Indium-111-Antimyosin Uptake in Acute and Remote Myocardial Infarction: Comparison with Pathohistologic Findings

Nataša V. Budihna, Metka Mičinski, Dunja Latifić-Jasnič, and Anton Cerar

Departments of Nuclear Medicine and Cardiology, University Medical Centre, and Department of Pathology, Medical Faculty, Ljubljana, Slovenia

Indium-111-Fab antimyosin antibody accumulation was studied in an 81-yr-old patient who was treated twice for unstable angina on ECG, signs of apicoseptal infarction, anterolateral and inferior ischemia without clinical evidence of an acute coronary event. During the last hospitalization, 9 and 3 mo after the previous ones, additional ischemia in the inferoposterior wall was demonstrated. Antimyosin was administered to detect acute infarction but pump failure developed and the patient died. Autopsy confirmed all stages of infarction on the anterior and lateral walls, predominant fibrosis in the apicoseptal region and predominant acute necrosis in the inferior wall. Macroscopic and scintigraphic examinations of transverse slices gave concordant results. A mixture of infarctions and normal tissue was confirmed by histologic findings. Antimyosin antibody accumulation was seen in areas of acute necrosis or bordering areas of reduced uptake in myocardium with remote damage, probably caused by prolonged episodes of unstable angina without evident acute coronary event.

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Inconclusive electrocardiographic changes without diagnostic enzymatic evidence of infarction need additional investigation to confirm possible myocardial necrosis. Moreover, immunoscintigraphy may be useful for obtaining valuable data (*1*). The accumulation of infarct-avid ^{111}In-labeled monoclonal antimyosin antibodies in acute myocardial infarction is proportional to myocardial damage (*2*). The precise value of immunoscintigraphy in subacute and remote infarction is not well determined (*3,4*). We recently studied a patient with suspected acute infarction who died 24 hr after injection. The following case report can add to the understanding of antimyosin antibody uptake in remote and in coexistent acute myocardial infarction.

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For reprints contact: Dr. Nataša V. Budihna, Nuclear Medicine Department, University Medical Centre, Zaloška 7, 61000 Ljubljana, Slovenia.

CASE REPORT

Our patient, an 81-yr-old female with longstanding arterial hypertension and diabetes mellitus, treated with peroral therapy, was followed from June 1990 to March 1991. She was admitted the first time pulseless and cyanotic after chest oppression lasting two days for which cardiopulmonary reanimation was required. High anterolateral ischemia together with electrocardiographic evidence of anteroseptal fibrosis, sinus arrest with nodal escapes and interventricular conduction aberration were present after resuscitation. No elevation of serum creatine kinase over the upper normal limit was revealed upon admission. The patient was discharged on antihypertensive therapy after an uneventful recovery.

Six months later she was readmitted because of severe progressive retrosternal pain. Additional ischemic ST-elevation in the inferior wall leads of the left ventricle were detected on ECG along with the preexistent abnormalities consistent with ischemia and anteroseptal fibrosis anterolateral wall leads. Unstable angina, with some of the episodes lasting up to 30 min, persisted for 2 wk in spite of intravenous and peroral antianginal treatment. Dynamic ST-T changes on the anterior and inferior walls were present during her hospitalization on repeated ECGs, but were inconclusive for abrupt coronary occlusion. No elevation of serum creatine kinase over the upper normal limit was confirmed. The patient was discharged on antianginal treatment after stabilization, but progressive worsening of angina pectoris occurred at home and she was again hospitalized.

This hospitalization was precipitated by severe prolonged chest pain at rest, which persisted almost continuously in spite of intravenous antianginal therapy. Moderate additional ischemic changes in the inferolateral leads of the left ventricle were discovered along with previously existing abnormalities. Serum creatine kinase elevation in accordance with acute myocardial necrosis was detected for the first time with values up to 7.6 μcat/liter (normal range 0.17–2.08 μcat/liter). The Fab fraction of murine monoclonal antibody (Myoscint; Centocor Europe, Leiden, The Netherlands) in a 0.5-mg dose labeled with 90 MBq of ^{111}In was administered intravenously to determine if acute infarction had occurred. Right and left ventricular failure developed, cardiogenic shock lasted 3 hr and the patient died despite all therapeutic interventions more than 24 hr later. Imaging was not performed because of the deterioration of her clinical condition.

