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CYTOMORPHOLOGICAL MARKERS OF REMOTE NEUROLOGICAL COMPLICATIONS OF THE POSTMENINGITIC PERIOD IN CHILDREN

Djurabekova Aziza Takhirovna
Doctor of Medical Sciences, Professor, Head of the Department of Neurology, Samarkand State Medical University

Niyozov Shukhrat Tashmirovich
Doctor of Medical Sciences, Associate Professor of the Department of Neurology, Samarkand State Medical University

Isanova Shoira Tulkinovna
Candidate of Medical Sciences, Associate Professor, Department of Neurology, Samarkand State Medical University

Xudoyberdiyev Sherzod Egamberdi Ugli
Master of the Department of Neurology, Samarkand State Medical University

Abstract: Childhood cerebrospinal fluid disorders are a heterogeneous group of pathological conditions characterized by impaired physiological processes of production, circulation, and resorption of cerebrospinal fluid. This pathology is one of the most pressing problems in modern pediatric neurology, neurosurgery, and neonatology, due to the high frequency of occurrence, the polymorphism of clinical manifestations, and the potential severity of consequences for the developing child's body.

Key words: cerebrospinal fluid, intracranial pressure, prognostic criteria, pediatric neurology, pediatric neurosurgery.

Introduction. Epidemiological data indicate that congenital hydrocephalus occurs with a frequency of 0.48-4.6 cases per 1000 newborns, while acquired forms of cerebrovascular disorders are diagnosed in 5-15% of children with various central nervous system diseases. It is particularly concerning that in the structure of children's disability due to nervous system diseases, cerebrovascular disorders occupy one of the leading positions, accounting for up to 25% of all cases of permanent loss of working capacity in this age group.

The pathophysiological mechanisms of cerebrodynamic disorders in children are characterized by the complex interaction of numerous factors, including impaired cerebrospinal fluid production in the vascular plexuses of the ventricles, obstruction of cerebrospinal fluid pathways at various levels, insufficient cerebrospinal fluid resorption through paxion granulation, and changes in brain tissue compliance. In children, these processes occur against the backdrop of ongoing morphogenesis of the central nervous system structures, which determines the peculiarities of the clinical manifestations and course of the disease.

The etiological structure of cerebrospinal fluid disorders in childhood is characterized by significant diversity. Congenital forms can be caused by genetic syndromes, chromosomal aberrations, developmental anomalies of the neural tube, intrauterine infections. Acquired cerebrospinal fluid disorders develop due to craniocerebral injuries, neuroinfections, brain tumors, intraventricular and subarachnoid hemorrhages, especially in premature newborns.

The clinical manifestations of cerebrospinal fluid disorders in children vary significantly depending on the patient's age, the rate of development of the pathological process, the degree of compensation, and

the localization of the main pathological focus. In newborns and infants, the leading symptoms are the enlargement of the head, tension and bulging of the greater fontanelle, divergence of the skull sutures, and eye symptoms. In older children, intracranial hypertension symptoms come to the forefront: headache, nausea, vomiting, retinal congestion, impaired consciousness and cognitive functions. It is particularly difficult to predict the course of cerebrospinal fluid disorders in children, which is due to the high variability of clinical manifestations, various compensation mechanisms, and individual characteristics of the developing brain. The lack of clear prognostic criteria makes it difficult to choose the optimal management tactics for patients, determine indications for surgical treatment, and assess the long-term outcomes of the disease.

Modern approaches to the diagnosis of cerebrospinal fluid disorders in children are based on the integrated use of clinical, laboratory, and instrumental research methods. Neurovisualization, including brain ultrasound, computed tomography, and magnetic resonance imaging, allows for the assessment of morphological changes in the cerebrospinal fluid system and the surrounding brain structures. Functional research methods such as intracranial pressure monitoring, cerebral vascular dopplerography, and electroencephalography allow for the assessment of the functional state of the nervous system and compensatory mechanisms.

Laboratory studies of cerebrospinal fluid play an important role in diagnosing and predicting the course of cerebrospinal fluid disorders. Analysis of the protein composition, cellular elements, biochemical indicators, and specific biomarkers of the cerebrospinal fluid allows for the identification of inflammatory processes, assessment of the permeability of the blood-brain barrier, and prediction of complications. Despite significant progress in the diagnosis and treatment of cerebrospinal fluid disorders, the problem of predicting the course of the disease in children remains largely unresolved. Existing classifications and scales for assessing the severity of the condition do not always allow for adequate assessment of the disease prognosis and optimal treatment tactics. There is no unified approach to interpreting the results of various diagnostic methods from the perspective of prognostic significance.

