Clinicopathologic Study of Persistently Positive Technetium-99m Stannous Pyrophosphate Myocardial Scintigrams and Myocytolytic Degeneration After Myocardial Infarction

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SUMMARY In a select series of 46 patients studied by serial myocardial scintigraphy, 19 (41%) retained persistent, usually low grade (2+)

positive technetium-99m stannous pyrophosphate (99mTc-PYP) myocardial scintigrams for at least 3 months after acute myocardial infarction. The one major difference between patients with positive and negative postinfarct 99mTc-PYP myocardial scintigrams was a more symptomatic postinfarct course in the former group, characterized by severe angina pectoris in 16 of the 19 patients and by severe congestive heart failure with angina in three patients. In a separate clinicopathologic series of seven patients, persistently positive 99mTc-PYP myocardial activity was associated with prominent myocytolytic degeneration involving muscle cells which had survived initial episodes of infarction in 5 patients (three with ventricular aneurysms) and with extensive myocardial fibrosis in one patient with recurrent angina pectoris. One patient with a negative postinfarct 99mTc-PYP myocardial scintgram had transmural fibrosis without residual myocardium in a resected ventricular aneurysm. It is concluded that a persistently positive 99mTc-PYP myocardial scintigram frequently correlates with progressive myocardial damage and muscle loss and that this scintigraphic finding may be an important prognostic indicator of a complicated and symptomatic postinfarct clinical course.

IN OUR EXPERIENCE, MYOCARDIAL SCINTIGRAPHY with technetium-99m stannous pyrophosphate (99mTc-PYP) has proven to be an effective and sensitive method for detection of acute myocardial infarction in patients and experimental animals.1-13 The test also has been positive in approximately one third of patients with unstable angina pectoris.3, 13 Review of the literature reveals a generally similar experience.14 Myocardial scintigraphy with 99mTc-PYP also detects muscle necrosis due to etiologies other than coronary heart disease, including trauma, repeated cardioversion, and metastatic tumor.14-17 In addition, positive 99mTc-PYP scintigrams with uptake in heart and other soft tissues may occur in patients with metastatic calcification.16, 18, 19 Autoradiographic studies in experimental acute myocardial infarcts have shown that radiopharmaceutical concentration occurs predominantly in frankly necrotic myocardium as well as in a small population of damaged border zone muscle cells admixed with necrotic muscle cells.20 Experimental studies also have shown that approximately 3 g of necrotic myocardium is needed for the test to maintain a high degree of sensitivity;21 however, a similar determination has not been made in humans.

The usual sequence with 99mTc-PYP myocardial scintigraphy is for the scintigram to become positive at 12 to 18 hours after onset of acute myocardial infarction, to increase in intensity over the first 72 hours, and thereafter to decrease in intensity and frequency to become negative by the end of the first 1 to 2 weeks after development of myocardial infarction.1, 2, 6 Nevertheless, we have observed that some patients maintain persistently positive 99mTc-PYP myocardial scintigrams for weeks to months after an episode of acute myocardial infarction.14, 20 Other workers also have observed persistently positive myocardial scintigrams in patients with ventricular aneurysms and in those without evidence of aneurysm.21-24 The present study was performed to characterize the clinical and scintigraphic features of patients with persistently positive scintigrams. In addition, myocardial tissue obtained at surgery or necropsy from seven patients was studied to obtain information regarding pathologic correlates of persistently positive 99mTc-PYP myocardial scintigrams.

Patients Studied and Methods

Clinical Studies

The clinical series consisted of 46 patients studied at Parkland Memorial Hospital of Dallas, Texas, over a 20 month period (March, 1975 to October, 1976). Criteria for inclusion in the study were 1) acute myocardial infarction documented by clinical, electrocardiographic, serum enzymatic, and 99mTc-PYP scintigraphic criteria at the time of initial study and 2) serial examination with 99mTc-PYP myocardial scintigraphy during the first two weeks after diagnosis of acute myocardial infarction until initially positive 99mTc-PYP myocardial scintigrams reverted to negative in the hospital or, if positive at discharge, again at least 3 months after infarction. Although these criteria limited the size of the study group, they were selected with the goal of obtaining detailed information regarding the clinical and scintigraphic features of persistently positive 99mTc-PYP myocardial scintigrams.

