

Positive indium-111 leukocyte imaging in post myocardial infarction syndrome

Kiyomitsu IKEOKA,* Hitoshi NARUSE,* Seinosuke KAWASHIMA,* Mitumasa OHYANAGI,*
Hiroyuki MAEDA,* Aya MIYOSHI,* Kazuhiro FUJITANI,* Tadaaki IWASAKI*
and Minoru FUKUCHI**

**The First Department of Internal Medicine, Hyogo College of Medicine*

***The Department of Nuclear Medicine, Hyogo College of Medicine, Nishinomiya, Hyogo, Japan*

The diagnosis of post myocardial infarction syndrome (PMIS) is sometimes difficult because of the absence of a specific test. We report a 68-year-old man with PMIS who had a persistent accumulation of indium-111 oxine labeled leukocytes in the infarcted myocardium for 1 month. The uptake of leukocytes preceded the appearance of the main symptoms and disappeared with the clinical improvement after the therapy with steroids. Leukocyte imaging has a potential as a useful tool for early diagnosis, evaluation of therapy and assessing the mechanism of PMIS.

Key words: indium-111 leucocyte imaging, post myocardial infarction syndrome

INTRODUCTION

THE POST myocardial infarction syndrome (PMIS) initially described by Dressler¹ is still of unknown etiology. It is characterised by pleuropericardial pain, fever, pleural effusions, friction rubs and a high erythrocyte sedimentation rate. Typically, these symptoms have a tendency to recur during a few weeks or months after a myocardial infarction. Diagnosis is sometimes difficult because of the variation in complaints and the lack of a specific test. In particular, there has been no graphic approach that helps to diagnose PMIS.

Since it was introduced by Thakur et al. in 1976,² indium-111 (¹¹¹In) oxine labeled leukocyte imaging (leukocyte imaging) has been found to be highly sensitive and specific for the detection of inflammation in humans. We report a patient with PMIS diagnosed by his clinical features, in whom persistent

inflammation was proved by leukocyte imaging in the infarcted myocardium for about 1 month.

CASE REPORT

A 68-year-old man was admitted to Hyogo College of Medicine Hospital because of acute antero-septal myocardial infarction confirmed by electrocardiograms with positive enzyme studies. On admission, 6 hours from the onset, physical examination revealed a regular pulse of 80/min and a blood pressure of 118/80 mmHg. The electrocardiogram showed an abnormal Q wave with ST increase in V1-4. Emergency coronary angiography showed a complete occlusion at the proximal site of the left anterior descending coronary artery. Intracoronary thrombolysis with Urokinase 960,000 units resulted in no recanalization. Cross sectional echocardiography showed a dyskinetic movement in the anterior wall of the left ventricle. On the 7th day of hospitalization, pericardial friction rub was audible at the left mid-sternal border. The electrocardiography showed a persisted increase in the ST segment in chest leads, indicating ventricular aneurysm. The echocardiography denied the presence of pericardial effusion.

Received March 19, 1990; revision accepted May 28, 1990.

For reprints contact: Kiyomitsu Ikeoka. The First Department of Internal Medicine, Hyogo College of Medicine, Mukogawa-cho 1-1, Nishinomiya 663 JAPAN.

Two days later, leukocyte imaging was performed with single photon emission computed tomography (SPECT) anticipating visualization of the pericarditis. Autologous leukocytes were isolated and labeled with ^{111}In using minor modifications of the technique of Thakur et al.³ The patient was injected with 430 μCi (15.91 MBq) of ^{111}In labeled leukocytes, and cardiac imaging was performed 24 hours after the injection. Simultaneous dual-peak imaging was performed with 20% windows around both photon peaks (173 and 247 KeV) of ^{111}In , and the sampling time was 180 seconds. Planar images were collected in the anterior position and 45 degree right and left anterior oblique positions. The SPECT was performed with 32 planar acquisitions for 30 seconds sampling each over a 180 degree extending from the 45 degree right anterior oblique to the 45 degree left posterior oblique position. A Maxi Camera 400 A/T (General Electric) was used for data acquisition, and a minicomputer system (Maxi Star) was used for data analysis. Using a filtered back projection, transaxial slices 6 mm thick were reconstructed parallel to the vertical and horizontal long axis and the short axis of the left ventricle. Leukocyte imaging demonstrated positive accumulation within the area of the infarcted myocardium which was represented as a defect on SPECT with thallium-201 (^{201}Tl) performed at the same time (Figs. 1, 2). The uptake of leukocytes was not diffused over the pericardium but localized in the infarcted myocardium. The reattack or extension of the myocardial infarction was not detected by the enzyme study. Two

weeks after admission (5 days after the first leukocyte imaging), the patient complained of pleuritic pain accompanied by shortness of breath and fever (37.5°C). The chest X-ray showed a small right pleural effusion. The peripheral leukocyte count was 9,700 with 83% granulocytes. The blood sedimentation rate was 32 mm/h and CRP was 3+. Examination of the pleural effusion revealed that the fluid was straw-coloured and exudative without any bacteria. The symptoms and increase in inflammatory reactants tended to decrease but persisted for a while. Leukocyte imaging (amount of ^{111}In : 460 μCi (17.02 MBq)) was performed again on the 26th hospital day. The accumulation of leukocytes was still seen

