than biopsy (*8,13*).

These findings suggest that ^{111}In-antimyosin Fab imaging may be useful in additional conditions associated with myocardial damage. This report describes two cases of antimyosin uptake due to cardiac involvement in systemic lupus erythematosus.

CASE REPORTS

Patient 1

A 64-yr-old woman was diagnosed as having diabetes mellitus in 1972 and has been insulin-dependent since 1975. In 1986, mitral valve replacement was performed due to mitral stenosis. Since 1989, the patient had complained of recurrent chest pain. In May 1989, left cardiac catheterization showed normal extramural coronary arteries, normal left ventricular function and a competent mitral valve prosthesis. At that time, the patient had an elevated erythrocyte sedimentation rate of 85/115 mm which decreased spontaneously. In October 1989, the patient was examined at another hospital for recurrent chest pain. Her erythrocyte sedimentation rate was 75/115 mm, hemoglobin 11.1 g/dl; antinuclear antibodies were slightly positive, antibodies to double-stranded DNA were 10.3 mg/dl (normal < 5) and anti-Sm antibodies were 34.3 U/liter (normal < 25). Systemic lupus erythematosus was suspected and temporary immunosuppressive therapy performed.

In April 1990, the patient was readmitted at our institution for complaints of recurrent chest pain. Her erythrocyte sedimentation rate was 80/110 mm, hemoglobin 10.9 g/dl (reticulocytes 18%); the LE cell preparation was positive, antibodies to native DNA negative, antinuclear antibodies negative, anticardiolipin antibodies negative; complement C3c was 59 mg/dl (normal 55–120) and complement C4 17 mg/dl (normal 20–50). There was massive proteinuria of 11.6 g/24 hr. Her creatinine clearance was reduced to 47 ml/min. Her ECG showed nonspecific anterolateral ST-T changes.

Standard quantitative planar ^{201}Tl myocardial scintigraphy was performed and showed persistently reduced tracer accumulation in the anterior and anteroseptal wall as well as inferior redistribution (Fig. 1). In addition, planar images were recorded 48 hr after intravenous administration of 2 mCi (74 MBq) ^{111}In-antimyosin Fab. Anterior, 40° and 75° left anterior oblique (LAO) views were

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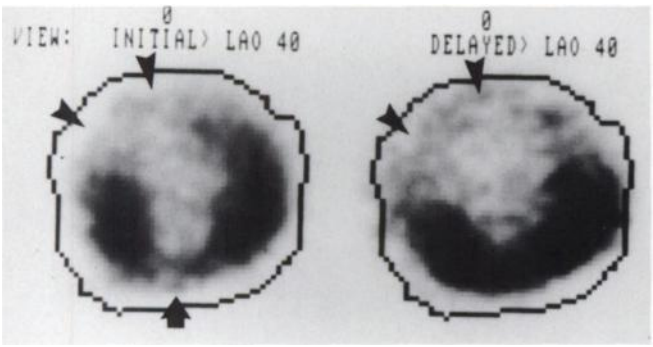

FIGURE 1. Thallium-201 myocardial scintigraphy in a 64-yr-old woman with chest pain and systemic lupus erythematosus (Patient 1). Planar 40° LAO views obtained after exercise (left) and at rest 3 hr later (right). There is persistently reduced tracer uptake in the anterior and anteroseptal left ventricular wall (arrow heads). In addition, there is decreased tracer accumulation in the inferior region on the initial scan (arrow) with redistribution on the delayed image.

obtained collecting 400,000 to 600,000 counts each into 128 × 128 matrices for 10 to 15 min per view using both photopeaks of ^{111}In (173 and 247 keV) and a medium-energy collimator. The antimyosin scans demonstrated diffuse tracer accumulation in projection to the heart (Fig. 2). The heart-to-lung ratio was 1.68 (normal < 1.50), the count density index (square of the count density over the myocardium divided by the count densities over the right lung plus sternal manubrium) was 1.70 (normal < 1.20). Therefore, left ventricular endomyocardial biopsy was performed and revealed myocardial small-vessel disease and focal myocellular necrosis consistent with myocardial involvement in systemic lupus erythematosus. Immunosuppressive therapy with cyclophosphamide relieved the patient's chest pain. Renal function, however, deteriorated progressively over the next 2 yr and hemodialysis treatment was necessary by October 1992.