For all studies, 99mTc-PYP was freshly prepared by complexing 99mTc with stannous pyrophosphate (Mallinkrodt Chemical Works) according to the manufacturers instructions. Frequent checks by standard chromatographic techniques were made to ensure proper labeling. The 99mTc-PYP was injected intravenously and at least one hour cir-
culation time was allowed prior to scintigraphy. Scintigrams were obtained in at least three projections (anterior, left lateral and left anterior oblique) using a Searle Pho-Gamma III scintillation camera with high resolution collimator. The scintigrams were read according to a previously described grading system ranging from 0 to 4+ with 2+ representing definite myocardial activity less than bone activity, 3+ as myocardial activity equal to bone activity, and 4+ as myocardial activity greater than bone activity. The positive scintigrams were further classified according to intensity (2-4+) and degree of localization. Special attention was given to differentiation of positive scintigrams from diffuse blood pool images, which were read as artificial or un-interpretable scintigrams (fig. 1).

Morphologic Studies

For clinicopathologic studies, a total of 40 patients were collected over a two year period (June, 1974 to October, 1976) who had undergone 99mTc-PYP myocardial scintigraphy prior to autopsy or surgical resection of myocardium. Detailed study of the timing of scintigraphy identified seven patients who had at least one myocardial scintigram performed past the first six weeks after onset of clinically suspected acute myocardial infarction. The other 33 patients were studied scintigraphically only at the time of initial hospital admission and are not included in this report. Only one of the seven patients in the pathology series was also included in the clinical series because of the more stringent criteria for serial myocardial imaging in the latter series.

Tissue blocks from seven patients were processed for standard histologic examination. Tissue obtained from three of the seven patients at surgery also was fixed in a modified Karnovsky's solution (2.5% glutaraldehyde and 2% paraformaldehyde in 0.1 M cacodylate buffer) and processed for detailed cytologic and electron microscopic examination.

Results

Clinical Studies

Clinical findings in the 46 patients are shown in table 1. A total of 19 (41%) of the 46 patients retained persistently positive 99mTc-PYP myocardial scintigrams after acute myocardial infarction; the mean duration of persistent positivity at the time of this analysis was 9 months. In 27 patients, the 99mTc-PYP myocardial scintigrams became negative. In the two groups, there were no significant differences in age, sex, history of previous myocardial infarct, location of acute infarct, or peak serum creatine kinase (CK) at the time of acute infarction.

Scintigraphic findings in the 19 patients with persistently positive 99mTc-PYP myocardial activity are summarized in table 2 and illustrated in figures 1 and 2. Scintigrams in the postinfarct period were graded as 4+ in one patient, 3+ in four patients and 2+ in 14 patients. In ten of the 19 patients, comparison of initial and follow-up scintigrams revealed a definite reduction in grade of positivity in the follow-up scintigrams obtained during the postinfarct period (fig. 2). Furthermore, a general tendency was noted toward decreased myocardial activity in the persistently positive