At autopsy, acute pericarditis was seen in the posterior wall of the right ventricle and in the inferoposterior wall of the left

ventricle. Ex vivo scintigraphy of the integral heart preparation was performed with a Siemens Basicam gamma camera equipped with a medium-energy collimator. Both photopeaks of ^{111}In (173 and 247 keV) were used with 20% windows. Extensive uptake of ^{111}In was present in the major part of the heart. It was not possible to separate the left and the right ventricles nor grade uptake intensity in separate ventricular walls. Transverse slices, approximately 1.5 cm thick, were made thereafter parallel to the atrioventricular junction. All coronary arteries were severely stenosed and a 90% stenosis of the anterior interventricular branch of the left coronary artery was found. Extensive atherosclerotic stenosis with occlusive thrombosis of the right coronary artery was demonstrated. Macroscopic examination of the transverse slices revealed areas of necrotic ventricular muscle merging with intact tissue in the anteroapical, septal, lateral and posterior walls of the left ventricle and in the anterior part of the right ventricle (Fig. 1). Predominant fibrotic tissue was present in anterior and apical walls adjacent to the interventricular septum. The slices were scanned on the gamma camera immediately afterwards. Low-grade uptake, representing viable myocardium, was shown only in minor portions of the subepicardial and subendocardial layers of the left ventricle. Intense radioactivity was seen in the majority of the left ventricular wall, with gradual nonuniform increase in intensity on the consecutive slices from the atrioventricular junction towards the apical region. Increased tracer uptake also was demonstrated in a portion of the right ventricular muscle (Fig. 2).

Histologic examination of tissue samples taken from the inferior and anteroapical portions of the left ventricle was performed. Viable muscular fibers in subendocardial and subepicardial parts were detected adjacent to the necrotic muscular tissue. Small and larger areas of necrosis with bands of vital myocardium were detected, especially at the marginal ends of the tissue sample (Fig. 3A). Intense neutrophilic infiltration dominated the periphery of necrotic myocardium. Young connective tissue rich with capillaries and fibroblasts and partly matured hyalinized older fibrotic islands were surrounded with necrotic tissue in some areas of the specimen (Fig. 3B). Furthermore, three samples were taken from the myocardium adjacent to the specimens for histologic examination and one from the fat tissue for *quantitative* evaluation of antimyosin uptake. The percentage of the applied radioactivity per gram of tissue was calculated. The following results were obtained: radioactivity in the epicardial fat tissue was 0.0056%, in macroscopically normal heart muscle 0.014%, in macroscopically fibrotic myocardial wall 0.032%, and in necrotic tissue 0.024%.

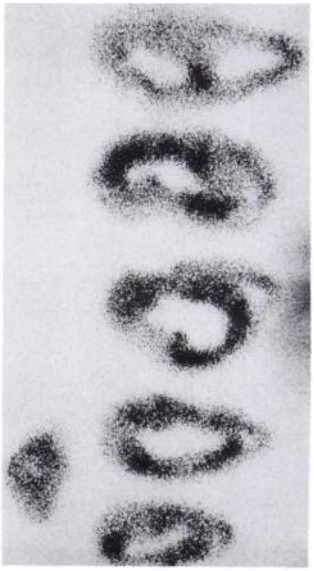

FIGURE 2. In this scintigram of myocardial slices, increased uptake of antimyosin ^{111}In-Fab is seen in the major part of the anterior wall (upper side of the slices), septum and lateral wall (left) of the left ventricle and in the anterior and lateral walls of the right ventricle.

DISCUSSION

Radioimmunoimaging with antimyosin antibodies is a highly specific method for myocardial necrosis confirmation (*2*), in which an inverse relationship between antibody accumulation and residual perfusion was demonstrated (*3*). Some authors believe that remote infarction does not accumulate ^{111}In-antimyosin antibodies (*4,5*). Tamaki et al. (*6*) also showed uptake in remote infarctions with intensity of tracer accumulation in an inverse relationship

FIGURE 1. Representative slice of the heart is shown. Patchy areas of necrotic tissue are interspersed with viable myocardium of anterior (top), septal (right), posterior (bottom) and lateral walls (left) of the left ventricle.

