Clinical application of Indium-111 antimonyosin antibody and Thallium-201 dual nuclide single photon emission computed tomography in acute myocardial infarction

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The significance of indium-111 antimonyosin antibody and thallium-201 dual nuclide single photon emission computed tomography (SPECT) was evaluated in 7 patients with acute myocardial infarction (AMI) who underwent emergency coronary angiography with successful revascularization by intracoronary thrombolysis. Indium-111 antimonyosin antibody and thallium-201 dual nuclide SPECT was performed 11 to 36 days after the onset of AMI. Antimonyosin SPECT images delineated areas of myocardial necrosis in all 7 patients (100%), but planar images detected necrotic areas in only 4 of 7 patients (57%). Peak CPK-MBs of the 3 patients in which no necrotic area was detected by indium-111 planar image showed a tendency to be smaller. Indium-111 antimonyosin antibody/thallium-201 overlap was observed in all patients. The area of overlap was at the center of necrosis in 4 patients (2 anterior infarction, 1 inferior infarction, 1 inferolateral infarction) and at the peripheral portion in 3 patients (all 3 had inferior infarction). Indium-111 antimonyosin antibody and thallium-201 dual nuclide SPECT is useful in identifying the localization of myocardial infarction and the overlap of these tracers might reflect the presence of salvaged myocardium adjacent to the necrotic myocardium.

Key words: 111Indium-AMA, 201Thallium, overlap, acute myocardial infarction

INTRODUCTION

ANTIMYOSEN antibody is a Fab fragment of monoclonal antibody that binds with myosin exposed in irreversibly damaged myocytes. Labeled with indium, the antibody is taken up into acutely necrotic tissue and can be imaged by planar or single photon emission computed tomography (SPECT) techniques.1 Using antimonyosin with thallium-201, we can identify the localization and quantification of necrotic myocytes exactly.2

Dual nuclide SPECT techniques with technetium-99m stannous pyrophosphate and thallium-201 have been developed to detect and to quantify myocardial infarction.3 But several animal experiments have shown that the uptake of pyrophosphate into infarcted tissue is not inversely related to regional blood flow and that maximal uptake occurs at the infarct periphery where some viable tissue remains.4,5

This clinical study evaluated the significance of indium-111 antimonyosin antibody and thallium-201 dual nuclide SPECT in 7 consecutive patients with acute myocardial infarction who underwent emergency coronary angiography with successful revascularization.

MATERIAL AND METHODS

Study patients
We consecutively studied 7 patients (5 men and 2 women, with a mean age of 67, ranging from 62 to
77 years old) admitted to our hospital because of precordial chest oppressive sensation due to cardiac ischemia of at least 30 minutes duration, with electrocardiographic ST elevation of at least 2 mm in 2 or more adjacent leads. None of the patients had a previous history of myocardial infarction. All 7 patients were transferred to the catheter laboratory immediately after arrival and emergency coronary angiography was performed. All the infarction-related arteries had been totally or subtotally occluded. Urokinase was infused into the infarct-related arteries at a rate of 24,000 U/min, until a dose of 960,000 U had been given to each patient. All patients showed rapid anterior opacification of the coronary artery involved. In all cases, the interval from the onset of myocardial infarction to revascularization was within 6 hours. Four of the 7 infarction-related arteries were the proximal right coronary artery, 2 were the proximal left anterior descending artery, and 1 was the proximal circumflex artery. After successful intracoronary thrombolysis, all patients were transferred to the coronary care unit. Swan-Ganz catheters were inserted and hemodynamic and electrocardiographic monitoring were performed. Hemodynamics were stable and no fatal arrhythmias occurred in any of the patients.

