CLINICAL SYMPTOMS OF THE BRAIN OF INFANTS WITH INTRAUTERINE HERPES CYTOMEGALOVIRUS INFECTION

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The main subject that has been discussed in this article is about children born from TORCH (Toxoplasmosis, Others, Rubella, Cytomegalovirus, Herpes) infected mothers and its result in developing the subependymal cysts in the brain in newborns and its detection on neurosonography. All children with subependymal cysts had different localization of cysts in the brain with various sizes. According to our results, TORCH infection caused not only subependymal cysts but also polymorphic defeat in other organs like involvement of respiratory system, prolonged jaundice with hyperbilirubinemia, hepatomegaly and edema. Newborns of two groups had immunotherapy with different immunoglobulins (Cytotect, pentaglobin), and only 3 children had immunochemotherapy (Cytotect, viroleks). The therapeutic effect was observed for all the children in these groups

Keywords: herpes, cytomegalovirus (CMV), neonates, ultrasound, subependimal cyst, intrauterine infection.

Currently, there is a large increase in intrauterine herpes infection and the increasing number of infected infants. Etiology of herpes infections has the highest prevalence of cytomegalovirus (CMV) and herpes viral infection caused by the herpes simplex viruses (HSV) I and II. In neonates 85% of herpes viral infections are caused by HSV type II. Outcome of these infections even in asymptomatic form during pregnancy can cause serious consequences in the fetus: lesions in various organs and systems, congenital malformations, the most serious of which is brain damage.

A clinical manifestation is observed only in 10% in the neonatal period of ante-or intrapartum infected children, the remaining intrauterine infection in the neonatal period are asymptomatic. Mortality in children with generalized cytomegalovirus and herpes virus infection in the absence of chemotherapy is 95%; 55% of the survivors had severe neuropsychiatric outcomes [1-3].

Fast and reliable decoding of the etiology of the disease in the newborn is of particular relevance in connection with emerging in recent years, the possibility of a causal therapy.

The main method of diagnosis of these diseases is an immunological method. But it is not all available due to the high cost, complexity, considerable time required for definitive diagnosis. In addition, this method does not allow establishing involvement in the pathological process of the brain that is crucial for choosing therapeutic interventions. Therefore, currently the main diagnostic method in the first stage is echoencephalography in addition to clinical methods in order to assess the degree of involvement of the brain and other internal organs in the process.

On the basis of brain ultrasound and disease clinical symptoms, newborns can begin to be treated like children "on suspicion". In the future, these children will constitute a group for complex immunological studies, in the result of which the diagnosis will be updated.

From literature data, children with intrauterine herpes cytomegalovirus infection most often Echoencephalography detected choroid plexus cysts of the lateral ventricles and (or) Subependymal cysts [4]. It is shown that when choroid plexus cysts isolated (without analyzing their causes) forecast of neuropsychiatric development of children generally favorable [5]. When subependymal cysts have infectious origin the result is uncertain: from normal development to severe cerebral deficits [6-8]. In this regard, the objective of this study was to assess the psycho-neurological status of children with choroid plexus cysts and (or) Subependymal cysts with intrauterine herpes cytomegalovirus infection, confirmed by complex immunological research.

Materials and methods. From a group of infants (45 infants with subependymal cysts and 26 with choroid plexus cysts) 22 children were selected (after the completion of the observation period) by us with confirmed herpes cytomegalovirus infection with the help of immunological methods, which were subjected to dynamic echoencephalography and clinical examination for 1-12

months. Indications for immunological study in the first phase were structural changes in the brain revealed by the ultrasound, indirectly indicating the presence of intrauterine infection.

Immunological diagnosis was to identify specific antigen enzyme immunoassay and immunofluorescence techniques, DNA fragments by polymerase chain reaction detection of specific antibodies in biological fluids. Material for studies in children were blood and urine, mothers - blood. Survey of mothers was conducted to improve the reliability of diagnosis in their children.

All children underwent dynamic echoencephalography the first 1-12 months of life.

Results and discussion. Of the 16 we observed children 4 children (I group) had isolated choroid plexus cysts of the lateral ventricles. All these children were full-term (2 boys, 2 girls) with a body weight of 2592 to 3825 g; 2 were born by spontaneous labor, 2 child recovered via cesarean section. Apgar score at 1 min. was 8 points, 5 min. 8-9. According complex immunological examination, 2 of 4 children set mixed herpes cytomegalovirus, in 1 – herpes viral infection and 1 – cytomegalovirus

The clinical picture in 2 children showed the CNS depression syndrome, which is expressed in the reduction of cerebral and motor activity, muscle tone and inhibition of physiological reflexes of newborns; these children revealed involvement in the pathological process of the respiratory system with the development of pneumonia. In 2 newborns with jaundice prolonged marked hepatosplenomegaly, in 2 – edema. At 4th child neurological symptoms was absent, he had revealed changes in the internal organs in the form of prolonged jaundice and hepatosplenomegaly.

