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Myocarditis in Patients With Clinical Presentation of Myocardial Infarction and Normal Coronary Angiograms

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OBJECTIVES The aim of this study was to assess the diagnosis of myocarditis in patients presenting with acute myocardial infarction (MI) and normal coronary angiograms.

BACKGROUND Most often in these patients, the etiologic diagnosis remains unclear once they are found to have normal coronary arteries. The diagnosis of myocarditis mimicking MI is clinically relevant, because numerous arguments suggest a relation between myocarditis and dilated cardiomyopathy. Myocardial indium-111 (^{111}In)-antimyosin antibody (AMA)/rest thallium-201 (^{201}Tl) imaging allows noninvasive detection of myocarditis.

METHODS Forty-five patients admitted to three intensive care units for suspicion of acute MI, with normal coronary angiograms, were investigated. Indium-111–AMA planar images and then a dual-isotope rest AMA/^{201}Tl tomographic study were performed. Six-month echocardiographic follow-up was obtained in 80% of the patients with initial left ventricular (LV) wall motion abnormalities.

RESULTS In eight patients, AMA and ^{201}Tl scintigraphy were negative. In two patients, a matched ^{201}Tl defect and focal AMA uptake suggested acute MI (due to prolonged vasospasm or spontaneously reperfused coronary occlusion). In 17 patients, diffuse AMA uptake over the whole LV suggested diffuse myocarditis. In 18 patients, focal AMA uptake with a normal ^{201}Tl scan suggested diffuse but heterogeneous, or focal myocarditis. Complete functional recovery was observed in 81% of the patients with a pattern of myocarditis.

CONCLUSIONS Among 45 patients presenting with acute MI and normal coronary angiograms, 38% had diffuse myocarditis and 40% had a scintigraphic pattern of heterogeneous or focal myocarditis. Short-term follow-up showed complete LV functional recovery in 81% of these patients. (J Am Coll Cardiol 2001;37:786–92) © 2001 by the American College of Cardiology

Currently, much attention is paid to the diagnosis and treatment of myocarditis, because clinical and experimental arguments suggest a relation between infectious cardiac disease and dilated cardiomyopathy (1–5). Deleterious immune phenomena identical to those found in idiopathic dilated cardiomyopathy (IDC) persist for many weeks after the virus has disappeared in myocarditis. The long-term outcome of patients with myocarditis may be as poor as that in IDC (6,7). Very recent studies focused on clinical or biologic (anticardiac autoantibodies) prognostic factors (7,8).

Clinically, myocarditis can mimic myocardial infarction (MI) (9–14), and so it is suspected in patients with clinical and electrocardiographic (ECG) evidence of acute coronary syndrome, and having normal coronary angiograms (~3% of patients with presentation of MI) (15,16). However, the prevalence of myocarditis in these patients is unknown. In most cases, MI secondary to coronary vasospasm or spontaneously reperfused coronary occlusion is suggested, but no definitive diagnosis is sought when the patient is found to have normal coronary arteries. Endomyocardial biopsy is rarely performed because of its poor risk/benefit ratio, due to low sensitivity (17–19). Indium-111 (^{111}In)-antimyosin antibody (AMA) scintigraphy, which allows specific detection of myocytic necrosis, has been widely reported as a useful tool to diagnose myocarditis, particularly those cases mimicking acute MI (11,20–22).

In this study, AMA scintigraphy coupled with rest thallium-201 (^{201}Tl) myocardial imaging was prospectively performed in 45 patients presenting with acute MI and normal coronary angiograms.

METHODS

Patients. Forty-five patients were prospectively included in this study during a 31-month period. They were referred by the intensive care units of three cardiology departments. The inclusion criteria were recent onset of acute, prolonged (>30 min) chest pain, ischemic ECG abnormalities during the acute phase, serum elevation of creatine kinase (CK) or

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Abbreviations and Acronyms

AMA = antimyosin antibody
CK = creatine kinase
HLR = heart to lung ratio
IDC = idiopathic dilated cardiopathy
^{111}In = indium-111
LV = left ventricle or left ventricular
LVEF = left ventricular ejection fraction
MI = myocardial infarction
SPECT = single photon emission computed tomography
^{201}Tl = thallium-201

troponin I, or both, and normal coronary angiograms (no significant coronary stenosis, no visible coronary thrombus or unstable plaque, no vasospasm). Patients with typical presentation of myopericarditis were excluded on the basis of young age, no cardiac risk factors but recent acute febrile illness, chest pain characteristic of pericardial involvement or pericardial friction rub, diffuse ST segment changes but no Q waves on the ECG and pericardial fluid but no segmental wall motion abnormalities on the echocardiogram obtained within 24 h after the onset of chest pain. During the study period, 1,280 patients were admitted for MI in the three study centers; 4% of them had normal coronary angiograms.

