

Case Report

Transient Left Ventricular Wall Thickening in a Child with Systemic Lupus Erythematosus and Myositis

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ABSTRACT

An 11-year-old girl presenting with clinical signs and laboratory markers consistent with systemic lupus erythematosus (SLE) and an associated secondary skeletal myositis, was found to have circumferential left ventricular wall thickening (LVWT) by echocardiography, with normal left ventricular function. There was no history of hypertension or other heart disease to account for ventricular thickening. The findings may have represented an early form of myocarditis. Over a six month period the LVWT completely resolved. Although cardiac abnormalities are common in childhood-onset SLE, transient LVWT with preserved systolic function has not been previously described.

INTRODUCTION

A number of cardiac abnormalities, including pericarditis, myocarditis, valvular heart disease and abnormalities of coronary perfusion have been described in children and adolescents with systemic lupus erythematosus (SLE) or SLE overlap syndromes^[1]. Hypertrophic cardiomyopathy (HCM) and left ventricular hypertrophy (LVH) have been reported in adults with SLE or SLE overlap syndromes^[2-9]. A single study has reported left ventricular wall thickening (LVWT) in 2 children with SLE. However, the etiology and the outcome of this finding were not described^[10].

We present a case of transient LVWT with preserved systolic function in association with childhood-onset SLE and secondary skeletal myositis.

CASE REPORT

An 11-year-old girl with a family history of scleroderma and rheumatoid arthritis developed symptoms of Raynaud's phenomenon during the summer of 2003. Three months later she noted increasing upper back pain, bilateral arm weakness, generalized fatigue, decreased appetite, perceptible weight loss, and hair loss. Shortly thereafter, she developed swelling and redness of her fingertips and toes, a rash on her nose and upper eyelids, and facial swelling. She was subsequently admitted to our hospital with high fever, chills and extreme fatigue.

On admission, examination revealed a temperature of 39.9°C, a malar rash, vasculitic changes of her fingers and toes, generalized lymphadenopathy, and muscle weakness in the neck and upper arms. Over the next 24 hours, she also developed arthritis of all proximal interphalangeal joints and myalgia in the lower limbs. On cardiovascular examination, resting tachycardia, a hyperdynamic precordium with a gallop rhythm, and a grade 2/6 pulmonary flow murmur were noted. There was no jugular venous distention or hepatomegaly. Blood pressure was 109/68 mmHg.

Laboratory evaluation showed relative leukopenia ($4.3 \times 10^9/L$) with lymphopenia ($1.0 \times 10^9/L$), autoimmune hemolytic anemia (100 g/L) with a positive direct Coomb's test, normal platelet count ($213 \times 10^9/L$), an elevated erythrocyte sedimentation rate (ESR) (58 mm/hr), and normal renal function (blood urea nitrogen 5.8 mmol/L and creatinine 59 $\mu\text{mol/L}$). Urinalysis showed trace protein, 3-5 red blood cells and no white blood cells, with 24 hour urine protein of 0.068g. Serum biochemistry revealed elevated levels of aspartate aminotransferase (94 U/L), alanine aminotransferase (39 U/L), lactate dehydrogenase (1525 U/L), aldolase (18.8 U/L), and creatinine kinase (CK) (3160 U/L), with a creatinine kinase-muscle brain (CK-MB) of 51 U/L (CK-MB fraction of 1.6%). Immunological studies revealed low complement factors (C3 0.31 g/L and C4 0.03 g/L), positive antinuclear antibody with speckled pattern, and positive anti-DNA antibodies with 67% DNA binding (Farr assay). Antibodies to extractable nuclear antigens (ENA) were elevated, with anti-Ro (SSA) antibody 177 IU, anti-La (SSB) antibody 209 IU, anti-Sm antibody 155 IU, and anti-RNP antibody 183 IU. Antiphospholipid antibodies were negative. An electromyogram and magnetic resonance imaging of the thighs and shoulders demonstrated changes consistent with inflammatory myositis.

