Role of Noninvasive Antimyosin Imaging in Infants and Children with Clinically Suspected Myocarditis

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Endomyocardial biopsy is an invasive procedure, often performed on children for the diagnosis of myocarditis, and is not without risk. Therefore, a noninvasive test of adequate diagnostic accuracy is highly desirable. We evaluated the role of antimyosin scintigraphy in infants and children with clinically suspected myocarditis. **Methods:** Forty patients (age range, 2 mo to 14 y) with suspected myocarditis underwent ^{111}In-antimyosin scintigraphy. All patients were clinically followed for 29 ± 17 mo; 21 patients underwent serial antimyosin scans (3.8 ± 1.7 per patient). The antimyosin uptake was assessed by heart-to-lung ratio (HLR). The scan results were compared with endomyocardial biopsy results in 22 patients. **Results:** Thirty-five of the 40 patients showed abnormal antimyosin findings; 17 patients showed intense myocardial antimyosin uptake (HLR > 2). The HLR was higher in patients presenting within the first 2 mo of illness (2.09 ± 0.43 vs. 1.74 ± 0.34, $P = 0.01$). Of 22 patients with endomyocardial biopsy, 17 demonstrated myocarditis. All 9 patients who had an HLR > 2 and underwent endomyocardial biopsy had histologic evidence of myocarditis. Of the remaining 13 patients with HLR < 2, 8 had biopsy-verified myocarditis (62%). The intensity of antimyosin uptake was the major determinant of survival in children, with a relative risk of 18 (confidence interval, 1.34–242; $P = 0.027$). High antimyosin uptake (HLR > 2) seen within 2 mo of the onset of symptoms was associated with a higher mortality rate. The survivors with an HLR > 2 and those with an HLR < 2 showed a high likelihood of complete functional recovery. Furthermore, the patients with serial antimyosin scans having persistently positive findings showed a poor clinical outcome. **Conclusion:** Intense myocardial uptake of antimyosin antibody is a reliable indicator of myocarditis in infants and children. Severe myocardial damage detected in the early phase of disease is associated with a higher mortality rate. The persistence of antimyosin uptake is associated with poor clinical outcomes.

Myocarditis is a histologic diagnosis comprising a combination of myocardial inflammation and myocyte necrosis (1). Acute myocarditis in children can be a fulminating illness and may result in significant morbidity and mortality (2–8). The clinical presentation of myocarditis is highly variable and predominantly includes ventricular dysfunction and ventricular arrhythmias. Endomyocardial biopsy is often performed for the diagnosis of myocarditis (2–8). The diagnosis of myocarditis early after clinical presentation predicts a significant recovery of left ventricular systolic function and has been used in critically ill children to avoid premature consideration of transplantation (2). However, endomyocardial biopsy is an invasive procedure and is not without risk in the pediatric age group (2); therefore, a noninvasive diagnostic test of adequate sensitivity and specificity is highly desirable.

[111]In-Antimyosin imaging has been used for the diagnosis and prognosis of myocarditis in adults (9–13). Antimyosin antibody injected intravenously selectively localizes in necrotic myocytes, which have lost the integrity of their sarcolemma and have exposed intracellular myosin to the extracellular milieu (14,15). If labeled appropriately, the localization of antimyosin antibody in regions of myocardial necrosis can be noninvasively visualized by radionuclide imaging (15). Because myocyte necrosis in myocarditis is multifocal, diffuse antibody uptake occurs in the cardiac region (11). The results of antimyosin scanning have been reported to be almost always positive when the biopsy is positive for myocarditis, and negative antimyosin findings are almost never associated with a positive biopsy (12). The feasibility of this noninvasive technique for the detec-

tion of myocarditis in the pediatric age group has not been evaluated.

In the present study, we evaluate the role of ^{111}In-anti-myosin scintigraphy in children with clinically suspected myocarditis. We also evaluated the impact of the severity of myocardial damage detected at the time of presentation on survival and recovery of systolic ventricular function. The evolution of myocardial damage was also examined by repeated antimyosin scanning.

MATERIALS AND METHODS

From January 1988 to December 1995, 40 children (15 male and 25 female; mean age [±SD], 39 ± 48 mo; range, 2 mo to 14 y) presenting with symptoms suggestive of myocarditis were evaluated by ^{111}In-antimyosin antibody scanning. Of the 40 patients, 35 presented with congestive heart failure (87%) and 7 with serious ventricular tachyarrhythmias (17%). Four children (10%) presented in the emergency room with cardiogenic shock. A history suggestive of preceding viral illness or fever was recorded for 22 patients (55%). Eleven patients (28%) presented with weight loss and failure to thrive. Nonspecific electrocardiographic abnormalities were observed in 29 patients (72%). The mean left ventricular fractional shortening at echocardiography was 0.18 ± 0.07; only 5 patients had normal left ventricular systolic function. None of the patients had any systemic or familial illness, metabolic disorder, or structural cardiac disease at echocardiography. The interval between the onset of symptoms and initial presentation was 2.67 ± 3 mo. Of the 40 patients, 28 presented for medical attention within 2 mo of the onset of illness.