The characteristics of the study group on hospital admission are described in Table 1. Eight patients had more than one coronary risk factor, and 23 had one risk factor. Sixteen patients had a fever. Two patients had clinical left ventricular (LV) failure. The ECG findings included Q waves in 12 patients, ST segment elevation in 29 and ST segment depression in 4. The biologic findings included elevated peak serum CK levels in 41 patients, elevated CK-MB fraction titer alone in 1 and elevated troponin I level alone in 3.

Table 1. Patient Characteristics on Hospital Admission

	Study Group (n = 45)
Age (yrs)	43 ± 18
Gender ratio (M/F)	29/16
Chest pain	45 (100%)
Cardiac risk factors	31 (70%)
Recent history of viral illness	22 (49%)
ECG changes	
ST segment elevation	29 (64%)
ST segment depression	4 (9%)
Pathologic Q-waves	12 (27%)
Mirror ST segment changes	17 (28%)
Peak serum CK level (UI/liter)	595 ± 469
CRP >10 mg/liter	30 (67%)
Normal coronary arteries	45 (100%)
Thrombolytic therapy	3 (7%)
Delay between admission and angiography	
<6 h	15 (33%)
<24 h	28 (62%)
<72 h	35 (78%)

Data are presented as the mean value ± SD or number (%) of patients.
CK = creatinine kinase; CRP = C-reactive protein; ECG = electrocardiographic; F = female; M = male.

Fifteen patients had angiography of the coronary arteries within 6 h of hospital admission, and three patients had thrombolytic therapy. The other patients were not considered for thrombolysis or coronary angioplasty on hospital admission because of pregnancy (n = 1), delayed appearance of Q waves and segmental wall motion abnormalities leading to re-evaluation of the initial diagnosis (from pericarditis to MI or myocarditis, n = 2) or late admission (>6 h after the beginning of chest pain, n = 24). They all received anti-ischemic therapy.

Coronary angiography. All patients underwent coronary angiography for suspicion of coronary artery disease responsible for acute MI. The scans were normal in all patients. A vasoconstrictor ergonovine test was performed in three patients and was always negative. Right ventricular endomyocardial biopsy was performed in two patients.

Two-dimensional echocardiography was also performed in all patients within 24 h of hospital admission (directly on admission in 31), according to the recommendations of the American Society of Echocardiography.

Indium-111–AMA/^{201}Tl scintigraphy. Coupled ^{111}In-AMA and rest ^{201}Tl scintigraphy was performed in all patients at a mean time of 11.1 ± 6.4 days after the onset of chest pain. The imaging procedure was the same as previously described (23,24). First, 74 Mbq of ^{111}In-AMA was injected intravenously (whole-body radiation dose: 19.2 mSv). Forty-eight hours later, planar thoracic images (anterior and oblique anterior views) were acquired, with a 20% window centered on the 173- and 247-keV photopeaks of ^{111}In and a preset time of 10 min. Then, 111 MBq of ^{201}Tl was injected, and dual-isotope single-photon emission computed tomography (SPECT) was performed 30 to 60 min later, with 20% windows fitted on 74-, 173- and 247-keV photopeaks. The two data sets (^{201}Tl-SPECT and ^{111}In-SPECT) were simultaneously, identically and automatically processed, centered and reoriented along the three axes with the help of ^{201}Tl acquisition as a landmark. Corresponding slices for each SPECT acquisition were displayed simultaneously and could be superimposed for better ^{111}In-AMA uptake localization.

Data analysis. On angiography and echocardiography, the extent of wall motion abnormalities was semiquantified as the number of hypokinetic or dyskinetic segments, after LV segmentation in nine segments (apical and basal parts of the anterior, inferior, lateral and septal walls, plus the apex).

The planar and tomographic scintigrams were scored in blinded manner by two investigators from the Department of Nuclear Medicine. A consensus reading was made in case of disagreement. Indium-111–AMA scintigraphy was scored as normal or abnormal on planar images, both visually and after calculating a heart to lung ratio (HLR), by using two regions of interest—one in the cardiac area and the other in the right lung. Left ventricular AMA uptake was considered significant when the HLR was >1.8. This

JACC Vol. 37, No. 3, 2001
March 1, 2001:786–92

threshold value was previously determined on the basis of the mean HLR value ± 2 SD in six healthy volunteers (25). Significant AMA uptake was scored as diffuse or regional on the basis of tomographic data, and its extent was quantified after LV segmentation identical to that used for quantification of wall motion abnormalities.

The etiologic interpretation was done as follows: 1) diffuse myocarditis in case of diffuse AMA uptake throughout the whole LV myocardium (no matter what the ^{201}Tl uptake was); 2) MI due to prolonged vasospasm or spontaneously reperfused coronary occlusion in case of segmental AMA uptake and matched ^{201}Tl defect; and 3) focal myocarditis in case of a mismatched pattern associating focal AMA uptake with normal ^{201}Tl uptake.

