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ORIGINAL ARTICLE

Correlation between various clinical parameters of systemic lupus erythematosus and levels of anti-histone and anti-chromatin antibodies

Soha Mostafa El Desouky [a], **Iman Ibrahim El-Gazzar** [a,*], **Laila Ahmed Rashed** [b], **Nehal Mohamed Salama** [a]

[a] *Department of Rheumatology and Rehabilitation, Faculty of Medicine, Cairo University, Cairo, Egypt*
[b] *Department of Medical Biochemistry, Faculty of Medicine, Cairo University, Cairo, Egypt*

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KEYWORDS

Systemic lupus erythematosus (SLE);
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Clinical manifestations;
SLE Disease Activity Index (SLEDAI)

Abstract *Background:* Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by the production of auto-antibodies leading to a spectrum of clinical findings. Among these auto-antibodies are anti-chromatin and anti-histone antibodies in which researches showed a renewed interest in the last few years.

Aim of the work: The aim of our study was to assess the serum levels of anti-chromatin and anti-histone antibodies in patients with SLE, and to correlate them with clinical features of the disease.

Patients and methods: The study included 60 female SLE patients and 13 normal females as controls. Patients were subjected to full history taking, clinical examination, and laboratory tests. Serum anti-chromatin and anti-histone antibodies were detected using enzyme linked immunosorbent assay (ELISA) in patients and controls.

Results: Anti-chromatin antibodies showed 100% sensitivity and 66.7% specificity, while anti-histone antibodies showed 100% sensitivity and 53.3% specificity. A statistically significant difference was elicited between SLE patients and controls regarding the serum levels of both antibodies. Serum levels of anti-chromatin antibodies in SLE patients were significantly correlated with the occurrence of hematological manifestations, duration of steroid therapy, and also dose and duration of hydroxychloroquine (HCQ) therapy. However, no significant correlation was found between anti-histone antibodies and other parameters.

* Corresponding author at: 14 Shehab Street, From Gameat Al Dewal Al Arabeyya Street, Mohandesseen, Giza, Egypt. Mobile: +20 1001313069.
E-mail address: imanalgazzar@hotmail.com (I.I. El-Gazzar).
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Conclusion: Anti-chromatin and anti-histone antibodies are both sensitive and specific for SLE and can be used not only for its diagnosis, but also for following therapeutic progress. Further studies on a large scale are needed to elucidate the effect of therapy on the serum levels of these antibodies in SLE patients.

1. Introduction

Systemic Lupus Erythematosus (SLE) is often described as the classical systemic autoimmune disease due to its wide spectrum of clinical and immunological abnormalities [1]. It is the most diverse of the autoimmune diseases and it is characterized by the production of multiple auto-antibodies with a complex and wide spectrum [2,3]. Even though the presence of autoantibodies in SLE has been known, for more than 60 years, still nowadays a great effort is being made to understand the pathogenetic, diagnostic, and prognostic meaning of such autoantibodies [3]. The prominent feature of immunological defects in SLE is the production of autoantibodies to nuclear antigens including deoxyribonucleic acid (DNA), histones and ribonucleoprotein (RNP) [4].

Anti-double stranded DNA (anti-dsDNA) antibodies are considered useful for the diagnosis of SLE, to monitor the disease activity, and correlate with renal and central nervous involvements [3]; they are found only in 50% of SLE patients and do not always correlate with disease activity [5].

On the other hand, antinuclear antibodies (ANA), the most prevalent antibodies, have low specificity for the diagnosis of SLE because they are found in most systemic autoimmune diseases and even in healthy individuals. Thus, it is important to look for other auto-antibodies that may be useful in the diagnosis and assessment of the disease activity in SLE patients [6].

Autoantibodies directed to chromatin components date back to the discovery of the LE cell with subsequent evidence that major components were chromatin and histones in particular. Over time, immunoassays ranging from ELISA and line immunoassays to more modern bead-based assays incorporated histone and DNA mixtures, purified histones, and purified nucleosomes leading to a more thorough understanding of the genesis and pathogenetic relationships of antibodies to chromatin components in SLE and other autoimmune conditions [7]. Anti-nucleosome antibodies are an excellent marker for SLE and good predictors of flares in quiescent lupus and anti-histone antibodies characterize drug-induced lupus [3].

Methods to detect anti-nucleosome antibodies have been available for more than 10 years and the test has demonstrated its good sensitivity and high specificity in diagnosing SLE. Despite these data produced through clinical and laboratory research, the test is little used. Data from the metanalysis have shown that anti-nucleosome antibodies have equal specificity but higher sensitivity and prognostic value than anti-dsDNA antibodies in the diagnosis of SLE. The use of anti-nucleosome antibodies appears more efficacious than anti-dsDNA [8]. Anti-histones were associated with a higher proportion of proliferative renal disease and poorer outcome in lupus nephritis patients [9].

The aim of the present study was to assess the serum levels of anti-chromatin and anti-histone antibodies in SLE patients and to correlate their serum levels with various clinical features of SLE.

2. Patients and methods

2.1. Patients

The present study was carried out on 60 SLE patients fulfilling the 1982 American College of Rheumatology (ACR) revised criteria for the classification of SLE [10,11] in addition to 13 apparently healthy age and sex matched subjects as the control group. All patients were selected from the outpatient clinic of Rheumatology and Rehabilitation Department, Cairo University Hospitals. 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 patients have been subjected to:

1. *Comprehensive history taking and thorough clinical examination:* general, cardiopulmonary, abdominal, neurological and musculoskeletal system.
2. *Routine laboratory investigations:* complete blood count (CBC), erythrocyte sedimentation rate (ESR), liver and kidney functions and urine analysis, in addition to estimation of total albumin in 24 h urine, blood glucose, immunological assays as anti-nuclear antibodies (ANA), anti-double strand DNA (anti-dsDNA) antibodies, anti Ro, anti La, anticardiolipin (aCL) antibodies and serum complement levels (C3 and C4).
3. *Assessment of disease activity using Systemic Lupus Erythematosus Disease Activity Index (SLEDAI):* Grading of disease activity to mild (1–10), moderate (11–20), severe (21–45), and very severe (>45) [12]. A final weight total SLEDAI score is then calculated with possible theoretic score of 105 [13].
4. *Radiological Investigations:* X-ray for any affected joint and Chest X-ray for detection of chest problems as pleural effusion, or interstitial lung disease.
5. *Electrocardiography (ECG):* for detection of ischemia, pericardial effusion, valvular abnormalities, pericarditis, myocarditis or endocarditis.
6. *Renal biopsy* and histopathological assessment in cases with renal involvement.

Serum anti-chromatin and anti-histone antibodies were detected in patients and controls as follows:

Determination of serum anti-chromatin (anti-nucleosome) and anti-histone antibodies using QUANTA-lite™ chromatin