The 40 patients were clinically followed for 29 ± 17 mo (range, 1–67 mo) for the assessment of mortality rate, need for transplantation, and persistence of or complete recovery of left ventricular systolic dysfunction.

Antimyosin Antibody Scintigraphy

Of the 40 patients, 3 infants needed chloral hydrate for sedation before the antimyosin scan was obtained. A dose of 125–250 µg of monoclonal antimyosin antibody coupled with diethylenetriamine pentaacetic acid (R11D10-Fab-DTPA; Centocor) was labeled with 18.5–37.0 MBq of ^{111}In-chloride and administered intravenously. Imaging was undertaken at 48 h using a conventional large-field-of-view camera with a high-resolution medium-energy collimator and a 20% window centered on the 247- and 173-keV energy peaks. A minimum of 500,000 counts between 5 and 10 min was collected, and analog and digital images in a 128×128 matrix were stored for subsequent analysis. Radiation-absorbed dose in the myocardial wall with standard doses is estimated as 0.0153 Gy and to the total body dose as 0.0086 Gy (Centocor). An independent observer who was unaware of the clinical data interpreted the antibody studies. Semiquantitative estimation of antimyosin antibody uptake was performed by calculation of the heart-to-lung ratio (HLR) to allow objective assessment of the images and comparison of the serial antimyosin scans (13). An HLR of 1.58 was used as the cutoff point to differentiate antimyosin studies with normal findings from those with abnormal findings. The cutoff value was derived from the mean HLRs observed in the visually normal studies + 2 SDs.

All 40 patients underwent antimyosin scintigraphy at the time of initial presentation. All patients who demonstrated positive scan findings were advised to undergo follow-up scanning at 3, 6, and 12 mo and then once every year. Informed parental consent for serial scanning was obtained for 21 patients. These patients were followed for 30 ± 14 mo, with 3.8 ± 1.7 follow-up antimyosin scans per patient.

Endomyocardial Biopsy

Right ventricular endomyocardial biopsy of the ventricular septum was performed with a Cordis bioptome through the right femoral vein. Five to 7 biopsy specimens averaging 1.5 mm in diameter were obtained and processed conventionally for light microscopy. Histologic sections from paraffin-embedded specimens were stained with hematoxylin and eosin and the Masson stain and analyzed for inflammation, myocyte necrosis, myocardial hypertrophy, and interstitial fibrosis. Specimens were considered to show myocarditis if they contained mononuclear cell infiltration surrounding or adjacent to necrotic myocytes, as defined by the Dallas criteria (1). A focal increase in interstitial mononuclear cells without associated myocyte necrosis was reported as borderline myocarditis. No procedure-related complications occurred.

Of the 40 children, 22 with abnormal antimyosin findings underwent right ventricular endomyocardial biopsy for histologic confirmation of the disease. Endomyocardial biopsy was not suggested to the patients with negative antimyosin findings. We decided not to perform biopsy on these children because negative antimyosin findings are highly predictive of absence of myocarditis in adult patients (12).

Immunosuppressive Treatment and Follow-up

The attending physicians decided whether to treat with immunosuppressive agents predominantly on the basis of the clinical status of congestive heart failure, the intensity of antimyosin findings, and evidence of myocarditis or borderline myocarditis if endomyocardial biopsy samples were available for examination. Of 40 patients, 16 were treated with immunosuppressive treatment comprising azathioprine and prednisone for 3 mo. Azathioprine was used orally at doses of 2 mg/kg of body weight and was further titrated on the basis of the white blood cell count. Prednisone was administered at 1 mg/kg of body weight as a single daily dose. The clinical outcomes of these 16 patients were compared with the those of the remaining 24 patients to assess the efficacy of immunosuppressive therapy.

Of the 16 patients who were treated with immunosuppression, 13 had histologic evidence of myocarditis or borderline myocarditis. All 16 patients had positive antimyosin findings; 15 had congestive heart failure with a mean left ventricular fractional shortening of 0.16 ± 0.04. These 16 patients had presented for medical attention 2.72 ± 2.5 mo after the onset of symptoms. Of 24 patients who did not receive immunosuppression, only 3 had histologic evidence of myocardial inflammation and 16 demonstrated positive antimyosin findings. Twenty-two of the 24 patients had congestive heart failure (P = not statistically significant [NS]) with left ventricular fractional shortening of 0.19 ± 0.09 (P = NS) and had presented at the hospital within 2.65 ± 3.4 mo of the onset of symptoms.

Statistical Analysis

Myocardial uptake of antimyosin antibody was semiquantitatively assessed by calculation of HLR and is represented as mean ± SD. The significance of differences in antimyosin uptake in various groups classified on the basis of time of presentation and clinical outcomes were initially tested by nonparametric analysis using the Mann–Whitney or Wilcoxon test. Serial changes in

antimyosin uptake and echocardiographic variables in individual patients were compared by 2-way ANOVA. The determinants of clinical outcome were analyzed by the univariate and multivariate Cox regression models, and the survival curves and probability of temporal resolution of left ventricular systolic dysfunction was evaluated by the Kaplan–Meier statistic. χ^2 was used to compare proportional figures.