Follow-up. Repeated clinical and ECG studies were performed during follow-up (6 ± 8 months) in 32 (71%) of 45 patients. Echocardiography was also repeated in 27 (77%) of 35 patients with initial LV wall motion abnormalities. Scintigraphic follow-up with delayed AMA scans was done 2 to 16 months (mean 5 ± 5) after the first evaluation in seven patients with significant myocardial AMA uptake on the initial scan.

Statistical analysis. Descriptive continuous variables were expressed as the mean value ± SD. A comparison of mean values was performed using the Student unpaired *t* test and chi-square analysis. Significant differences were considered at $p < 0.05$.

RESULTS

Initial wall motion studies. Normal global and segmental LV function was found in 10 patients (22%), global hypokinesia without regional abnormalities in seven patients (16%; mean LV ejection fraction [LVEF] 40.8 ± 11.5%) and regional wall motion abnormalities in 28 patients (62%; decrease in LVEF [mean value 49.5 ± 3.9%], n = 4). None of the patients had LV dilation (mean end-diastolic LV diameter 50.5 ± 4.0 mm). Mild pericardial effusion was found in seven patients with localized ischemic ECG abnormalities or pathologic Q waves (n = 1).

Scintigraphic results. Coupled ^{111}In-AMA and rest ^{201}Tl scintigraphy was performed at a mean time of 11.1 ± 6.4 days after the onset of angina. The intraobserver and interobserver reproducibilities of the image reading were 90% and 85%, respectively. The mean difference in HLR values between the two observers was 5.12%. Eight patients (18%) had negative AMA scintigraphy (HLR 1.53 ± 0.30 [range 1.40 to 1.70]), and the ^{201}Tl scan was normal in all eight patients. Thirty-seven patients (82%) showed significant LV AMA uptake (HLR 2.14 ± 0.33 [range 1.82 to 3.2]).

Seventeen patients (38%) had diffuse AMA uptake involving the whole LV myocardium (and also the right ventricle in two patients), suggesting diffuse myocarditis without a ^{201}Tl defect in 14 patients (Fig. 1) and with a ^{201}Tl defect involving four and six segments in two patients.

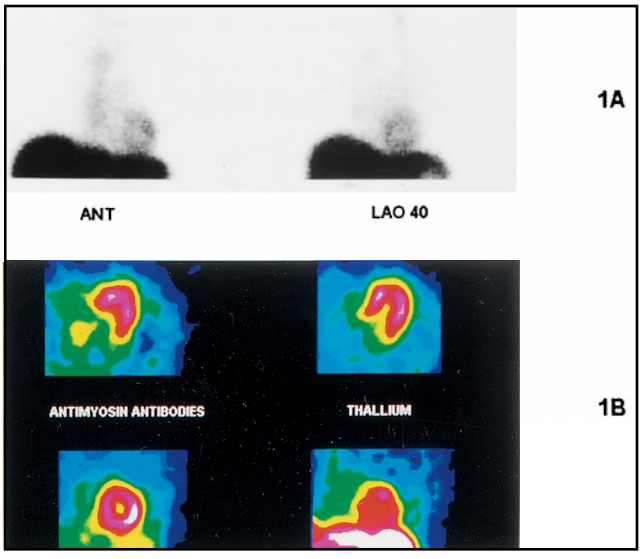

Figure 1. Scintigraphic pattern of diffuse myocarditis. The AMA planar images **(A**, HLR 2.1) and ^{111}In-AMA/^{201}Tl SPECT data **(B**, corresponding ^{111}In-AMA and ^{201}Tl slices) show diffuse AMA uptake throughout the whole LV myocardium, as well as normal ^{201}Tl uptake. ANT = anterior; LAO = left anterior oblique.

In eight of these patients, AMA uptake was more pronounced in one particular region. Eighteen patients (40%) showed focal AMA uptake without a ^{201}Tl defect (Fig. 2). The territories affected by AMA uptake were systematized in 11 patients (apical in 7, lateral in 1, inferior in 1 and inferolateral in 2) and not systematized, involving the apex and part of or all of the lateral wall, in the other seven

