Myocardial Distribution of Indium-111-Antimyosin Fab in Acute Inferior and Right Ventricular Infarction: Comparison with Technetium-99m-Pyrophosphate Imaging and Histologic Examination

Tomoaki Nakata, Tohru Sakakibara, Tetsuya Noto, Tetsuro Shoji, Takatoshi Tsuda, Masahiro Kubota, Atsuo Hattori, and Osamu Iimura

Second Department of Internal Medicine, Division of Emergency and Critical Care, Department of Radiology, and Department of Pathology, Sapporo Medical College, Sapporo, Japan

In a postmortem study of a 69-yr-old female patient who had suffered 2 yr previously a non-Q-wave anterior infarction and who had sustained just seven days earlier a left inferior and right ventricular infarction, the distribution of ^{111}In-antimyosin Fab was compared to the results of ^{99m}Tc-pyrophosphate imaging and histologic examination. Indium-111-antimyosin Fab imaging could not be performed because of cardiogenic shock. However, postmortem gamma scintillation counting revealed increased activities of antimyosin Fab in the infero-apical and right ventricular infarcted regions in which ^{99m}Tc-pyrophosphate positive imagings were observed; in contrast, a histologically confirmed old subendocardial anterior infarction had no definite activity. Thus, the myocardial distribution of ^{111}In-antimyosin Fab corresponded well to the results of ^{99m}Tc scintigrams and histologic examinations in a human heart, suggesting that this technique could be useful in vivo for detecting several-day-old myocardial infarction of the right ventricle as well as the left ventricle. Tissue from the 2-yr-old infarction was not identified by this technique.

J Nucl Med 1991; 32:865–867

It has been demonstrated that immunoscintigraphy using antimyosin monoclonal antibody Fab labeled with ^{111}In is highly sensitive and specific for detecting acutely infarcted myocardium (*1–5*), and the accuracy of this imaging technique during the first 2–4 days after acute myocardial infarction has been established by several clinical studies (*2,3,6*). However, histologic analysis using human cardiac specimens is limited (*7*), and it has not been established how old an infarct can be and still be detected by this imaging technique (*8*). In addition, it has not been demonstrated that antimyosin Fab scintigraphy can detect right ventricular infarction reliably. We describe the pattern of distribution of ^{111}In-antimyosin Fab and compare myocardial radioactivity with the results of histologic examination using postmortem specimens from a patient with acute left ventricular inferior and right ventricular infarction who had sustained a non-Q-wave anterior infarction 2 yr previously.

Received Aug. 3, 1990; revision accepted Oct. 11, 1990.
For reprints contact: Tomoaki Nakata, MD, Second Department of Internal Medicine, S-1, W-16, Chuo-ku, Sapporo 060, Japan.

CASE REPORT

A 69-yr-old woman was admitted with prolonged severe chest pain. At the age of 67, the diagnosis of non-Q-wave anterior infarction and postinfarction angina was established. Electrocardiograms showed ST-segment elevation in leads III, a VF, and the right precordial leads V1 and V3R to V6R, and reciprocally depressed ST-segments in leads I, a VL, and V2 to V6. Two-dimensional echocardiography revealed severe hypokinesis of the left ventricular inferior wall and dilatation and hypokinesis of the right ventricle. Serum creatinine kinase increased progressively up to 3463 IU/l. Three days after admission, ^{99m}Tc-pyrophosphate (740 MBq) planar and tomographic scans were performed using a large field of view gamma camera (Searle LFOV, with a low-energy, all-purpose, parallel-hole collimator) and a rotated gamma camera (Siemens ZLC 75, with a high-resolution parallel-hole collimator), respectively. Increased activity was observed in the left ventricular inferior wall, inferior septum, and the right ventricle (Fig. 1). From these findings, the clinical diagnosis of acute left ventricular inferior and right ventricular infarction was established.

When the patient was stable, she was given 0.5 mg of murine monoclonal antimyosin Fab (R11D10, Centocor Inc., Malvern, PA) labeled with ^{111}In (74 MBq) intravenously after a negative skin test on the seventh day following infarction. Twenty-four hours later, reinfarction occurred in the same inferior wall of the left ventricle and antimyosin imaging could not be performed because of her critical condition. Eight days after the administration of ^{111}In-antimyosin Fab she died of pulmonary edema and pump failure; an autopsy was performed 8 hr after death.