RESULTS

Antimyosin Uptake and Histologic Evidence of Myocarditis

Thirty-five of the 40 patients (87%) demonstrated abnormal antimyosin findings (Fig. 1). The scintigraphic studies had normal findings in the remaining 5 patients. The mean HLR of antimyosin uptake in the patients with abnormal findings was 2.08 ± 0.42. Of the 35 patients with abnormal findings, 17 demonstrated intense myocardial antimyosin uptake, with an HLR > 2, and the remaining 18 demonstrated an HLR < 2. Antimyosin uptake was significantly higher in patients presenting with cardiogenic shock (mean HLR, 2.4 ± 0.53 vs. 1.94 ± 0.4; $P = 0.04$) (Table 1). In addition, the patients who presented within 2 mo of the onset of illness demonstrated higher antimyosin uptake (mean HLR, 2.09 ± 0.43) than did those presenting during the later phase (mean HLR, 1.74 ± 0.34; $P = 0.01$) (Fig. 2A).

Endomyocardial biopsy results were available for 22 patients. Of these, 17 had biopsy samples demonstrating histologic evidence of myocarditis ($n = 11$; Fig. 1) or borderline myocarditis ($n = 6$); no diagnostic abnormality was observed in the remaining 5 patients. Although a higher prevalence of myocarditis was observed in the first 2 mo

(86%) than in the later phase of the disease (63%), the difference was not significant statistically. All 9 patients who had an HLR > 2 and underwent endomyocardial biopsy demonstrated histologic evidence of myocarditis ($P < 0.01$). In contrast, 13 patients had an HLR < 2 and 8 had biopsy-verified myocarditis (62%) (Fig. 2B).

Antimyosin Uptake, Clinical Outcomes, and Survival Trends

Univariate and multivariate analyses of various clinical and investigative variables were undertaken to identify determinants of clinical outcome (Table 2). Left ventricular fractional shortening, cardiogenic shock, and HLR were the only determinants of survival on univariate analysis. Upon multivariate analysis, fractional shortening (relative risk, 90.897; 95% confidence interval, $4.4-\infty$; $P = 0.02$) and antimyosin HLR were the determinants of survival (relative risk, 6.6; 95% confidence interval, $1.2-36$; $P = 0.02$). However, if the patient presented during the first 2 mo of illness, HLR was the sole prognostic determinant in univariate as well as in multivariate analysis (relative risk, 18; 95% confidence interval, $1.34-242$; $P = 0.027$) (Figs. 3A–3C).

Twenty-eight patients had presented within the first 2 mo of disease. Of these, 16 demonstrated an HLR > 2 (mean HLR, $2.42 \pm 0.0.27$). Six of these 16 patients died of congestive heart failure, and 1 patient continued to demonstrate left ventricular dysfunction, whereas 9 patients achieved complete recovery of left ventricular systolic function. The remaining 12 of the 28 patients presenting during the first 2 mo had an HLR < 2 (mean HLR, 1.71 ± 0.17;
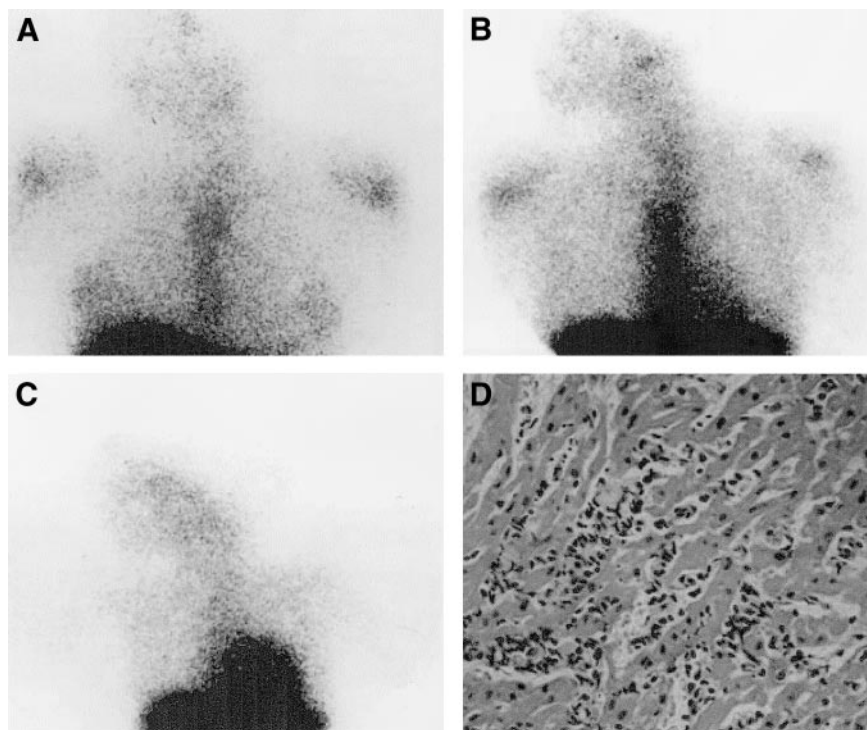

FIGURE 1. (A) Absence of myocardial antimyosin uptake (HLR = 1.4) in a scan with normal findings. (B) Moderate myocardial antimyosin uptake (HLR = 1.8) in a patient with myocarditis. (C) Intense myocardial antimyosin uptake (HLR = 2.5) in a patient with biopsy-verified myocarditis. (D) Right ventricular endomyocardial biopsy demonstrating a central focus of necrotic myocytes surrounded by lymphomononuclear cell infiltrate (arrows) diagnostic of myocarditis (hematoxylin and eosin, ×200).