A 12-lead electrocardiogram demonstrated sinus rhythm with low voltages and right axis deviation. Chest radiography was normal. Echocardiography (Figure 1A) revealed concentric LVWT (posterior wall end-diastolic thickness of 12.3 mm, normal < 9.7mm) and mild right ventricular wall thickening. There was normal left ventricular systolic function (fractional shortening 40%, ejection fraction 72%) and qualitatively normal right ventricular systolic function. There was no left ventricular dilation (left ventricular end-diastolic dimension 4.17 cm, normal 3.51-4.84 cm), and no outflow tract obstruction or systolic anterior motion of the mitral valve. There was trace mitral regurgitation and a trivial pericardial effusion. A 24-hour ambulatory electrocardiogram (Holter monitor) showed isolated atrial premature beats, but no ventricular ectopy.

Figure 1A. Echocardiographic images from the parasternal long-axis view.



A) At diagnosis, there was concentric left ventricular wall thickening. Biventricular systolic function was normal.

LA: left atrium, LV: left ventricle, Arrow: left ventricular posterior wall, Arrowhead: interventricular septum

On day 3 of admission, she was documented to fulfill 5 American College of Rheumatology criteria for the classification of SLE and was started on pulse methylprednisolone (1000mg) for three days, followed by daily prednisone (20 mg bid) and hydroxychloroquine (200 mg qhs). She was discharged a week later with marked improvement of all symptoms and clinical signs. Repeat echocardiography at this time showed no significant change.

At two-month follow-up, she had persistent proximal muscle weakness but was able to return to school full-time. On physical examination, the sequelae of vasculitis on her fingertips were resolving, and her malar rash was almost gone. Her neurological evaluation was normal, but there was persisting muscle weakness and new bilateral knee effusions. On laboratory evaluation, the hematologic disorder had corrected, inflammatory markers had improved with an ESR at 15 mm/hr, and there was no evidence of renal involvement. However, the muscle enzymes remained elevated, with a CK at 791 U/L and aldolase at 40.4 U/L. The Childhood Myositis Assessment Scale score^[11] showed mild impairment at 46/53. Immunologic studies revealed normal complement levels, persistently elevated ENA (Ro 169 IU, La 119 IU, Sm 91 IU and RNP 122 IU), and DNA binding of 32%. The overall picture was still consistent with SLE with secondary myositis, although the resolution of most clinical signs and the persistence of myositis suggested the evolution to a SLE overlap syndrome. Repeat echocardiography at this time demonstrated reduced LVWT (posterior wall end-diastolic thickness 10.6 mm). The patient's parents and brother underwent echocardiography, and had normal studies. Treadmill testing revealed poor exercise tolerance, attributed to muscular pain. Her heart rate and blood pressure response to exercise were normal, without arrhythmia or ischemic changes.

At six-month follow-up, the echocardiographic examination was normal, showing complete resolution of the previously noted LVWT (Figure 1B). Three months later, while on a weaning schedule of prednisone,

she had a flare-up of myositis without clinical and laboratory signs of SLE. Repeat echocardiography at this time was normal.

Figure 1B. Echocardiographic images from the parasternal long-axis view.



B) Six months following initial presentation, the left ventricular wall thickening had completely resolved. LA: left atrium, LV: left ventricle, Arrow: left ventricular posterior wall, Arrowhead: interventricular septum

DISCUSSION

Our patient is a previously healthy 11 year-old girl who presented acutely ill with features consistent with a diagnosis of SLE with secondary myositis. The acute SLE features resolved but myositis persisted, suggesting the evolution to a SLE overlap syndrome. Although she had no cardiovascular symptoms, her clinical findings suggested cardiac involvement. Echocardiographic examination revealed moderate LVWT with preserved left ventricular function and chamber size, and a trivial pericardial effusion. Over a six month period the LVWT completely resolved. The transient nature of this finding was not consistent with true myocardial hypertrophy. Therefore, LVWT is a more accurate term than LVH in this patient.

The prevalence of clinical heart disease among children with SLE ranges from 32 to 68%^[10,12]. Subclinical disease, as demonstrated by echocardiography and autopsy studies, is also common^[10]. Pericarditis is the most common cardiac abnormality, but there may be involvement of the endocardium, myocardium, valves, conducting tissue, or coronary arteries^[1]. There are no studies of the prevalence of clinical heart disease among children with SLE overlap syndromes.

