The Egyptian Heart Journal (2013) 65, 281–288

Egyptian Society of Cardiology

The Egyptian Heart Journal

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ORIGINAL ARTICLE

Early detection of premature subclinical coronary atherosclerosis in systemic lupus erythematosus patients

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Received 23 September 2012; accepted 15 December 2012
Available online 5 February 2013

KEYWORDS
Coronary calcification;
Calcium score;
Atherosclerosis;
SLE

Abstract *Objective:* To elucidate early coronary atherosclerotic changes in premenopausal systemic lupus erythematosus (SLE) female patients without clinical cardiovascular manifestation using a 64-slice Multi-detector computed tomography (MDCT) scan to detect coronary calcification and measure coronary calcium score (CCS), and to find out its correlation to some traditional and non-traditional risk factors.

Methodology: Sixty consecutive premenopausal SLE female patients, and sixty age and sex matched healthy subjects without known systemic, immunological, or cardiovascular disease (served as a control group) underwent clinical examination, serological analysis, and 64-slice MDCT-based coronary calcium scoring. All the clinical, serological, and MDCT parameters of the patients were correlated.

Results: Coronary calcification (CC) was seen in 21 patients (35%), the number of atherosclerotic calcified plaques ranged from 0 to 19. Calcium scores ranged from 0 to 843. In contrast to control subjects, SLE patients had significantly higher erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), total cholesterol level, low-density lipoprotein (LDL), immunoglobulin G (IgG) and IgM anti-cardiolipin antibodies, serum intracellular adhesion molecule (sICAM) and E-selectin levels. SLE patients had highly significantly more atherosclerotic plaques (3 ± 0.66 compared to 0.1 ± 0.07, $p < 0.001$) and higher CCS (59.2 ± 20.3 compared to 2.6 ± 1.85, $p < 0.001$). Significant positive correlation was found between both number of atherosclerotic plaques and CCS

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Peer review under responsibility of Egyptian Society of Cardiology.

Production and hosting by Elsevier

http://dx.doi.org/10.1016/j.ehj.2012.12.003

and total cholesterol level, LDL, cumulative prednisone dose, SLE disease activity index (SLEDAI), ESR, CRP, sICAM-1, E-Selectin, and anti-cardiolipin antibodies ($p < 0.05$ in all).

Conclusion: Pre-menopausal SLE female patients free from clinical atherosclerotic vascular disease have an increased number of atherosclerotic plaques and CCS, which correlate positively with SLEDAI disease activity score, serum CRP, anticardiolipin antibodies, sICAM-1, E-Selectin, LDL level, total cholesterol level, and cumulative prednisone dose. In addition, we conclude that MDCT is a non-invasive, sensitive, reproducible, and reliable tool for accurate measurement of coronary calcification.

1. Introduction

Systemic lupus erythematosus (SLE) is a systemic inflammatory disease that affects primarily women and causes chronic vascular inflammation.[1] Women with SLE have a high frequency of coronary artery disease (CAD) and exhibit high rates of myocardial infarction that are up to 52 times higher than in women without SLE in the age between 35 and 44 years.[2] As treatments for lupus itself have generally improved, direct mortality rates have declined and cardiovascular co-morbidities have become a growing clinical problem. Circulatory diseases are today a leading cause of mortality among SLE patients.[3] Several studies of subclinical atherosclerosis have identified that 30–40% of women with SLE have myocardial perfusion abnormalities.[4–6]

There has been a growing interest in the hypothesis that atherosclerosis may be an immune-inflammatory disease; in this regard, SLE is an interesting model because it represents an inflammatory disease of autoimmune origin.[7]

The mechanism of accelerated atherosclerosis in SLE is not clear. Several factors have been implicated for the high prevalence of premature CAD; these factors are a mixture between traditional risk factors and factors associated with the disease itself or its treatment. SLE patients have increased prevalence of conventional risk factors like hypercholesterolemia, diabetes mellitus, obesity, hypertension, and sedentary life.[8] Risk factors related to SLE and its treatment include the presence of anti-phospholipid antibodies like anti-cardiolipin antibodies (aCL), which are considered as an independent risk factor for myocardial infarction,[9] corticosteroid therapy either due to their direct atherogenic effects or through enhancement of traditional risk factors such as hyperlipidemia, hyperglycemia, hypertension, and obesity.[10,11] Also having SLE is considered an independent risk factor for cardiovascular disease[2]; the ongoing inflammatory process accompanying multiple immunological and procoagulant abnormalities in SLE[12], and the underlying genetic susceptibility to develop accelerated atherosclerosis in patients with SLE may play a role.[13]

Coronary calcium is closely associated with the presence and extent of atherosclerotic plaque and therefore constitutes a potential marker for early stages of coronary atherosclerosis in asymptomatic subjects.[14]

Therefore, this study was planned to elucidate early coronary atherosclerotic changes in premenopausal SLE female patients without clinical cardiovascular manifestation, using a 64-slice MDCT scan to detect coronary calcification and measure coronary calcium score, and to find out its correlation to some traditional and non-traditional risk factors.

2. Patients and methods

Between June 2010 and April 2012, sixty consecutive premenopausal SLE female patients fulfilling the criteria of the American College of Rheumatology (ACR) for the classification of SLE[15] were studied. We included only premenopausal women in order to avoid the strong confounding effect of low estrogen levels on the risk of vascular disease. We excluded patients with juvenile onset SLE; patients with other connective tissue diseases; clinical atherosclerotic vascular disease (previous cardiac, cerebral, or peripheral vascular affection); family history of premature CAD; diabetes mellitus; arterial hypertension; current smoking habit; or birth control using oral contraceptive pills so that we can limit the causes of early atherosclerotic changes in premenopausal female patients to the effect of SLE and/or its therapy. A group of sixty healthy female subjects of matched age (age is a known strong predictor of atherosclerosis) without known systemic, immunological, or atherosclerotic vascular disease served as a control group. The Royal Commission Hospital Ethics and Research Committee approved the study on March 2010.

At the time of the study, detailed disease and medication history (steroid intake duration, dosage, and frequency); calculation of body mass index (BMI) according to the following equation: BMI = Body weight in kg/Height in m.^{2} assessment of disease activity using the SLE Disease Activity Index (SLEDAI) according to Bombardier et al. (1992)[16]; laboratory assessment of complete blood count (CBC) using Coulter Counter T660, erythrocyte sedimentation rate (ESR) using the Westergren method, C-reactive protein (CRP) using the ELISA technique, antinuclear antibodies (ANA) by indirect immune-florescence using Kallestad kit, anti-double stranded DNA by the indirect immune-fluorescence technique, anti-cardiolipin antibodies (IgG and IgM) by enzyme linked immunosorbent assay (ELISA) according to Harris et al. (1987),[17] and 12 h fasting lipid profile (including total cholesterol, triglycerides, LDL-cholesterol, and HDL-cholesterol) using CX5 system (Beckman US) were performed.

2.1. Coronary calcium scoring protocol

Patients were scanned using a 64-slice CT scanner (General Electrics LightSpeed VCT, Milwaukee, WI, USA). A non-enhanced low-dose ECG-gated scan covering the whole heart during a single breath hold was performed at 70–75% of the R–R interval using the following scan parameters: detector coverage 1.25 mm; gantry rotation time 350 ms; tube voltage 120 kV; and tube current 180–200 mA. Datasets were reconstructed from the retrospectively gated raw data. Images were