Case report

Resolution of lupus-related left ventricular wall thickening and interstitial lung disease in a child with pulsed steroids and cyclophosphamide

Cardiopulmonary involvement is one of the important manifestations of systemic lupus erythematosus (SLE) that tends to be more common in adults than children with SLE. SLE-related cardiopulmonary affection ranges from subclinical to life threatening condition. Although increased left ventricular mass and interstitial lung disease have been reported in association with SLE, the reversibility of such conditions with treatment of SLE was not sufficiently reported. Herein, we describe a female adolescent with SLE and lupus nephritis class III who presented as well with moderate dyspnea, tachycardia in absence of heart failure and hypertension. She had also productive cough of whitish sputum, no fever and both sputum and blood cultures were negative. Her echocardiography revealed left ventricular wall hypertrophy with preserved systolic function, electrocardiogram showed sinus tachycardia. Her pulmonary function tests revealed mild restrictive pattern and high resolution computed tomography revealed veiling of both lungs with increased attenuation and interstitial nodules with bilateral mild pleural effusion. She received full dose prednisone and intravenous monthly cyclophosphamide in addition to intravenous pulsed methylprednislone. She gradually improved with complete resolution of her cardiopulmonary disease and significant reduction of her proteinuria. In conclusion, cardiopulmonary involvement in relation to SLE could be reversible with adequate treatment leaving no residual damage.

Keywords: SLE, left ventricular hypertrophy, interstitial lung disease.

Dalia H. El-Ghoneimy, Omneya I. Youssef*

Pediatric Allergy and Immunology Unit, Pediatric Cardiology Unit, Pediatrics Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt.*

Correspondence:
Dr. Dalia El-Ghoneimy, Lecturer of Pediatrics, Ain shams University, Abbassiah, Cairo, Egypt.
E-mail:
dalia.elghoneimy@gmail.com

INTRODUCTION

The most common form of cardiac involvement in pediatric patients with systemic lupus erythematosus (pSLE) is pericardiatis with pericardial effusion, and less commonly, endo-or myocarditis or valvular disease[1]. Clinical or subclinical pleuropulmonary disease is also a frequent manifestation of childhood SLE[2]. The clinical spectrum includes pleuritis, pneumonitis, infectious pneumonia, pulmonary hemorrhage, pulmonary hypertension and pneumothorax. Uncommon manifestations are diaphragmatic involvement, vasculitis, and pulmonary embolism[1]. Diffuse interstitial lung disease occurs occasionally in pSLE[3]. However, pulmonary involvement was found frequent among a group of Egyptian children with SLE and tended to correlate with disease severity[4]. We describe a female child with SLE who developed left ventricular hypertrophy and interstitial lung disease that resolved completely three months after treatment.

CASE PRESENTATION

A twelve-year-old female patient of consanguineous parents presented to the emergency room of the Children's Hospital, Ain Shams University complaining of high remittent fever and bilateral lower limbs swelling of gradual onset and one week duration. The parents reported that their child's illness started one month ago with bouts of unexplained high fever, malaise, decreased appetite and weight loss. Shortly after, a non-itchy erythematous rash appeared on her nose and cheeks with exacerbation on sun exposure with painful swelling of both knees and ankles; her condition was poorly responding to repeated doses of antipyretics and analgesics.

On admission, physical examination revealed that the patient was feverish (38.5°C), had a malar rash, she was tachycardiac (HR: 120/min) and dyspneic (RR: 40/min), her blood pressure was normal (110/60mmHg). There was no jugular venous congestion or hepatomegaly. Cardiac and chest examination were free. Patient had arthritis of