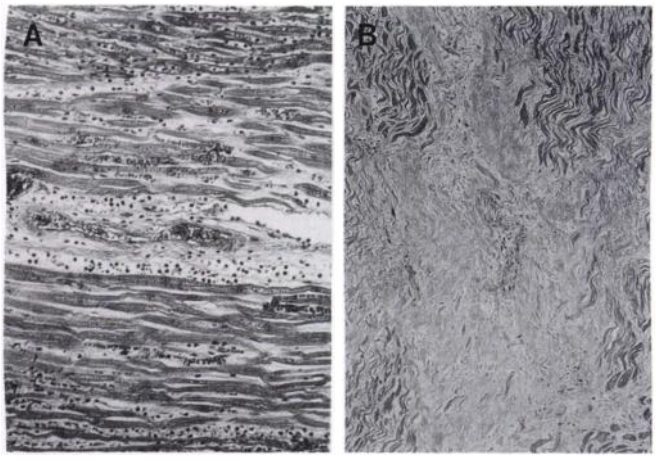

FIGURE 3. (A) Bands of vital myofibers surround edematous and inflammatory infiltrated interstitium (in the central region). Necrotic tissue is seen in the upper and lower margins of the specimen taken from the inferior wall of the left ventricle. Hematoxylin-eosin stain; original magnification 50x. (B) Scar tissue with necrotic vessel in the center; wavy necrotic myofibers at the periphery of the figure. Anterior wall of the left ventricle. Hematoxylin-eosin stain; original magnification 20.5x.

with time between the acute event and imaging. Prolonged breakdown of myosin after acute infarction or ongoing necrosis were proposed as possible causes, although the precise mechanisms remained unknown.

Only a few reports on the postmortem evaluation of ^{111}In-antimyosin distribution in the infarcted myocardium are available. Jain and coworkers (*7*) demonstrated close correlation between in vivo, postmortem scintigraphic images and infarct-specific staining in a patient with a 6-day-old infarction. Nakata and coworkers (*8*) presented a patient's postmortem analysis with proven uptake of antibody fragments in a recent but noncoexistent remote infarction.

Although no elevation of serum creatine kinase over the upper normal limits was detected in our patient during the first and the second hospitalizations, we believe that consecutive events of nontransmural necrosis occurred. Serial electrocardiographic changes suggest that the first major coronary event on the anterolateral and septal walls and the second one involving the anterolateral and inferior walls probably occured 9 and 3 mo, respectively, before the last hospitalization. The final event developed due to thrombotic occlusion of a severely stenotic right coronary artery and marked underperfusion with ischemic damage in the remaining coronary artery supply areas. Macroscopic examination of the heart confirmed ischemic damage of different ages in all myocardium. Scars, necrotic areas and vital myocardium were merging and presented as mixed infarction (*9*). Furthermore, predominant fibrosis with less vital and recently necrotic islands was found in the anteroapical region, and prevalently vital and recently necrotic areas with scarce islands of fibrosis were demonstrated in inferior parts of the left ventricle on histological examination. Since cardiogenic shock developed shortly before death, its influence on the myocardial injury is likely; we believe that all different stages of myocardial damage confirmed with autopsy and histological examination would be present, even following sudden cardiac death during the last hospitalization. Thus, the accumulation of antimyosin antibodies in infarction, clinically considered to be remote, can result from recent necrosis of preserved islands of viable myocardium inside the prevalent fibrotic tissue. This mechanism could also explain the lower intensity of antimyosin accumulation observed in some acute myocardial infarction patients from other studies (*2*). Uptake quantitation revealed higher uptake in macroscopically fibrotic tissue than in macroscopically necrotic tissue. This apparently paradoxical finding is in fact in accordance with histologic findings of merged vital, acutely damaged and mature fibrotic tissue, which made the definite visual macroscopic separation of acute and old infarction impossible. Unfortunately, histologic examination of the same samples was not performed. Because this patient's myocardial damage was so widespread, it is possible that the structure of those two samples was similarly mixed (the structure of adjacent histologically analyzed myocardium).

Immunoscintigraphy remains the most sensitive method for confirmation and quantitation of myocardial necrosis, especially for acute and well-delineated transmural lesions. However, slowly developing myocardial necrosis due to chronic underperfusion without evident acute coronary event can result in diffuse antimyosin antibody uptake. Although uneventful recovery is wished for all myocardial infarction patients, additional histologic evaluation of myocardial changes in patients with similar clinical courses would add useful information to the subset of patients with unstable angina and negative cardiac enzymes who do not have electrocardiographic changes indicative of acute myocardial infarction and would increase our understanding of the complex mechanisms involved in mixed-type myocardial infarction.

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