Echoencephalography of children found a group of 1 to 3 isolated cystic structures (cannot be combined with other structural changes) with a diameter of 0.3-0.5 cm located at the top of the body or the choroid plexus of the right lateral ventricle . For 3 of these children ventriculometry source data matched normal values. At the 1st child was a slight (0.5 cm) extension of interhemispheric fissure

and subarachnoid spaces on the surface of the brain and convexital symmetrical moderate increase in the width of the frontal horns (mostly) and the height of the lateral ventricles bodies (up to 0.6 cm).

At the end of the observation period, which ranged from 1 to 7 months, In 2 children choroid plexus cysts were former size and number; ventriculometry, as the first ultrasound, was age-adequate. One child with choroid plexus cyst decreased in size from 0.4 to 0.1 cm; further by Echoencephalography was noted symmetrical expansion of the lateral ventricles (their width and height of the frontal horns bodies increased from 0.6 to 0.8 cm) and interhemispheric fissure and subarachnoid spaces convexital on the brain surface from 0.5 to 0.8 cm. In one child at 7 months of life, choroid plexus cyst could not be detected, but it was symmetrical widening of the frontal horns (mostly) and the height of the lateral ventricles bodies up to 1 cm and expansion of subarachnoid spaces convexital on the brain's surface to 0.6 cm in follow-up, only this child revealed slight delay in psychomotor development, in 3 other children group signs of cerebral deficits were not marked.

II group consisted of 6 neonates with subependymal cysts; in 2 of them Subependymal cyst was combined with choroid plexus cysts. Of the 6 children in this group was 4 girls, 3 boys; All infants were full-term, with a birth weight of 2494 to 4740, the 3 of them infants recovered by cesarean section, 3 - were born in spontaneous labor. Apgar score at 1st min was 7-8, 5th min – 8-9.

According to complex immunological examination, in 3 children has been established mixed herpes cytomegalovirus, in 1 – and cytomegalovirus 2 – herpes viral infection. The clinical picture of this group of patients revealed polymorphic defeat with a predominance of symptoms of disorders of the nervous system in all children: mostly syndrome oppression – in 4, hyper excitability – in 2. The involvement of respiratory noted in 3 infants, prolonged jaundice with hyperbilirubinemia – the 6, hepatomegaly – in 2, edema – in 3 children.

Children in this group in the first Echoencephalography study were identified with subependymal cystic structure located at thalamo-caudal notch

(TCN) and (or) anterior to it in diameter from 0.4 to 1.0 cm. In some newborns Subependymal cysts were presented with single cavity with homogeneous or heterogeneous content, these structures resembled a cell, i.e., consisted of a variety of fluid inclusions surrounded by echo-positive rim. These structural features of subependymal cysts, apparently were due to the different stages of resorption. In 4 children Subependymal cysts were located in symmetric areas of both hemispheres, in 2 infants - only in the left hemisphere. In 3 children, in addition subependymal cysts located in thalamo-caudal clipping and (or) anterior to it, further revealed Subependymal slit cystic structure at the average level

All infants in this group the original data ventriculometry matched normal values. At the end of the observation period of 1 to 11 months. Size of the ventricular system in 4 children remained at normal values in 2 children had moderate (up to 0.8 cm), symmetrical widening of the frontal horns (mostly) and the height of the lateral ventricles bodies . In addition, one child showed expansion of interhemispheric fissure and subarachnoid spaces on the surface of the brain convexital to 0.8 cm during follow. Subependymal cysts decreased in size in 5 children (fully resorbed at the end of the observation period in 4 of them) and only in 1 child unilateral subependymal cyst increased to 2 months of life of from 0.5 to 1 cm

Newborn Group I and II had immunotherapy with different immunoglobulins (Cytotect, pentaglobin), 3 children – immunochemotherapy (Cytotect, viroleks). The therapeutic effect was observed for all the children in these groups.

Effectiveness of treatment was assessed by maturity out of a grave condition, elimination or reduction the phenomena of infectious toxicosis, buildup of body weight, according to the dynamic of Echoencephalography and laboratory parameters. At catamnestic follow-up, psycho-emotional and motor development in children 3 of Group II corresponded to the age norm. Other three children in this group during the first half had a lack of psychomotor development in varying

degrees (third of them had ventriculomegaly). By the end of the first year of life, signs of cerebral deficits was gone.

As in group I children, we found no clear link between the number, localization, and dynamics of subependymal cysts by complex immunological studies, and clinical manifestations of the disease in the early neonatal period and at the end of the observation period.

