Assessment of Environmental Impact on the Prevalence of Allergic Diseases in the Region

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ABSTRACT

In recent years, more and more data have appeared showing that the pathology of two systems - immune and nervous - can be one of the potential mechanisms mediating the development of a wide range of mental disorders, and, above all, neurodevelopmental disorders (attention deficit and hyperreactivity syndrome, autism spectrum disorders) (ASD), schizophrenia spectrum disorders. Among neurodevelopmental pathologies, ASD is of the greatest concern, due to high heterogeneity and steady growth in the last 20 years, which cannot be explained only by increased awareness and improved clinical diagnostics, which complicates the diagnosis and treatment of this pathology

Keywords: environment, allergic diseases, immune system, pathology of the nervous system.

The authors have shown that neuroimmune disorders in the central nervous system (CNS) associated with the activation of microglia and astrocytes in various brain regions can be a key factor in the development and maintenance of ASD. Prolonged activation of microglia and its production of a wide range of pro-inflammatory cytokines leads to the death of neuronal cells and the loss of synaptic connections, which determines cognitive impairment and the core symptom of ASD - difficulties in social adaptation.

At the same time, pre/perinatal inflammation of the CNS in ASD creates the conditions for the formation of chronic inflammation that supports the dysfunction of the main regulatory systems of the body: the immune, neuroendocrine and microbial communities of the intestine, which, due to the complexity and complexity of interactions, are combined into an axis "intestinal microbiota - the immune system is the brain" [73, 79]. Within the framework of the axis, the immunoregulatory effect on the CNS is mediated by resident immunocompetent brain cells, T-lymphocytes, autoreactive to brain antigens, the autonomic nervous system, through sympathetic innervation, as well as peripheral cytokines, which normally enter the brain through areas with a specialized capacity of the blood-brain barrier. Intestinal bacteria, and, above all, the endogenous microbiota of the small intestine, being an important component of the metabolism of the human body, through the intestinal nervous and immune systems, or directly, through metabolites, participate in neurotransmission to the CNS (serotonin system), acting as modulators of brain plasticity, cognitive functions and behavior in general. The reverse regulation of immune responses and intestinal microbiota is carried out systemically - through hormonal cascades (the hypothalamic-pituitary-adrenal axis (HPA axis) and the sympathetic-adrenomedullary (SAM) system), regionally - through the nerve pathways to the lymphoid organs, and locally - through neurotransmitters (including dopamine and oxytocin). Obviously, the effects of dysregulation of the “intestinal microbiota-immune system-brain” axis will manifest itself

as an imbalance of peripheral signaling molecules: pro/anti-inflammatory cytokines, stress hormones, neurotransmitters, and metabolites of microorganisms. A comprehensive one-stage assessment of peripheral signaling molecules of the "gut microbiota – immune system – brain" axis and their biological variations can expand the understanding of the mechanisms involved in the development of ASD, determine biological markers of various clinical ASD phenotypes, and indicate new therapeutic targets.

Research methods: Violations of the functioning of the nervous system can occur under the influence of both exogenous (hypoxic, infectious, traumatic, toxic, psychogenic) and endogenous factors (genetic), as well as their combination and interaction. The clinical diagnosis of these conditions, especially at an early age, is far from always sufficient to predict the further development of the disease and assess the possible compensation of the identified disorders. Difficulties in diagnosis are often associated with the non-specific clinical picture of the disease due to the immaturity of the nervous system, as well as the nosological heterogeneity of mental illness.

In connection with the foregoing, an important and relevant aspect is the search for biological markers associated with certain characteristics of the disease and objectively reflecting the characteristics of the clinical condition of patients (clinical and biological correlations). Of great importance is also the possibility of using these indicators as predictors, allowing to reliably assess the likelihood of positive or negative dynamics of the development of the disease even during the initial clinical examination.A large amount of data has been accumulated in the literature that indicates the regulatory effect of the immune system on the nervous system, and the involvement of immune mechanisms in the formation of disorders in the functioning of the nervous system has been proven.