<table>
<thead>
<tr>
<th>Table 1. Patients with Acute Myocardial Infarcts Followed with Serial 99mTc-PYP Myocardial Scintigrams (N = 46)</th>
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<tbody>
<tr>
<td>I. Patients with persistently positive 99mTc-PYP myocardial scintigrams (N = 19)</td>
</tr>
<tr>
<td>1) Age: 61 ± 2.7 years</td>
</tr>
<tr>
<td>2) Sex: 11 male, 8 female</td>
</tr>
<tr>
<td>3) Types of infarcts: 6 subendocardial, 5 anterior and 8 inferior</td>
</tr>
<tr>
<td>4) Peak serum CK: 312 ± 72.3 units</td>
</tr>
<tr>
<td>5) Cath. results: 5 patients have severe 3 vessel coronary artery lesions</td>
</tr>
<tr>
<td>6) Previous known infarcts: 2 patients</td>
</tr>
<tr>
<td>7) Died suddenly: 2 patients</td>
</tr>
<tr>
<td>8) Subsequent course: 7 patients readmitted 3 or more times during next 15 months for severe chest pain</td>
</tr>
<tr>
<td>II. Patients developing negative 99mTc-PYP myocardial scintigrams (N = 27)</td>
</tr>
<tr>
<td>1) Age: 57 ± 2.7 years</td>
</tr>
<tr>
<td>2) Sex: 16 male, 11 female</td>
</tr>
<tr>
<td>3) Types of infarcts: 5 subendocardial, 6 anterior, 14 inferior, 1 lateral and 1 with left bundle branch block</td>
</tr>
<tr>
<td>4) Peak serum CK: 319 ± 61 units</td>
</tr>
<tr>
<td>5) Cath. results: 2 patients have significant 3 vessel and 1 has 2 vessel coronary artery lesions</td>
</tr>
<tr>
<td>6) Previous known infarcts: 0</td>
</tr>
<tr>
<td>7) Died suddenly: 1 patient</td>
</tr>
<tr>
<td>8) Subsequent course: No patient readmitted 3 or more times during next 15 months with severe chest pain</td>
</tr>
</tbody>
</table>
scintigrams even if the follow-up scintigrams were assigned the same grade as the initial scintigrams. Myocardial scintigrams in the 2-3+ grades tended to have less discrete activity than scintigrams in the 3-4+ categories. All positive scintigrams, however, exhibited more localized activity than blood pool images which are characterized by a large, globular appearance in all projections (fig. 1).

In the 19 patients with persistently positive \textsuperscript{99m}Tc-PYP myocardial scintigrams, no interim acute myocardial infarction was documented clinically to explain the persistently positive tests. Five of the 19 patients were studied by cardiac catheterization, and all five had severe three vessel coronary artery disease; none had evidence of a left ventricular aneurysm. In the group without persistently positive scintigrams, three were catheterized, and two had triple vessel disease and one exhibited significant narrowing of two coronary arteries. Sudden death occurred in two patients with persistently positive myocardial scintigrams and in one patient without a persistently positive test.

Three patients have undergone revascularization surgery in the group with persistently positive scintigrams; one has subsequently developed a negative myocardial scintigram, but the scintigrams remained positive shortly after operation in the other two patients.

The one major difference between the two groups related to the subsequent clinical course of the 19 patients with persistently positive scintigrams. The major clinical problem in 16 of the 19 patients was recurrent, severe and limiting angina pectoris, and three patients had severe congestive heart failure with recurrent angina. Two of the latter three patients had 3-4+ persistently positive scintigrams and the other patient had persistent 2+ activity. Seven of the 19 patients have been readmitted to the hospital three or more times over a period of 15 months and 12 patients have been readmitted two or more times over a four month follow-up period for evaluation of severe chest pain. In contrast, none of the 27 patients in the negative group has been readmitted for evaluation of chest pain three or more times during a 15 month follow-up period. The difference in frequency of hospital admissions for evaluation of chest pain is significant ($P < 0.01$; group t-test).

**Morphologic Studies**

Six of the seven patients in the separate morphology series had at least one positive \textsuperscript{99m}Tc-PYP myocardial scintigram indicative of persistently positive activity (table 3). Five of these six patients had clinically documented previous myocardial infarcts. All six patients had episodes of recurrent chest pain associated with the persistently positive scintigrams, and two of the patients were judged to have unstable angina pectoris at some point in their course.

In three patients (1-3) with persistently positive scintigrams and ventricular aneurysms, study was made of the resected aneurysm walls. The resected portions of the left ventricular walls exhibited marked thinning and replacement fibrosis; however, the specimens contained many foci of muscle cells which had survived the initial infarction (fig. 3). Many of these muscle cells showed degenerative changes of variable severity which may be classified under the general designation of myocytolysis. Some muscle cells appeared markedly swollen (hydropic change) and showed marked separation of stained cytoplasmic components. Other muscle cells showed a decrease or complete loss of stained cytoplasmic components apparently due to lysis of myofibrils. Von Kossa stains for calcium salts were negative both in the scar tissue and in the muscle cells with degenerative changes. None of the aneurysms were associated with mural thrombi. Examination of tissue obtained from one patient with a ventricular aneurysm and a negative postinfarct scintigram showed that the aneurysm wall was completely devoid of surviving muscle cells and consisted entirely of dense fibrous tissue (fig. 4).