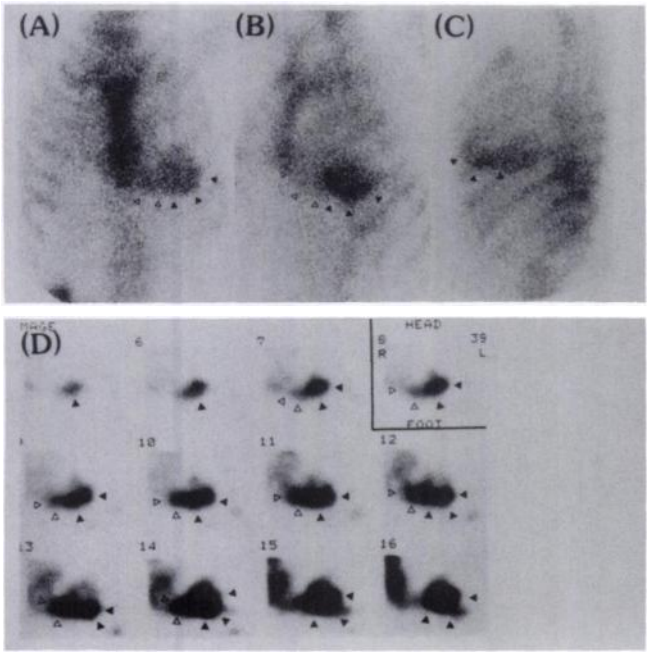

FIGURE 1. Technetium-99m-pyrophosphate scintigrams from anterior (A), left anterior oblique (B), and left lateral (C) views, and coronal tomograms (D) demonstrate increased activity in the inferoapical region of the left ventricle (▲), inferior septum, and right ventricle (△).

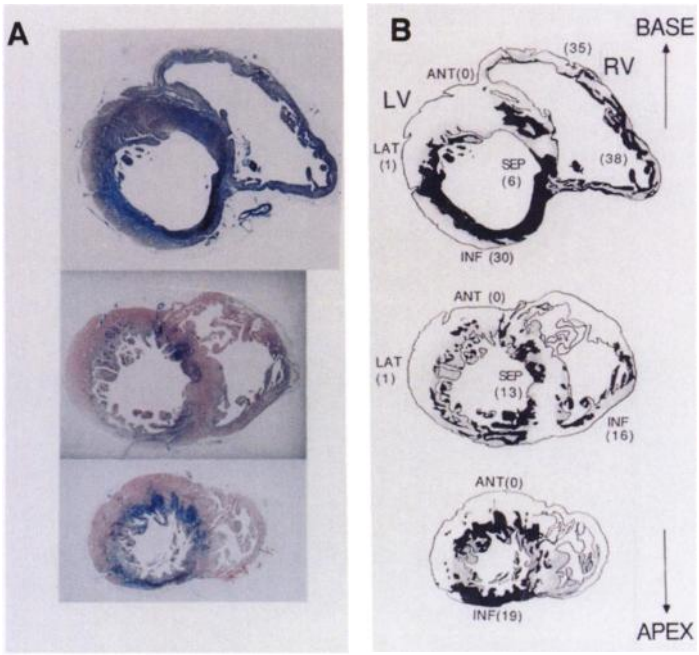

FIGURE 2. AZAN-stained heart slices (A) from base (upper) to apex (lower) and their corresponding illustrations (B) demonstrate right ventricular infarction, subendocardial infarction in the anteroseptal walls, and transmural inferior infarction of the left ventricle. Myocardial activities (cpm) of ^{111}In-antimyosin Fab shown in parentheses are greater in the left ventricular inferior wall, apex, and right ventricle, compared with those in the older anterior subendocardial infarction.

Pathologic Examination

On gross examination, the heart showed marked thinning of the left ventricular inferior wall and right ventricular dilatation in addition to old subendocardial scarring in the anteroseptal wall of the left ventricle. The basal, midventricular, and apical short-axis slices stained by AZAN showed infarcted myocardium and myocardial scar tissue which were delineated as pale or blue regions in Figure 2 (left panel). In addition to subendocardial anterior infarction and transmural inferior infarction of the left ventricle, right ventricular infarction was observed in the upper two slices. Illustrations of the stained heart slices (Fig. 2, right panel) demonstrated myocardial scar tissue and highly necrotic myocardium as black regions and other forms of myocardial damage such as wavy myocardial fibers, interstitial edema, and contraction bands as gray. Thus, both macroscopic and microscopic findings supported the clinical diagnosis of acute left ventricular inferior and right ventricular infarction, and the presence of an older anterior subendocardial infarction also was confirmed.