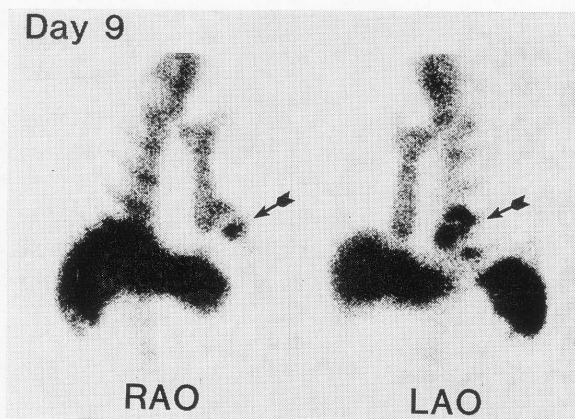


Fig. 1 Planar images on the 9th day showing the multiple uptake of ^{111}In labeled leukocytes in the anterior wall of the left ventricle (arrowed) and normal uptake in the liver and spleen.

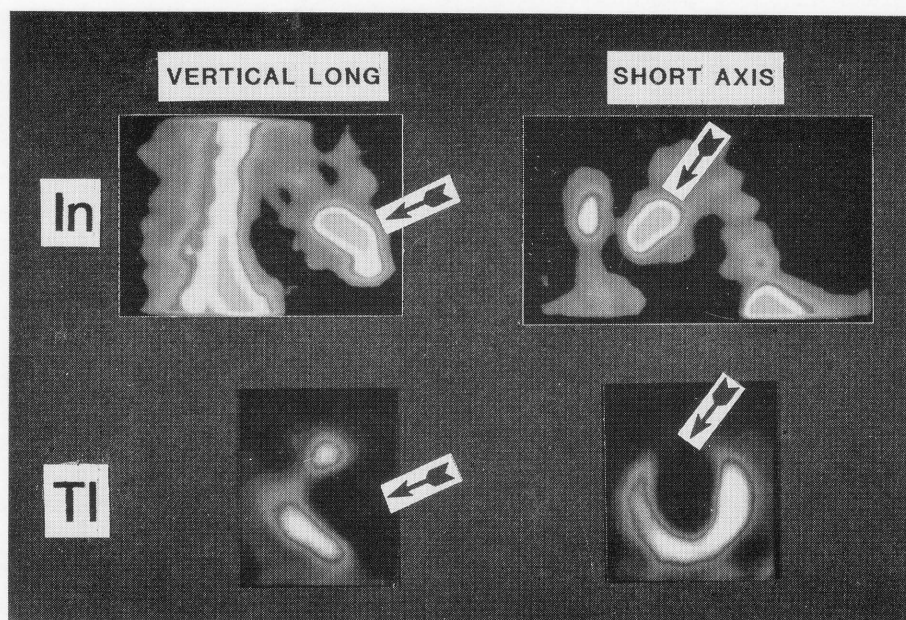


Fig. 2 Simultaneous single photon emission computed tomographic images in the two transverse planes. The ^{201}Tl images show a defect in the anterior wall of the left ventricle. The ^{111}In images show the uptake that coincides with the defect in ^{201}Tl images (arrowed).

in the infarcted myocardium and there was a change in the shape and site of the lesion compared with the previous study (Figs. 3, 4). After that, left pleural effusion suddenly appeared on the 40th hospital day. It was accompanied by leukocytosis ($10,800/\text{mm}^3$) with eosinophilia (10%) and an accelerated sedimentation rate (50 mm/h). Two-dimensional echocardiography demonstrated moderate pericardial effusion that was not seen in the earlier study. The patient was started on treatment with prednisolone 40 mg/day. The viral antibody titers suggested no acute infection at that time. No autoimmune antigen test showed positive findings, and no serum circulating autoantibodies to heart muscle were detected either. After the administration of prednisolone, the patient showed a remarkable clinical improvement. Two

weeks later he had no sign of pleuritis or pericarditis. The signs of inflammation and the positive result in the immunological studies became negative. No accumulation of leukocytes was detected in the myocardium on the third leukocyte imaging (amount of ^{111}In : $390 \mu\text{Ci}$ (14.43 MBq)) performed on the 59th day from the onset of myocardial infarction (Fig. 5).