TABLE 1
Clinical Features Associated with Antimyosin Uptake and Correlation with HLR

| Parameter | Presence of uptake | | Absence of uptake | | P | r |
	n	HLR (mean ± SD)	n	HLR (mean ± SD)		
Clinical feature						
Shock	4	2.40 ± 0.53	36	1.94 ± 0.40	0.04	
CHF	35	1.98 ± 4.40	5	1.90 ± 0.40	NS	
Dyspnea	22	2.09 ± 0.38	18	1.92 ± 0.50	NS	
Orthopnea	9	2.16 ± 0.44	31	1.97 ± 0.43	NS	
Gallop rhythm	17	2.09 ± 0.43	23	1.96 ± 0.43	NS	
Hepatomegaly	30	2.06 ± 0.44	10	1.88 ± 0.39	NS	
Sweat/edema	16	2.12 ± 0.46	24	1.94 ± 0.46	NS	
Tachyarrhythmia	7	1.91 ± 0.46	33	2.04 ± 0.43	NS	
Fever	22	2.02 ± 0.43	18	2.00 ± 0.46	NS	
Preceding respiratory illness	6	1.71 ± 0.18	34	2.07 ± 0.45	NS	
Failure to thrive	11	1.75 ± 0.27	29	2.11 ± 0.45	0.016	
Altered repolarization	29	2.00 ± 0.40	11	2.02 ± 0.45	NS	
Low QRS voltage	10	2.27 ± 0.40	30	1.93 ± 0.42	0.03	
CTR > 60	35	2.05 ± 0.44	5	1.77 ± 0.29	NS	
LVH	7	2.00 ± 0.36	33	2.02 ± 0.45	NS	
LVD	36	2.00 ± 0.43	4	2.14 ± 0.51	NS	
RVD	5	2.19 ± 0.20	35	2.00 ± 0.45	NS	
MR	30	2.05 ± 0.43	10	1.90 ± 0.44	NS	
Correlation with HLR						
Age (mo)					NS	0.036
Time interval					0.016	−0.377
Cardiac rate					0.05	0.296
LV fractional shortening					NS	0.086
LV ejection fraction					NS	−0.001

CHF = congestive heart failure; CTR = cardiothoracic ratio; LVH = left ventricular hypertrophy; LVD = left ventricular dilatation; RVD = right ventricular dilatation; MR = mitral regurgitation.

$P < 0.0001$). Of these 12, 11 patients demonstrated complete resolution of left ventricular function and only 1 patient had a persistently low ejection fraction (Fig. 4).

The remaining 12 of the 40 patients presented for medical attention more than 2 mo after the onset of illness. Clinical outcome was variable in these patients. Eleven patients had an HLR < 2; 2 of these patients died, 4 continued to show left ventricular dysfunction, and 5 recovered. The only patient with an HLR > 2 recovered completely.

Evolution of Myocardial Damage in Myocarditis

Twenty-one patients were followed for 30 ± 14 mo with serial antimyosin scanning. Of these, 4 patients died or underwent heart transplantation and 3 had persistent left ventricular dysfunction. In the remaining 14 patients, left ventricular function recovered.

Clinical outcomes were more favorable in patients showing complete resolution of myocardial antimyosin uptake ($P = 0.01$) (Fig. 5). Fifteen patients demonstrated complete resolution of antimyosin uptake in 14 ± 7 mo; the resolution of antimyosin uptake was accompanied by normalization of left ventricular systolic function in 13 patients (Fig. 5, middle panel). Of the remaining 6 patients who continued to demonstrate persistently positive scan results, 2 died awaiting transplantation and 3 continued to have severe left

ventricular systolic dysfunction (Fig. 5, bottom panel). Left ventricular function normalized completely in 1 remaining patient despite mildly positive antimyosin findings.

Impact of Immunosuppressive Therapy

Clinical outcomes were compared for 16 patients who received and 24 who did not receive immunosuppressive therapy. In the group receiving immunosuppressive therapy, 3 deaths occurred, compared with 5 in the untreated group. The number of patients with persistent left ventricular dysfunction was 2 and 4, respectively, in the 2 groups. Eleven and 15 patients, respectively, of the 2 groups completely recovered. However, the differences were NS (Kaplan–Meier probability = 0.79).