Left ventricular wall thickening in association with childhood-onset SLE, has been previously reported in a single study in only 2 patients^[10]. However, the authors did not specify if any factors predisposing to LVWT were present. It is also unclear whether the echocardiographic abnormality resolved at follow-up.

Signs and symptoms of myocarditis occur in less than 10% of children with SLE^[13]. Significant myocarditis has also been described in children with SLE overlap syndromes^[14]. Left ventricular wall thickening due to interstitial edema has been reported in the setting of acute myocarditis^[15]. Since

echocardiography in our patient showed no ventricular dilation or dysfunction, the findings were considered atypical for myocarditis. It is possible that our findings represented a very early form of myocarditis, however asymptomatic myocarditis is an ill-defined entity in children. Among 4 asymptomatic schoolchildren who were found to have abnormal screening electrocardiograms and evidence of myocarditis by endomyocardial biopsy, 1 had moderate left ventricular dysfunction, 1 had left ventricular dilation, and 2 had normal echocardiograms; none had LVWT^[16].

Another cause of LVWT is hypertrophic cardiomyopathy (HCM), characterized by abnormal ventricular hypertrophy in the absence of an identifiable primary cause^[17]. The association of HCM with SLE or SLE overlap syndrome has been previously described^[2-4]. However, all patients in those studies were adults and had longstanding illness. None had resolution of the ventricular hypertrophy. Our patient, initially thought to have HCM, had complete resolution of LVWT, which excludes this diagnosis.

Prevalence studies of cardiac abnormalities in adults with SLE, as detected by echocardiography, identified LVH in 7 to 14% of patients^[5-9]. All had longstanding illness and most were on corticosteroid therapy. The LVH in these patients may correspond to the common occurrence of hypertension and premature coronary atherosclerosis in SLE, which may be secondary to the effects of steroids^[18,19]. Crozier et al also demonstrated increased interventricular septal and posterior left ventricular wall thickness and left ventricular mass in adults with SLE versus controls^[6]. However, they found no significant relation between these variables and SLE duration, disease activity, blood pressure or dose or duration of prednisone therapy. The LVH in SLE may therefore be due to direct myocardial involvement, as both fibrinoid and cellular infiltration and increased myocardial fibrous tissue are seen in SLE^[19,20]. Myocardial lymphocytic infiltration and fibrosis is also found in adults with SLE overlap syndrome^[21], but LVH has never been described in this entity. Left ventricular hypertrophy has not been reported in children with SLE or SLE overlap syndromes.

CONCLUSION

Cardiac abnormalities occur frequently in children with SLE and SLE overlap syndromes. We have described a patient who had transient LVWT in association with SLE and a secondary myositis, which subsequently evolved into what may be a SLE overlap syndrome. To our knowledge, this has not been previously reported. The LVWT may have represented a mild form of myocarditis, but the absence of ventricular dilation or dysfunction is unusual with this diagnosis. Since echocardiography is essential in identifying structural cardiac abnormalities, it should be used routinely for new-onset childhood SLE and SLE overlap syndromes.

REFERENCES

1. Cassidy JT, Petty RE. Systemic lupus erythematosus. In: Cassidy JT, Petty RE, editors. Textbook of Pediatric Rheumatology, 4th ed. Philadelphia: WB Saunders; 2001:396-438.
2. Asherson RA, Ames D, Coltart J, Byrne C, Hughes GR. Hypertrophic cardiomyopathy in systemic lupus erythematosus and "lupus-like" disease. Chance association? A report of 2 cases. J Rheumatol.

1992;19:1973-7.