DISCUSSION

Since the original description by Dressler, PMIS remained an ill-defined clinical entity, with difficulty in diagnosing it because of the variation in complaints and the absence of a specific test. Laboratory investigation of PMIS is characterized by non specific signs of inflammation and thus suffers from the lack

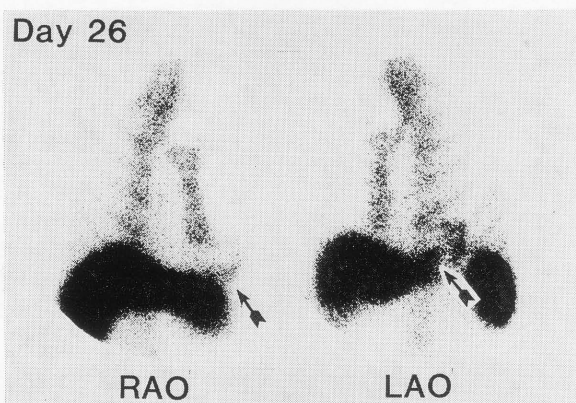


Fig. 3 Planar images on the 26th day show the accumulation of ^{111}In labeled leukocytes in the apex of the heart (arrowed).

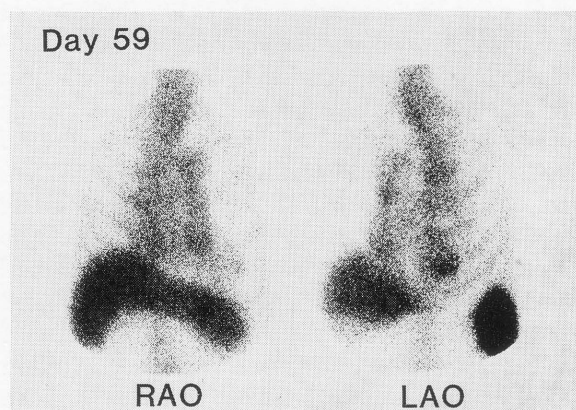


Fig. 5 Planar images on the 59th day. There is no abnormal uptake in the heart.

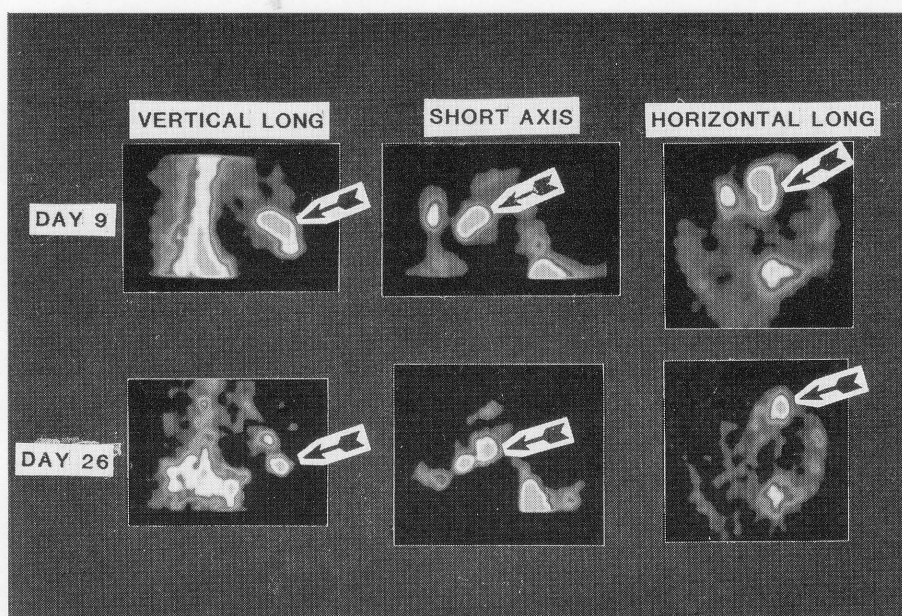


Fig. 4 Single photon emission computed tomographic images of ^{111}In on the 9th and 26th days. The changes in uptake in the shape and the site are obvious (arrowed).

of a simple, readily definable marker. The anti-heart muscle antibody screening was thought to be a reliable marker, but it is realized that antibodies are not present in all patients with PMIS and can be seen in many other cardiac conditions.^{4,5} And it is known that the antigen made from human infarct myocardium is more sensitive than that from the intact heart of other animals.⁶ In our hospital we used the antigen made from rat myocardium, and that might be one reason for the negative result in our patient. In spite of the negative result obtained with the anti-heart muscle antibody, this patient demonstrated protracted fever, recurrent pleuritis with exudative pleural effusion and pericarditis accompanying the laboratory findings of inflammation and leukocytosis with eosinophilia. In addition, a dramatic improvement in symptoms and laboratory findings including the leukocyte imaging were observed after prednisolone therapy. On the basis of these findings, we diagnosed his case as PMIS.

