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Optimization of the Diagnosis of Cytomegalovirus Infection in Young Children in an Outpatient Setting

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Relevance A feature of modern pathology in young children is the wide prevalence of herpesvirus group infections, which can be activated against the background of impaired immune defense, thereby providing an additional immunosuppressive effect and causing general sensitization of the body Cytomegalovirus infection (CMVI) is caused by the opportunistic intracellular herpesvirus type 5 (HHV-5) [2].

The prevalence of CMV in most studies was studied by the frequency of detection of specific IgG antibodies to the virus, as an indicator of infection in the population. The level of seropositivity of the population to this infection varies significantly even within one country, depending on ethnic and socio-economic factors. Thus, in Europe and the USA, 40-60% of the adult population is seropositive for CMV; in developing countries, the prevalence of CMV is even higher - 80.0% of children and almost the entire adult population. In the work of American scientists conducted in the last decade when studying the prevalence of serological markers of CMV in children, the following age trends were identified: among children aged 12 months, seropositivity was 12%, at the age of 2 years - 21%, at 5 years - 31% [1].

It is now considered proven that in the first months of life, the main source of infection for the newborn is the mother, who excretes the virus in urine, saliva and breast milk. About 20% of seropositive mothers have cytomegalovirus in breast milk and 30-60% of their children are infected [3].

Sources of CMV infection can be cytomegalovirus carriers or patients. The virus is transmitted both horizontally, through biological fluids and secretions, and vertically (hematogenously) . According to the concept of the pathogenesis of an infectious disease expressed by domestic scientists (Uchaikin V.F., Shamsheva O.V., 2013), it is fundamentally important to distinguish the route of transmission and, accordingly, the entrance gate of the infection, as well as to determine the tropic organ where the pathogen is most fully realizes its capabilities as a factor of aggression, and where the first meeting with all factors of the immune response occurs [8-27]. Cytomegalovirus has a pronounced tropism for lymphocytes, blood monocytes, and epithelial cells of the ducts of the salivary glands, where it is able to slowly multiply without damaging cells [4].

Purpose of the study. Clinical and laboratory variants of active cytomegalovirus infection in children of the main group.

Material and research methods. Among children with symptoms of ARI, various markers of CMV were detected in 77% (351/455) of children, the active stage of CMV was determined in 14% (65/455). Among clinically healthy patients, CMV markers were identified in 71% (46/65) of children, without signs of activation. The study groups were recruited from 455 people with ARI according to the inclusion/non-inclusion criteria: the main group consisted of 65 children with markers of active CMV (32 patients with acute primary CMV, 33 with reactivation of

CMV), the comparison group consisted of 43 children without markers of active CMV. The control group of conditionally healthy patients consisted of 46 people with markers of latent CMV infection.

All children of the main group were examined on an outpatient basis, with a referral from the local pediatrician in 64.6% (42/65) of cases.

The characteristics of the antenatal and early postnatal period of children of the main group were retrospectively studied. A burdened obstetric history was recorded in 40.0% (26/65) of mothers and was represented by such conditions as long-term infertility (16.9% (11/65)), previous miscarriages (15.4% (10/65)) and missed pregnancies (9.2% (6/65)). In all cases, the cause of these pathological conditions was not finally established. Threatened miscarriage occurred in 60.0% (39/65) of cases, of which 15.4% (10/65) occurred during the second half of pregnancy.

When studying the anamnesis, it was found that 23% (15/65) of children of the main group had a history of recurrent otitis media, 9% (6/65) laryngotracheitis and 11% (7/65) broncho-obstructive syndrome, and recurrent respiratory infections were noted in 63. 0% (41/65). 32% (21/65) of children in the main group had a history of mild hypochromic anemia. In the main group, the frequency of ARI over the previous 6 months was 3-8 episodes: average IR value = 0.51 ± 0.13. Hospitalization over the past six months was required by 20% (13/65) of children, with an average duration of 9.7 ± 1.6 days (CI 8.0; 11.3). Bacterial complications of ARI occurred in 69% (45/65) of cases and were represented by bronchopneumonia - 9% (6/65) and bronchitis - 18.5% (12/65); acute otitis media – 41.5% (27/65); acute tonsillitis – 3% (2/65). Over a 6-month retrospective analysis, the number of courses of antibiotic therapy was 2.8±0.2 (CI 2.5; 3.0), 126 cases of antibiotic therapy were documented, of which 108 were in outpatient settings, 18 in inpatient settings.