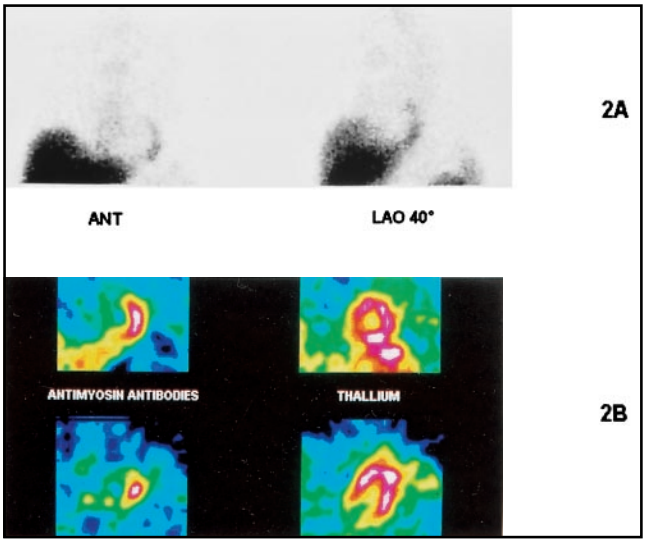

Figure 2. Scintigraphic pattern of focal myocarditis. The AMA planar images **(A**, HLR 2.4) and ^{111}In-AMA/^{201}Tl SPECT **(B**, corresponding AMA and ^{201}Tl slices) show focal AMA uptake on the apex and the lateral LV wall, as well as a normal ^{201}Tl scan. In this patient, coronary angiography and intracoronary contrast echocardiography performed during intense chest pain were normal, except for hypokinesia of the inferior and lateral walls. The chest pain persisted 6 h despite anti-ischemic therapy. Three months later, the ECG was normalized, and echocardiography showed mild global hypokinesia (LVEF 50%) without segmental wall motion abnormalities. ANT = anterior; LAO = left anterior oblique.

Table 2. Electrocardiographic and Echocardiographic Characteristics of the Patients (n = 45) According to Scintigraphic Patterns

	AMA Negative (n = 8)	Diffuse AMA Uptake (n = 17)	Focal AMA Uptake/Normal Tl Scan (n = 18)	Focal AMA Uptake/Matched Tl Defect (n = 2)
ECG changes				
Q waves	2	7	3 (3*)	0
ST segment elevation	4	9	14 (10*)	2 (2*)
ST segment depression	2	1	1 (1*)	0
Wall motion studies				
Normal LV function	2	2	5	1
Global LV hypokinesia (no regional abnormalities)	1	6	0	
Regional wall motion abnormalities	5	9	13	1
Decreased LVEF	1	7	4	0

*Number of patients in whom the location of AMA uptake corresponded with that of ECG abnormalities.
AMA = antimyosin antibody; ECG = electrocardiographic; LV = left ventricular; LVEF = left ventricular ejection fraction; Tl = thallium.

patients. The mean extent of AMA uptake was 2.4 ± 0.7 segments (range 1 to 5). Two patients (4%) showed matched focal AMA uptake (HLR 1.84 and 2.4) and a ^{201}Tl defect in the inferior wall (extent of three and four segments), a pattern highly suggestive of acute inferior MI. The results of ECG changes and LV wall motion studies according to scintigraphic patterns are reported in Table 2.

Right ventricular endomyocardial biopsy performed in two patients with focal AMA uptake (apical/inferior) and a normal ^{201}Tl scan revealed lymphocytic myocarditis according to the Dallas criteria (26).

Follow-up. During the hospital period, chest pain persisted despite anti-ischemic therapy in most patients (>2 h in 68%, mean duration 5.7 ± 6.4 h). The mean chest pain duration was lower in patients with a negative AMA scan versus a positive scan (1.5 ± 1.3 h vs. 10.5 ± 8 h, p = 0.03). In the 32 patients without pathologic Q waves on hospital admission, the ECG abnormalities did not evolve into a pattern of typical acute MI. During follow-up (Table 3), echocardiography revealed persistent wall motion abnormalities in 4 (15%) of 27 patients (global LV hypokinesia in one patient [LVEF 50%], only segmental abnormalities in three patients). The three patients with initial ST segment depression who were followed showed ECG and echocardiographic normalization. In six of seven patients with scintigraphic follow-up, the delayed AMA scan became negative (HLR 1.60 ± 0.25), with still normal ^{201}Tl uptake in five patients and a larger inferior ^{201}Tl defect in one patient (with an initial pattern suggestive of acute MI). In one patient, the HLR decreased but was not normalized (from 2.5 to 1.9) after three months, and the ^{201}Tl scan was still normal.

DISCUSSION

This study reports on 45 patients with initial clinical presentation of acute MI, normal coronary angiograms and a pattern of ^{111}In-AMA/^{201}Tl uptake highly suggestive of myocarditis in 35 of them.