The patients with an HLR > 2 were also separately analyzed, since they were likely to have myocarditis based on the results shown above. Of the 17 patients with an HLR > 2, 9 received immunosuppressive therapy (mean HLR, 2.45 ± 0.3). Two of these 9 patients died, and 7 recovered completely. In contrast, 8 of the 17 patients did not receive immunosuppression (mean HLR, 2.43 ± 0.24; $P = NS$). Of these 8 patients, 4 died or received a transplant, 1 continued to show systolic dysfunction, and 3 recovered completely.
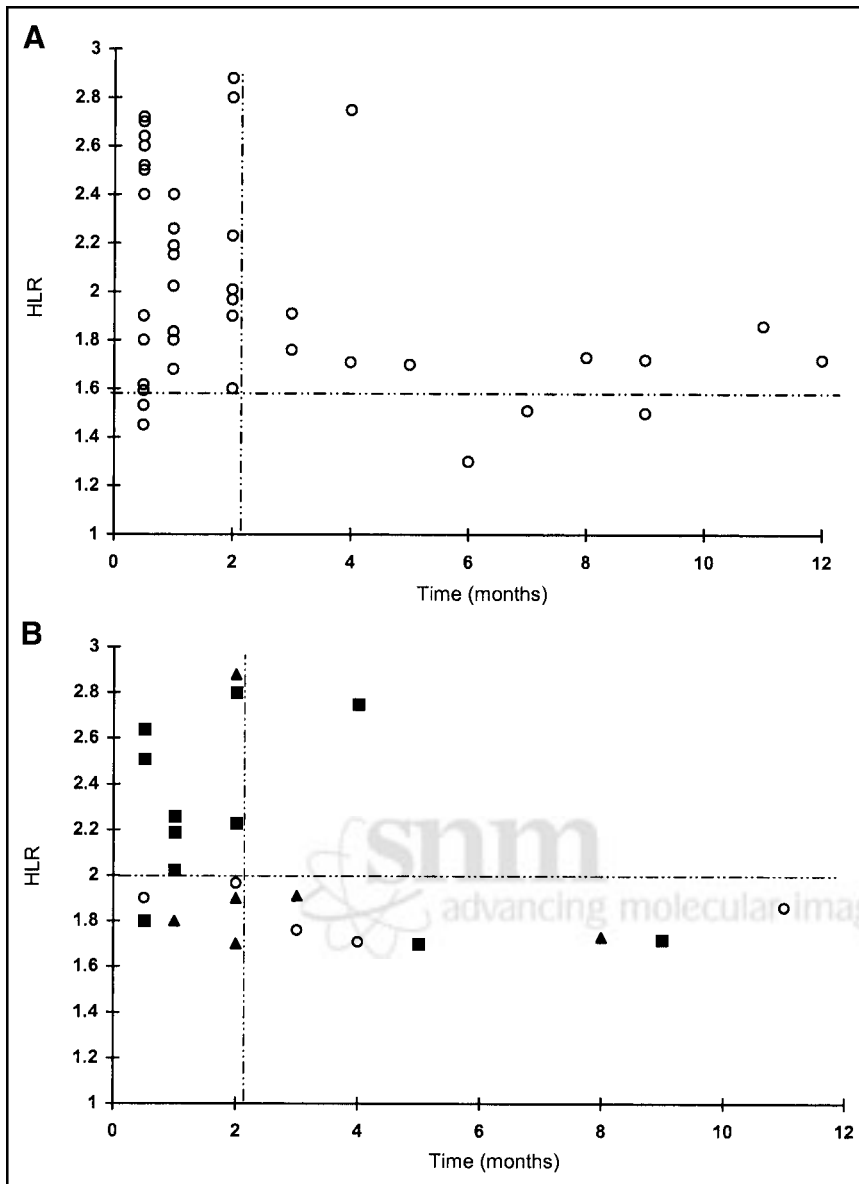
FIGURE 2. (A) Distribution of myocardial antimyosin uptake by the interval between the onset of symptoms and scintigraphy. The intensity of antimyosin uptake is presented as heart-to-lung uptake ratio, and the abnormal antimyosin result is defined by the dashed horizontal line at HLR > 1.58. A relatively higher HLR was observed in patients evaluated within 2 mo of illness (dashed vertical line). (B) Histologic findings from 22 patients who underwent endomyocardial biopsy, and comparison with intensity of antimyosin uptake and interval from onset of symptoms. The myocarditis is represented by ■ and borderline myocarditis by ▲; nondiagnostic biopsy is shown as ○. All patients with an HLR > 2 had histologic evidence of myocardial inflammation.

DISCUSSION

A viable cell must have an intact cell membrane that does not allow passage of macromolecules and maintains an osmotic gradient between the intracellular and extracellular milieus (*14*). Loss of cell membrane integrity allows cell swelling and heralds cell necrosis. In cardiomyocytes, loss of sarcolemma allows soluble intracellular macromolecules (such as troponin, creatine kinase, and myosin light chains) to wash out in the bloodstream and be measured as an indicator of severity of necrosis. On the other hand, the

TABLE 2
Univariate Regression Analysis Using the Cox Proportional Hazards Model

Parameter	Total			<2 Mo			≥2 Mo		
	RR	95% CI	P	RR	95% CI	P	RR	95% CI	P
Shock	6.2	1.12–34.4	0.034	5.4	0.9–33	0.06	—	—	—
LVFS	22,115	3.9–∞	0.02	1,535	0.2–∞	0.1	0.15	0–∞	0.15
HLR	6.6	1.2–36	0.02	18	1.34–242	0.027	0.92	0.03–27	0.96