The action of any damaging factor, both exogenous and endogenous, including components of damaged, infected or modified cells of one's own body, triggers the activation of the immune system both in the brain and in the periphery. The developing pathological process is nonspecific character, manifesting itself in the brain in the form of neuroglia activation, synthesis pro-inflammatory factors, changes in the microvasculature and migration to the site of damage of peripheral immune cells, primarily neutrophils - the main effectors of inflammation. Degranulation of neutrophils in the focus of inflammation is accompanied by the release of proteolytic enzymes and neutralization of the focus of damage. Activation of inflammatory factors is also observed in the periphery. Further aggravation of neuroinflammation processes leads to impaired permeability of the blood-brain barrier, penetration of peripheral cytokines into the brain, damage/death of neurons, and release of neuroantigens into the bloodstream, accompanied by the synthesis of appropriate autoantibodies, i.e. the development of autoimmune reactions.

Among the numerous immunological indicators, those that are interconnected with the characteristics of the clinical condition of patients are of the greatest interest. Such indicators include, for example, indicators reflecting the state of innate immunity - leukocyte elastase (LE) and its inhibitor - α1-proteinase inhibitor (α1-PI). LE is a serine protease released into the extracellular space from azurophilic granules of neutrophils due to degranulation. The substrates of LE are collagen types I, II, III, IV, elastin, fibrinogen, fibrin, and the basal membrane of the vascular endothelium, and therefore, in some cases, LE is considered as a factor involved in the violation of BBB permeability [2,111]. α1-PI is an acute phase protein of inflammation that limits the proteolytic activity of LE and performs an important function in the regulation of inflammatory reactions [283]. The level of autoantibodies to neuroantigens is one of the indicators that reflect the state of acquired immunity and are interconnected with the characteristics of the clinical condition. Determined in the blood serum of patients with various neuropsychiatric diseases, it is considered as a marker of the severity of their clinical condition. However, until now, a

comparative analysis of a comprehensive assessment of the state of the immune system (inflammatory and autoimmune reactions), reflecting the relationship between innate and acquired immunity, in patients with impaired functioning of the nervous system (both exogenous and endogenous) has not been carried out. In addition, the direction associated with the search for immunological markers in terms of predicting the further development of the disease is extremely relevant. Such studies are undoubtedly a promising direction and are of significant practical interest for the diagnosis, therapy, and prognosis of the further development of these conditions.

The aim of this study was a comparative analysis of inflammatory and autoimmune reactions in the pathogenesis of disorders of the functioning of the nervous system of exogenous and endogenous nature in children with the consequences of perinatal CNS lesions, autism spectrum disorders and adolescents with schizophrenia.

Research objectives: Determine the indicators characterizing the state of innate immunity (inflammatory factors - the activity of leukocyte elastase and a1-proteinase inhibitor) and acquired immunity (autoimmune reactions to neuroantigens, nerve growth factor and myelin basic protein), in children with the consequences of perinatal CNS lesions, autism spectrum disorders and adolescents with schizophrenia before and after treatment.To investigate the clinical and immunological relationships between these indicators and the clinical assessment of the condition of patients according to the corresponding psychometric scales within each nosology. Assess the possibility of using each of these indicators, as well as their complex, as predictors of the further development of the disease in each group of patients.

For the first time, a comparative assessment of the indicators of innate and acquired immunity in patients with various forms of dysfunction of the nervous system (PN CNS, RAS, schizophrenia) in dynamics (before and after treatment) was carried out. Differences in the degree of activation of the immune system depending on the clinical condition of the patient and the severity of the disorder within each nosology were revealed. It has been shown that in all the studied forms of disorders of the functioning of the nervous system, LE activity is interrelated with the severity of the current pathological process, and the level of AAT to neuroantigens is related to its severity. For the first time, an assessment was made of the possibility of using the studied immunological parameters to predict the assessment of the further development of the disease for each examined nosological group. It is shown that the most predictive is the complex determination of the studied immunological parameters.

The results obtained expand the understanding of the role of the immune system in the pathogenesis of diseases of the nervous system, and also indicate that inflammatory and autoimmune reactions are common pathogenetic links in various forms of dysfunction of the nervous system.

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