Which diagnosis in patients presenting with acute MI and normal coronary angiograms? The diagnosis of myocarditis is particularly misleading, although such a clinical presentation mimicking acute MI has been widely reported (9–14,27,28). Furthermore, there is a lack of reliable tools for the positive diagnosis of myocarditis, which is based on histologic Dallas criteria (26). Endomyocardial biopsy is invasive, induces significant cardiovascular risk and is insensitive because of sampling error related to the patchy distribution of the disease, as well as high interobserver variability on histologic analysis: 10% to 22% sensitivity according to some investigators (17–20,29,30). In 34 patients presenting with MI and normal coronary angiograms, Dec et al. (10) reported a 30% rate of histologically proven myocarditis; this prevalence is probably underestimated for the same reasons. Immunohistologic techniques seem more sensitive (31). However, this is still an invasive technique that is not routinely used, especially during the acute phase of MI. The other main etiologic hypothesis in these patients is acute MI, which is difficult to diagnose in the absence of visible coronary spasm or thrombus on the angiogram. In practice, after coronary angiography has

Table 3. Electrocardiographic, Echocardiographic and Scintigraphic Follow-Up Data (n = 45)

	AMA Negative (n = 8)	Diffuse AMA Uptake (n = 17)	Focal AMA Uptake/Normal Tl Scan (n = 18)	Focal AMA Uptake/Matched Tl Defect (n = 2)
ECG normalization	4/6 (75%)	8/11 (73%)	9/13 (69%)	2/2 (100%)
Echocardiographic normalization	5/5 (100%), 1*	8/10 (80%), 5*	9/11 (82%), 2*	1/1 (100%), 1*
Scintigraphic normalization		2/3 (66.6%)	4/4 (100%)	

*Number of patients with an abnormal initial echocardiogram who were lost to follow-up.
Abbreviations as in Table 2.

JACC Vol. 37, No. 3, 2001
March 1, 2001:786–92

been performed, a reliable noninvasive tool for assessing myocardial damage is required.

Diagnostic role of AMA scintigraphy. Indium-111–AMA scintigraphy, using antibodies specific for damaged myocytes, allows in vivo detection of recent myocytic necrosis, no matter what the cause and mechanism of cell damage (32). Although this cannot prove myocardial inflammation, it was shown to be a reliable noninvasive technique for the diagnosis of myocarditis by demonstrating myocytic damage induced by the inflammatory process. Compared with histologic analysis alone, it has 80% to 100% sensitivity and an apparent lack of specificity (~60%) (20,21). Compared with coupled histologic and immunohistologic data, Kühl et al. (31) reported a sensitivity of 66% and a good specificity of 71%. Indium-111–AMA scintigraphy also allows detection of MI (>90% sensitivity) (33). Besides myocarditis and MI, the other main causes of positive AMA scintigraphy are toxic cardiac injury and IDC, which do not concern our study patients (34–36). In our study, AMA scintigraphy detected myocardial damage in 82% of patients.

Indium-111–AMA/^{201}Tl scintigraphic pattern of MI. Acute MI, whatever its mechanism (coronary occlusion with spontaneous reperfusion or prolonged coronary spasm), implies a no-flow phenomenon in a coronary artery. Therefore, the resulting myocardial necrosis is confluent, occurs in the area depending on the infarct-related artery and induces intense segmental AMA uptake and a matched perfusion and metabolism defect, as previously reported (37,38). None of these mechanisms can explain diffuse LV (or right ventricular) myocardial AMA uptake (38% of our patients) or focal and poorly systematized AMA uptake without a matched ^{201}Tl defect (40% of our patients). It is of little clinical value that no spastic episode occurred in any of the patients, neither before the time of the study nor during the follow-up period. Also, no coronary thrombus or spasm was observed in six patients who had coronary angiography during chest pain; one of them (Fig. 2) also had intracoronary contrast echocardiography, which did not show evidence of any flux abnormality of the microvasculature.

A normal ^{201}Tl scan can be observed after rapidly reperfused MI (20% of patients in a previous study done at our institution) (39). However, in such cases, myocytic necrosis is probably not detectable with AMA scintigraphy 11 ± 6 days after the acute episode, for two reasons: 1) these cases probably correspond with limited nontransmural MI with mild myocytic necrosis, because, according to Khaw et al. (40), there is an inverse correlation between the intensity of AMA uptake and that of early and late ^{201}Tl uptake; and 2) 11 ± 6 days after this transient and mild necrotic process, AMA uptake is probably not significant, because part of the necrosed myocytes has been removed by macrophages. In our experience, in patients with a recent acute MI and angioplasty during the acute phase, only two scintigraphic patterns were observed: a ^{201}Tl defect with matched focal AMA uptake or a normal ^{201}Tl scan with a negative AMA scan. Finally, in this study, a scintigraphic pattern typical of acute MI was observed in only two patients.