both knees and ankles together with bilateral lower limb edema up to the knees. Her laboratory evaluation revealed normal leukocytic count (8.8x 10^9/L), mild normocytic normochromic anemia (9.2 gm/dl), normal platelet count (301x10^9/L), an elevated erythrocyte sedimentation rate (100 mm/hr), hypoalbuminemia (2.6 gm/dl) and normal renal functions (blood urea nitrogen: 18 and serum creatinine: 0.3 mg/dl). Her thyroid profile was normal. Urine analysis showed albuminuria (+3 by dipsticks), hematuria (>100/HPF), pyuria (20-25/HPF) and granular casts, the urine culture was negative. The 24-hour urinary proteins was 1.5 grams/24 hours. Immunological studies showed positive ANA (titer: 1/640, homogenous pattern), anti-ds DNA was positive (400 IU/ml) with consumed C3 and C4 (27mg/dl and 7mg/dl respectively). Both lupus anti-coagulant and anti-cardiolipin antibodies were negative. Renal biopsy revealed lupus nephritis class III (focal proliferative glomerulonephritis). Thus, our patient was a case of SLE and lupus nephritis. She was placed on full dose steroids (60 mg/day) and started monthly cyclophosphamide at a dose of 500 mg/m^2. Four days after starting steroids, her cardiac evaluation included 12 lead electrocardiogram revealing sinus tachycardia, an echocardiography showing increased left ventricular wall thickening (LVWT) with preserved systolic function (ejection fraction: 67%) and mild pericardial effusion (figure1a). A 24-hour-ambulatory Holter monitoring showed sinus tachycardia and infrequent premature ventricular contractions.

While on full dose steroids, patient developed in addition to the persistent dyspnea, frequent non-productive cough, her chest examination revealed only few bibasilar fine crepitations. So evaluation of pulmonary involvement was carried out showing pulmonary infiltrates on plain chest x-ray, sputum and blood cultures were both negative for organisms. Pulmonary function tests showed mild restrictive pattern and high resolution computed tomography (HRCT) of the chest revealed veiling of both lungs with increased attenuation and interstitial nodules with bilateral mild pleural effusion (figure 2a).

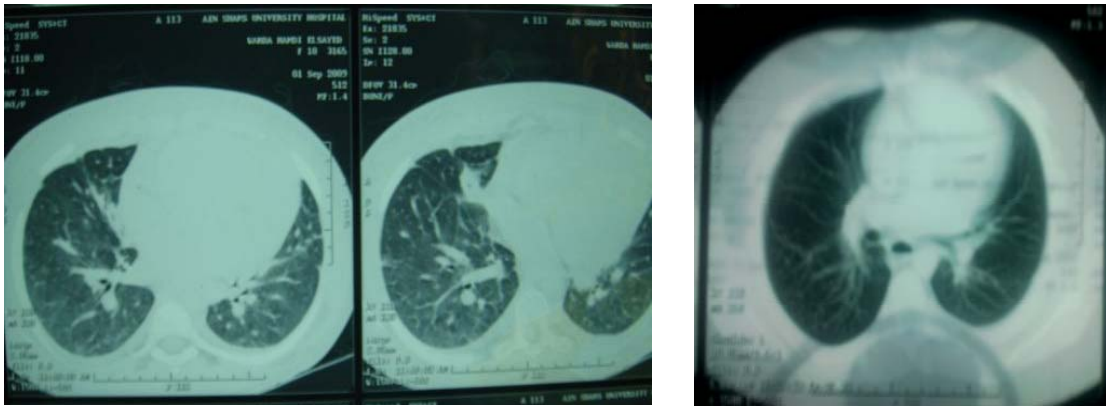
In view of the marked nephrosis that was not responding adequately to oral steroids and pulsed monthly cyclophosphamide, and the cardiopulmonary involvement, monthly methyl prednisolone (30mg/kg maximum1gm) was added. An angiotensin receptor blocker and diuretics were added to control the newly developed hypertension (140/90 mmHg) and edema. Her condition gradually improved concerning renal and cardio-pulmonary involvement. At 3-months follow-up, the patient had no constitutional symptoms with resolution of dyspnea and tachycardia, her laboratory evaluation showed normalization of C3 and C4 and negative anti-ds DNA with marked decrease in proteinuria.