The problem of prediction is especially relevant in young children, when clinical manifestations can be minimal or nonspecific, and the compensatory capabilities of the developing brain are high. Under these conditions, the role of objective diagnostic criteria increases, allowing for the detection of early signs of decompensation and predicting the further course of the disease.

The development of modern neuroimaging technologies, including functional magnetic resonance imaging, diffusion-tensor imaging, positron emission tomography, opens up new possibilities for studying the pathophysiological mechanisms of cerebrospinal fluid dynamic disorders and developing new prognostic criteria. The integration of data from various research methods using modern statistical methods and artificial intelligence allows for the creation of multifactorial prognostic models.

The study of molecular biomarkers of cerebrospinal fluid dynamics disorders is of great importance. Studies of proteins, neurotransmitters, inflammatory products, and other biologically active substances in cerebrospinal fluid and blood open up new prospects for early diagnosis and disease progression prognosis.

The socio-economic significance of the problem is due to the high cost of treating and rehabilitating children with cerebrospinal fluid disorders, as well as significant losses due to the disability of patients. The development of effective prognostic criteria will optimize patient management tactics, reduce the frequency of complications, and improve long-term outcomes.

The relevance of this study is due to the need to develop a comprehensive system of clinical and diagnostic criteria for predicting the course of cerebrospinal fluid disorders in children based on the integration of modern clinical, laboratory, and instrumental research methods. This will allow personalized treatment approaches, optimize the timing and volume of surgical interventions, and improve the quality of life of children with this pathology.

The aim of the study is to assess the clinical significance of cytological changes in cerebrospinal fluid in the formation and severity of neurological symptoms in children in the long-term period of meningitis.

Materials and methods of research. The study included 31 children aged 3 to 7 years who were examined and treated in the pediatric neurology and neurosurgery departments of the Multidisciplinary Clinic of Samarkand State Medical University with a diagnosis of the consequences of meningitis; Samarkand City Multidisciplinary Children's Hospital; Samarkand City Private Clinics, for the period 2022-2025. The average age of the examined children was 5.1±1.2 years.

The inclusion criteria in the study were: the presence of clinical and neurological symptoms of a residual nature (cerebrasthenic syndrome, seizures, motor, cognitive, and autonomic disorders), confirmed by clinical and instrumental examination methods; documented confirmation of the fact of meningitis; the presence of informed consent of parents or legal representatives for the child's participation in the study.

Exclusion criteria were: combined severe developmental defects of the central nervous system incompatible with life; tumor processes of the central nervous system; pronounced somatic diseases in the decompensation stage, preventing a comprehensive clinical and laboratory examination.

The diagnosis of the consequences of meningitis was established in accordance with the International Classification of Diseases of the 10th revision (ICD-10: G03.9, G09). The distribution of children by age was as follows: children aged 3 to 5 years constituted 45.2% (n=14), 5 to 7 years - 54.8% (n=17). By sex, the main group consisted of 61.3% boys (n=19), 38.7% girls (n=12). Taking into account the etiological factors of the meningitis, patients were distributed as follows: bacterial meningitis was noted in 48.4% of children (n=15), viral nature was noted in 38.7% (n=12), meningitis of unknown etiology was detected in 12.9% (n=4).

Analysis of cerebrospinal fluid disorders showed that 41.9% of children (n=13) had signs of moderate cerebrospinal fluid disorders, 29.0% (n=9) had pronounced disorders, while 29.1% of patients (n=9) had no significant cerebrospinal fluid deviations during the examination period.

The control group consisted of 22 conditionally healthy children, comparable to the main group in age and gender, who underwent a preventive examination in outpatient settings. The children of the control group did not have clinical and instrumental signs of central nervous system pathology, nor did they have anamnestic data on past neuroinfectious diseases.

Result. All children included in the study underwent a comprehensive examination using clinical, neurological, laboratory, and instrumental methods that comply with modern management standards for patients with meningitis complications.

Clinical and neurological examination included a detailed collection of anamnestic data with clarification of the features of the course of the acute period of meningitis, recovery periods, and the presence of residual symptoms. The neurological status was assessed by analyzing the severity of diffuse and focal symptoms, the state of cranial nerves, muscle tone, tendon reflexes, movement coordination, as well as the presence of convulsive, cognitive, and autonomic syndromes. The nature and severity of clinical and neurological manifestations were assessed taking into account the age characteristics of the examined children.

Instrumental methods included electroencephalography to detect epileptiform activity and functional changes in brain bioelectric activity. Based on the indications, neuroimaging studies (brain magnetic resonance imaging) were conducted, aimed at identifying residual-organic changes, signs of post-inflammatory complications, and cerebrospinal fluid dynamics disorders.

