Comparative Clinical Signs of Herpetic Infection Coupled with HIV Infection

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Abstract

The article represents the results of the observation oft he comparative clinical examination of herpetic infection coupled with HIV infection in 57 children aged 1 to 15 years. There have been 41 boys (71,93%) and 16 girls(28,07%). The comparison group included 23 children oft he same age infected with HIV without herpetic infection.

The following laboratory research method have been used: a general analysis of blood, urine, feces, the study of the immune status, level of CD4 cells; Serological: by ELISA method antibodies to CMV and HSV (Herpes Simplex Virus) have been detected in blood. The results obtained indicate that coexisting diseases with the formation of complications and immunodeficiency development have been worsening the course of herpetic infection in HIV infected children and leading to a severe relapsing course.

Keywords: *Herpeticinfection, HIV infection, children, Herpes Simplex Virus.*

Introduction

The most significant group of opportunistic infections in HIV-infected children is the herpes group[3]. Infections caused by herpetic viruses draw attention by high prevalence in the human population. The most significant group of opportunistic infections in HIV-infected children is the herpes group[3]. Infections caused by herpetic viruses attract attention with a high prevalence in the human population. Among human viral diseases, herpetic infection (HI) occupies one of the leading places, which is explained by its ubiquitous transmission[4]. Herpeticinfectionis a group of diseases caused by herpes simplex viruses (HSV) of type 1 and 2. Atherpeticinfectionnotonlyepithelial, hematopoietic, nerve cells are affected, but also T-lymphocytes, which leads to the development of secondary immunodeficiency and generalized forms of the disease[5]. Herpes viruses are widespread in the human population, they are able to infect almost all organs and systems of the host organism, causing latent, acute and chronic forms of infection[3]. The cytopathogenic effect of herpes viruses is enhanced against the background of immunodeficiency condition. HIV infection is accompanied by the development of opportunistic diseases, among which herpes viruses take one of the leading places. The most common among them are lesions associated with herpes simplex viruses, zoster varicella, cytomegalovirus[1]. Herpes viruses can activate HIV, which is in the provirus stage, and is a cofactor in the progression of HIV infection and AIDS. In this regard, herpetic infection (HI) is one of the important AIDS-indicator disease. AIDS currently ranks third in the world in the group of deaths after diseases

of the cardiovascular system and neoplasms, and among children with HIV/AIDS it is the leading cause of death. The incidence of HI in the general population is 650-720 per 100 thousand population. Among HIV-positive, the same indicator is almost 10 times higher[2]. The viral etiology of the herpes group causes anabnormality of the functions of the immune system, resulting in the progression of immunopathological reactions, which reduces the control of virus replication, causing a manifestation or relapse of the disease[6].With herpes, immunodeficiency states develop due to the insufficiency of various parts of the immune system and its inability to eliminate the virus from the body. Persistent throughout life, sometimes in considerably high titres, virus-neutralizing antibodies if rather embarrass the spread but do not prevent the occurrence of relapses[6].

The urgency of the problem is determined by the high mortality rate of HIV-infected children with herpes infection, the absence of clear criteria for the diagnosis itself, as well as the natural difficulties in establishing this diagnosis.

The aim of the researchis to study the comparative clinical signs of herpes infection coupled with HIV infection.

Materials and Method

A clinical examination of herpetic infection in HIV-infected children has been conducted. 57 patients aged 1 year to 15 years registered at the Research Institute of Virology of the Ministry of Health of the Republic of Uzbekistan were under the supervision. Primary HIV diagnosis: a) Serological studies - the determination of antibodies to the human immunodeficiency virus has been carried out in the laboratory of the AIDS Center of the Ministry of Health of the Republic of Uzbekistan. The diagnosis of HIV infection has been verified in accordance with the National Protocol of the Republic of Uzbekistan, No. 117 as of March 17, 2005. The comparison group included 23 children of the same age infected with HIV withouth erpeticinfection. The results of repeated HIV tests were negative. Laboratory research method included a general analysis of blood, urine, feces, the study of the immune status, level of CD4 cells; Serological method: by ELISA, antibodies to CMV and herpes simplex virus (HSV) have been determined in the blood.

