İLAÇ KULLANMAYAN ŞİZOFRENİKLERDE ANTİNÜKLEER ANTİKORLAR

ANTINUCLEAR ANTIBODIES IN DRUG-FREE SCHIZOPHRENICS

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Özet

Otoimmun fenomen ve şizofreni arasındaki ilişkinin biçimi tam anlamıyla açık değildir. Şizofren hastaların otoimmun durumlarını tanımlamak amacıyla, hastalar ve sağlıklı kontrollerin serumları antinukleer antikorlar(ANA), anti-double-stranded DNA(anti-dsDNA), anti-Ro(SS-A) ve anti-La(SS-B) gibi anti-single-stranded DNA(anti-ssDNA) için test edilidi. Bu otoantikorların analizi sensitive enzyme-linked immunosorbent assay(ELISA) yöntemiyle yapıldı. 70 hastanın hiçbirinin serumunda ANA, anti-dsDNA ve anti-ssDNA pozitifliği yoktu. ANA, anti-dsDNA ve anti-ssDNA açısından şizofrenikler ve kontroller arasında fark yoktu ($p>0.05$). Şizofreni etyolojisinde otoimmun temele ait delillerin belirsiz olarak kaldığı yorumu yapıldı.

Anahtar kelimeler: *Antinukleer antikor, Oto-immunite, Şizofreni*

Summary

The nature of the association between auto-immune phenomena and schizophrenia is not entirely clear. In an attempt to define the auto-immune status of patients with schizophrenia, sera of patients and healthy controls were tested for antinuclear antibodies (ANA), anti-double-stranded DNA (anti-dsDNA), anti-single-stranded DNA (anti-ssDNA), as anti-Ro (SS-A) and anti-La (SS-B). The analysis of these autoantibodies were done with sensitive enzyme-linked immunosorbent assay (ELISA). None of the sera of 70 patients was positive for the presence of ANA, and anti-dsDNA and anti-ssDNA. There was no significant difference between schizophrenics and controls in terms of ANA, anti-dsDNA and anti-ssDNA ($p>0.05$). It was concluded that evidence of auto-immune basis for schizophrenia etiology remains unclear.

Key words: *Antinuclear antibody, Auto-immunity, Schizophrenia*

Introduction

The auto-immune hypothesis in the etiology of schizophrenia is first advocated by Fessel (1). The relationship of auto-immunity and schizophrenia is not completely obvious (2). Antibodies to nuclear antigens (ANA, dsDNA, ssDNA), for instance, are almost invariably found in patients with Systemic Lupus Erythematosus (SLE) a subset of whom have a variety of psychiatric abnormalities (3) including psychosis, delirium, depression, and dementia (4). Furthermore, some patients even present with severe disease manifestations without clear evidence of other clinical signs of SLE (5). ANA occurred more often and in higher titers in schizophrenia (5-8), but anti-DNA antibodies were not found (9). ANA have also been found in schizophrenic patients treated with chlorpromazine and other psychotropic drugs (7,10-13). In an attempt to clarify this issue, we aimed to investigate the frequency of autoantibodies of different specificities in sera of schizophrenic patients and healthy controls.

Materials and Methods

Subjects

Seventy consecutive patients with schizophrenia and 20 normal controls were included in the study. Patients were categorized according to DSM-IV(14). Their conditions were diagnosed with aid of Structured Clinical Interview for DSM-IV version(15). None had evidence of SLE or other autoimmune-related disorders. Schizophrenics were free of psychotropic drugs for at least one month prior to hospital admission. Twenty similarly age-and sex-matched healthy volunteers, without history of psychiatric or vascular events and without history of chronic medication, were taken as the control group. Serum samples: After an overnight fasting, ten milliliters of heparinized venous blood was drawn and allowed to clot at room temperature. The sera were separated on the same day and stored at -80 ^{0}C until analysis. Detection of ANA, anti-dsDNA, anti SS-A and anti SS-B: ANA, anti-dsDNA, SS-A and SS-B were semiquantitatively detected with ELISA by using commercially available kits (Clark Laboratories Inc.). Firstly, control and serum samples were diluted with the diluent solution, then 100 µl of diluted serum control and standard samples were pipetted into the wells. The plates were incubated at room temperature (18-25^{0}C) for 30 minutes, then were washed four times with washing buffer. After this treatment, 100 µl of enzyme conjugate (goat anti-human IgG immunoglobulin conjugated with horseradish peroxidase) were added in to the wells. The plate was incubated at room temperature (18-25^{0}C) for 30 minutes. The washing procedure was repeated. 100 µl of substrate solution (solution A: hydrogen peroxide, solution B: tetramethyl benzidine) was dispersed into the wells, then incubated at room temperature (18-25^{0}C) for 15 minutes. 50 µl of stopping solution (1N H_2SO_4) was added into the wells. Optical density (OD) was read on multiscan spectrophotometer (microplate autoreader EL 309) at 450 nm. The intensity color developed is proportional to the concentration of serum ANA.

Statistical Analysis

All statistical analysis were performed by SPSS 7.0 statistical program (16). Comparisons were determined by χ^2 test. P value less than 0.05 was accepted as significant.

Results

Of the schizophrenic patients, 38 were paranoid, 14 were undifferentiated and 18 were disorganized. There was no significant difference (χ^2 =7.05, df=5, p=0.38) in terms of age between the study groups; mean (SEM) 33.3 ($\pm$2.57) years for the controls, 38.2 ($\pm$3.98) years for the schizophrenics. There was no significant difference in male to female ratio between these groups: controls: 10/10, schizophrenic disorder: 33/37. None of the schizophrenic patients and controls had positive test for ANA. All serum samples of patients were negative for anti-dsDNA, SS-A and B. Of the control individuals, 2 had positive serum test for anti-dsDNA. There were no significant relationships between age, sex and ANA, anti-DNA and a correlation was not found between serum ANA and anti-DNA antibody tests with the psychiatric diagnosis.

Discussion

We did not find any difference between schizophrenics and controls for ANA, anti-dsDNA and anti-ssDNAs; that finding was consistent with the study of de Vires et al (5). Another study revealed that a subgroup of schizophrenics had several significant immunological abnormalities, including increased prevalence of autoimmune diseases and ANA (17). Spivak et al (18) determined the significantly higher frequency of positive ANA among chronic schizophrenic patients when compared with the controls. No antinative DNA autoantibodies were detected in either schizophrenic patients or controls. In their study, positive sera for ANA was 20% in chronic

schizophrenics. In our study, absence of difference between schizophrenics and controls may have been due to the number of chronic patients (n=15) which was relatively fewer. Positive tests for ANA determined in other studies may be the result of drug use for a long time in chronic patients. It was determined that particularly those concerning a positive association between chlorpromazine and ANA (10,19). Our patients have not been taking any drug at least for a month and the number of chlorpromazine users were relatively fewer. In other studies, it was reported that positive sera for ANA was independent from disease, and it seemed to be seen in older ages, especially over the 60 years (5,19). The low mean age of our patients may explain the absence of positive sera for ANA. The auto-immune basis for schizophrenia has been investigated for the last 60 years. Although numerous immune abnormalities have been reported, there is much skepticism because most of the studies have failed to control for extraneous factors that may have influence the findings (17). In conclusion, we emphasize that autoantibody response may have multifactorial origin in psychiatric patients. Therefore further studies are needed, especially those having a longitudinal design and including drug-naive patients and with larger groups.

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