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RESEARCH ARTICLE

Systemic Lupus Erythematosus Reactive Antibodies in Sudanese Psychiatric Patients

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ABSTRACT

Background: the relationship between neuropsychiatric manifestations and systemic lupus erythematosus (SLE) reactive autoantibodies is controversial and was not investigated before in Sudanese psychiatric patients.

Aim: to determine the association between psychiatric manifestations and several SLE reactive autoantibodies regardless of the presence of other SLE manifestations.

Material and Methods: the study involved a test group of one hundred psychiatric patients and age/gender matched control group of one hundred apparently healthy subjects. Antinuclear antibodies (ANA), anti-double stranded DNA (anti-dsDNA) antibodies and ANA profile3 concentrations were measured for each studied subject using ELISA method. The association between various SLE reactive antibodies and psychiatric illnesses were assessed using Mid-P extract test. $P < 0.05$ was considered significant.

Results: all subjects in the control group were ANA and dsDNA negative, however, only one (1%) was positive for anti-histone antibody (ANA profile3). Regarding patients with psychiatric diseases, 6% were ANA positive, 2% were dsDNA and 6% ANA profile3 positive. In contrast to dsDNA, there were significant associations between psychiatric diseases and ANA and/or ANA profile3 antibodies ($P = 0.007$ for ANA, $P = 0.0.125$ for dsDNA and $P = 0.033$ for ANA profile3).

Conclusion: Sudanese patients with psychiatric diseases tend to have positive SLE reactive autoantibodies especially for ANA and ANA profile3 antibodies.

Keywords: ANA, anti-dsDNA, ANA profile3, autoantibodies, neuropsychiatric, SLE.

1. INTRODUCTION

Characteristically complications of systemic lupus erythematosus (SLE) can involve any system in the human body including central nervous system, which explain the high prevalence of neuropsychiatric manifestations among SLE patients in children [1] as well as adults [2]. Neuropsychiatric SLE manifestations are wide ranging and they include cognitive and mood disorders, anxiety disorder, depression and psychosis [3, 4].

The etiology of Neuropsychiatric SLE manifestation is controversial but there are evidences that SLE-associated cerebral vasculitis, the cross-reaction of lymphocytotoxic antibodies with brain tissue and blocking of neurotransmission by noncytotoxic antibodies are involved in the pathogenesis [5]. The diagnosis of neuropsychiatric SLE is practically difficult because of the diversity of its clinical manifestations and the poor sensitivity and specificity of the laboratory tests commonly used for that purpose. Several attempts were made to link Neuropsychiatric SLE manifestations to certain auto-antibodies like antinuclear antibodies (ANA) and anti-double stranded DNA (anti-dsDNA) [6, 7]. The results of the previous studies in this regards showed great unexplained

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variability. This study was conducted to determine the association between psychiatric manifestations and several SLE reactive autoantibodies regardless of the presence of the other SLE manifestations. This in turn may give cues regarding participation of these autoantibodies in the pathogenesis of psychiatric disorders and whether SLE patients were admitted into psychiatric hospitals without being diagnosed as having SLE.

2. MATERIAL AND METHODS

The study was conducted during the period from December 2009 to November 2011 in the three major psychiatric hospitals in Khartoum state – Sudan. The ethical approvals were received from the institutional review board of the hospitals of concern.

The study involved a test group of 100 psychiatric patients selected randomly from psychiatry hospitals and age/gender matched control group of 100 apparently healthy subjects. Thorough medical history and clinical examination were conducted for all studied subjects.

Antinuclear antibodies (ANA) and anti-double stranded DNA (anti-dsDNA) antibodies concentrations were measured for each studied subject using ELISA method [8, 9]. The normal ranges for ANA and anti-dsDNA were <1.2 IU/ml and < 45 IU/ml respectively. Westernblot technique for ANA profile3 was used for detection of autoantibodies against cell nuclei, namely: nRNP/Sm, Sm, Ro52, ss-B, Scl-70, PM-Scl, Jo-1, CENP-B, dsDNA, nucleosomes, PCNA, Histones, Rib.P-protien and AMA-M2 (EUROIMMUN- Germany). The outcome of these results were evaluated by special ANA profile3 computer program (EUROBlotMaster and EUROLineScan). Statistical evaluation was performed using SPSS (SPSS for windows version 19) and OpenEpi version 2.3.1. The association between various SLE reactive antibodies and psychiatric illnesses were assessed using Mid-P extract test. $P < 0.05$ was considered significant.

3. RESULTS

61% of the psychiatric patients were males (age mean (M) ± standard deviation (SD) = 30.3±9.2 for the males and 32.5±12.2 for females). Alternatively, 57% of the control group were males (age M±SD = 30.0±8.9 and 32.0±7.4 for males and females respectively). The control group is well matched for age ($P = 0.794$) and gender ($P = 0.565$) with the test group.

All subjects in the control group were ANA and dsDNA negative, however, only one (1%) was positive for anti-histone antibody (ANA profile3). Regarding patients with psychiatric diseases, 6% were ANA positive, 2% were dsDNA and 6% ANA profile3 positive (table 1). In contrast to dsDNA, there were significant associations between psychiatric diseases and ANA and/or ANA profile3 antibodies ($P = 0.007$ for ANA, $P = 0.0.125$ for dsDNA and $P = 0.033$ for ANA profile3). Risk-based estimates and 95% confidence intervals (CI) of having SLE reactive auto-antibodies in patients with psychiatric diseases are summarized in table 2.

