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Anti-DNA Antibodies from Patients with Schizophrenia Hydrolyze DNA

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Abstract : Schizophrenia associated with dysregulation of neurotransmitter processes in the central nervous system and disturbances in the humoral immune system resulting in the formation of antibodies (Abs) to the various components of the nervous tissue. Abs to different neuronal receptors and DNA were detected in the blood of patients with schizophrenia. Abs hydrolyzing DNA were detected in pool of polyclonal autoantibodies in autoimmune and infectious diseases, such catalytic Abs were named abzymes. It is believed that DNA-hydrolyzing abzymes are cytotoxic, cause nuclear DNA fragmentation and induce cell death by apoptosis. Abzymes with DNAase activity are interesting because of the mechanism of formation and the possibility of use as diagnostic markers. Therefore, in our work we have set following goals: to determine the level anti-DNA Abs in the serum of patients with schizophrenia and to study DNA-hydrolyzing activity of IgG of patients with schizophrenia. Materials and methods: In our study there were included 41 patients with a verified diagnosis of paranoid or simple schizophrenia and 24 healthy donors. Electrophoretically and immunologically homogeneous IgGs were obtained by sequential affinity chromatography of the serum proteins on protein G-Sepharose and gel filtration. The levels of anti-DNA Abs were determined using ELISA. DNA-hydrolyzing activity was detected as the level of supercoiled pBluescript DNA transition in circular and linear forms, the hydrolysis products were analyzed by agarose electrophoresis followed by ethidium bromide stain. To correspond the registered catalytic activity directly to the antibodies we carried out a number of strict criteria: electrophoretic homogeneity of the antibodies, gel filtration (acid shock analysis) and in situ activity. Statistical analysis was performed in 'Statistica 9.0' using the non-parametric Mann-Whitney test. Results: The sera of approximately 30% of schizophrenia patients displayed a higher level of Abs interacting with single-stranded (ssDNA) and double-stranded DNA (dsDNA) compared with healthy donors. The average level of Abs interacting with ssDNA was only 1.1-fold lower than that for interacting with dsDNA. IgG of patient with schizophrenia were shown to possess DNA hydrolyzing activity. Using affinity chromatography, electrophoretic analysis of isolated IgG homogeneity, gel filtration in acid shock conditions and in situ DNAse activity analysis we proved that the observed activity is intrinsic property of studied antibodies. We have shown that the relative DNAase activity of IgG in patients with schizophrenia averaged 55.4±32.5%, IgG of healthy donors showed much lower activity (average of 9.1±6.5%). It should be noted that DNAase activity of IgG in patients with schizophrenia with a negative symptoms was significantly higher (73.3±23.8%), than in patients with positive symptoms (43.3±33.1%). Conclusion: Anti-DNA Abs of patients with schizophrenia not only bind DNA, but quite efficiently hydrolyze the substrate. The data show a correlation with the level of DNase activity and leading symptoms of patients with schizophrenia.

Keywords : anti-DNA antibodies, abzymes, DNA hydrolysis, schizophrenia
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