3. Ara J, Vivancos J, Soler-Carrillo J, Paré JC, Cervera R, Font J. Hypertrophic cardiomyopathy and systemic lupus erythematosus. *Clin Rheumatol*. 1998;17:531-3.
4. Anastasiadis GP, Moysakis I, Boki K, Kyriakidis M. Hypertrophic cardiomyopathy in systemic lupus erythematosus. *Mayo Clin. Proc* 2001;76:111.
5. Leung WH, Wong KL, Lau CP, Wong CK, Cheng CH. Cardiac abnormalities in systemic lupus erythematosus: a prospective M-mode, cross-sectional and Doppler echocardiographic study. *Int J Cardiol*. 1990;27:367-75.
6. Crozier IG, Li E, Milne MJ, Nicholls MG. Cardiac involvement in systemic lupus erythematosus detected by echocardiography. *Am J Cardiol*. 1990;65:1145-8.
7. Cujec B, Sibley J, Haga M. Cardiac abnormalities in patients with systemic lupus erythematosus. *Can J Cardiol*. 1991;7:343-9.
8. Kalke S, Balakrishanan C, Mangat G, Mittal G, Kumar N, Joshi VR. Echocardiography in systemic lupus erythematosus. *Lupus* 1998;7:540-4.
9. Barletta G, Brugnolo F, Del Bene R, Ricignolo G, Marchione T, Abbate R, Romagnani S, Fantini F, Emmi L. Heart involvement in systemic lupus erythematosus. *J Noninvasive Cardiol*. 1999;3:161-7.
10. Al-Abbad AJ, Cabral DA, Sanatani S, Sandor GG, Seear M, Petty RE, et al. Echocardiography and pulmonary function testing in childhood onset systemic lupus erythematosus. *Lupus* 2001;10:32-7.
11. Lovell DJ, Lindsley CB, Rennebohm RM, Ballinger SH, Bowyer SL, Giannini EH, et al. Development of validated disease activity and damage indices for the juvenile idiopathic inflammatory myopathies. II. The Childhood Myositis Assessment Scale (CMAS): a quantitative tool for the evaluation of muscle function. The Juvenile Dermatomyositis Disease Activity Collaborative Study Group. *Arthritis Rheum*. 1999;42:2213-9.
12. Guevara JP, Clark BJ, Athreya BH. Point prevalence of cardiac abnormalities in children with systemic lupus erythematosus. *J Rheumatol*. 2001;28:854-9.
13. Oshiro AC, Derbes SJ, Stopa AR, Gedalia A. Anti-Ro/SS-A and anti-La/SS-B antibodies associated with cardiac involvement in childhood systemic lupus erythematosus. *Ann Rheum Dis*. 1997;56:272-4.
14. Michels H. Course of mixed connective tissue disease in children. *Ann Med*. 1997;29:359-64.
15. Riera Sagrera M, Fiol Sala M, Perez Barcena J, Bergada Garcia J, Forteza Canellas C, Ibanes Juve J. Acute myocarditis and left ventricular "hypertrophy". *Echocardiography* 2000 Aug;17:567-70.
16. Nakagawa M, Sato A, Okagawa H, Kondo M, Okuno M, Takamatsu T. Detection and evaluation of asymptomatic myocarditis in schoolchildren: report of four cases. *Chest* Aug 1999;116:340-345.
17. Wynne J, Braunwald E. The Cardiomyopathies and Myocarditides. In: Braunwald E, Zipes DP, Libby P editors. *Heart Disease: A Textbook of Cardiovascular Medicine*, 6th ed. Philadelphia: WB Saunders; 2001:1760-74.
18. Doherty NE, Siegel RJ. Cardiovascular manifestations of systemic lupus erythematosus. *Am Heart J*. 1985;110:1257-65.
19. Bulkley BH, Roberts WC. The heart in systemic lupus erythematosus and the changes induced in

it by corticosteroid therapy. A study of 36 necropsy patients. *Am J Med.* 1975;58:243-64.

20. Brigden W, Bywaters EG, Lessof MH, Ross IP. The heart in systemic lupus erythematosus. *Br Heart J.* 1960;22:1-16.

21. Whitlow PL, Gilliam JN, Chubick A, Ziff M. Myocarditis in mixed connective tissue disease. Association of myocarditis with antibody to nuclear ribonucleoprotein. *Arthritis Rheum.* 1980;23:808-15.