Indium-111–AMA/^{201}Tl scintigraphic pattern of myocarditis. Diffuse myocardial AMA uptake is typical of diffuse myocarditis (10,20–22). Thallium-201 scintigraphy shows no defect in most of these cases because of the patchy distribution of the necrosed myocytes, which coexist with viable cells (23,24,41). Histologically proven myocarditis also has been previously reported in patients with focal AMA uptake but no ^{201}Tl defect, as found in two patients of our series (41). Other investigators have not mentioned this scintigraphic pattern in myocarditis. However, their study group and methodology were different from ours, with a higher proportion of patients with decreased LVEF (associated with diffuse AMA uptake [Table 2]) and no tomographic AMA acquisitions, which are needed to precisely determine the topography of AMA uptake (10,22). The main hypothesis for this scintigraphic pattern is that we detect only part of a diffuse but heterogeneous process of myocardial injury at the site where it is intense and/or recent enough to be detected. Thus, 50% of our patients with diffuse AMA uptake had markedly increased uptake in one particular region corresponding to the ECG and regional wall motion abnormalities; two of these patients had a ^{201}Tl defect. Focal confluent necrosis in diffuse myocarditis has previously been reported in a study with postmortem histologic examination (42). The hypothesis of strictly focal myocarditis has also been suggested. Experimental viral infections and meticulous attention at necropsy and biopsy frequently confirm myocarditis to be a focal or multifocal myocardial lesion (27,28,43–45). It is worth noting that initial and residual segmental wall motion abnormalities, as well as the presence of coronary artery disease, do not exclude the diagnosis of myocarditis (9–14,27,28,42–44).

In our study, focal AMA uptake was preferentially seen in the lateral and apical LV walls, suggesting that the necrotic process is more intense in these segments. In a previous autopsy study, gross myocardial lesions were more often seen in the LV free wall than in the septal wall (46). In a study using percutaneous cardioscopy, the authors performed biopsy in the three wall segments that did not exhibit normal brown color, usually the apical, lateral and inferobasal segments in each patient; this may suggest that these locations were preferentially involved by the process (47). Methodologic reasons may explain a lack of detection of focal inferior AMA uptake—that is, because of high liver AMA activity, which is just close to the inferior wall of the LV. However, they cannot clearly explain an eventual lack of detection in the anterior or septal walls or false positive images in the apex. As an indirect confirmation of apical involvement in our cases of pure apical or apicolateral AMA uptake (n = 14), it is worth noting that wall motion abnormalities, when present (10 of 14 patients), always concerned the apex.

Patients with negative scintigraphy. Scintigraphy was performed in the same delay in patients with AMA-negative and AMA-positive scans (9.5 ± 5.2 vs. 11.4 ± 6.9 days; p = NS).

The initial characteristics and follow-up data of patients with AMA-negative scans suggest that, like the others, they had experienced an acute episode of myocardial injury, but less intense and too mild to be detected by ^{111}In-AMA/^{201}Tl scintigraphy. It could be mild or limited myocarditis (reported sensitivity of AMA scintigraphy is 66% to 100%) or transient troncular ischemia or occlusion leading to a limited nontransmural myocardial necrosis.

Prognosis of patients. Short-term follow-up of patients with a pattern of myocarditis showed a favorable course of the disease in the majority, but not all, of them; there was complete LV functional recovery in 81% and scintigraphic normalization in six of seven patients. Given some data previously reported in patients with MI and normal coronary angiograms, and because numerous arguments suggest a relation between myocarditis and IDC, more attention should be paid to the long-term follow-up of these patients (1–5,48). It is worth noting that in one of our patients, the control scintiscan showed persistent AMA uptake while echocardiography was normalized at the same time; this suggests that a milder but chronic process of myocardial damage persisted even though the acute episode had been resolved.

Study limitations. Endomyocardial biopsy was not performed in most cases because the risk was considered too high in these patients who potentially had acute MI. We did not perform systematic ergonovine testing because of the absence of legal authorization at the time of the study.

Conclusions. In this prospective series of 45 patients presenting with MI and normal coronary angiograms, the clinical, ECG, scintigraphic and follow-up data were conclusive for diffuse myocarditis in 17 patients (38%) and suggested diffuse heterogeneous or focal myocarditis in 18 patients (40%). Short-term follow-up showed complete LV functional recovery in 81% of these patients. Because many arguments suggest a relation between myocarditis and IDC (especially identical immune phenomena), these findings prompt us to pay more attention to the anticardiac autoimmune status and to long-term follow-up of these patients (1–5,8).

