Anti-Ro/SS-A and anti-La/SS-B antibodies associated with cardiac involvement in childhood systemic lupus erythematosus

Andrew C Oshiro, Stephen J Derbes, Aluizio R Stopa, Abraham Gedalia

Abstract

***Objectives*—To determine the frequency and type of cardiac manifestations in children with systemic lupus erythematosus (SLE) and investigate whether cardiac involvement of SLE in children was associated with any autoantibody pattern.**

***Methods*—Retrospective analysis of the medical records of all children with SLE (31 patients) seen between January 1984 and January 1994 by the paediatric rheumatology service at Children's Hospital in New Orleans. All patients satisfied the American College of Rheumatology criteria for the diagnosis of SLE. Paediatric SLE patients with cardiac manifestations based on echocardiogram were identified. Autoantibody tests at diagnosis were identified retrospectively by chart review, and the correlation between autoantibodies and cardiac involvement was analysed using the two tailed Fisher's exact test.**

***Results*—Thirteen (42%) of 31 SLE patients had cardiac manifestations of SLE. Seven (22%) had pericarditis without myocarditis, five (16%) had pericarditis and myocarditis, and one (3%) had myocarditis without pericarditis. Two patients (6%) with pericarditis had cardiac tamponade. Cardiac manifestations of SLE usually occurred at the time of diagnosis or within six months. Anti-Ro/SS-A antibodies were present in serum samples of nine of 11 (82%) patients with cardiac involvement and in five of 15 (33%) without cardiac involvement (p=0.02). Anti-La/SS-B antibodies were present in serum samples of six of 10 (60%) patients with cardiac involvement and two of 15 (13%) without cardiac involvement (p=0.03). Anti-Sm and anti-RNP antibodies showed no correlation with the presence of cardiac disease.**

***Conclusions*—Cardiac involvement in our paediatric SLE population was frequently found and correlated significantly with the presence of anti-Ro/SS-A and anti-La/SS-B antibodies.**

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Divisions of Rheumatology and Cardiology, Department of Pediatrics, Louisiana State University Medical Center and Children's Hospital, New Orleans, Louisiana, USA
A C Oshiro
S J Derbes
A R Stopa
A Gedalia

Correspondence to:
Dr A Gedalia, Department of Pediatrics, LSUMC, 1542 Tulane Avenue, New Orleans, LA 70112-2822, USA.

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Systemic lupus erythematosus (SLE) is a multi-system organ disease, and involvement of the heart is a common manifestation. As the diagnosis of cardiac diseases has changed a great deal in the past 10 years because of improved resolution and increased availability of echocardiography, we sought to determine the frequency and type of cardiac manifestations of SLE in our paediatric population.

In addition, we investigated whether cardiac manifestations of childhood SLE were associated with any autoantibody pattern, as the presence of specific autoantibodies has been associated with particular disease manifestations of adult SLE. Neonatal lupus associated with anti-Ro/SS-A and anti-La/SS-B antibodies is well established.[1–3] In adult patients with SLE, an association between anti-Ro antibodies and myocarditis or cardiac conduction defects has been described.[4] However, studies in childhood onset SLE are lacking, and no association of specific autoantibodies with cardiac involvement has been reported previously.

Methods

The inpatient and outpatient medical records of all children (<18 years old) with SLE (31 patients) seen between January 1984 and January 1994 by the paediatric rheumatology service at Children's Hospital of New Orleans were reviewed retrospectively. All SLE patients who satisfied the American College of Rheumatology criteria for the diagnosis of SLE[5] and had echocardiograms were included in the study. Since 1991, based on our new protocol, echocardiograms were routinely done for all our SLE patients. Paediatric SLE patients with cardiac involvement as confirmed by echocardiogram were identified. Pericarditis and myocarditis were defined by the presence of characteristic echocardiographic findings—that is, presence of fluid in the pericardial sac was the characteristic findings of pericarditis, and decreased myocardial function was the characteristic finding in myocarditis. A paediatric cardiologist read all echocardiograms. Autoantibody tests at diagnosis were identified retrospectively by chart review. Before December 1990, anti-Ro/SS-A, anti-La/SS-B, anti-Sm, and anti-RNP antibody tests were done by double immunodiffusion; enzyme linked immunosorbent assay (ELISA) was used thereafter. In the measurement of these antibodies, IgG isotype was determined. The anticardiolipin antibody (aCL) test (ELISA) was routinely done on patients with childhood SLE only during the last two years of the study. Correlations between autoantibodies and cardiac involvement were analysed using the two tailed Fisher's exact test.