Cytological examination of cerebrospinal fluid was conducted according to the standard methodology. The total number of cellular elements, the nature of cellular composition (lymphocytic, neutrophilic, mixed), the presence of residual inflammatory process signs, as well as qualitative changes in cellular

elements were assessed. The obtained cytological indicators were analyzed in comparison with clinical and neurological symptoms and instrumental data.

A key feature of this study was a comprehensive correlation analysis of clinical and neurological syndromes and cytological indicators of cerebrospinal fluid in children in the long-term period of meningitis. For the first time, within the framework of this sample, a systematic assessment of the relationship between the severity of individual clinical symptoms (convulsive syndrome, cognitive and motor impairments, signs of cerebrospinal fluid disorders) and the nature of cytological changes in cerebrospinal fluid was carried out, which allowed us to consider cytological indicators not only as a reflection of the past inflammatory process, but also as potential prognostic markers of residual damage to the central nervous system.

Statistical processing of the obtained results was carried out using variational statistics methods on an individual computer. To assess intergroup differences, parametric and non-parametric analysis methods were used depending on the nature of data distribution. The relationship between clinical and neurological manifestations and cytological indicators was assessed using correlation analysis. Differences were considered statistically significant at a significance level of $p<0.05$.

Instrumental methods confirmed the presence of functional and organic changes in the central nervous system. Pathological changes in brain bioelectrical activity according to EEG data were registered in 61.3% of children in the main group, while epileptiform activity was detected in 35.5% of patients. According to MRI data, residual organic changes of a post-inflammatory nature were noted in 45.2% of children, and in 29.0% - signs of cerebrospinal fluid dynamics disorders, which indicates persistent structural and functional damage to the CNS in the long-term period of the disease.

Cytological analysis of cerebrospinal fluid revealed significant differences between the main and control groups. In children with consequences of meningitis, a significant increase in the total number of cellular elements in the cerebrospinal fluid was noted compared to the control group ($p<0.001$). The lymphocytic nature of pleocytosis prevailed, which may indicate persistent immuno-inflammatory activity in the central nervous system. In 38.7% of patients in the main group, signs of residual inflammation were detected, while in most children in the control group, cytological indicators corresponded to age norms. The obtained data confirm that cytological changes can persist in the long-term period of the disease and reflect the depth of CNS damage.

The conducted correlation analysis revealed statistically significant relationships between clinical manifestations, instrumental, and cytological indicators. A positive correlation was established between the presence of convulsive syndrome and the severity of lymphocytic pleocytosis ($r=0.56$; $p<0.01$), as well as between the pathological changes in EEG and an increase in the total number of cellular elements in the cerebrospinal fluid ($r=0.48$; $p<0.05$). A moderate correlation was noted between residual organic changes according to MRI data and signs of residual inflammation in the cerebrospinal fluid ($r=0.52$; $p<0.01$). Furthermore, the severity of cognitive impairments was reliably associated with combined cytological changes in the cerebrospinal fluid ($r=0.44$; $p<0.05$). A detailed analysis of the correlations indicates that the cytological indicators of cerebrospinal fluid are closely related to both the clinical picture and instrumental signs of central nervous system damage, which confirms their prognostic and diagnostic significance in assessing the consequences of meningitis in children.

Conclusions: The obtained results confirm that the consequences of meningitis in children are characterized by persistent clinical and neurological disorders that persist in the long-term period of the disease, despite the completion of the acute phase of the inflammatory process. The identified range of clinical manifestations from cerebrostenic syndrome to seizures and cognitive impairments aligns with data from foreign and domestic studies indicating the polymorphism of residual lesions of the central nervous system after neuroinfections. At the same time, a key feature of this study is the identification of reliable relationships between clinical manifestations, instrumental changes, and cytological indicators of cerebrospinal fluid. Unlike most previously published works focused primarily on the acute period of meningitis, this study shows that cytological changes in the

cerebrospinal fluid can persist for a long time and reflect the depth of the inflammatory damage to the CNS. Of particular importance is the established correlation between convulsive syndrome, pathological activity according to EEG data, and signs of residual inflammatory process in the cerebrospinal fluid, which indicates their general pathogenetic mechanisms. Similarly, the relationship between cognitive and motor impairments and residual-organic changes according to MRI data emphasizes the role of structural and functional brain damage in the formation of the clinical picture. Thus, the research results expand the understanding of the pathogenesis of the consequences of meningitis in children and justify the expediency of a comprehensive clinical, instrumental, and cytological approach to assessing the condition of patients in the long-term period of the disease. The identified patterns can be considered as a basis for improving diagnostic and prognostic algorithms, as well as for individualizing subsequent observation and rehabilitation of this category of patients.

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