Of the three patients (3-6) with persistently positive \textsuperscript{99m}Tc-PYP myocardial scintigrams studied at necropsy, none had ventricular aneurysms. One patient (4) showed degenerative changes of myocytolysis involving muscle cells in regions adjacent to areas of healing transmural myocardial infarction. Another patient (5) showed changes of myocytolysis, atrophy, acute necrosis and fibrosis scattered throughout the left ventricular subendocardium (fig. 5). The final patient (6) with a persistently positive \textsuperscript{99m}Tc-PYP myocardial scintigram had a history of severe, initially unstable, recurrent angina pectoris but had never had a clinically documented acute myocardial infarct. This patient had multiple scattered areas of replacement fibrosis as well as involvement of the intramural coronary arteries by amyloid deposits. Von Kossa stains for calcium salts were negative in the three patients studied at necropsy.

Detailed light and electron microscopic study of three operatively removed aneurysm specimens confirmed and amplified the findings observed in routine paraffin sections (figs. 6 and 7). Fine structural study revealed marked swelling and separation of organelles without disruption of

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**Table 2. Patterns of Persistently Positive \textsuperscript{99m}Tc-PYP Myocardial Scintigrams in Nineteen Patients**

<table>
<thead>
<tr>
<th>Number of Patients</th>
<th>Initial Scintigrams</th>
<th>Follow-up Scintigrams</th>
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<tbody>
<tr>
<td>1</td>
<td>4+</td>
<td>4+</td>
</tr>
<tr>
<td>1</td>
<td>4+</td>
<td>2+</td>
</tr>
<tr>
<td>4</td>
<td>3+</td>
<td>3+</td>
</tr>
<tr>
<td>9</td>
<td>3+</td>
<td>2+</td>
</tr>
<tr>
<td>4</td>
<td>2+</td>
<td>2+</td>
</tr>
</tbody>
</table>

Total: 19

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**Figure 2. Typical scintigraphic findings in a patient with persistently positive \textsuperscript{99m}Tc-PYP myocardial activity.** The initial myocardial scintigram obtained shortly after onset of acute myocardial infarction shows 4+ positive myocardial activity located lateral to the tip of the sternum. Follow-up scintigram shows reduced 2+ positive activity in the same region as the initial myocardial scintigram.
Table 3. Clinical and Morphological Findings in Seven Patients

<table>
<thead>
<tr>
<th>Pt No</th>
<th>Interval since AMI</th>
<th>Postinfarct Scintigrams*</th>
<th>Source of Tissue</th>
<th>Morphologic Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) B.B.</td>
<td>3 mo</td>
<td>2+, apical</td>
<td>Operative resection of ventricular aneurysm</td>
<td>Healed infarct, myocytolysis</td>
</tr>
<tr>
<td>2) N.P.</td>
<td>3 1/2 mo</td>
<td>3+, anterior</td>
<td>Operative resection of ventricular aneurysm</td>
<td>Healed infarct, myocytolysis</td>
</tr>
<tr>
<td>3) C.D.</td>
<td>9 mo</td>
<td>3+, apical</td>
<td>Operative resection of ventricular aneurysm</td>
<td>Healed infarct, myocytolysis</td>
</tr>
<tr>
<td>4) R.F.</td>
<td>1 1/2 mo</td>
<td>2+, apical</td>
<td>Autopsy (no aneurysm)</td>
<td>Healed infarct, myocytolysis</td>
</tr>
<tr>
<td>5) D.B.</td>
<td>3 1/2 yr</td>
<td>2+, apical</td>
<td>Autopsy (no aneurysm)</td>
<td>Healed subendocardial infarctes of papillary muscles; circumferential subendocardial myocytolysis, atrophy, necrosis and fibrosis</td>
</tr>
<tr>
<td>6) W.F.</td>
<td>Not documented clinically</td>
<td>2+, apical</td>
<td>Autopsy (no aneurysm)</td>
<td>Multifocal fibrosis</td>
</tr>
<tr>
<td>7) H.H.</td>
<td>mos</td>
<td>Negative</td>
<td>Operative resection of ventricular aneurysm</td>
<td>Transmural fibrosis without myocytolysis</td>
</tr>
</tbody>
</table>

