Myocardial Uptake of Indium-111-Labeled Antimyosin in Acute Subendocardial Infarction: Clinical, Histochemical, and Autoradiographic Correlation of Myocardial Necrosis

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Indium-111-labeled antimyosin has been utilized in the diagnosis and localization of acute transmural myocardial infarction. The present report describes a patient who presented with a massive subendocardial infarction. Two days after the injection of antimyosin, the patient's clinical status markedly deteriorated and he expired. Postmortem examination demonstrated severe three-vessel coronary artery disease with extensive myocyte death in the endocardium. Autoradiography and histochemical staining of the prosected heart demonstrated high correlation for myocardial necrosis and corresponded to clinical evidence for diffuse subendocardial infarction.

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Imaging with indium-111-labeled monoclonal antimyosin antibody (^{111}In-antimyosin) has been used to detect, localize, and quantitate myocardial necrosis in experimental and clinical myocardial infarction (*1–3*). This detection and localization of irreversibly damaged myocardium with the monoclonal antibody (Fab fragments) correlates well with histologic and histochemical evidence for transmural myocardial necrosis (*4–6*). However, the specificity of this method for subendocardial infarction is unknown.

The present report describes a patient who presented with an acute subendocardial infarction and was part of a local cohort of a multicenter investigation using indium-labeled antimyosin for the diagnosis of acute chest pain. After the study, clinical deterioration ensued and the patient died 2 days later. Autoradiography was performed in the prosected heart and correlated with histologic and gamma well counting techniques.

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CASE REPORT

The patient was a 74-yr-old man with a history of hypertension and chronic stable angina pectoris since 1979 who presented, on January 31, 1988, with a 3.5-hr history of heavy chest pain with radiation to both shoulders, associated with diaphoresis and dyspnea. He experienced no relief with four sublingual nitroglycerin. He had previously undergone exercise testing, which was reportedly positive, and during the preceding month prior to admisssion experienced chest pain at rest. His past medical history was remarkable for hypertension and recurrent pyelonephritis requiring a left nephrectomy. Medications on admission included propranolol, isosorbide dinitrate, diltiazem, hydrochlorothiazide, and naprosyn.

Physical examination revealed a blood pressure 120/90 mmHg and a heart rate of 72 bpm. A right carotid bruit was present as was a left nephrectomy scar. The chest X-ray suggested a right middle lobe infiltrate and the initial electrocardiogram demonstrated widespread ST segment depression consistent with diffuse subendocardial injury or ischemia (Fig. 1).

Treatment was initiated with i.v. nitroglycerin and lidocaine. He subsequently ruled in for an acute myocardial infarction with creatinine kinase peaking at 986 IU (17% MB fraction). Forty-eight hours following the onset of chest pain and after obtaining informed consent, the patient was injected with 2.05 mCi of ^{111}In labeled to 0.5 mg Fab fragment of antimurine monoclonal myosin antibody (Myosint; Centocor, Malvern, PA). The patient's clinical deterioration necessitated that imaging on the following day (2/2/89) would be performed with a portable small field of view gamma camera (equipped with a low-energy, high-resolution collimator, Fig. 2A). This methodology was recognized to be less than optimal for imaging ^{111}In, but can yield diagnostic studies (*7*).

On February 2, 1989, the patient had recurrent ischemia and developed new electrocardiographic changes. Dyspnea and hypotension ensued requiring endotracheal intubation

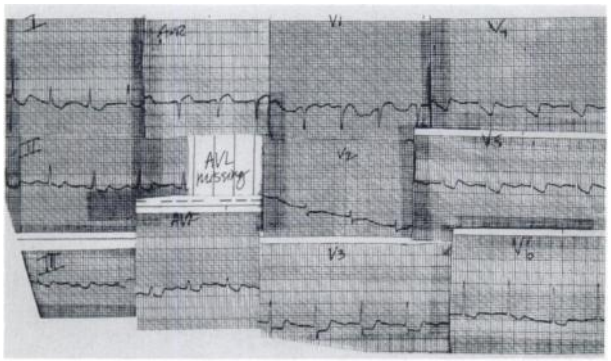

FIGURE 1
Electrocardiogram obtained shortly after the initial presentation demonstrating diffuse ST segment depression, consistent with subendocardial ischemia or injury.