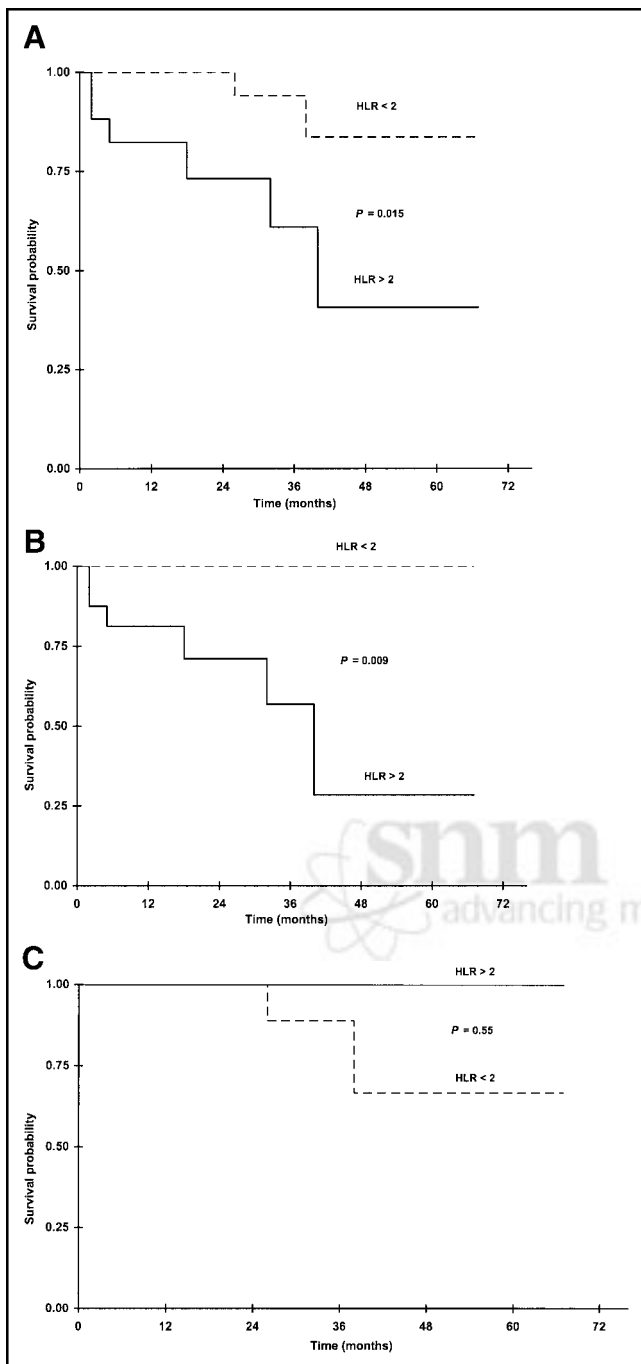RR = relative risk; CI = confidence interval; LVFS = left ventricular fractional shortening.

FIGURE 3. Kaplan–Meier curves for survival outcome (survival/heart transplantation) based on the intensity of antimyosin uptake in all patients (A), in patients evaluated within the first 2 mo of onset of illness (B), and in patients evaluated later (C).

insoluble macromolecules (such as heavy chains of myosin) remain immobilized until removed by the scavenger cells. An antibody specifically directed against the heavy chain of myosin (antimyosin antibody) allows differentiation of necrotic cells (with disintegrated sarcolemma) from viable cells (with intact sarcolemma) (15). The necrotic myocardial regions, which allow binding of antimyosin antibody to the exposed myosin heavy chain, can be noninvasively

localized by radionuclide imaging if the antibody is appropriately labeled with a γ-emitter and is administered intravenously. Antimyosin antibody has been successfully used for the detection of myocardial necrosis associated with acute myocardial infarction (16–18). Antibody uptake in infarction occurs discretely in the myocardial territory supplied by the occluded coronary artery (11). Cardiovascular disorders characterized by multifocal myocardial necrosis, such as myocarditis and cardiac allograft rejection, show diffuse antibody uptake in the cardiac region (9–13,19–21). All patients with histologically verified myocarditis have positive antimyosin scan findings representing high sensitivity (12). In contrast, no antimyosin-negative patients have biopsy evidence of myocarditis. Therefore, antimyosin antibody has been recommended as a useful screening tool in adults with suspected myocarditis (12). The feasibility of using antimyosin scintigraphy in children with clinically suspected myocarditis has not been investigated.

The present study revealed the significant diagnostic and prognostic utility of antimyosin scintigraphy in infants and children with suspected myocarditis. Intense myocardial uptake of antimyosin antibody with an HLR > 2 is almost invariably associated with biopsy-verified myocarditis. Of patients with an HLR < 2, almost half had histologic evidence of inflammation (Fig. 2).