Blood was drawn every 2 hours for 24 hours from the onset of infarction, and every 4 hours for the next 24 hours to estimate peak CPK and peak CPK-MB. Standard 12-lead electrocardiography was recorded every 4 hours. Four to 5 weeks later, second-looking coronary arteriography and left ventriculography were performed to evaluate the left ventricular function and the coronary artery lesions. (Table 1)

Radionuclide studies
Two to 5 weeks after the onset of myocardial infarction (range 11–36 days), scintigraphy with thallium-201 and indium-111 monoclonal antimonyosin antibody was simultaneously performed at the nuclear medicine laboratory. In order to detect hypersensitivity to the radiolabeled antibody, 0.1 ml of indium-111 labeled antimonyosin antibody solution was administered intradermally. If no wheal and no flare were observed in the next 15 minutes, 74 MBq indium-111 antimonyosin antibody was injected intravenously. Forty-eight hours after the injection, imaging was performed with a rotating single-head digital gamma camera equipped with a medium-energy, high-resolution, parallel-hole collimator (SHIMADZU SNC-500R). This gamma camera was interfaced to a dedicated computer (SHIMADZU Scintipac 700). At first, planar images were obtained for 10 minutes in anterior, 45-degree left anterior oblique, and 75-degree left anterior oblique views. Two 10% windows were used centered over the 173 keV and 240 keV photopeaks characteristic of indium-111. Then 74 MBq thallium-201 was injected. After a 5-minute equilibration period, 32 projections were obtained over 180 degrees, from 45-degree right anterior oblique to 45-left posterior oblique. Each projection image was acquired at a preset time of 60 sec. Tomographic data were acquired in a 64 x 64 matrix with a 1.3 x hardware zoom factor. There is an energy overlap between the high peak (163 keV) of thallium-201 and the low peak (173 keV) of indium-111 at a simultaneous dual energy SPECT, so energy discrimination was set at 80 keV with a 10% window for thallium-201, and at 240 keV with a 10% window for indium-111. Each projection data was given 200,000 to 240,000 counts of thallium-201 and 30,000 to 50,000 counts of indium-111. On average, 9% of these respective counts per pixel were within the myocardial region with indium and thallium activity. Finally a planar image of thallium-201 was acquired for 5 minutes in the same projections as with indium-111, using 80 keV photopeak with a 10% window. The image display of SPECT was a vertical long axis, a horizontal long axis, and a short axis. SPECT and planar images were visually interpreted by two nuclear medicine specialists who were not given any clinical information. Accuracy in revealing the presence, site, and extent of acute myocardial infarction was compared in planar and SPECT images of indium-111 antimonyosin antibody. Quantification of infarction area was evaluated by peak CPK-MBs. The infarced area was identified by serially obtained electrocardiograms, the territory of the infarction-related artery, and thallium-201 SPECT images. Overlap between indium-111 antimonyosin antibody and thallium-201 was investigated on dual nuclide SPECT images.

Immune response to antimyosin antibody
Blood was drawn to measure human antimonouse antibody titers 3 and 8 weeks after the injection of indium-111 antimonyosin antibody.

RESULTS

SPECT vs planar images of indium-111 antimonyosin antibody
Indium-111 antimonyosin antibody accurately accumulated in the infarcted area in all 7 patients on SPECT images corresponding with the electrocardiograms and the territory of the infarction-related artery. In the planar image, only faint accumulation was noted in 3 of 7 patients (Fig. 1). The infarcted area was inferior in 2 of these 3 patients (case No. 3 and 4), and was inferolateral in 1 patient (case No. 7). Peak CPK-MBs of these 3 patients showed a tendency to be lower than the others (Table 1 & 2).
Fig. 1 Planar thallium-201 (upper panel) and indium-111 antmyosin (bottom panel) scans acquired in anterior, 45 degree left anterior oblique and 75 degree left anterior oblique view of inferior myocardial infarction (Case No. 4). The uptake of thallium was normal and indium uptake was obscured by liver attenuation.