57 children aged 1 to 15 years have been under our examination: 41 boys(71,93%)and 16girls (28,07%).57 HIV-infected children with herpesvirus infection who have been HIV positive and herpesvirus infection has been serologically confirmed. The control group consisted of 23 children with HIV infection without herpes virus. Observations and general clinical studies have been conducted on the basis of the Research Institute of Virology of the Ministry of Health of the Republic of Uzbekistan. In terms of age, the children have been divided as follows: from 1 year to 6 years – 34children (59.65%), from 6 years to 10 years - 13 children(22.81%) and from 10 to 15 years - 10 children (17.55%). The diagnosis of HIV infection has been established on the basis of epidemiological, clinical and laboratory tests, confirmed by double detection of antibodies (AB) to HIV by enzyme-linked immunosorbent assay (ELISA). The diagnosis of HI has been established on the basis of the disclosed changes in the organs and systems taking into account the polytropy of the pathogen and the generalized nature of the lesions in the terminal stage of the disease. For each child, an examination card has been filled out, in which the passport part, the date of admission of the child, a detailed clinical diagnosis, medical history, infection routes, therapeutic measures, as well as the results of laboratory and instrumental research method throughout the observation period have been noted. Clinical and laboratory examination included: examination, thermometry, ultrasound of the abdominal organs, a general blood test, a biochemical blood test to determine the content of total protein, bilirubin and its fractions, AlAT, AsAT, sedimentary sample.

Statistical processing of the results has been carried out using the STATISTIKA V.5.5A program with the Student's t-criterion. The etiological interpretation of HI has been based on the results of polymerase chain reaction (PCR). A comparative analysis of the severity of the disease has been carried out with HIV-infected patients without HI[23], having similar HIV infection experience and similar sex and age characteristics. This group of patients (HIV + HI)[57] has undergone a comprehensive clinical and laboratory examination.

Results

The results of there search haves how nth at in the structure of coexisting diseases in young children frequent acute respiratory viral infections prevail with the formation of complications (18.7%), digestive tract infections (27.1%), fungal skin lesions (2.1%), in the group of children from 7 to 15 years there has been less

complications (p<0,05) rather than in younger children. An analysis of the results has disclosed that the most common in HIV-infected children without herpes infection are coexistingdiseases in the form of anemia in 19 (82.61%) cases, damage to the nervous system in 16 cases (69.57%), 14 cases of pneumonia(60.87%), 10 cases of tuberculosis (43.48%), 9 cases of intrauterine infection (39.13%), as well as 7 cases of chronic viral hepatitis B + C (30.44%),5 cases of thrombocytopenia (21.74%), 3 cases of sepsis (13.05%), 3 cases of chronic viral hepatitis C (13.05%), 2 cases of chronic viral hepatitis B (8.70%), 1 case of syphilis (4.35%). As HIV infection progresses, the severity of herpetic lesions worsens, which requires timely diagnosis[33] and therapeutic antiviral therapy[43]. From the epidemiological data, the identification of children at risk has been of great importance[75]. The characteristics of the children included in the researchhave been based on the classification of herpetic infection proposed by V.F. Uchaykin. The severity of the course of RHI has been determined by the frequency of relapses (Masyukova S.A. and others. 2007). The results of the research have shown that herpes simplex type 1 and type 2 occurred in 59.65–80.71% of HIV-infected people without herpes infection, causing mucocutaneous ulcerative lesions, diseases of the nervous system[14]. Herpes zoster is observed in 15.79–31.58% of patients with HIV infection and is one of the earliest markers of immunosuppression[12]. Coexisting diseases such as anemia (54 cases - 94.74%), nervous system damage (41 cases - 71.93%) pneumonia (38 cases - 66.67%), tuberculosis (33 cases - 57.90 %), toxoplasmosis (28 cases - 49.13%), intrauterine infection (26 cases - 45.62%), as well as chronic viral hepatitis B + C (24 cases - 42.11%), sepsis (20 cases - 35.09%), thrombocytopenia (15 cases - 26.32%), trichomoniasis (11 cases - 19.30%), chronic viral hepatitis C (10 cases - 17.55%), chlamydia (7 cases - 12.28%), syphilis (6 cases - 10.53%) are the most frequently met in HIV-infected children with herpesvirus infection[32]. The simultaneous action of such unfavorable factors as an early age at the time of infection, premorbid background, intensive parenteral loads exacerbated the course of herpes virus infection in HIV-infected children and also led to an early lethal outcome[50].

Discussion

An analysis of the clinical stages of HIV-infected patients with clinical signs of herpes virus infections shows that most of them 78.96% have been at stage 2 (stage 2B - 36.85%, stage 2C - 8.78%).

Studies conducted have shown that the prevailing form of relapse of herpetic infection in HIV-infected children is herpes of skin (52.64%).