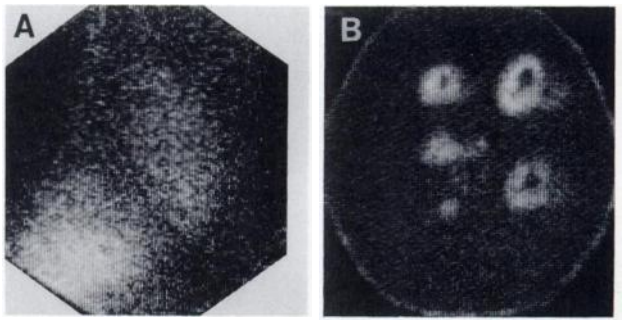

FIGURE 2
(A) In vivo left anterior oblique 24 hr postinjection of antimyosin demonstrating global myocardial activity. While this may represent blood-pool activity, the absence of the right ventricle and great vessels suggests left ventricular uptake and localization. (B) Serial sections along the long-axis of the subject's heart placed on a gamma scintillation camera.

and the use of vasopressors. Cardiac enzymes (creatine kinase and creatine kinase-MB) once again increased (infarct expansion) and hemodynamic monitoring revealed findings consistent with biventricular failure. On the following day, his cardiac index was noted to be markedly reduced (1.3 l/min) and he developed a new left bundle branch block and first-degree AV block. A radionuclide ventriculogram revealed marked global depression of left ventricular function with an ejection fraction of 0.20. Later than day, he sustained an asystolic cardiac arrest and all efforts of resuscitation were futile.

Postmortem examination revealed an acute circumferential, subendocardial myocardial infarction with 100% occlusion of the left circumflex coronary artery by a fresh thrombus. Additionally, the left anterior descending coronary artery was totally occluded and there was a significant stenosis of the right coronary artery. Signs of congestive heart failure and pulmonary edema were also present. Histologic examination revealed extensive myocyte death in the endocardium in a circumferential manner.

The heart was then sliced into multiple sections each 1–2 cm in width perpendicular to the long-axis. Images were obtained by positioning the various slices on a gamma camera equipped with a medium-energy collimator (Fig. 2B). These images revealed ^{111}In-labeled antimyosin uptake concentrically in all portions of the heart slices (comparable to Fig. 2A). Autoradiography was also performed by placing the slices directly onto a Lanex cassette for eight days loaded with Kodak (TMAT) double-emission film (Fig. 3A). These images revealed activity within the entire slice, specifically concentrated in the endocardial sections.

Biopsy specimens were also obtained from various locations within each slice (100–300 mg each) and were analyzed in a scintillation counter. After subtraction of the background counts, all values were reported in cpm/gram. Approximately 2–4 biopsies were obtained from the endocardial layer and a corresponding section of the epicardium from each slice. The right ventricle was also sampled. Table 1 depicts the ratios of endocardium-to-epicardium and the endocardium-to-right ventricle proceeding from base to apex. The endocardial activity was substantially greater than that of the epicardium and almost three times that of the right ventricle, indicating extensive localized uptake of the ^{111}In-labeled antimyosin in this region. However, some antimyosin uptake was present in the entire slice. Individual corresponding regions of endocardium and epicardium were compared by count ratios and demonstrated an average two-fold increase in activity in the endocardium compared with the epicardium (range of 1.23 to 3.15; mean = 2.17).

