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Original Article

Echocardiographic findings in systemic lupus erythematosus and its relation to disease activity and damage index

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ABSTRACT

Aim of the work: To assess the echocardiographic changes using Trans Thoracic Echocardiograghy in systemic lupus erythematosus (SLE) patients with and without antiphospholipid syndrome (APS) and to study the relation of the changes to the disease activity and damage.

Patients and methods: This study was conducted on 50 SLE patients (25 with and 25 without APS) and 50 controls. The SLE disease activity index (SLEDAI) and Systemic Lupus International Collaborating Clinics Damage index (SLICC/DI) were assessed. Laboratory investigations were performed and transthoracic echocardiography (TTE) was done.

Results: The mean age of the patients was 27.7 ± 8.5 years and disease duration 4.1 ± 3.7 years; 44 females and 6 males; 7.3:1. There was a high frequency of mitral (64%), aortic (22%) and tricuspid (24%) valve regurges as well as pericardial effusion (22%). Left ventricular hypertrophy and atrial dilation was present in 10% of the patients. The frequency of mitral, aortic and tricuspid regurge in SLE patients with APS tended to be higher (84%, 32% and 36%) than in those without (44%, 12% and 12%, respectively). There was a significant correlation between SLEDAI and pericardial effusion ($p = 0.001$), between the SLICC/DI with the left ventricular diastolic dysfunction (LVDD) ($p = 0.001$), the presence of lupus nephritis with the ejection fraction ($p = 0.02$) and between hypertension with the LVDD ($p = 0.001$).

Conclusion: All SLE patients especially those with APS should be screened for the presence of structural cardiac abnormalities. TTE can be helpful as a noninvasive diagnostic tool for early detection of the abnormalities, resulting in earlier treatment and reduction in mortality and morbidity.

1. Introduction

Systemic lupus erythematosus (SLE) is a heterogeneous autoimmune disease that may involve many different organs and display a variable clinical course. The diagnosis of SLE is based on characteristic clinical findings of the skin, joints, kidneys, heart and the central nervous system, as well as on serological parameters such as antinuclear antibodies (ANA), in particular antibodies to double stranded deoxyribonucleic acid (dsDNA). The various clinical symptoms do not always occur simultaneously and may develop at any stage of the disease [1]. The heart is frequently involved in SLE: very sensitive methods of cardiovascular investigation have found the prevalence of cardiac involvement to be > 50% [2]. Dyslipidemia was associated with a decrease in the quality of life in SLE patients and obesity increased the risk of development of atherosclerosis [3]. Effective management of metabolic syndrome would help control SLE activity, damage, and the future development of cardiovascular events especially in the absence of symptoms of cardiovascular disease (CVD) [4].

Cardiac involvement substantially contributes to the morbidity and mortality of SLE patients. Multiple pathogenic mechanisms have been reported; non-organ-specific autoantibodies have been implicated in immune complex formation and deposition as the initial triggers for inflammatory processes responsible for Libman–Sacks verrucous endocarditis, myocarditis and pericarditis. Anti-phospholipid (aPL) antibodies have been associated with thrombotic events in coronary arteries, heart valve involvement and intra-myocardial vasculopathy in the context of primary and secondary APS. Antibodies-SSA/Ro and anti-SSB/La antigens also play a major pathogenic role affecting the heart conduction tissue leading to the electrocardiographic (ECG) abnormalities [5]. Cardiac manifestations are often mild and asymptomatic

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that can be recognized by echocardiography and other non-invasive tests [6]. All three layers of the heart (pericardium, myocardium and endocardium) can be involved by lupus. Pericarditis, although often not evident clinically, is included in the American College of Rheumatology (ACR) classification criteria for SLE [7]. Myocarditis is clinically found in 3–15% SLE patients and was subclinically reported [6]. Heart valve lesions (vegetation, valve thickening and dysfunction) are frequently reported in APS patients with and without SLE [8] and in those with aPL alone [9].

The aim of the present study was to assess the echocardiographic changes using Trans Thoracic Echocardiograghy (TTE) in SLE patients with and without APS and to study the relation of the changes to the disease activity and damage.

2. Patients and methods

This study included 50 SLE patients; 25 with APS and 25 without, collected from the Rheumatology and Rehabilitation Department, Beni-Suef University Hospital from May 2016 to December 2016 and were diagnosed according to the Systemic Lupus International Collaborating Clinics (SLICC) classification criteria for SLE [10]. 50 age and sex matched healthy unrelated subjects served as control. The study conforms to the 1995 Helsinki declaration and was approved by Cairo University Hospitals' ethical committee. Informed consent was obtained from all patients.

Patients were subjected to clinical and investigational work-up including full history thorough clinical examination with special attention to the chest and cardiac examination. Laboratory work-up included complete blood picture (CBC), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) concentrations (> 6 mg/l was considered positive), serum complement 3 (C3) and 4 (C4), antinuclear antibody (ANA) and anti-ds DNA, urine analysis and 24 h urinary proteins. Radiological investigations (if indicated) as chest X-ray, and ECG were done. Systemic Lupus erythematosus Disease Activity Index (SLEDAI) score was assessed [11]. A SLEDAI score of > 6 was considered an active disease. The disease damage was assessed according to the SLICC damage index (SLICC DI) [12].