The prognostic utility of antimyosin scanning was observed only when the test was performed during the first 2 mo of the disease (Fig. 3). Patients with evidence of severe myocardial damage as represented by an HLR > 2 had a bimodal outcome. Either these patients succumbed to severe congestive heart failure, or the survivors showed complete recovery of left ventricular function. It has been proposed that necrotic myocytes in myocarditis are associated with a large population of viable but functionally depressed myocytes (22). Whereas antimyosin-positive necrotic myocytes may determine an adverse outcome, viable and functionally depressed cells should contribute to functional recovery (Fig. 4). Similar outcomes of high antimyosin uptake have also been reported in doxorubicin hydrochloride cardiotoxicity (23), heart transplant rejection (21), and dilated cardiomyopathy in adults (24).

Compared with the bimodal outcome in patients with an HLR > 2, complete functional recovery was demonstrated in almost all patients who presented within 2 mo of illness but had an HLR < 2. The discriminatory value of antimyosin scintigraphy was lost if scanning was performed after 2 mo. Almost all patients had an HLR < 2 after 2 mo. It seems logical to propose that patients presenting relatively later in the course of disease have a more smoldering variety of cardiomyopathic process and are more likely to show persistent left ventricular dysfunction.

Myocyte damage is an integral component of various cardiovascular disorders and is an important determinant of long-term outcome. The resolution of myocardial damage observed in the present study was associated with complete functional recovery. On the other hand, most patients in
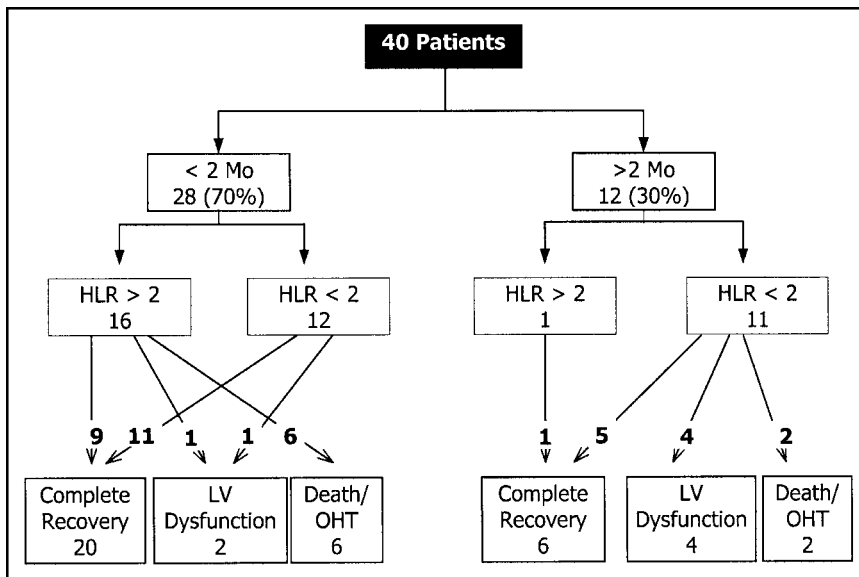
FIGURE 4. Schematic representation of clinical outcomes (death/heart transplantation [OHT], persistent left ventricular dysfunction, and complete recovery) based on the dichotomous distribution by intensity of antimyosin uptake and interval between onset of illness and scintigraphy.

whom antimyosin uptake did not resolve either died, received a transplant, or continued to show persistent left ventricular dysfunction (Fig. 5). A logical hypothesis would be that in patients with prolonged episodes or recurrences of myocardial damage, more irreversible damage of myocardial tissue will eventually develop and clinical outcome will be poor.

The present results describing the role of antimyosin imaging in children were predominantly similar to reported experience with adults. Almost all adults presenting within 4 wk of symptom onset had abnormal antimyosin findings regardless of initial left ventricular function (*24*). Similar to the pediatric population, 30% of the adult population had variable rates of resolution of myocardial damage, 25% had persistent low-grade myocardial damage, and the rest had frequent cycles of recurrence of myocardial damage (*24*). Resolution of myocardial damage was associated with improved left ventricular function, but the degree of resolution was not proportional to the extent of improvement in left ventricular ejection fraction. Recurrence of myocardial damage was not accompanied by significant depression of left ventricular function, and episodes of reactivation were largely asymptomatic.

The only significant difference between the 2 populations was the better correlation of positive antimyosin results with endomyocardial biopsy results in the pediatric population. In adults with clinically suspected myocarditis, no more than half the scans with positive findings were associated with a biopsy positive for myocarditis (*10,12*). This lack of correlation has been attributed to sampling error in the biopsy, because only a limited area of the right ventricular apex can be sampled. The sampling error in biopsies of children has been considered to be lower, but the reason for this lower error is unknown (*2*). Furthermore, immunosuppressive treatment has been shown ineffective for adult myocarditis. The statistical estimates in the present study

showed immunosuppression to have no significant impact on mortality from pediatric myocarditis either.

Noninvasive diagnosis is especially important in the pediatric population. Radiation burden and risk of immunologic reaction should be considered before clinical indication is established. Radiation-absorbed dose in the myocardial wall with standard doses in children (0.0153 Gy) is substantially lower than that received during cardiac catheterization and endomyocardial biopsy. The total-body dose of an antimyosin scan (0.0086 Gy) is also comparable to that of radiologic procedures currently widely used in pediatric diagnosis. Furthermore, the administration of 125–250 μg of the Fab fragments is not likely to carry any risk of immunologic reaction. The higher doses of this antibody fragment have been used extensively in different patient populations, and allergic reactions have not been reported even in patients injected up to 10 times (*20,21*).