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REFERENCES

1. Dec GW, Palacios IF, Fallon JT, et al. Active myocarditis in the spectrum of acute dilated cardiomyopathies. N Engl J Med 1983;312:885–90.
2. Sole MJ, Liu P. Viral myocarditis: a paradigm for understanding the pathogenesis and treatment of dilated cardiomyopathy (abstr). J Am Coll Cardiol 1993;22 Suppl A:99A–105A.
3. Kasper EK, Agema WRP, Hutchins GM, Deckers JP, Hare JM, Baughman KL. The causes of dilated cardiomyopathy: a clinicopathologic review of 673 consecutive patients. J Am Coll Cardiol 1994;23:586–90.
4. Why HJ, Meany BT, Richardson PJ, et al. Clinical and prognostic significance of enteroviral RNA in the myocardium of patients with myocarditis or dilated cardiomyopathy. Circulation 1994;89:2582–9.
5. Luppi P, Rudert WA, Zanone MM, et al. Idiopathic dilated cardiomyopathy: a superantigen-driven autoimmune disease. Circulation 1998;98:777–85.
6. Grogan M, Redfield MM, Bailey KR, et al. Long-term outcome of patients with proven myocarditis: comparison with idiopathic dilated cardiomyopathy. J Am Coll Cardiol 1995;26:80–4.
7. McCarthy RE, Boehmer JP, Hruban RH, et al. Long-term outcome of fulminant myocarditis as compared with acute (nonfulminant) myocarditis. N Engl J Med 2000;342:734–5.
8. Lauer B, Schannwell M, Kühl U, Strauer BE, Schultheiss HP. Antimyosin autoantibodies are associated with deterioration of systolic and diastolic left ventricular function in patients with chronic myocarditis. J Am Coll Cardiol 2000;35:11–8.
9. Costanzo-Nordin MR, O'Connel JB, Subramanian R, Robinson JA, Scanion PJ. Myocarditis confirmed by biopsy presenting as acute myocardial infarction. Br Heart J 1985;53:25–9.
10. Dec GW, Waldman H, Southern J, Fallon JT, Hutter AM, Palacios I. Viral myocarditis mimicking acute myocardial infarction. J Am Coll Cardiol 1992;20:85–9.
11. Narula J, Khaw BA, Dec W, et al. Brief report: recognition of acute myocarditis masquerading as acute myocardial infarction. N Engl J Med 1993;328:100–4.
12. Silverman AJ, Kapadia N, Borin AJ. Acute myocarditis presenting as acute myocardial infarction. J Am Osteopath Assoc 1995;95:278–80.
13. Raev D. Acute staphylococcal myocarditis masquedaring as an acute myocardial infarction. Int J Cardiol 1997;60:95–8.
14. Galiuto L, Enriquez-Sarano M, Reeder, et al. Eosinophilic myocarditis manifesting as myocardial infarction: early diagnosis and successful treatment. Mayo Clin Proc 1997;72:6–10.
15. Betriu A, Pare JC, Sanz GA, et al. Myocardial infarction with normal coronary arteries: a prospective clinical-angiographic study. Am J Cardiol 1981;48:28–32.
16. Lindsay J, Pichard AD. Acute myocardial infarction with normal coronary arteries. Am J Cardiol 1984;54:902–4.
17. Chow LH, Radio SJ, Sears TD, McManus BM. Insensitivity of right endomyocardial biopsy in the diagnosis of myocarditis. J Am Coll Cardiol 1989;14:915–20.
18. Mason JW, O'Connel JB, Herskowitz, et al. A clinical trial of immunosuppressive therapy for myocarditis. N Engl J Med 1995;333:269–75.
19. Davidson CJ, Fishman RF, Bonow RO. Cardiac catheterization. In: Braunwald E, editor. Heart Disease. Philadelphia: W.B. Saunders, 1997:1202–4.
20. Dec GW, Palacios IF, Yasuda T, et al. Antimyosin antibody cardiac imaging: its role in the diagnosis of myocarditis. J Am Coll Cardiol 1990;16:97–104.
21. Narula J, Khaw BA, Dec W, et al. Diagnostic accuracy of antimyosin scintigraphy in suspected myocarditis. J Nucl Cardiol 1996;3:371–81.
22. Lambert K, Isaac D, Hendel R. Myocarditis masquerading as ischemic heart disease: the diagnostic utility of antimyosin imaging. Cardiology 1993;82:415–22.
23. Sarda L, Georges C, Assayag P, et al. Utility of ^{111}In-antimyosin scintigraphy for the diagnosis of myocardial damage in systemic sclerosis. J Nucl Med 1997;38:1759–61.
24. Sarda L, Georges C, Assayag P, et al. ^{111}Indium antimyosin antibody imaging of primary myocardial involvement in systemic diseases. Ann Rheum Dis 1999;58:90–5.
25. Le Guludec D, Lhote F, Weinmann P, et al. New application of myocardial antimyosin scintigraphy: diagnosis of myocardial disease in polymyositis. Ann Rheum Dis 1993;52:235–8.
26. Aretz HT. Myocarditis: the Dallas criteria. Hum Pathol 1987;18:619–24.
27. Olsen ECJ. Myocarditis: a case of mistaken identity? Br Heart J 1983;46:1227–34.
28. Spodick DH. Infection and infarction: acute viral (and other) infection