*Interval between the last scintigraphic study and tissue sampling was 10 days for patient #6 and 1 day for the other 6 patients. Abbreviations: AMI = acute myocardial infarction.

myofibrillar architecture in some muscle cells (fig. 6). Other muscle cells showed variable degrees of disruption and disorganization of myofibrils (fig. 6). Damaged muscle cells exhibited focal mitochondrial swelling, but did not show inclusions characteristic of mitochondrial calcification or amorphous matrix (flacculent) densities characteristic of irreversible damage following acute ischemic injury. Many of the muscle cells were interspersed between bundles of collagen fibers and appeared to have lost intracellular connections with adjacent muscle cells. Some of these cells exhibited severe atrophy (figs. 6 and 7). These cells were markedly reduced in size and contained aggregates of sarcoplasmic reticulum and masses of filaments but were devoid of organized myofibrils (fig. 7).

Discussion

This study has shown that: 1) persistently positive 99mTc-PYP myocardial scintigrams occurred in 19 (41%) of 46 patients in a select series followed with serial scintigrams after acute myocardial infarction; 2) persistently positive 99mTc-PYP myocardial scintigrams were characterized by a high incidence (14 of 19 patients) of low grade (2+ positive) activity and by a general tendency for decreased activity as compared to initial scintigrams; 3) patients with persistently positive 99mTc-PYP scintigrams had a more symptomatic clinical course than patients without persistently positive scintigrams, and 4) persistently positive 99mTc-PYP myocardial scintigrams correlated with presence of significant myocardial degeneration, myocytolysis, and fibrosis in a series of seven patients studied morphologically.

Other clinical investigators also have observed a relatively frequent occurrence of persistently positive 99mTc-PYP myocardial scintigrams following acute myocardial infarction. The overall incidence, however, of persistently positive 99mTc-PYP myocardial scintigrams is probably lower than the reported incidence since the data have been obtained in subpopulations available for follow-up study. From the present and previous studies, it appears that persistent positivity of 99mTc-PYP myocardial scintigrams is associated with mildly increased (2+) activity in the vast majority of patients. It is also clear that persistently positive

Figure 3. Histologic findings in a patient with a ventricular aneurysm and 3+ persistently positive 99mTc-PYP myocardial scintigram. A) The operatively resected aneurysm wall exhibits extensive replacement fibrosis (F), and adipose tissue invasion (fatty replacement) (FR), but contains foci of myocardium (M) which have survived the initial infarction. B) These foci of myocardium show interstitial fibrosis as well as degeneration of muscle cells ranging from edema to complete loss of stained cytoplasmic constituents. Mason trichrome stains; A, ×9, B, ×240.

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FIGURE 4. Histologic findings in a patient with a ventricular aneurysm and a negative post-infarct 99mTc-PYP myocardial scintigram. The operatively resected aneurysm wall consists of dense fibrous tissue and is devoid of myocardium. Compare with figure 3. Mason trichrome stain, ×60.