On an outpatient basis, 19% (21/108) were prescribed penicillins per os, 32% (34/108) – protected penicillins per os, 27% (29/108) III generation cephalosporins per os and intramuscularly, 23% (24/108) 108) oral macrolides were prescribed. In a hospital setting, the vast majority (89% (16/18)) of children received injectable forms of third-generation cephalosporins, rarely (11% (2/18)) - macrolides per os. Allergic pathology occurred in 35.4% (23/65) of children. Atopic dermatitis manifested itself from the first months of life in 24.6% (16/65) of children.

Using a laboratory examination, it was established that 49.2% (32/65) of children in the main group suffered primary CMV infection (PCR+ blood, IgM±, IgG-). During follow-up, all these children developed a picture of typical infectious mononucleosis. In the remaining 50.8% (33/65) of children in the main group, CMV reactivation was laboratory determined (PCR+ blood, IgM±, IgG+) and an acute respiratory disease with prolonged fever and lymphadenopathy was diagnosed.

In accordance with clinical recommendations for the management and treatment of ARI in children [8], all children in the main group had a moderate form of the disease.

Acute primary CMV infection in all cases occurred in the form of infectious mononucleosis. The clinical diagnosis was established based on a set of clinical and laboratory data, including lymphadenopathy, hepatosplenomegaly, damage to the nasopharynx and oropharynx, changes in white blood in the form of lymphocytosis with the appearance of atypical mononuclear cells. All patients with CMV mononucleosis had active replication of the virus in blood lymphocytes, which was confirmed by detection of CMV DNA in the blood.

The results of the study and their discussion. The onset of the disease in all children was acute, catarrhal syndrome was practically absent. The duration of fever, which in most cases (75%, 24/32) was febrile, was more than 7 days in all patients; low-grade fever syndrome persisted after illness for up to 14 days in 71% (23/32) of children. Lymph nodes were enlarged in all children, mainly submandibular and posterior cervical, no more than 2 cm in size, painless on

palpation; there were no cases of generalized lymphadenopathy. In 12.5% (4/32) of children, sialadenitis syndrome was noted, with severe pain when chewing and palpation of the parotid salivary glands. All children had moderate difficulty in nasal breathing, but without complete obstruction na general blood test, neutrophilic leukocytosis was noted in 28.1% (9/32) of cases; in the remaining children, the number of leukocytes was normal (16%, 5/32) or reduced from 4.0 to 3.5 109 cells/l (56%, 18/32), neutropenia (decrease in the absolute number of neutrophils below 1500 cells) - in 50.0% (16/32) of cases, absolute lymphocytosis was noted in all cases, monocytosis - in 84.3% (27/32) cases, atypical mononuclear cells were found in 56.2% (18/32) of children in the first - second week of illness in an amount from 4 to 20.0%, the ESR level was normal in 31.0% (10/32) of children, or moderate accelerated (from 15 to 20 mm/hour) in all other cases.

An immunological study indicated a deficiency of the humoral component of immunity, namely, a decrease in IgG occurred in 72.0% (23/32) and Ig A in 28.0% (9/32) of children of the main group who had infectious mononucleosis. A biochemical blood test revealed that markers of liver damage were detected in 44.0% (14/32) of children: an increase in ALT no more than 2-3 times, simultaneously with AST in all cases. Anti-CMV IgM was detected in 66.6% (24/32) of children who had a clinical picture of typical mononucleosis.

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