### Table 1 Patient’s characteristics

<table>
<thead>
<tr>
<th>Pt</th>
<th>Age (yrs)</th>
<th>Sex</th>
<th>Infarct related artery</th>
<th>Residual diameter stenosis (AHA %)</th>
<th>Peak CPK-MB (IU/L)</th>
<th>Collateral circulation</th>
<th>Interval from onset to reperfusion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Acute</td>
<td>Chronic</td>
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<tr>
<td>1</td>
<td>65</td>
<td>M</td>
<td>RCA</td>
<td>99</td>
<td>99</td>
<td>767</td>
<td>0</td>
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<tr>
<td>2</td>
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<td>F</td>
<td>RCA</td>
<td>75</td>
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<tr>
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<td>70</td>
<td>F</td>
<td>LAD</td>
<td>99</td>
<td>99</td>
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<td>2</td>
</tr>
<tr>
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<td>LAD</td>
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<td>90</td>
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<tr>
<td>7</td>
<td>66</td>
<td>M</td>
<td>LCX</td>
<td>90</td>
<td>90</td>
<td>371</td>
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</tr>
</tbody>
</table>

Abbreviations: RCA = right coronary artery; LAD = left anterior descending coronary artery; LCX = left circumflex coronary artery; AHA = american heart association; Peak CPK-MB = peak creatininekinese-MB; H = hour; collateral scoring: 0 = absent; 1 = poor; 2 = relevant.

### Table 2 Comparison of infarction detected by planar antmyosin, SPECT antmyosin and the site of overlap between SPECT antmyosin and SPECT thallium

<table>
<thead>
<tr>
<th>Pt</th>
<th>ECG location</th>
<th>Planar AMA</th>
<th>SPECT AMA</th>
<th>Overlap site between TI and AMA</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Inf</td>
<td>Intense</td>
<td>Intense</td>
<td>Peripheral</td>
</tr>
<tr>
<td>2</td>
<td>Inf</td>
<td>Intense</td>
<td>Intense</td>
<td>Peripheral</td>
</tr>
<tr>
<td>3</td>
<td>Inf</td>
<td>Faint</td>
<td>Intense</td>
<td>Central</td>
</tr>
<tr>
<td>4</td>
<td>Inf</td>
<td>Faint</td>
<td>Intense</td>
<td>Peripheral</td>
</tr>
<tr>
<td>5</td>
<td>Ant</td>
<td>Intense</td>
<td>Intense</td>
<td>Central</td>
</tr>
<tr>
<td>6</td>
<td>Ant</td>
<td>Intense</td>
<td>Intense</td>
<td>Central</td>
</tr>
<tr>
<td>7</td>
<td>Inf-lat</td>
<td>Faint</td>
<td>Intense</td>
<td>Central</td>
</tr>
</tbody>
</table>

Abbreviations: AMA = indium-111 antmyosin antibody; SPECT = single photon emission computed tomography; TI = thallium-201; Inf = inferior; Ant = anterior; Inf-lat = inferolateral.

**Overlap between indium-111 antmyosin antibody and thallium-201 on dual nuclide SPECT images**

In all 7 patients, indium-111 and thallium-201 overlap was noted in SPECT imaging. Four patients had an overlap at the central portion of necrosis (2 anterior infarction, 1 inferior infarction, and 1 inferolateral infarction), and 3 patients had an overlap at the peripheral portion (all 3 had inferior infarction). (Fig. 2, Fig. 3, and Table 2). There were no differences in peak CPK-MBs, the interval to recanalization, and the left ventricular function at chronic phase between these two subgroups with different overlap areas.

**Further ischemic events**

Among our patients, two patients went on to show evidence of ischemia. One patient had total occlusion
at the identical site 2 months after the first myocardial infarction (case No. 2). The other had recurrent chest pain and underwent percutaneous transluminal coronary angioplasty (case No. 7). The other 5 patients were free from chest pain with intensive medical treatment.

Immune response to antimonyosin antibody
No allergic reaction to antibody injection occurred, nor was there documented a significant increase in human antimouse antibody titers postinjection.