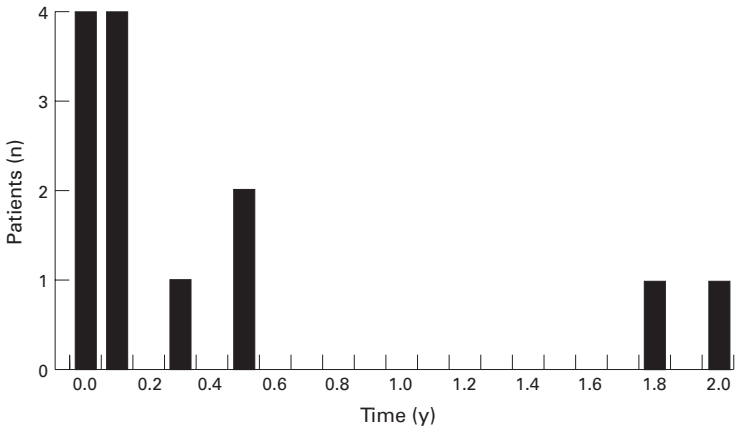

Figure 1 Time (y) of the first cardiac manifestations of lupus after diagnosis.

Results

Thirty one children with SLE were included in the study, of whom 26 were female and five were male. Twenty seven patients were African-American, three were white, and one was native American. The mean age of the patients at diagnosis was 12.1 years (range 5-17). Of the 31 patients identified, 13 (42%) had cardiac involvement. Seven (22%) had pericarditis without myocarditis, five (16%) had pericarditis and myocarditis, and one (3%) had only myocarditis without pericarditis. Two of our patients with pericarditis (6%) presented with cardiac tamponade. One patient with myocarditis had concurrent mitral valve insufficiency; one patient with pericarditis had concurrent mitral and tricuspid insufficiency. Valvular vegetation or thickening was not seen in any of the patients. Of the 12 patients with pericarditis, four had recurrent episodes. Statistical analysis using the two tailed Fisher's exact test showed that cardiac involvement correlated significantly with the presence of anti-Ro/SS-A and anti-La/SS-B antibodies (table 1). Anti-Ro/SS-A antibodies were present in the serum of nine of 11 (82%) patients with cardiac involvement and five of 15 (33%) without cardiac involvement (p=0.02). Similarly, anti-La/SS-B antibodies were present in serum of six of 10 (60%) patients with cardiac involvement and in only two of 15 (13%) without cardiac involvement (p=0.03). Presence of anti-Sm and anti-RNP antibodies showed no correlation with cardiac involvement (p=0.12 and p=1.00, respectively). The aCL antibody test was performed on nine patients of whom only four were positive (three of IgG isotype and one of IgA isotype). Of the four patients with positive aCL antibody test, only one had cardiac involvement (pericarditis).

At the time of diagnosis, cardiac manifestations of SLE were present in four of our patients (fig 1). Within six weeks of the diagnosis of SLE, an additional four had cardiac manifestations of SLE, and within six months, an additional three had a cardiac manifestations of SLE. Two patients had initial cardiac manifestations 1.8 years after being diagnosed with SLE. The 13 patients with cardiac manifestations were followed up for 3.8 years (range 0.1-8.5); 18 patients without cardiac manifestations were followed up for an average of 3.4 years (range 0.1-8.2).