Biodistribution

Thirty days later, 21 samples were obtained from heart, lung, spleen, liver, and kidney tissue, which had been fixed in 10% buffered formalin. The radioactivities of ^{111}In-antimyosin Fab were counted for 40 min in a gamma scintillation counter and calculated as cpm/g after correction for background count rate. The myocardial specimens were taken from region adjacent to the sections presented in Figure 2. The myocardial activities are plotted in the illustrations of the histologic preparations in Figure 2 (right panel) and the biodistribution is shown in Figure 3. Greater activities were observed in the apex, inferior, and posterior walls of the left ventricle and the right ventricular walls as seen in the liver, spleen, and kidney. The ratios (relative to the activity of the lung) of ^{111}In-antimyosin Fab were 4.3 in the right ventricle, 3.4 in the left ventricular inferior wall, and 4.1 in the apex, while the ratios were less than 1.0 in the anterior and lateral walls of the left ventricle.

DISCUSSION

There was a good correlation between the histologically determined myocardial damage and ^{111}In-antimyosin Fab localization, suggesting that ^{111}In-antimyosin Fab might be useful for detecting damage a week after myocardial infarction. However, since neither antemortem nor postmortem scans by ^{111}In-antimyosin Fab could be undertaken, it is unclear whether or not a high-quality in-vivo image can be obtained, especially in the case of right ventricular infarction. Although monoclonal antimyosin Fab is highly specific, the amount of infarcted myocardium in the right ventricle might not be sufficient to be detected in vivo (*1*). Further clinical experience is necessary to determine whether or not this tracer is as useful in right ventricular infarction as ^{99m}Tc-pyrophosphate.

Increased activity of ^{99m}Tc-pyrophosphate (Fig. 1) and ^{111}In-antimyosin Fab (Figs. 2–3) was demonstrated in recently infarcted regions of the left and right ventricles (as confirmed by AZAN staining), while there was no increase in activity in the scarred region presumably infarcted 2 yr earlier. These results suggest that the myocardial uptake of ^{111}In-antimyosin Fab depends upon infarct age or, pre-

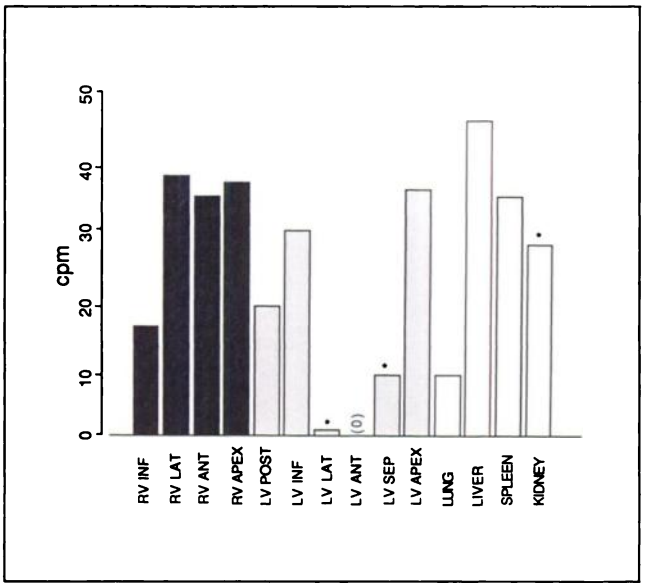

FIGURE 3. Biodistribution of ^{111}In eight days after administration of ^{111}In-antimyosin Fab. Closed columns = activities in the right ventricle; dotted columns = activities in the left ventricle; and open columns = activities in the other organs. *Values are presented as the mean of two or three tissue samples. ANT = anterior, INF = inferior, LAT = lateral, LV = left ventricular, POST = posterior, RV = right ventricular, and SEP = septal.