The present study did not allow the specificity of antimyosin scintigraphy to be defined, since biopsies were not performed on patients with normal scan findings. The decision not to perform an invasive procedure such as biopsy on scan-negative patients was based on the very high predictive value of negative antimyosin scintigraphy results for excluding a diagnosis of myocarditis in adults. Another limitation of the study arose from the nonrandomized decision to treat with immunosuppressive agents. Evaluation of the efficacy of immunosuppression in the pediatric population was not the major objective of the present study and needs to be addressed by an independent prospective study. Furthermore, the intention to treat did not affect the diagnostic and prognostic implications of the study.

CONCLUSION

Imaging with ^{111}In-monoclonal antimyosin antibody provides a noninvasive means to reliably detect myocarditis.
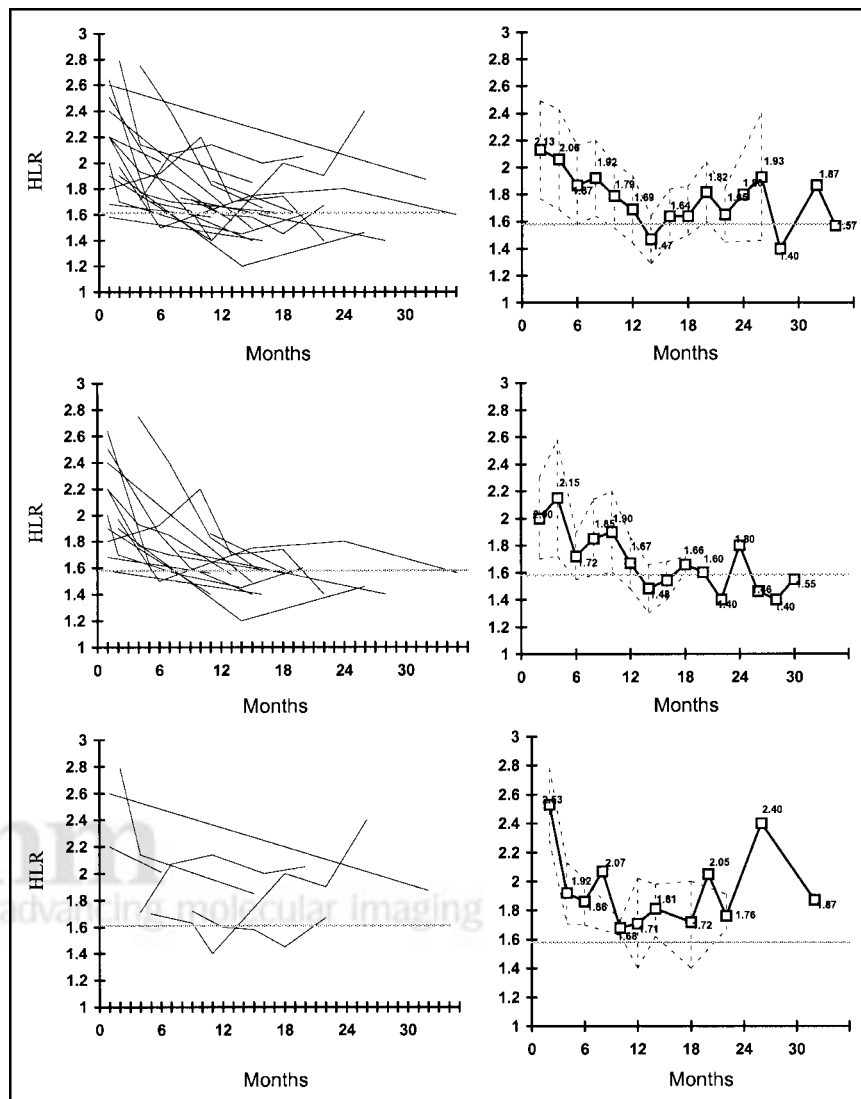
FIGURE 5. Evolution of myocardial damage in children with myocarditis as represented by the intensity of serial antimyosin scans. The graphs show data from individual patients (left) and the evolution of mean HLR with ±1 SD (right). Data are represented for all patients (top), patients who showed complete resolution of antimyosin uptake (middle), and patients who continued with persistent antimyosin uptake over time (bottom). The persistence of antimyosin uptake was associated with poor clinical outcomes and resolution with left ventricular functional recovery.

Severe myocardial damage with an HLR > 2 is almost invariably associated with histologic evidence of myocarditis. Severe myocardial damage with an HLR > 2 seen within 2 mo of the onset of symptoms is also associated with a higher mortality rate. Survivors with high antimyosin uptake or with an HLR < 2 almost always achieve complete functional recovery. Antimyosin scanning has no significant prognostic value if performed more than 2 mo after the onset of symptoms. Antimyosin imaging also allows sequential evaluation of the extent of myocellular damage after an acute presentation and suggests that persistence or recurrence of myocardial damage may be associated with a poor outcome.

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