On the status of autoimmunity in the disorders of schizophrenic and depressive spectra*

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The immunopathological process is known to be a typical facet for many disorders of the nervous system. In this study, quantitative and functional parameters were used to assess the immune system status in patients with schizophrenia, affective disorders, organic brain diseases with psychotic disorders, and multiple sclerosis. The results confirm the possible role of autoimmune reactions in the structure of the pathogenesis of endogenous mental disorders. The immunological profiles in schizophrenia and affective disorders were very similar. Patients with later onset of schizophrenia have shown higher levels of C-reactive protein. It may indicate its important role in the development of schizophrenia in this particular group of patients. Also, patients with schizophrenia having higher levels of neuron-specific enolase and C-reactive protein suffered from more severe thinking impairment.

Keywords: autoimmunity, schizophrenic disorders spectrum, depressive disorders spectrum, neuron-specific antigens, galactocerebrosides, S-100 protein, neuron-specific enolase, glial fibrillary acidic protein.

Introduction

The question of autoimmunity involvement in the pathogenesis of many psychiatric disorders has become the most relevant in the last decade. Yet, despite the presence of many studies in the field of interrelation between the immune system, autoimmune process, and mental disorders, the pathophysiology of psychoses remains not fully understood [1].

Materials and methods

The immune status in 57 patients with schizophrenic spectrum disorders and in 57 patients with multiple sclerosis was evaluated to study the role of the autoimmune component and pathophysiology of endogenous mental disorders.

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The following quantitative and functional parameters were used to assess the immune system status:

1. Lymphoid cells subpopulation share (in %) — CD3+; CD4+; CD8+; CD20+; CD4+/CD8+ ratio, immune regulatory index (IRI);
2. Plasma levels of immunoglobulins (IgA, IgG, IgM);
3. The neutrophil bactericidal activity — according to the NBT test;
4. Spectrum and level of neuron-specific antigens in blood sera: S-100 protein, neuronal membrane antigen, myelin basic protein (MBP), C-I type galactocerebrosides (GalC);
5. Plasma levels of circulating immune complexes;
6. Interferon status and cytokine profile.

The assessment of interferon status was provided in the Laboratory of the development of antiviral drugs and interferon inductors at the Research Institute of Influenza (St. Petersburg). The evaluation of cytokines' levels (IL-4, IL-6, IL-8, and INF-γ) was carried out using the enzyme-linked immunosorbent assay with a test system (LLC "Protein circuit").

The choice of diseases was made taking into account the following:

1. Multiple sclerosis may be used as a model of interaction of nervous and immune systems in autoimmune pathology.
2. The development of multiple sclerosis and schizophrenia (both are multifactorial disorders) may be associated with genetic predisposition and interaction between environmental factors, epigenetic modifications, and an implemented polygenetic system [3].
3. Multiple sclerosis and schizophrenia both may be characterized by a progressive course of the disease.

The processes underlying the pathogenesis of schizophrenia and depression are similar. That is why patients with affective disorders were also included in the research. A large spectrum of the research results in this field was currently accumulated. It allows us to affirm, that depression syndrome is an integral part of schizophrenia and may be registered in any clinical form and on any step of the course of this disease [5].

The inclusion of patients with organic brain diseases in the study was due to the fact that immunodeficiency may occur in almost all forms of these disorders.

Results

This allows us to compare the immune system reactivity depending on whether the aetiological factor is endo- or exogenous (Table 1).

The occurrence of neuron-specific antigens in the peripheral blood may be a marker of the destructive process in the nervous system. This includes alterations in astrocytes and oligodendroglia elements (S-100, MBP, GalC-1), myelin sheath of axons (MBP) or neuron membranes (MemAg). An increased level of inflammatory markers such as C-RP plays a similar role. The release of brain tissue proteins in a bloodstream provides the development of increased autoimmune reactions.

We investigated serum samples of 91 patients with schizophrenia (34.6 ± 9.9 years, 51 men и 40 women). The NSE, S100B, and hs-CRP levels were measured with Abbott and Roche automatic test systems (Table 2).

Table 1. **Comparison of data on immune status in mental disorders and multiple sclerosis with the normal values**

Immune status parameter	Schizophrenia (F2 by IDC-10)	Affective disorders (F3 by ICD-10)	Organic brain diseases with psychotic disorders (F06.8 — F06.9 by ICD-10)	Multiple sclerosis (G35 by ICD-10)
CD3-T (%)	▼	▼	▼	▼
CD4-TH (%)	▼	▼	▼	▼
CD8-TS (%)	▼	▼	▼	▼
IRI	▲	▲	▲	▼
NBT-spontaneous (%)	▲	▲	▲	—
NBT-stimulated (%)	▼	▼	▼	—
Rc NBT (%)	▼	▼	▼	—
CD20-B (%)	▲	▲	▲	▲
IgA (g/l)	▲	▲	▲	▲
IgG (g/l)	▲	▼	▼	▲
IgM (g/l)	▲	▲	▲	▲
S100 (i. a.)	▼	▼	▼	▼
MemAg (i. a.)	Norm *	▲	▼	▼
MBP (i. a.)	▲	▲	▲	▼
GalC (i. a.)	▲	▼	▲	▼

Notes: ▼ — statistically significant decrease; ▲ — statistically significant increase; * — during the analysis of the parameter in various nosological forms, its significant fluctuations observed.

Table 2. **NSE, S100B и hs-C-RP serum levels in patients with schizophrenia**

	NSE (ng/ml)	S100B (ng/l)	C-RP (mg/l)
M±m	6.44 ± 3.55	43.8 ± 21.4	1.83 ± 1.67
Min	3.86	20	0.07
Max	16.04	130	13.65

One-third of patients have shown C-RP levels between 3 and 10 mg/l, what indicates the presence of systemic inflammation. Patients with treatment resistance had higher levels of NSE (n = 34, 9 ± 3.1 versus 5.1 ± 3.0 ng/ml). Patients with family history of mental diseases have shown significantly higher levels of S100B (0.046 ± 0.026) compared with patients without a family history of mental illness (0.038 ± 0.015 mcg/l, p = 0.026). The positive correlation between levels of NSE, S100B and a number of hospitalizations was observed (r = 0.281, p = 0.012 and r = 0.289, p = 0.010 respectively).

The data analysis, aforementioned in Table 1 showed:

1. discovered trends in deviations of immune system parameters in schizophrenia and affective disorders follow very similar courses. This allows us to consider these disorders immunologically belonging to one group of mental pathology;
2. study witnessed in favor of a hypothesis long existing in literature, which emphasizes the immunopathological process as a typical pathogenetic link for many disorders of the nervous system. This allows using a similar neuroimmune approach for the analysis of various disorders.

The analysis of results, aforementioned in Table 2 showed the following:

1. higher levels of NSE and S100B were typical for patients with more severe disorder course, who also have undergone more exacerbations in a shorter time;
2. family history of mental disorders played a significant role in patients with increased levels of S100B protein. At the same time patients with later onset of the disease have shown higher levels of C-RP, which may indicate its important role in the development of schizophrenia in this particular group of patients;
3. patients with higher levels of NSE and C-RP suffered from more severe thinking impairment.

Conclusion

The research confirms the possible role of autoimmune reactions in the pathogenesis of endogenous mental disorders and deepens and specifies the conception. Practically it helps us to consider the new approaches to therapy (i.e. immunomodulatory treatment), directed against autoimmune manifestations in patients with endogenous mental disorders.

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