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# CLINICAL AND LABORATORY- INSTRUMENTAL FEATURES OF MIXED HERPESVIRAL MENINGITES IN CHILDREN WHICH CAUSED BY COMBINATION OF HERPES SIMPLEX VIRUS AND CYTOMEGALOVIRUS

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**Abstract.** *The children of pre-school and school age with the burdened premorbid background, the average physical and physiological neuropsychic development more often have mixed herpesviral meningitis, caused by the combination of the virus of herpes simplex with the cytomegalovirus, somewhat more frequent in spring and in summer. The clinical picture was characterized by the symptoms of intoxication, catarrhal, general cerebral, gepato- or gepatolienal syndromes. In the peripheral blood of patients more there are found lymphocytosis, increase of ESR, anemia; in the urine of half of patients there is detected protein, of third part – acetone; in the liquor there is moderate lymphocytic cytositis, decrease of level of sodium and calcium. On electrocardiogram of children there are revealed sinus arrhythmia and disturbances of repolarization processes. On the echoencephalogram of the overwhelming majority of patients it is recorded normotension.*

**Keywords:** *children, virus meningitis, the virus of herpes simplex, cytomegalovirus, clinical picture.*

Viral meningites in children are some of the most severe neuroinfectious diseases according to frequency and evidence of severe consequences. In 15-60% of cases from the general morbidity by the viral affections of central nervous system viral meningitis finished by death of those patients [1,2]. In 85-96% of cases of herpesviral meningites take place neurologic deficiency [2,3]. All of them becomes to reason of invalidization and social disadaptation of reconvalescents. Among the

etiologic factors of viral meningites in the first place there are found the viruses of family Herpesviridae [1,6]. Some authors show that in 60-70% of cases herpesviral infection occurs not as mono- but mixed infectious pathology of nervous system caused more often by combination with virus of herpes simplex and other viruses of this family [1,2,6]. Detection of mixed affections of nervous system which caused by viruses of this family in the early stages of disease is important part of diagnostic process [3,6]. That is permit to quickly correction of therapy for decrease of severity and frequency of rezidual neurologic disturbances. Thus, the question of diagnostics of viral meningitis in children is one of the most prevalent problems of neuroinfectious pathology [4,5].

The aim of the research: improvement of diagnostics of meningites in children caused by the association of herpes simplex virus with cytomegalovirus, on basis of the study of their clinical picture, analysis of the results of standard laboratory and instrumental methods of diagnostics.

### **Materials and methods of the investigation**

The clinical picture and the results of the standard laboratory-instrumental methods of diagnostics of 15 children with mixed herpesviral meningites which caused by association of herpes simplex virus and cytomegalovirus, who hospitalized into the regional children's infectious clinical hospital of Kharkov was analyzed.

The verification of diagnosis was accomplished by the founding of specific antibodies to viruses (IgM and IgG) by the method of immune-enzyme analysis (ELISA-test), DNA of viruses in the blood serum and the liquor by the polymerase chain reaction, specific cytomegaloviral cells in the liquor by microscopic method.

### **Results and discussion of investigation**

Under the observation was 15 children in age 1 month - 15 years old with viral meningites, which caused by association of herpes simplex virus with cytomegalovirus: 2 (13,3%) - untill 1year old, 3 (20,0%) - 1-3 years old, 4 (26,7%) -

4-6 years old, 2 (13,3%) - 7-11 years old, 4 (26,7%) - 12-15 years old. Among of them was 7 boys and 8 girls (53,3%).

In winter 3 cases (20,0%) of disease was registered, in spring - 4 (26,7%), in summer - 5 (33,3%), in autumn - 3 (20,0%).

Analysis of anamnesis vitae of children of first three years old showed that in all cases pregnancy was complicated by gestosis I and/or II half pregnancy, and from early age has artificial feeding.

2 children (13,3%) in anamnesis vitae has manifestations of allergy. 11 children (73,3%) has experienced in the past one or more diseases: 9 (60,0%) - acute respiratory infections, 1 (6,7%) - bronchitis, 1 (6,7%) - pneumonia and in 2 children (13,3%) - intestinal infection. Neurologic-and-behavioral development in 14 patients (93,3%) conform to age, in 1 (6,7%) - was his delay.

In 3 children (20,0%) physical development was below average ( $<1$ ), 9 (60,0%) - average ( $\pm 1$ ), 3 (20,0%) - above average ( $> 1$ ).

Children entered to hospital on first-second day of disease beginning.

General condition of 13 children (86,7%) was moderately severe, of 2 (13,3%) - severe.

The clinical picture of meningitis was characterized by symptoms of intoxication, catarrhal, general cerebral, gepato- or hepatolienal syndromes (Tab. 1).

Fever in the first three-five days were recorded in all patients, including 5 children (33,3%) - up to  $38,0^{\circ}\text{C}$ ; 8 (53,3%) - up to  $39,0^{\circ}\text{C}$ ; 2 (13,3%) - above  $39,0^{\circ}\text{C}$ .