A follow up echocardiography was done and it revealed normalization of LVWT (figure 1b). A pulmonary function tests become normal on follow up, with the resolution of HRCT scan findings of the chest (figure 2b).

So, cardiopulmonary affection was one of the presenting manifestations in this patient with SLE that resolved completely 3 months after aggressive therapy leaving no residual damage.

(a) (b)

Figure 1. Echocardiography (long axis parasternal view) of the patient showing: a- Left ventricular hypertrophy with no chamber dilatation at presentation, b- Resolution of the left ventricular hypertrophy 3 months after immunosuppressive therapy.



(a) (b)

Figure 2. High resolution computed tomography (HRCT) of the chest showing: a- Veiling of both lungs with increased attenuation and interstitial nodules at presentation, b- Clear both lung fields (three months after immunosuppressive therapy).

DISCUSSION

Cardiovascular involvement is the third most common reason of death in patients with SLE[5]. Prevalence of clinical heart disease among SLE children ranges from 32 to 68 %[6]. Subclinical disease as demonstrated by echocardiography and autopsy studies are also common[7].

Our patient was a previously healthy 12 years old girl who presented acutely with features consistent with SLE. The only clinical cardiovascular finding was tachycardia out of proportion to fever, Echocardiographic examination revealed increased LVWT with preserved systolic function (ejection fraction was 68%) and chamber size with minimal pericardial effusion. Alterations in left ventricular (LV) structure and function have been reported among the cardiac manifestations of SLE in adults[8]. A direct disease related effect of SLE on LV structure has been suggested[9].

LVWT become normal within three months, making this finding a transitional one not consistent with myocardial hypertrophy. Transient LVWT has been described in a child with SLE and myositis[10].

Since the patient's echocardiography showed no ventricular dilatation or dysfunction, these findings were considered atypical for myocarditis. LVWT 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[11].

Chronic interstitial lung disease characterized by chronic nonproductive cough, recurrent pleuritic chest pain, and dyspnea on exertion have been reported children and adults with SLE[12,13]. Physical examination may show fever, cyanosis, and bibasilar crackles. Clubbing is less common in SLE than in idiopathic ILD[14]. HRCT findings in SLE-induced ILD include interlobular and intralobular septal thickening, air-space nodules, and architectural distortion[15]. This is in addition to pulmonary function test abnormalities. Restrictive pattern of pulmonary function tests was reported in 62% of children with SLE with the most frequent HRCT findings were ground glass appearance, pleural irregularity, bronchial wall thickening and pulmonary nodules[4].

Bronchoalveolar lavage (BAL) is considered to be an effective and relatively safe method of obtaining inflammatory cells and secretions in patients with pulmonary disease where lymphocyte predominance was found in symptomatic patients while both lymphocytes and neutrophils infiltrates exist in those with only radiographic changes of ILD[16]. Although diagnosis of primary lung disease may only be made by lung biopsy, with appropriate microbiological and histopathological investigation[15]. Our patient had no clinical or laboratory evidence of infective pulmonary disease, the HRCT finding of the chest and the restrictive pattern of the pulmonary function tests suggested SLE-related interstitial lung disease.

Our patient's chest condition represented an initial stage of insidious onset of SLE-induced interstitial lung disease which might progress to more severe form if inadequately treated. High-dose corticosteroids is the mainstay of treatment for diffuse ILD; although other agents such as cyclophosphamide, azathioprine, intravenous gamma globulin, and plasmapheresis have been used with varying degrees of success[16]. Previous studies on the pleuropulmonary manifestations of pSLE reported the occurrence of chronic interstitial

lung disease associated with SLE activity with variable response to treatment and outcome[17]. Our patient showed excellent response to the pulsed monthly methylprednisolone and cyclophosphamide with clinical recovery and normalization of the HRCT scan of the chest and the pulmonary function tests. In conclusion, unexplained dyspnea and tachycardia in SLE patients should be thoroughly investigated for early diagnosis and treatment and hence better outcome.

