Cytomegalovirus infections in neonates

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Abstract. This article presents the results of clinical and laboratory studies of 155 newborns with congenital cytomegalovirus infection. The following clinical manifestation have the greatest diagnostic value: jaundice, pallor, expressed hepatosplenomegaly. It's difficult to diagnose cytomegalovirus infection in premature babies for various reasons: frequent nonspecific clinical symptoms, subclinic or clinically asymptomatic picture. The presence and the level of immunoglobulins (antibodies) G and M and an increase in their titres is the crucial point in the diagnosis of CMV as well as positive polymerase chain reaction. Treatment of cytomegalovirus infection is effective on the background of comprehensive therapy (80%) and administration of NeoCytotect.
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Keywords: Cytomegalovirus infection, preterm infants, city children's clinical hospital, subclinic or clinically asymptomatic picture.

Introduction

Cytomegalovirus (CMV) infection is a viral infectious disease caused by DNA-containing virus *Human herpesvirus 5* (HCMV, or Cytomegalovirus hominis, or human cytomegalovirus) from the family of herpesviruses *(Herpesviridae)* [1,2]. Being in the family *Herpesviridae* HCMV belongs to the subfamily *Betaherpesvirinae* which also includes cytomegaloviruses, pathogenic viruses of other mammals [3]. Although viral particles can be found throughout the whole body, HCMV is often detected in the salivary glands. The virus does not manifest itself in a healthy human organism. However it can be fatal for people with immune deficiencies: HIV-infected patients, transplant recipients, newborns. After infection HCMV can latently persist in the body for a long time. Eventually this can lead to the development of mucoepidermoid carcinoma and other malignancies [4]. HCMV is found in all parts of the globe and in all socio-economic groups. Infection rate in the USA varies between 50% and 80% of adult people. Approximately 40% of people are infected all over the world that can be judged by the presence of antibodies in most of the population all over the world. The proportion of seropositive people depends on the age: in the age over 6 years more than 58.9% of individuals are infected, while after 80 years this figure is equal to 90.8% [6]. HCMV most commonly affects developing fetus being the most common viral cause of congenital defects in industrialized countries. It is more common in developing countries and among people with low socio-economic status. Virus considerably affects the immune system in later life and may cause increased morbidity and mortality [7].

Congenital infections result from prenatal (antenatal and intranatal) infection of a fetus. In the majority of cases mother is the source of infection to the fetus [8]. In recent years the use of invasive methods of prenatal diagnosis and treatment (amniocentesis, puncture of the umbilical vessels and others) and intrauterine administration of drugs through the blood vessels of the umbilical cord (transfusion of packed RBCs in hemolytic disease), as well as prolongation of pregnancy for preterm rupture of membranes predispose to iatrogenic fetal infection of the fetus. Along with this we can see an increasing number of people infected with sexually transmitted infections due to objective and subjective reasons. Therefore in the present time the number of infected women of childbearing age has increased [9]. However there's no single point of view on the issues of diagnosis and treatment in the intrauterine and early extrauterine periods [10]. At the same time in the republic there's no monitoring system for such a contingent of people. That's why the proportion of intrauterine infection in neonatal (early and late) mortality tends to grow [11].

Research objectives

Improve the quality of research methods and treatment of cytomegalovirus infection in newborn infants.

Material and methods

We have analyzed 155 medical records of infants treated at the City Children's Clinical Hospital of Aktobe diagnosed with intrauterine infection.

Results and discussion

The results of analysis of medical cases showed that mothers of 124 (80%) children revealed positive ELISA analysis during pregnancy for various intrauterine infection: CMV, HSV, toxoplasmosis, listeriosis, and others. In 80 (51.6%) mothers there were spontaneous abortions before the current pregnancy. 62 of the surveyed children (40%) were full-term, while the rest were preterm (60%).