FIGURE 5. Histologic findings in a patient with ischemic cardiomyopathy and a 2+ persistently positive 99mTc-PYP myocardial scintigram. The patient had a history of subendocardial infarction, recurrent angina pectoris and progressive congestive heart failure. Necropsy revealed severe three vessel coronary disease, cardiac hypertrophy (450 g) and marked left ventricular dilatation. A) The thinned left ventricular wall exhibits extensive myocardial fibrosis (F). B) Muscle cells adjacent to the areas of fibrosis show marked vacuolization (small arrowheads) and atrophy (large arrowheads). C) Fragments of severely damaged muscle cells blend into the fibrous tissue (arrowheads). Mason trichrome stains; A, ×6; B, ×36; C, ×90.
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FIGURE 6. Detailed cytologic features of myocardial degeneration in patients with ventricular aneurysms and persistently positive 99mTc-PYP myocardial scintigrams. A) Many muscle cells in an area of interstitial fibrosis show partial to complete loss of myofibrils. One relatively normal muscle cell (N) with well preserved myofibrils also is present. B) Another fibrotic area contains markedly atrophic muscle cells with vacuolated cytoplasm and few myofibrils. Semithin (one micron) epoxy sections, toluidine blue stains, both ×640.

myocardial scintigrams can occur in patients with and without ventricular aneurysms. Available observations from the present study and a previous study suggest that moderately increased (3+) activity on persistently positive 99mTc-PYP myocardial scintigrams may occur more frequently in patients with ventricular aneurysms than in those without aneurysms.

Some investigators have questioned the significance of a 99mTc-PYP myocardial scintigram with mildly increased activity (2+) when the activity appears poorly localized or diffuse. We originally used the 2+ diffuse designation to characterize the typical 99mTc-PYP myocardial scintigraphic pattern observed in many patients with clinically documented subendocardial infarcts and in one third of patients with unstable angina pectoris. The diffuse designation was meant to convey difficulty in precise localization due to a combination of factors, including relatively low levels of 99mTc-PYP activity and difficulty in visualization of activity in every scintigraphic projection. In our experience, however, a distinction generally can be made between true myocardial uptake, even if relatively poorly localized, from very diffuse artifactual blood pool images since the blood pool images tend to occupy larger, globular areas on every scintigraphic projection and to significantly overlap the sternum (fig. 1). Our practice for handling equivocal cases is to perform delayed and repeat scintigraphic study in order to ensure technically satisfactory scintigrams. It is helpful on repeat scintigraphic study to ob-

FIGURE 7. Electron micrograph shows a muscle cell with features of marked degeneration and atrophy (diameter 5.5 microns). The muscle cell is surrounded by collagen fibers and contains numerous filaments but only a few disorganized remnants of myofibrils. ×17,200.
tain blood pool and delayed images for comparative study (fig. 1). Others also have reported resolution of equivocal cases with delayed or repeat imaging protocols.27

Findings in the present study suggest that a persistently positive 99mTc-PYP myocardial scintigram correlates with a symptomatic clinical course following acute myocardial infarction. All 19 patients with persistently positive scintigrams had exertion limiting angina pectoris; seven of the 19 patients have been readmitted to the hospital three or more times over the past 15 months and 12 of the 19 patients had been admitted two or more times over a 4 month follow-up period for evaluation of severe chest pain. The major clinical problem in 16 of the 19 patients was recurrent, severe and limiting chest pain, while the major problem in three patients was severe congestive heart failure with intermittent angina pectoris. The latter three patients appeared to fit into the clinicopathologic spectrum of ischemic cardiomyopathy.28,29

Our morphological studies demonstrate that a persistently positive 99mTc-PYP myocardial scintigram frequently correlates with significant myocardial degeneration involving muscle cells which survive the initial acute myocardial infarctions. The observed pattern of myocardial degeneration has the features of myocytolysis as described in the classic paper by Schlesinger and Reiner.30 Various stages or forms of myocytolysis have been observed in a variety of human and experimental cardiac diseases.31-33 Distinctive features of myocytolysis associated with acute and chronic coronary heart disease appear to be the involvement of relatively large numbers of muscle cells which frequently are localized in discrete regions of the myocardium, namely, the border zone regions of recent or old myocardial infarcts.30,31 We have also observed myocytolysis associated with patchy acute necrosis or fibrosis in patients with positive 99mTc-PYP myocardial scintigrams and unstable angina pectoris.7 Indeed, two patients in the morphology series of the present study had persistently positive 99mTc-PYP myocardial scintigrams and unstable angina pectoris. Although the one patient in the morphology series with a negative postinfarct scintigram did not show myocytolysis, it seems likely that myocytolysis is not a specific pathologic correlate of positive 99mTc-PYP myocardial scintigrams, but that the positive scintigram is related to quantitative factors, such as extent of muscle damage and blood flow for delivery of radio-nuclide to such areas.