Conclusion. As you know, Subependymal cysts arising from infection are the result of damage of subependymally located germinal matrix by infectious agent. At the beginning of the process the damage zone necrosis occurs in the germinal matrix portion, to the extent to its resorption in 3-4 weeks it transformes into a cystic cavity [9]. Complete resorption of the cyst, as shown by our study is the end of 2-4 months of child's life (more cystic cavity, the longer the process of resorption). Since in all our sonographic observations of the brain have been identified Subependymal cysts, we can say that the damage to the germinal matrix occurred in utero.

Of 26 neonates with subependymal cysts only one child had gestational age 30 weeks. Overwhelming number of newborns (87.9%) were full-term. Knowing the time required for the formation of cysts in the subependymal zone of necrosis, we can assume that in most cases the damage of the matrix occurred at the end of the II - beginning of III trimester of pregnancy.

Same structural changes in the brain in newborns as subependymal cysts, apparently, are the outcome of damage to the germinal matrix in the process of regression (after completion of its primary function). Rejection or confirmation of this assumption could be done by screening ultrasound of fetal brain, conducted at the beginning of the II trimester of pregnancy, a highly qualified specialist using transvaginal transducer.

The similarity of the clinical picture of the disease in newborns in groups I and II, the etiology of the process established by the immunological method and a high therapeutic effect using the same drugs indicate that not the choroid plexus or Subependymal cysts are crucial in the clinical picture of the disease, but apparently

similar pathologic changes occurring in the brain influenced by infection that is undetectable by Echoencephalography. Choroid plexus and Subependymal cysts – are just markers of pathological processes. At the same time, identification with ultrasound of choroid plexus cysts and (or) subependymal cysts with clinical picture characteristic of intrauterine viral infections gives reason for immunochemotherapy even before the results of immunological research, which leads to a decrease in severe brain disorders in children at an early age.

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РЕЗЮМЕ

КЛИНИЧЕСКОЕ ТЕЧЕНИЕ ВНУТРИУТРОБНОЙ ГЕРПЕС-ЦИТОМЕГАЛОВИРУСНОЙ ИНФЕКЦИИ ГОЛОВНОГО МОЗГА У НОВОРОЖДЕННЫХ

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Основной темой, которая обсуждалась в этой статье было о детях, рожденных от матерей, инфицированных TORCH (Toxoplasmosis, Others, Rubella, Cytomegalovirus, Herpes) инфекцией и его результат в развитии субэпендимальных кист в головном мозге у новорожденных и его обнаружения на нейросонографии. При размещении всех детей с субэпендимальными кистами имели различную локализацию кист в головном мозге с различными размерами. Согласно нашим результатам, TORCH инфекция, вызвала не только субэпендимальные кисты, но и полиморфное поражение в других органах и системах, такие как вовлечение дыхательной системы, длительная желтуха с гипербилирубинемией, гепатомегалии и отеки. Новорожденные с двух групп имели иммунотерапию с различными иммуноглобулинами (Цитотек, Пентаглобин), и только 3 детей были на иммунохимиотерапии (Цитотек, Вайролекс). Терапевтический эффект наблюдался для всех детей в этих группах
Ключевые слова: герпес, ЦМВ, новорожденные, ультразвук, субэпендимальные киста, внутриутробная инфекция.

XÜLASƏ

YENİDOĞULMUŞLARDA BAŞ BEYNİN BƏTNDAXİLİ HERPES-SİTOMEQALOVİRUS İNFEKSİYASININ KLİNİK GEDİŞİ

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Təqdim edilmiş məqalədə müzakirə edilən əsas mövzu TORCH (Toxoplasmosis, Others, Rubella, Cytomegalovirus, Herpes) infeksiyası olan analardan doğulan uşaqlar, bu infeksiyanın yenidoğulmuşların baş beynində subependimal sistlərin inkişafında rolu və bu sistlərin neyrosonoqrafiya ilə aşkarlanması olmuşdur. Bütün uşaqlarda subependimal sistlərin baş beyində lokalizasiyası və ölçüsü müxtəlif olmuşdur. Bizim tədqiqatın nəticələrinə əsasən TORCH infeksiyası təkcə subependimal sistin yaranmasına deyil, həm də tənəffüs sisteminin cəlb edilməsi, hiperbilirubinemiya ilə uzunmüddətli sarılıq, hepatomeqaliya və ödemlər kimi digər orqan və sistemlərin polimorf zədələnməsinə səbəb olmuşdur. İki qrupa bölünmüş yenidoğulmuşlar müxtəlif immunoqlobulinlərlə (Sitotek, Pentaqlobin) immunoterapiya almışdırlar və yalnız 3 uşaq immunkimyəvi terapiya keçmişdir (Sitotek, Viroleks). Terapevtik effekt bu qruplarda olan bütün uşaqlarda müşahidə edilmişdir.
Açar sözlər: herpes, SMV, yenidoğulmuşlar, ultrasəs, subependimal sistlər, bətndaxili infeksiya.

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