Table 1 Autoantibodies in children with SLE

Type of antibodies present	*With cardiac involvement*	*Without cardiac involvement*	*p Values**
Ro/SSA (n tested)	9 (11)	5 (15)	0.02
La/SSB (n tested)	6 (10)	2 (15)	0.03
Sm (n tested)	8 (11)	6 (16)	0.12
RNP (n tested)	6 (11)	8 (17)	1.00

n = number, * Fisher's exact test.

Discussion

The incidence of clinically diagnosed pericarditis in adult SLE was 25-30%, and this frequency was even higher in a necropsy series of adult SLE patients.[6] Pericarditis with cardiac tamponade occurred in 2.5%.[7] Cardiac manifestations among children with SLE are common. In studies of paediatric populations with SLE published after 1980, the incidence of pericarditis has ranged from 5-24%, and myocarditis from 2-6%.[8–10] With the exception of case reports,[8 11] no mention of the frequency of cardiac tamponade in childhood onset SLE has been published in the medical literature.

In our study, the incidence of cardiac involvement was higher than that recently reported[10]; pericarditis was found in 38% (12 of 31), and myocarditis in 19% of children with SLE. The incidence of cardiac tamponade in our study was 6% (2 of 31), which is higher than the 2.5% (10 of 395) reported by Kahl *et al* in a study of adult SLE patients.[7] These differences are probably because cardiac involvement in our study was based only on echocardiography, which is much more sensitive than are physical examamination and radiology in detecting cardiac disease, especially pericarditis. In addition, our paediatric population probably faces a high risk of severe disease because it is comprised of a large percentage of African-Americans, a population that has been found to have higher death rates from SLE than white people.[12] Referrals to our centre are drawn from a population comprised of 60% African-Americans.

Cardiac manifestations of SLE in our paediatric study usually occurred as an initial manifestation of the disease or within six months after the diagnosis of SLE. An initial occurrence beyond this period was uncommon. These findings have not been described previously. Recurrence of pericarditis after an initial episode was common.

Anti-Ro/SS-A antibodies have been associated with the finding of myocarditis or cardiac conduction defects in adults with SLE.[4] No such association has been previously reported in children with SLE. Anti-cardiolipin antibodies have been associated with abnormal intracardiac anatomy (valvular lesions, pericardial involvement, or myocardial dysfunction) in adults with SLE. In addition, anti-cardiolipin antibodies have also been associated with isolated left ventricular dysfunction, verrucous valvular thickening, global valvular thickening and dysfunction, mitral regurgitation, and aortic regurgitation in adults with SLE.[13] Apart from a recent fatal case report of myocardial

infarction in a child with SLE, no such association has been previously reported in children with SLE.[14]

Our study demonstrated an association between cardiac manifestations of SLE and anti-Ro/SS-A antibodies (p=0.02) and anti-La/SS-B antibodies (p=0.03) (table 1). This represents the first reported association, in children, of cardiac manifestations of SLE and autoantibodies. Moreover, our findings also represent the first association of anti-La antibodies with cardiac manifestations of SLE, in both children and adults. Anti-Sm and anti-RNP showed no correlation with the presence of cardiac disease. The aCL antibody test was done in nine patients only; therefore the sample size was too small for statistical analysis. This study is a retrospective one, and, accordingly some bias in the selection of patients may exist; we believe this is minimal, however.

It is well accepted that maternal anti-Ro/SS-A and anti-La/SS-B antibodies are associated with congenital heart block.[1–3] Experimental evidence supporting a direct role for anti-Ro/SS-A and anti-La/SS-B antibodies in cardiac involvement comes from a rabbit model.[15] It remains to be determined whether the same mechanisim exists in childhood onset SLE.

In summary, cardiac manifestations of childhood SLE are common. Our data suggest that these manifestations are associated with anti-Ro/SS-A and anti-La/SS-B antibodies. The pathophysiology involved is not yet fully understood. Although a similar association is found between these antibodies and cardiac involvement in the neonatal lupus syndrome, the cardiac manifestations are somewhat different than those of paediatric SLE.

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