In 11 patients (73,3%) revealed changes in the upper respiratory tract: discharge from the nose were recorded in 4 children (26,7%), hyperemia of the mucous membranes of the oropharynx - 11 (73,3%).

In 5 patients (33,3%) was observed moderate enlargement of the liver size, 1 (6,7%) - the liver and spleen.

8 patients (53,3%) at onset of the disease complained of intense headache.

In 3 children (20,0%) in the first day recorded short-term klonik-tonic convulsions.

In 5 patients (33,3% ) during the first two days of the disease was observed vomiting: in 2 of them (40,0%) it was ones, 3 (60,0 %) - many times.

Table 1.

The principal clinical manifestations of mixed herpesviral meningites at onset of the disease

Clinical manifestations	Number of patients	
	abs.	%
Fever:	15	100
up to 38 <sup>0</sup>	5	33,3
38,1-39 <sup>0</sup>	8	53,3
39,1-40 <sup>0</sup>	2	13,3
Mucous discharge from the nose	4	26,7
Hyperemia of mucous membranes of the oropharynx	11	73,3
Enlargement of the liver	6	40,0
Enlargement of the spleen	1	6,7
Headache	8	53,3
Convulsions	3	20,0
Vomiting:	5	33,3
single	2	40,0
multiple	3	60,0
Positive meningeal signs	4	26,7

Positive meningeal symptoms (rigidity of occipital muscles; upper, middle and lower Brudzinsky's symptoms; Kernig's symptom; Lessage's symptom in infants) found in 4 children (26,7 %).

In the peripheral blood in 10 children (66,7%) lymphocytosis was recorded, in 4 (26,7%) - acceleration of ESR, in 3 (20,0%) - anemia.

In the urine of 8 patients (53,3%) the protein is occurred, in 3 (20,0%) - acetone.

In the liquor of all patients pleocytosis (211±17,3 cells in 1 mkl) was registered. Biochemical indices of liquor characterized by decreased level of sodium and calcium and normal concentration of protein, glucose, potassium, chlorine.

On electrocardiogram of 3 children (20,0%) sinus arrhythmia and in 2 (13,3%) disorder of repolarization process was register. On echoencephalography in 11 children (73,3%) normotension, 4 (26,7%) - hypertension was revealed.

### **Conclusions:**

1. Mixed herpesviral meningitis, which caused by combination of herpes simplex virus and cytomegalovirus, occurs more frequently at children of 1-3 years old (20%), 4-6 years old (27%), 12-15 years old (27%) with compromised premorbid background, normal neurologic-and-behavioral development (93,3%) and average physical development (60%), more frequently in spring and summer (27% and 33% accordingly).
2. The clinical picture of disease mainly registered in moderately severe (87%) forms and are characterized by the presence of symptoms of intoxication (100%), catarrhal (73%), general cerebral (55%), hepato- or hepatolienial (40%) syndromes.
3. In peripheral blood of patients in 67% of cases registered lymphocytosis, 27% - increased ESR, 20% - anemia. In half patients in urine protein is detected, in thirds - acetone.
4. In liquor of sick children moderate lymphocytic cytolysis is registered, level of sodium and calcium is decreased, level of protein, glucose, potassium and chloride is physiological.
5. 73% of patients has liquor normotension on echoencephalography; 20% - sinus arrhythmia and 13% - disorder of repolarization process on electrocardiogram.

### **References.**

1. Aurelius E. Neurological morbidity after herpes simplex virus type 2 meningitis: a retrospective study of 40 patients / E. Aurelius, M. Forsgren, E. Gille // Scandinavian journal of infectious diseases. – 2012. – 34(4). – . 278-283.
2. Caviness A.C. The prevalence of neonatal herpes simplex virus infection compared with serious bacterial illness in hospitalized neonates / A.C.

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- Caviness, G.J. Demmler, Y. Almendarez // The journal of pediatrics. – 2012. – 153(2). – . 164-169.
3. Celum C. The interaction between Herpes simplex virus and human immunodeficiency virus / C. Celum // Herpes. – 2004. – 11 (Sup 1. 1). – . 36-44.
4. Ihekweba U.K. Clinical features of viral meningitis in adults: significant differences in cerebrospinal fluid findings among herpes simplex virus, varicella zoster virus, and enterovirus infections / U.K. Ihekweba, G. Kudesia, M.W. McKendrick // Clinical infectious diseases. – 2013. - 15. – . 783-789.
5. Kimberlin D. Herpes simplex virus, meningitis and encephalitis in neonates / D. Kimberlin // Herpes. – 2004. – 11 (Suppl. 2). – . 65A-76A.
6. Tyler K.L. Herpes simplex virus infections of the central nervous system: encephalitis and meningitis, including Mollaret's syndrome / K.L. Tyler // Herpes. – 2004. – 11 (Suppl. 2). – . 57A-64A.

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