Virtually all analyzed children had icteric staining of the skin and mucous membranes. In 102 subjects (66.7%) we revealed gray earthy skin. Skin turgor was reduced in 113 (73.3%) children. Clinical manifestation of pneumonia was noted in 124 (80%) children. In 51 children (33.3%) we revealed tachycardia. In 134 children (86.7%) there was bleeding from injection sites. In all subjects there was enlargement of the liver by 2-3 cm, and in some children we stated enlarged spleen.

Biochemical blood analyses detected hyperbilirubinemia mainly due to direct bilirubin fraction. An increased concentration of bilirubin was in the range from 130 mmol/L to 350 mmol/L. Liver transaminases were also increased in all 155 children: GPT within 8-60 U/L in 20%, from 68 to 124 U/L in 80%, GOT in all children was within 72-102 U/L. In half of the children there were elevated CRP levels that can indicate an activity of the process. All the children were tested for uterine infection by ELISA method. The former study gave positive results in all the surveyed children: in 124 (80%) children we detected anti-CMV IgG, in 20% children we detected anti-CMV IgM, and in 62 children (40%) we detected both (IgG, IgM) anti-CMV immunoglobullins. The level of IgG exceeded the permissible limits more than 10 times.

PCR was positive in 134 children (66.7%). Complete blood count revealed different degrees of anemia in all subjects. In 41 children there were indications for packed RBC infusion. In 20 children there was recurring administration of packed RBC. Fresh frozen plasma was used in half of the children in order to normalize coagulation system. In 35 children fresh frozen plasma was used repeatedly. In 1/3 of children there was expressed cerebral hemorrhage. These children underwent neurosonography and computed tomography of the brain. 2/3 of children along with overall therapy received etiotropic treatment: NeoCyotect. The drug was used at the dose of 1.9 ml/kg with an injection rate of 0.08 ml/kg body weight/hour. NeoCyotect was administered 3 times every other day as i.v. drip. Effectiveness of the drug was tested by the clinical manifestations in the form of improved color and elasticity of the skin, reducing in the sized of liver and spleen, and improving of biochemical parameters. All the children at different stages of the treatment demonstrated normalization of the clotting time, bilirubin level (direct and indirect fractions).

Five of 155 children died, and the others were rescued. For example, a child O. aged 1.5 months was diagnosed with congenital CMV hepatitis and referred to the regional children's infectious diseases hospital. The etiotropic treatment (NeoCyotect) wasn't carried out due to financial difficulties and at the age of 7 months the child was repeatedly admitted with cirrhosis, portal hypertension and died from profuse gastrointestinal bleeding. The diagnosis was confirmed by pathologist.

Second child K. aged 1.5 months was admitted in the ICU in critical condition, the child was diagnosed with intrauterine cytomegalovirus infection, congenital hepatitis. Hemorrhagic syndrome. Haemorrhage of the brain. Severe anemia. Morphofunctional immaturity.

In the biochemical blood analysis the level of common bilirubin was 113.6 mmol/L, direct bilirubin 52.5 mmol/L, indirect bilirubin 61.1 mmol/L, GOT 215 U/L, GPT 157 U/L.

ELISA analysis revealed: CMV-positive titers of JgG (OD serum 3.500; OD crit. 0.189). PCR analysis for CMV was positive. Along with intensive therapy we conducted etiotropic therapy, namely we administered NeoCyotect i.v. drip at the dose of 1 ml/kg/day with the infusion rate of 0.08 ml/kg/hour followed by the repeated administration in 48 hours twice more. The child's condition was stabilized on Day 20, in biochemical assays there was a decrease in total bilirubin down to 28 mmol/L, direct bilirubin down to 7.7 mmol/L, indirect bilirubin down to 20.3 mmol/L, GPT down to 69 U/L, GOT down to 55 U/L. PCR analysis for CMV was negative.

The child was discharged in satisfactory condition at home. All other children, besides those who died, received the same specific treatment and now all the children are alive and satisfactorily developed.

Conclusion.

Diagnosis of intrauterine cytomegalovirus infection requires objective evidence with mandatory polymerase chain reaction. Comprehensive treatment of the intrauterine infection affecting liver (hepatitis) requires antiviral treatment with NeoCyotectom.

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