In order to precisely define the exact relationship between myocytolysis and myocardial uptake of 99mTc-PYP, further work is required to determine whether actual concentration of 99mTc-PYP occurs in degenerating and myocytolytic cells and to elucidate mechanisms for this concentration. As in the case of acute myocardial infarction, complexing with elevated tissue calcium stores would appear to be a likely mechanism for concentration of 99mTc-PYP in areas of myocytolysis.3-10 Although foci of myocytolysis did not exhibit demonstrable calcification, these findings do not exclude the occurrence of elevated tissue calcium content in vivo since initial stages of pathologic calcium accumulation involve highly soluble forms of calcium which may not be preserved in routinely fixed and processed tissues.10,39,40 The observation of prominent cell swelling and edema in foci of myocytolysis suggests the possibility that the degenerative process is associated with electrolyte alterations resulting from altered membrane function.41,42 Indeed, in the case of experimental adriamycin cardiotoxicity, myocardial degeneration and myocytolysis have been shown to be associated with elevated myocardial sodium and calcium levels.37,38

Although our study suggests that concentration of 99mTc-PYP in areas of myocytolysis is a frequent cause of persistently positive scintigrams, other possible mechanisms for persistently positive scintigrams also may be operative. Cowley, Priest and associates have suggested that persistently positive scintigrams result from 99mTc-PYP uptake in metabolically abnormal muscle cells which exhibit only mild ultrastructural alterations, including mitochondrial inclusions of uncertain nature.39,44 It should be pointed out that the morphological observations reported by Cowley, Priest and associates were observed in small subepicardial biopsies removed at the time of myocardial revascularization. In the present study, transmural samples were available for examination and showed severe myocytolytic degeneration in deeper regions of the samples. Decrease or loss of cardiac activity on 99mTc-PYP myocardial scintigrams following revascularization of patients with persistently positive myocardial scintigrams3-4,13 could be explained by a reversal of early myocytolytic changes which typically accompany the more severely damaged muscle cells.30,31 Considerable evidence, however, indicates that myocytolysis does include an irreversible stage of damage since the end result of myocytolysis is complete dissolution of muscle cells and collapse fibrosis.30,31 Another possible mechanism for persistently positive 99mTc-PYP myocardial scintigrams may be concentration of 99mTc-PYP in foci of dystrophic calcification in scar tissue of old infarcts as well as in calcified portions of mural thrombi overlying the old infarcts.

Clinical interpretation of 99mTc-PYP myocardial scintigrams now must include awareness of the phenomenon of persistent positivity. Since most persistently positive 99mTc-PYP myocardial scintigrams exhibit 2+ activity, the diagnosis of acute myocardial infarction can still be made with reasonable confidence on the basis of a single, 3-4+ positive 99mTc-PYP myocardial scintigram in a patient with a compatible clinical history. Even in these patients, it is best to confirm the diagnosis with a repeat myocardial scintigram later in the course to document a decrease or loss of cardiac activity. In patients presenting with prolonged chest pain and 2+ positive 99mTc-PYP myocardial scintigrams, serial imaging will be necessary to establish the diagnosis of acute myocardial infarction scintigraphically. Nevertheless, our findings indicate that a positive 99mTc-PYP myocardial scintigram signifies the presence of significant myocardial pathology. Although the persistently positive uptake of 99mTc-PYP following acute myocardial infarction complicates the interpretation of the test, sequential 99mTc-PYP myocardial scintigraphy provides a mechanism for recognition of acute myocardial infarction and also for evaluating the course of patients with coronary heart disease. Further studies should help to elucidate the prognostic significance of a persistently positive 99mTc-PYP myocardial scintigram in larger numbers of patients followed for longer periods of time.
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