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ORIGINAL ARTICLE

Study of anti-apolipoprotein A-I antibodies and paraoxonase 1 activity in systemic lupus erythematosus patients; correlation with disease activity and damage indices

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KEYWORDS

Systemic lupus erythematosus (SLE);
Anti-apolipoprotein A-I antibody (anti-Apo A-I);
Paraoxonase 1 (PON1)

Abstract *Introduction:* Systemic lupus erythematosus (SLE) patients have an increased risk of atherosclerosis. Identification of at-risk patients and the pathogenesis of atherosclerosis in SLE remain elusive. Paraoxonase 1 (PON1) and anti-apolipoprotein A-I antibody (anti-Apo A-I) appear to have a potential role in premature atherosclerosis in SLE.

Aim of the work: To assess two novel risk factors of atherosclerosis in SLE patients; PON1 activity, and anti-Apo A-I antibody levels, in order to elucidate any possible correlation between both of them, and to demonstrate their relations to disease activity disease activity as well as disease related damage.

Patients and methods: Forty SLE female patients and 40 apparently healthy volunteers were included in this study. Anti-Apo A-I antibody levels and PON1 activity levels were assessed. Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) and Systemic Lupus International Collaboration Clinics (SLICC)/American College of Rheumatology (ACR) damage index were preformed to all patients.

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Results: Compared with controls, SLE patients showed significantly lower PON1 activity and significantly higher titers of anti Apo A-I. Anti-Apo A-I antibody titers correlated inversely with PON1 activity. Elevated titers of anti-Apo A-I antibody and reduced PON1 activity were related to increased SLEDAI and (SLICC/ACR) damage index scores.

Conclusion: There is a decreased PON1 activity and formation of anti-Apo A-I antibodies in SLE patients and both of them correlated with disease activity as well as disease-related damage. PON1 activity and anti-Apo A-I antibodies might be involved in the pathogenesis of premature atherosclerosis in SLE patients.

1. Introduction

Systemic lupus erythematosus (SLE) is a chronic autoimmune inflammatory disorder that primarily affects women and can involve virtually any organ in the body [1]. It is characterized by the presence of autoantibodies against multiple self antigens and immune complexes that target multiple organ systems [2].

With the increased life expectancy among SLE patients, accelerated atherosclerosis and subsequent cardiovascular disease (CVD) have emerged as a significant threat that significantly contributes to morbidity and mortality [3].

In recent years, there has been a growing interest in understanding the pathogenesis of accelerated atherosclerosis in SLE [4]. Traditional risk factors fail to account fully for the excess CVD events in SLE patients. Therefore, it has been suggested that patients possess additional SLE-related risk factors [5].

Epidemiological studies have demonstrated a strong inverse relationship between high density lipoprotein (HDL) level and risk for CVD [6]. HDL has a wide range of functions including: reverse cholesterol transport, antioxidant, anti-inflammatory, anti-thrombotic and anti-atherogenic activity [7]. The protective functions of HDL could be partly explained by its constituents mainly, apolipoprotein A-I (Apo A-I) and paraoxonase (PON1) [8].

Apo A-I is the major protein component of HDL and is widely considered to be responsible for the anti-atherogenic and anti-thrombotic effects of HDL by promoting cellular cholesterol efflux and exerting anti-oxidative and anti-inflammatory effects [8]. Apo A-I exerts anti-oxidant properties by stabilizing PON1 [9]. PON1 is an antioxidant enzyme attached to HDL. PON1 decreases systemic oxidative stress and is associated with a lower incidence of CVD [10].

There is an emerging evidence of the presence of anti-Apo A-I antibodies and the reduction in the plasma levels of PON1 in SLE patients, thus interfering with the protective functions of HDL favoring atherogenesis [11].

The aim of the present study was to assess two novel risk factors of atherosclerosis in SLE patients; PON1 activity, anti-Apo A-I antibody levels, to find any possible correlation between both of them, and to demonstrate their relations to disease activity as well as disease related damage.

2. Patients and methods

2.1. Patients

Eighty participants were included in this study; they were divided into two groups:

2.1.2. Group (A): patient group

Forty SLE premenopausal female patients were diagnosed according to the ACR revised criteria of SLE [12]. Their age ranged between 18 and 46 years and the SLE disease duration extended between 0.5 and 15 years. These patients were recruited from Rheumatology and Rehabilitation outpatient clinic and department of Kasr El-Aini hospitals (Cairo University). SLE patients with parameters known to influence the PON1 activity or induce premature atherosclerosis were excluded namely, smoking, diabetes mellitus, chronic renal failure or nephrotic syndrome, and antiphospholipid syndrome. Patients on lipid lowering drugs, known cases of primary dyslipidemia and hypothyroidism and family history of CVD were also excluded.

2.1.3. Group (B): control group

Forty apparently healthy, age – matched female volunteers served as the control group. Their age ranged between 18 and 47 years.

An informed consent was obtained from all participants in the study, and the study was approved by the Institutional Review Board (IRB) of faculty of medicine, Cairo University.

2.2. Methods

All participants were subjected to the following:

1. **Comprehensive history taking and thorough clinical examination;** general, cardiopulmonary, abdominal, neurological, and musculoskeletal system.
2. **Routine laboratory investigations** (CBC, ESR, liver and kidney functions, and urine analysis, in addition to estimation of total albumin in 24 h urine), lipid profile (triglycerides and total serum cholesterol, HDL, and LDL concentration), immunological assays (ANA, anti-dsDNA antibodies, anticardiolipin antibodies, and lupus anticoagulants), and serum complement levels (C3 and C4).
3. **Determination of anti-Apo A-I antibody levels in the plasma;** 96-well plates (PolySorp) were half-coated for 1 h at 37 °C with 10 g/ml human Apo A-I (Sigma–Aldrich) in 70% ethanol. Blocking was performed using phosphate buffered saline containing 1% albumin from bovine serum for 1 h at 37 °C. Hundred microliters of the samples (1:300 dilutions in blocking agent) and positive control were added to duplicate wells in both halves of the plate and kept for 1 h at 37 °C. After washing, alkaline phosphatase-conjugated anti-human IgG (1:1000 in the blocking agent) was added for 1 h. *p*-Nitrophenyl phosphate (1:5000 in