sumably, upon the antigenicity of the remaining cardiac myosin. During the reparative process of infarcted myocardium, cardiac myosin gradually disappears and is replaced by scar tissue over several weeks (*9,10*), suggesting that this tracer would be less sensitive during the later stages of acute myocardial infarction. However, there is little information on the effect of infarct age on the sensitivity of this agent. Jain et al. (*7*) reported a positive antimyosin image of a 6-day-old infarction and a recent study by Tamaki et al. (*8*) showed that antimyosin Fab scintigraphy detected infarction at various stages from 3 days to 9 mo after myocardial infarction in humans. The present study confirms previous reports (*7,8*) demonstrating that ^{111}In-antimyosin Fab can be used to identify 7-day-old infarcted myocardium with a high degree of specificity. However, it is not clear how well acutely necrotic tissue can be differentiated from that infarcted much earlier. Further clinical studies are necessary to define the interval during which the technique is useful, to establish a method for identifying the age of infarct, and to confirm its utility in detecting right ventricular infarction.

In conclusion, the present report demonstrates that ^{111}In-antimyosin Fab localization can identify myocardial necrosis of the left and also the right ventricle with a high degree of specificity and that this tracer may support the diagnosis of infarctions several days, but not years, old.

ACKNOWLEDGMENTS

The authors gratefully acknowledge the kind comments and advice of Nawal W. Derias, PhD, MRC Path., Department of Histopathology, St. Thomas' Hospital, London and the editorial assistance of Naomi M. Anderson, PhD, Calgary, Canada. We are also grateful to Daiichi Radioisotope Laboratories Ltd. for providing ^{111}In-antimyosin Fab.

REFERENCES

1. Khaw BA, Yasuda T, Gold HK, et al. Acute myocardial infarction imaging with indium-111-labeled monoclonal antimyosin Fab. *J Nucl Med* 1987;28:1671–1678.
2. Khaw BA, Gold HK, Yasuda T, et al. Scintigraphic quantification of myocardial necrosis in patients after intravenous injection of myosin-specific antibody. *Circulation* 1986;74:501–508.
3. Johnson LL, Seldin DW, Becker LC, et al. Antimyosin imaging in acute transmural myocardial infarctions: results of a multicenter clinical trial. *J Am Coll Cardiol* 1989;13:27–35.
4. Khaw BA, Fallon JT, Beller GA, Haber E. Specificity of localization of myosin-specific antibody fragments in experimental myocardial infarction. Histologic, histochemical, autoradiographic, and scintigraphic studies. *Circulation* 1979;60:1527–1531.
5. Khaw BA, Scott J, Fallon, JT, et al. Myocardial injury: quantitation of cell sorting initiated with antimyosin fluorescent spheres. *Science* 1982;217:1050–1052.
6. Khaw BA, Strauss HW, Moore R, et al. Myocardial damage delineated by indium-111-antimyosin Fab and technetium-99m-pyrophosphate. *J Nucl Med* 1987;28:76–82.
7. Jain D, Crawley JC, Lahiri A, Raftery EB. Indium-111-antimyosin images compared with triphenyl tetrazolium chloride staining in a patient six days after myocardial infarction. *J Nucl Med* 1990;31:231–233.
8. Tamaki N, Yamada T, Matsumori A, et al. Indium-111-antimyosin antibody imaging for detecting different stages of myocardial infarction: comparison with technetium-99m-pyrophosphate imaging. *J Nucl Med* 1990;31:136–142.
9. Mallory GK, White PD, Salcedo-Salgar J. The speed of healing of myocardial infarction: a study of the pathologic anatomy in 72 cases. *Am Heart J* 1939;18:647–671.
10. Fishbein MC, MacLean D, Maroko PR. The histopathologic evolution of myocardial infarction. *Chest* 1978;843–849.

EDITORIAL

Of Antimyosin Imaging and Histopathology of Myocardial Infarction: When, Where, and Why?

Antimyosin antibodies bind specifically to myosin exposed in myocardial cells that have lost their sarcolemmal integrity, thereby providing a noninvasive approach for the diagnosis of myocyte necrosis associated with acute myocardial infarction (MI) (*1–7*), acute myocarditis (*8,9*), and heart transplant rejection (*9,10*). This principle was demonstrated with cultured neonatal murine myocytes subjected to ischemic condition. Antimyosin antibody covalently linked to polystyrene spheres selectively adhered to necrotic cells that had intracellular contents herniating through

Received Jan. 9, 1991; accepted Jan. 9, 1991.

For reprints contact: B. A. Khaw, Division of Nuclear Medicine, Massachusetts General Hospital-East, Bldg. 149, 13th St., Rm. 5410, Charlestown, MA 02129.