No	Age	Gender	ANA	dsDNA	ANAprofile3result
1	34 Years	Female	Positive	Negative	Positive for SS-B(La)
2	60 Years	Female	Positive	Positive	Positive for DsDNA and Ro-52
3	29 Years	Male	Positive	Negative	Positive for AMA-M2
4	20 Years	Female	Positive	Negative	Positive for PCNA
5	48 Years	Male	Positive	Positive	Positive for Ro-52
6	26 Years	Female	Positive	Negative	Positive for Scl-70

Table-1: Distribution of age, gender and auto-antibodies profile among psychiatric patients with positive SLE reactive antibodies

	Risk in patients with psychiatric diseases	Risk in subjects without psychiatric diseases	Risk ratio	P (Mid-P Extract)
ANA	6 (CI = 2.5-12.7)	0 (CI = 2.5-12.7)	13 (CI = 0.7-227.7)	0.007
dsDNA	2 (CI = 0.1-7.4)	0 (CI = 0.0-4.4)	5 (CI = 0.2-102.8)	0.125
ANA Profile3	6 (CI = 2.5-12.7)	1 (CI = 0.0-5.9)	6 (CI = 0.7-48.9)	0.033

Table-2: Risk-based estimates having SLE reactive auto-antibodies

4. DISCUSSION

It is evident from the current results that psychiatric diseases increase the odds of having positive SLE reactive autoantibodies especially for ANA and ANA profile3 antibodies. These findings are comparable with some previous studies investigating SLE reactive autoantibodies among patients with psychiatric disorders [10, 11] but not others [12, 13].

By the end of the last century, it was noticed that half of the members of the Dutch Lupus Patients Society had experienced psychiatric complains before SLE was diagnosed [12]. This motivated van Dam and his group to investigate whether SLE patients were admitted into psychiatric hospitals without being diagnosed as having SLE. ANA were found in 3% of patients, as well as controls. Anti-DNA antibodies were found in 1% of both patients and controls. These two important results enforced van Dam *et al* to conclude that SLE is not an important cause of admission to psychiatric hospitals. The conclusion of Dam *et al* was further supported by another study investigating whether unrecognized systemic SLE might occur more frequently among psychiatric patients [13]. Positive tests for ANA were found in 7% of the psychiatric patients and 4% of the control group. Antibodies against dsDNA were not found in sera of the psychiatric patients. After categorizing both groups for age and sex, no difference was found as for the frequency of ANA positive

sera between both groups, indicating that on the basis of serology, no evidence exists that SLE might be underestimated among psychiatric patients [13]. However, in the current study the control group is well matched for age and gender with the psychiatric patients, yet ANA, but not dsDNA, seropositivity was significantly higher in the control groups.

On the other hand, the relatively high percentage of ANA seropositivity in patients of the current study is further supported by the results of a recent research investigating the tendency of major depressive disorder towards autoimmunity. In spite of the relatively small sample size, the results revealed high positive ANA rate among the patient compared to the control group [14]. In addition, Villemain *et al* examined the sera of 81 psychiatric patients (51 with schizophrenia and 30 with affective disorders) using several assays in parallel for the presence of non-organ-specific autoantibodies including ANA and anti-histone antibodies. Nine out of the all sera studied were positive for ANA. Moreover, in 15 patients, significant titers of anti-histone antibodies were detected [11]. Although the results Villemain *et al* could not demonstrate an association between autoantibodies titre and a specific class of drugs, other studies suggest the possibility of drug-induced, namely lithium carbonate, high levels of antinuclear antibodies [15]. Alternatively, an old study investigated the prevalence of positive ANA in a group of patients suffering from recurrent affective disorders who had been treated for more than one year with lithium carbonate. There was no increase of ANA in these patients (8%) as compared with a group of patients suffering from affective disorders (7.5%). According to same study, prevalence of ANA positivity in the general population was 9% which is more compared to the current study (6%) [16].

Most of the recent studies investigating SLE reactive antibodies in psychiatric patients concentrate on more specific antibodies like those against endothelial cells (AECA), Ro, Ro52 and ribosomal P protein [17]. Conti *et al* evaluate the prevalence of antibodies against AECA, cardiolipin, β2 glycoprotein I, Ro, Ro52, La, glial fibrillary acidic protein, ribosomal P protein, dsDNA, and nucleosomes in SLE patients with neurosychiatric syndromes. AECA were present in 64.7% of SLE patients with psychosis and mood disorders and in 29.4% of patients without psychiatric manifestations other than anxiety. Conversely, no significant correlation were found between the presence of the other autoantibodies studied and psychiatric involvement.

In conclusion and according to the results of the current study, Sudanese patients with psychiatric diseases tend to have positive SLE reactive autoantibodies especially for ANA and ANA profile3 antibodies. These findings agree with some previous studies but not others. Possible explanation for the lack of agreement is that most previous researches target patients with different types of neuropsychiatric syndromes. In addition, most of these studies failed to adjust for the possible confounding factors e.g. the effects of some anti-psychotic drugs on SLE reactive antibodies titre, ethnicity and age variations.

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Conflict of Interest: None Declared

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