Patient 2

A 47-yr-old man was diagnosed as having chronic discoid lupus erythematosus in May 1990. On November 8, 1993, the patient was admitted to our institution because of exacerbating skin lesions. At that time, the lupus band test revealed immune complex deposition with anti-IgG and anti-C3 fluorescence in skin biopsies from macroscopically unaffected parts of the forearm. Active systemic lupus was diagnosed and thalidomide therapy initiated. Early in the morning of November 20th, the patient was transferred to the cardiology department with chest pain of increased duration since the previous evening. There was no pericardial friction rub on physical examination. The ECG showed ST-segment elevations in lead I, II, aVL and V2 to V6. Echocardiographic findings were normal. Coronary angiography shortly after admission demonstrated normal extramural coronary arteries and perimyocarditis was diagnosed. Laboratory findings during the following days were as follows: erythrocyte sedimentation rate 70/110 mm, CRP 144 mg/liter; hemoglobin 12.2 g/dl (reticulocytes 10‰), leukocyte count 2,700/μl (bands 18%, lymphocytes 10%), thrombocyte count 133,000/μl; the LE cell preparation was positive, antinuclear antibodies positive (1:80), antibodies to native DNA 40.9 U/liter (normal < 7.0), antibodies to double-stranded DNA 56.9 U/ml (normal < 8.0), anti-Sm antibodies 27.3 U (normal < 25), anti-U1-n-RNP (70 kDa) 10.3 U (normal < 25); complement C3c 56 mg/dl (normal 55–120), complement C4 12 mg/dl (normal 20–50); urine protein 60 mg/l, normal creatinine clearance of 134 ml/min. Serial creatine kinase and troponine T values were not elevated. On November 22nd, the echocardigram showed slight pericardial effusion.

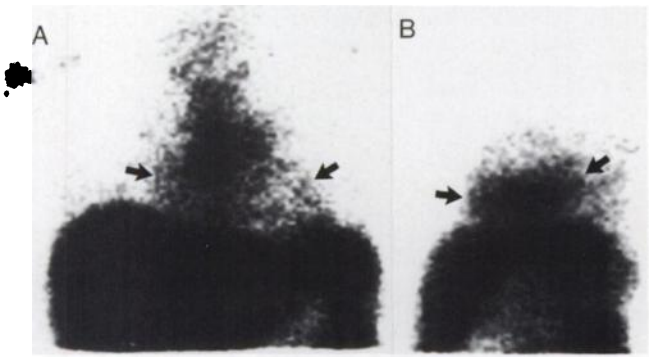

FIGURE 2. Indium-111-antimyosin Fab myocardial scintigraphy in Patient 1. (A) Planar anterior and (B) 75° LAO views obtained 48 hr postinjection demonstrate diffuse tracer accumulation in the projection to the heart with inferior predominance (arrows).

The patient was injected intravenously with 2 mCi (74 MBq) ^{111}In-antimyosin Fab. Planar scintigraphy in standard views was performed 48 hr postinjection and revealed diffuse myocardial tracer accumulation with apical and diaphragmal prominence (Fig. 3). The heart-to-lung ratio was 1.58 (normal < 1.50) and the count density index was 1.90 (normal < 1.20). Immunosuppressive therapy with methylprednisolone and cyclophosphamide was initiated. The patient's chest pain, pericardial effusion and ECG changes resolved within the next few days.

DISCUSSION

Myocardial Involvement in Systemic Lupus Erythematosus

Systemic lupus erythematosus is a recurrent autoimmune process which can affect multiple organs, including the cardiovascular system. Cardiovascular morbidity and mortality in this disease is increasing; cardiovascular involvement is now the third leading cause of death (*14,15*).

In autopsy series, nonbacterial Libman-Sacks endocarditis has been found in 13%–74% and pericarditis in 43%–83% of patients with systemic lupus erythematosus (*16*). The incidence of lupus myocarditis at necropsy varied between 8% and 78%, whereas clinical evidence for myocardial involvement has been found in 8%–10% (*16*). Hemodynamic measurements (*17*) and computer-assisted digital echocardiography (*18*), however, demonstrated diastolic and systolic left ventricular dysfunction in patients with systemic lupus without clinical signs of cardiac dysfunction.