Transthorathic echocardiography using (VividS5 machine) with performed for all patients for evaluation of the left ventricular internal dimensions, left ventricular ejection fraction, Pulmonary artery systolic pressure, resting wall motion abnormalities, presence of valvular regurgitation and its severity as well as assessment of diastolic function and pericardial effusion.

2.1. Statistical analysis

Statistical package for social science (SPSS) software version 20 was used. Results were described in the form of percentage distribution for qualitative data and (minimum, maximum, mean and standard deviation) calculation for quantitative data. Cross tabulation test was used for comparison between numerical values and Student *t*-test for comparison between means of two groups with a normal distribution. Mann-Whitney or Kruskall-Wallis tests were used to compare variables that were normal distribution. Significance was considered at $p < .05$.

3. Results

The study included 50 SLE patients; 25 with APS and 25 without as well as 50 matched control. The mean age of the patients was 27.7 ± 8.5 years and disease duration 4.1 ± 3.7 years; 44 females and 6 males; 7.3:1. Clinical manifestations, laboratory investigations, SLEDAI and SLICC in the SLE patients, with and without APS, are presented in Table 1. Comparisons of echocardiographic findings between SLE patients with and without APS are presented in Fig. 1 and with control in Table 2. None of the control had any echocardiographic findings except 2 with a grade 1 left ventricular diastolic dysfunction and 3 (6%) had mitral valve prolapsed (MVP). There was no significant difference between SLE patients and controls as regard of gender.

Correlation between echocardiographic findings with some clinical features, disease activity and damage in SLE patients are presented in Table 3. There was no significant correlation of the echocardiographic findings with malar rash, photosensitivity, oral ulcers, discoid rash, hematological disorders, serositis, arthritis, alopecia and fever.

4. Discussion

Systemic lupus erythematosus is a potentially severe autoimmune disease which demonstrates variations in incidence, prevalence, disease activity, and prognosis based on race and ethnicity [13]. The autoimmune process in SLE can cause myocarditis, pericarditis, endocarditis, valvular lesions, and defect in the conduction system. The most frequent valvular lesions reported in SLE patients were valve regurgitations with predilection to involve mitral and aortic valves [14]. Cardiovascular involvement in SLE might be associated with disease severity and activity [6]. Cardiac involvement as an initial manifestation of SLE is rare; however, in more than 50% of cases, cardiac involvement is associated with significant morbidity and mortality [15]. APS also can affect the cardiovascular system and contributes to many cardiopulmonary manifestations of SLE [16]. High levels of anticardiolipin (aCL) antibodies were strongly associated with cardiac abnormalities in SLE and other lupus-like syndromes [17]. Echocardiography is a sensitive and specific technique in detecting cardiac abnormalities and should be performed periodically in SLE patients [6].

In the current study, echocardiographic findings were significantly present in SLE patients including mitral, aortic and tricuspid regurgitation, pericardial effusion, left ventricular hypertrophy and left atrial dilation. In another study performed on 50 asymptomatic SLE patients [18] showed that mitral regurge (MR) was found in 32%, pericardial effusion in 32%, aortic regurge (AR) in 10% and tricuspid regurgitation (TR) in 20%. 22% of SLE patients had LVH and 8% had LVDD. The discrepancy in frequencies compared to the current work may be attributed to asymptomatic study design of their study. Another study [19] revealed MR in 8% of SLE patients, AR in 12% and pericardial effusion in 20%. In a study by Bourré-Tessier et al. [20] on 217 SLE patients 26% of SLE patients had MR, 3.7% AR and 4.6% had pericardial effusion. Several other studies, reported echocardiographic findings including valve regurge and pericardial effusion [21–25]. The female to male ratio in the present work was comparable to that in another study on Egyptian SLE patients [26]. In the present study, there was no significant difference between SLE patients and controls as regard of gender.

The present results confirm previous reports [18,21] on predilection towards the mitral valve cusps to be the most commonly affected in SLE patients followed by tricuspid valve In contrast to our study, mitral valve was followed by aortic valve in another 2 studies [9,22]. Moder and coworkers [27] suggested that valvular regurgitaion may be due to a combination of factors as Libman-Sacks endocarditis, fibrinoid degeneration, fibrosis, valvulitis, bacterial endocarditis and aortic dissection. Other contributing factors could be hypertension, prior rheumatic fever, an underlying bicuspid aortic valve and corticosteroid therapy. Bidani et al. [28] revealed that on histopathology, small pericardial blood vessels were surrounded by an infiltrate of lymphocytes, plasma cells, macrophages, and rare polymorphonuclear leukocytes. On immunofluorescence, IgG was present in a predominantly granular pattern around small pericardial vessels suggesting that immune complex deposition was the cause of pericarditis.

In this work there was a significant correlation between SLICC DI and LVDD. In agreement, Shang and coworkers [29] showed that SLICC DI ≥ 1 was independently associated with LVDD. This may suggest that the overall inflammatory burden in SLE, as reflected by SLICC DI is associated with the development of diastolic dysfunction. In the current study there was highly significant correlation between SLEDAI and