Bufalino et al.⁷ reported that Gallium-67 imaging was helpful in detecting the inflammation occurring in the post pericardiotomy syndrome, a condition which is pathophysiologically similar to PMIS. But there has been no graphic approach in diagnosing PMIS itself. Recent reports^{8,9} suggest that leukocyte imaging is positive in patients with acute myocardial infarction who had an injection of ¹¹¹In labeled leukocytes within 24 hours of the onset of symptoms. Our experience has also shown that early injection of leukocytes is more likely to produce positive imaging¹⁰ and no positive image has been obtained after 3 days from the onset of myocardial infarction. We performed the leukocyte imaging on positive patients again the following week, but there was no positive image in any patient. These results suggest that the stimulus for the activation and migration of leukocytes is transient in the early phase of acute myocardial infarction. In this case, the first leukocyte imaging demonstrated abnormal localization of activity on the 9th day after acute myocardial infarction. This is not a natural course for infarct patients with positive leukocyte imaging, and reinfarction was unlikely to exist at that time. Thereafter, the activity persisted with changes in the shape and the site in the infarcted myocardium for about 1 month. We do not yet know the meaning of these changes, but they may imply that the abnormal accumulation of leukocytes found in this patient did not occur in response to acute myocardial ischemia. The accumulation probably represents a chronic inflammatory immunological response which occurred in the infarcted myocardium. An immunological mechanism for PMIS has been postulated,^{6,11} but the cause remains unclear. Our findings are likely to reflect a part of the immunological disorder which is

related to the infarcted myocardium in PMIS. In addition, it is noteworthy that the findings of positive leukocyte imaging preceded the occurrence of main clinical symptoms. These findings might contribute important information concerning the etiology of PMIS.

Although PMIS is usually benign, it may be confused with more serious conditions such as pulmonary embolism and extension of infarction. Therefore, making a diagnosis of PMIS is important in deciding the therapeutic strategy. Leukocyte imaging has a potential as an excellent practical addition in diagnosing PMIS and may also be a useful research tool for further controlled, prospective evaluation of therapy and demonstrating the mechanism of this disease.

REFERENCES

1. Dressler WA: A post myocardial infarction syndrome. *JAMA* 160: 1379-1383, 1956
2. McAfee JG, Thakur ML: Survey of radioactive agents for *in vitro* labeling of phagocytic leukocytes. I. Soluble agents. *J Nucl Med* 17: 480-487, 1976
3. Thakur ML, Gottschalk A, Zaret BL: Imaging experimental myocardial infarction with indium-111-labeled autologous leukocytes: effects of infarct age and residual myocardial blood flow. *Circulation* 60: 297-305, 1979
4. Heine WJ, Friedman H, Mandell MS, et al: Auto-antibodies to cardiac tissue in acute ischemic heart disease. *Am J Cardiol* 17: 798-803, 1966
5. Kaplan MH, Frengley JD: Autoimmunity to the heart in cardiac disease. *Am J Cardiol* 24: 459-473, 1969
6. Itoh K, Ohkuni H, Kimura E, et al: Immuno-serological studies on myocardial infarction and post-myocardial infarction syndrome. *Jpn Heart J* 10: 485-502, 1969
7. Bufalino VJ, Robinson JA, Henkin R, et al: Gallium-67 scanning: a new diagnostic approach to the post-pericardiotomy syndrome. *Am Heart J* 106: 1138-1143, 1983
8. Davies RA, Mathew L, Thakur PD, et al: Imaging the inflammatory response to acute myocardial infarction in man using indium-111-labeled autologous leukocytes. *Circulation* 63: 826-832, 1981
9. Bell D, Jackson M, Millar AM, et al: The acute inflammatory response to myocardial infarction: imaging with indium-111 labelled autologous neutrophils. *Br Heart J* 57: 23-27, 1987
10. Ikeoka K, Naruse H, Terawaki K, et al: Imaging the inflammatory response to acute myocardial infarction using Indium-111-labeled autologous leukocytes. *Jpn Circ J* 52: 1067, 1988
11. Kennedy HL, Das SK: Postmyocardial infarction syndrome: report of a case with immunological and viral studies. *Am Heart J* 91: 233-239, 1976