DISCUSSION

The present report illustrates the high correlation between the clinical and pathologic evidence of extensive subendocardial necrosis and ^{111}In-labeled antimyosin uptake. The initial electrocardiogram is consistent with global subendocardial ischemia or injury, and the subsequent clinical events correspond with a massive circumferential myocardial infarction. Although the initial in vivo myocardial scans are suboptimal, they do suggest global uptake of antimyosin, which was confirmed by the necropsy specimen. A prior report also supports the finding that this pattern of extensive or diffuse myocardial update of ^{111}In-anti-

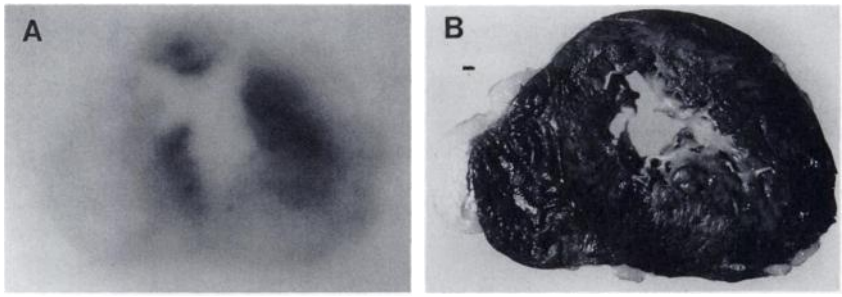

FIGURE 3
Autoradiography (A) and the corresponding gross specimen (B) of slices of the subject's myocardium. Panel A was prepared as described in the text. Panel B was stained with triphenyltetrazolium chloride (TTC), with the pale area representing infarction.

TABLE 1
Ratios of Endocardial, Epicardial, and Right Ventricular Biopsy Data (cpm/g)

Slice	Endo/Epi	Endo/RV
4	2.55	3.81
3	2.45	3.47
2	2.18	3.79
1	1.64	3.03

Endo = endocardium; Epi = epicardium; RV = right ventricle. Slice 4 to slice 1 (basal to apical).

myosin is associated with a poor prognosis (*8*). The autoradiographs correspond well to the histochemical evidence of myocardial necrosis and the individual biopsy samples demonstrate that the endocardial concentration of ^{111}In-labeled antimyosin is more than two-fold that of the epicardium consistent with diffuse subendocardial infarction.

The physiologic mechanism of antimyosin imaging is well established. When myocyte membrane integrity is lost, and necrosis ensues as with myocardial infarction, the Fab fragment of antimurine monoclonal antimyosin antibody may diffuse across the membrane and gain access to the proteins that are normally only cytosolic (*4*). The antibody then binds to cardiac myosin and the linkage with a radioactive substance permits the scintigraphic visualization of necrotic myocardium.

Earlier reports revealed a high degree of agreement regarding the presence, extent, and location of experimental myocardial infarction between histologic evidence of necrosis and ^{111}In-antimyosin uptake (*4*). Two postmortem case reports have confirmed a similar close relationship in humans (*5,6*). In these articles, histologic and histochemical evidence for a focal transmural infarct with myocardial rupture correlated well with autoradiography. Previous clinical studies have also demonstrated high sensitivity and specificity for diagnosis of acute myocardial infarction with antimyosin (*1,2*). The high sensitivity of this technique has been demonstrated even in the setting of non-Q-wave myocardial infarction (sensitivity = 84%) (*3*). This is particularly relevant to the present case, as the infarction was clearly subendocardial with a significant transmural gradient.

Monoclonal antibody imaging with ^{111}In-labeled antimyosin has been shown to detect, localize, and quantitate the amount of myocardial necrosis associated with infarction. The specificity of this technique is confirmed and the correlation of autoradiography to the histochemical detection of myocyte necrosis, as well as the biopsy confirmation of the endocardial location of the infarction in this case. It is therefore apparent that transmural necrosis may not be necessary for adequate uptake of the antimyosin. Furthermore, a scintigraphic pattern of generalized left ventricular antimyosin uptake may indicate extensive subendocardial damage.

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