CONSENT

An informed consent was taken from the parents of the patient for publication of this case report and accompanying images.

REFERENCES

1. **Benseler SM, Silverman ED.** Systemic lupus erythematosus. Ped Clin N Am 2005; 52: 443-67 .
2. **Cervera R, Font J, Pare C, Azqueta M, Perez-Villa F, Lopez-Soto A, et al.** Cardiac disease in systemic lupus erythematosus: prospective study of 70 patients. Ann Rheum Dis 1992; 51: 156-9.
3. **Petty RE, Laxer RM.** Systemic lupus erythematosus. In: Cassidy JT, Petty RE, Laxer RM, Lindsley CB, editors. Textbook of Pediatric Rheumatology. Philadelphia: PA, Elsevier Saunders, 5th ed, 2005. p.355.
4. **Abd El-Khalik KA, El-Sayed ZA, Faheem MS, Fouda E, Abdurrahman L, Abd El-Ghany S.** High resolution computed tomography and pulmonary function tests in childhood systemic lupus erythematosus and juvenile rheumatoid arthritis. Egypt J Pediatr Allergy Immunol 2004; 2(1): 8-15.
5. **Ostanek KL , Plonska E, Peregud-Pogozelska M , Mokryzychi K, Brzosko M, Fischer K et al.** Cardiovascular abnormalities in systemic lupus erythematosus patients in echocardiographic assessment. Pol Merkur lekarski 2006, 20:305-8 (Abstr.(.
6. **Guevara JP, Clark BJ, Athreya BH.** Point prevalence of cardiac abnormalities in children with systemic lupus erythematosus. J Rheumatol 2001; 28: 854-9.
7. **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 .
8. **Omdal R, Lunde P, Rasmussen K, Mellgren SI, Husby G.** Transesophageal and transthoracic echocardiography and Doppler-examinations in systemic lupus erythematosus. Scand J Rheumatol 2001; 30: 275–81.
9. **Pieretti J, Roman M J, Devereux RB, Lockshin M D, Crow MK, Paget SA, et al.** Systemic lupus erythematosus predicts increased left ventricular mass. Circulation 2007; 116: 419-26.
10. **Prsa M, Mackie AS, Chedeville G, Duffy CM.** Transient left ventricular wall thickening in a child with systemic lupus erythematosus and myositis. Pediatr Rheumatol Online J 2006; 1-7.
11. **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; 17: 567-70 .
12. **Beresford MW, Cleary AG, Sills JA, Couriel, Davidson JE.** Cardio-pulmonary involvement in juvenile systemic lupus erythematosus. Lupus 2005; 14: 152-8.
13. **Weinrib L, Sharma OP, Quismorio FP.** A long term study of interstitial lung disease in systemic lupus erythematosus. Semin Arthritis Rheum 1990; 16: 48-56 .
14. **Renzoni E, Rottoli P, Coviello G, Perari MG, Galeazzi M, Vagliasindi M.** Clinical, laboratory and radiological findings in pulmonary fibrosis with and without connective tissue disease. Clin Rheum 1997; 16: 570–7.
15. **Bankier AA, Kiener HP, Wiesmayer MN, Fleischmann D, Kontrus M, Herold CJ, et al** . Discrete lung involvement in systemic lupus erythematosus. Radiology 1995; 196: 835- 40.
16. **Cheema GS, Quismorio FP.** Interstitial lung disease in systemic lupus erythematosus. Curr Opin Pulm Med 2000; 6(5): 424– 9.
17. **Delgado EA, Malleson PN, Pirie GE, Petty RE.** The pulmonary manifestations of childhood onset systemic lupus erythematosus. Semin Arthritis Rheum 1990; 19: 2.