The etiology of lupus myocarditis is unknown. Bidani et al. demonstrated myocardial immune complex aggregates in nine of ten autopsy patients with systemic lupus erythematosus and hypothesized that immune complex deposition may lead to complement activation, inflammation and myocardial damage (*19*). These immunopathologic mechanisms may also be responsible for coronary vasculitis in systemic lupus (*20*), which result in small foci of myocardial necrosis adjacent to narrowed intramural coronary arteries (*21*). Vasculitis may even result in myocar-

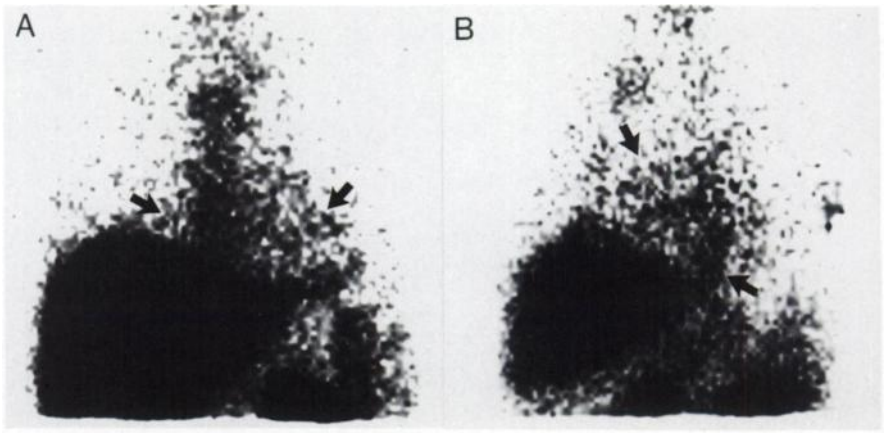

FIGURE 3. Indium-111-antimyosin Fab myocardial scintigraphy in a 47-yr-old man with systemic lupus erythematosus presenting after sudden onset of chest pain (Patient 2). Planar anterior (A) and 75° LAO (B) views acquired 48 hr postinjection show diffuse tracer uptake in the projection to the heart with posterolateral accentuation (arrows).

dial infarction when the larger extramural coronary arteries are involved (*20,22*).

Indium-111-Antimyosin Fab and Lupus Myocarditis

Both patients in this study had indications of systemic lupus erythematosus according to the revised American Rheumatoid Association criteria (*23*) with symptomatic myocardial involvement. Significant stenoses of extramural coronary arteries due to atherosclerosis or vasculitis were ruled out by coronary angiography in each patient.

Patient 1 had renal, hematologic and immunologic disorders as well as antinuclear antibodies indicating systemic lupus erythematosus (*23*). In this patient, however, proteinuria might also have been attributed to diabetic nephropathy and hemolytic anemia to mitral valve prosthesis. Indium-111-antimyosin Fab imaging demonstrated tracer accumulation in the projection to the heart and prompted endomyocardial biopsy. Histology was consistent with myocardial involvement in systemic lupus and provided further evidence of the diagnosis.

In Patient 2, the diagnosis of systemic lupus erythematosus was based on a discoid rash, serositis, hematologic and immunologic disorders as well as antinuclear antibodies (*23*). In addition, this patient had a positive lupus band test on skin biopsy. Lupus pericarditis was diagnosed because of characteristic electrocardiographic changes and mild pericardial effusion on echocardiography. Indium-111-antimyosin Fab imaging showed additional myocardial involvement and supported the decision for immunosuppressive therapy with methylprednisolone and cyclophosphamide in this patient.

Endomyocardial biopsy is the only recognized tool for in vivo diagnosis of lupus myocarditis. This procedure is invasive and subject to sampling errors. Antiphospholipid antibodies such as anticardiolipin were significantly associated with cardiac involvement in systemic lupus erythematosus (*24,25*). Their diagnostic accuracy in specifically revealing myocardial involvement has not been evaluated. Measurements of creatine kinase enzyme levels may be too insensitive. Troponin T release in lupus myocarditis has not been investigated. Electrocardiographic changes in lupus myocarditis are nonspecific. Routine echocardiography proved to be of low sensitivity to reveal wall motion abnormalities in systemic lupus (*18*). With MRI, the spin-lattice relaxation time T1 was significantly prolonged in patients with active systemic lupus erythematosus (*26*), although these findings have not been validated.

Patient 1 had an abnormal ^{201}Tl exercise study. In another study, three of six patients with clinically documented viral myocarditis also had abnormal ^{201}Tl scans with focal areas of reduced tracer accumulation at rest (*27*). It may be anticipated that the scintigraphic patterns in lupus myocarditis may resemble those of atherosclerotic coronary artery disease and, as such, be nonspecific.

CONCLUSION

Indium-111-antimyosin Fab is a specific marker for myocellular injury which has been evaluated in various conditions associated with localized or disseminated myocardial injury. This report demonstrates that ^{111}In-antimyosin Fab imaging can identify myocardial involvement in lupus myocarditis. This technique may provide valuable diagnostic information and influence patient management in active systemic lupus erythematosus. The sensitivity and specificity of ^{111}In-antimyosin Fab for myocardial involvement in systemic lupus have to be determined before its broad clinical use can be recommended.

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