in the onset, pathogenesis, and mimicry of acute myocardial infarction. Am J Med 1986;81:661–8.
29. Billingham MB. Acute myocarditis: a diagnostic dilemna. Br Heart J 1987;58:6–8.
30. Hauck AJ, Kearney DL, Edwards WD. Evaluation of post-mortem endomyocardial biopsy specimen from 38 patients with lymphocytic myocarditis: implications for role of sampling error. Mayo Clin Proc 1989;64:1235–45.
31. Kühl U, Lauer B, Souvatzoglou M, Vosberg H, Schultheiss HP. Antimyosin scintigraphy and immunohistologic analysis of endomyocardial biopsy in patients with clinically suspected myocarditis: evidence of myocardial cell damage and inflammation in the absence of histologic signs of myocarditis. J Am Coll Cardiol 1998;32:1371–6.
32. Khaw BA, Scott J, Fallon JT, Haber E. Myocardial injury quantitation by cell sorting method with antimyosin fluorescent spheres. Science 1982;217:1050–3.
33. Johnson LL, Seldin DW, Becker LC, et al. Antimyosin imaging in acute transmural infarctions: results of a multicenter clinical trial. J Am Coll Cardiol 1989;13:27–35.
34. Obrador D, Ballester M, Carrio I, Berna L, Pons-Llado G. High prevalence of myocardial antimyosin antibody uptake in patients with chronic idiopathic dilated cardiomyopathy. J Am Coll Cardiol 1989; 13:1289–93.
35. Carrio I, Estorch M, Berna L, Duncker C, Torres G. Cumulative dose of doxorubicin and severity of myocardial damage assessed by antimyosin monoclonal antibody studies. J Nucl Med 1991;32:1019–20.
36. Ballester MD, Marti V, Carrio I, et al. Spectrum of alcohol-induced myocardial damage detected by In-111–labeled monoclonal antimyosin antibodies. J Am Coll Cardiol 1997;2:160–7.
37. Johnson LL, Lerrick KS, Coromilas J, et al. Measurement of infarct size and percentage myocardium infarcted in a dog preparation with single-photon emission computed tomography, thallium-201, and indium-111 monoclonal antimyosin Fab. Circulation 1987;76:181–90.
38. Morguet AJ, Munz DL, Kreuzer H, Emrich D. Simultaneous double nucleotide scintigraphy with indium-111 antimyosin Fab and technetium sestamibi for evaluation of myocardial viability after experimental and clinical infarct. Z Kardiol 1996;85:388–94.
39. Faraggi M, Karila-Cohen D, Brochet E, et al. The relation between reverse redistribution in thallium scans, microvascular perfusion, myocardial viability and late regional wall motion after acute myocardial infarction. J Nucl Med 2000;41:393–9.
40. Khaw BA, Strauss W, Pohost G, Fallon JT, Katus AK, Haber E. Relation of immediate and delayed thallium-201 distribution to localization of iodine-125 antimyosin antibody in acute experimental myocardial infarction. Am J Cardiol 1983;51:1428–32.
41. Yamada T, Matsumori A, Tamaki N, Nohara R, Konishi J, Sasayama S. Indium-111 antimyosin antibody imaging: a comparative myocardial scintigraphic study using single-photon emission computed tomography in patients with myocarditis and dilated cardiomyopathy. Jpn Circ 1997;61:827–35.
42. Saffitz JE, Schwartz DJ, Southwork W, et al. Coxsackie viral myocarditis causing transmural right and left ventricular infarction without coronary narrowing. Am J Cardiol 1983;52:644–7.
43. Nicholls AC, Thomas M. Coxsackie virus infection in acute myocardial infarction. Lancet 1977;23:883–4.
44. Desa'Neto A, Bullington JD, Bullington RH, Desser KB, Benchimol A. Coxsackie B5 heart disease: demonstration of inferolateral wall myocardial necrosis. Am J Med 1980;68:295–8.
45. Parillo JE, Aretz HT, Palacios I, Fallon JT, Block PC. The results of transvenous endomyocardial biopsy can frequently be used to diagnose myocardial disease in patients with idiopathic heart failure: endomyocardial biopsy in 100 consecutive patients revealed a substantial incidence of myocarditis. Circulation 1984;69:93–101.
46. Shirani J, Freant LJ, Roberts WC. Gross and semiquantitative histologic findings in mononuclear cell myocarditis causing sudden death, and implications for endomyocardial biopsy. Am J Cardiol 1993;72:952–7.
47. Uchida Y, Nakamura F, Hirose J, et al. Cardioscopic spectrum of the left ventricular endocardial surface and its relation to histologic changes in idiopathic mocarditis. Am Heart J 1996;131:107–14.
48. Raymond R, Lynch J, Underwood D, Leatherman J, Razavi M. Myocardial infarction and normal coronary arteriography: a 10-year clinical and risk analysis of 74 patients. J Am Coll Cardiol 1988;11: 471–7.