DISCUSSION
Murine monoclonal antimonyosin antibody has been experimentally demonstrated to bind selectively to irreversibly damaged myocytes. Khaw and his coworkers proved that the uptake of antimonyosin antibody has an inverse exponential relation with regional coronary blood flow.\textsuperscript{4,6} This relation is present experimentally not only in infarcted hearts with a persistently occluded infarction-related artery, but also in successfully reperfused hearts.\textsuperscript{5} Clinically,
the sensitivity of antimony antibody uptake for detecting acute myocardial infarction is 76–92%. All of the patients reported here were confirmed to have infarctions by SPECT images. But in planar images of antimony antibody, the infarction area was demonstrated in only 4 of 7 patients. In the 3 patients with negative planar images, the infarct size tended to be smaller and the site of infarction was inferior or inferolateral. Reasons for the failure to detect inferoposterior infarction may include residual blood pool activity, overlying tissue attenuation, and high uptake in the liver. Partial volume effect and respiratory and/or cardiac motion might obscure a small-size infarction. All of these problems were reduced by the SPECT technique in our study. Simultaneous use of thallium-201 (dual energy SPECT) has made reconstruction of SPECT images easier, especially in small myocardial infarctions. Indium-111 and thallium-201 are well suited for simultaneous dual isotope imaging because the high photopeak of indium-111 is widely separated from the 80 keV photopeak of thallium-201 and the downscatter from indium activity to the thallium window is very small.

In all 7 patients there was an overlap uptake between indium-111 antimony antibody and thallium-201. Technetium-99m pyrophosphate accumulates both at reversible injured myocytes (jeopardized myocardium) and necrotic myocardium. So the area of accumulation of technetium-99m pyrophosphate tends to be larger than the necrotic area. Technetium-99m pyrophosphate/thallium-201 overlap is an index of early successful reperfusion and might reflect the presence of salvaged myocardium adjacent to the necrotic myocardium. On the other hand, Khaw and his coworkers reported that no work had shown antimony uptake by reversible injured cells, and that the accumulation of indium-111 antimony antibody should reflect the necrotic myocardium more exactly than that of technetium-99m pyrophosphate. The area where thallium-201 accumulated was thought to preserve viability. Johnson et al reported the significance of dual isotope SPECT imaging in identifying acute infarct patients at further ischemic risk. They classified three patterns of tracer uptake. Matches were defined as scans with only thallium-201 defects and corresponding indium-111 uptake; mismatches were defined as scans with thallium-201 defects without corresponding antimony uptake, in addition to matching regions corresponding to electrocardiographic infarct location; overlap was defined as scans with thallium-201 and indium-111 uptake in the same segments. Mismatched segments represented old myocardial scar or myocardium with reduced blood flow due to decreased supply (ischemia). Overlap segments could represent nontransmural necrosis occurring in the distribution of the infarct vessel. They concluded that patients with mismatched scans or overlap scans went on to have further ischemic events. In their study, 14 of 42 patients had mismatched scans and only 5 of 42 patients had overlap scans. Our study was very small, but all patients had overlap scans, which was very different from Johnson's study. There are two possible mechanisms to explain in the difference. Experimental and clinicopathological studies have shown that myocardial necrosis begins in the subendocardium and extends toward the epicardium. The salvage of the myocardium is dependent on the early restoration of coronary blood flow and sufficient collateral flow. Therefore, early reperfusion has salvaged epicardial tissue and thallium-201 might accumulate in that layer and indium-111 antimony antibody might accumulate in the necrotic subendocardial layers. Another mechanism that might explain the overlap is as follows. Autopsy studies have shown digestion of normal and necrotic tissue in the infarction area, especially in the border zone. Such histopathologic findings would be expected to be more common in patients that have undergone successful reperfusion. Therefore indium-111 and thallium-201 overlap was found in the infarcted areas in our patients who had all undergone successful intracoronary thrombolysis. Early restoration of the blood supply might have salvaged the myocardium, and overlap was noted in the infarcted area. In conclusion, indium-111 monoclonal antimony antibody and thallium-201 dual nuclide SPECT was useful for the evaluation of acute myocardial infarction, and indium-111 antimony antibody/thallium-201 overlap might reflect the presence of salvaged myocardium adjacent to the necrotic myocardium, especially in patients that have undergone successful revascularization.

ACKNOWLEDGEMENT

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REFERENCES

3. Hashimoto T, Kambara H, Fodo T, et al: Significance of technetium-99m/thallium-201 overlap on simultaneous dual emission computed tomography