The results of the researchhave shown that in children under 6 years of age complications have been significantly more likely to be detected than in the group of children from 7 to 15 years of age, where complications have been less common (p <0.05). Overcooling in 61.41% of cases, insolation in 8.78%, psychoemotional stress in 3.51%, acute respiratory viral infection in 57.90%, mechanical trauma to mucous membranes in 7.02%, and exacerbation of allergic dermatosis in 8.78% of cases have become provoking factors for the development of relapses of infection. Severe RHI course has been recorded more often in children under 6 years of age, the duration of relapse in children under 6 years of age has been significantly higher (p <0.05). The occurrence of relapse has been accompanied by intoxication signs, more pronounced in young children. The terms of epithelialization of defects have been delayed in children under 6 years of age by 7.4±1.7 days from the onset of the disease, and in the group of children from 7 to 15 years of age by6.4±2.8 days. The number of leukocytes in children under 6 years of age during the onset of relapse has been characterized by moderate leukopenia (5.0±1.76 *) (p <0.05) with relative lymphocytosis (64.9±1.40) (p <0.01) preserved in remission (61.4±1.82) (p <0.05). In the period of exacerbation of the disease in children over 7 years old, leukocytosis (6.4±2.15) (p <0.05) with relative lymphocytosis (40.1±1.22) (p <0.01) has been noted. The remission period has been also characterized by an increase in the percentage of lymphocytes (38.7±0.11) (p <0.05). The subpopulation composition in children from 1 year to 6 years of age with RHI during the period of exacerbation has been characterized by a pronounced decrease in the relative (22.6±1.35) and absolute (0.74±0.15) levels of CD4,% cells compared with the control group (37.7±1.47) (1.47±0.06) (p <0.001). During remission, their absolute number corresponded to (1.01±0.03) (p <0.05), the control group (1.47±0.06). In the group of children from 6 years to 15 years, there has also been a significant decrease in the relative content of SD4,% cells during periods of exacerbation (23.4±2.51) (p <0.001) and remission (27.3±3.09) (p <0.01). Their absolute number during exacerbation decreased moderately (0.63±0.12) (p <0.05), during remission it has corresponded to the norm (0.75±0.12). The indices of the absolute and relative content of T-cytotoxic lymphocytes during exacerbation

(40.1±1.22) and during remission (38.7±0.11) have not differed from the control values (34.2±1.35) in the group 6 years to 15 years. In children from 1 year to 6 years, there has been a significant increase in the relative content of SD8,% cells throughout the observation period (27.7±1.73) (p <0.01). Their absolute content has sharply increased during the exacerbation of the disease (1.14±0.17) (0.91±0.07) (p <0.001). In children from 1 year to 6 years, a decrease in the relative content of SD16,% cells during exacerbation (9.3±1.02) (p <0.01) and remission period (10.1±1.11) (p <0.05) of the disease has been noted. In children from 6 years to 15 years, the level of MK cells has decreased only during relapse (8.1±0.92) (p <0.05). The absolute number of CD16 cells in children from 1 year to 6 years and in the group from 6 years to 15 years has also decreased during the period of relapse (0.33±0.05) (0.26±0.06) (p <0, 05). In both groups, normal values of the relative number of B-cells have been recorded. Their absolute content has significantly decreased in children from 1 year to 6 years during remission (0.90±0.09) (0.51±0.03) (p <0.05).

The humoral immunity has been characterized by an increase in the values of all classes of immunoglobulins. The IgM level mg/μl in children from 1 year to 6 years has increased during the period of exacerbation of the disease (1.5±0.68) (p <0.05), and in remission period as well (1.5±0.19). In children from 6 years to 15 years, an increase in IgM mg/μl has been more pronounced during the exacerbation period (1.6±0.19) (p <0.01), normalizing during remission of the disease (1.3±0.15) (p <0.05). High values in children from 1 year to 6 years have been recorded throughout the course of the disease (p <0.01). In the group of children from 6 years to 15 years, an increase in the level has been observed only during exacerbation (p <0.01). The IgA content mg/μl in both groups has had a similar dynamics, increasing during an exacerbation of the disease (1.3±0.11) (1.8±0.22) (p <0.01). In remission, IgA hyperimmunoglobulinemia has persisted in both groups (1.2±0.26) (1.7±0.19) (p <0.05).

The results of the research have shown that in all HIV-infected children with herpes infection that we have observed, various forms of chronic HI have been diagnosed, the reactivation of which has occurred in 21 cases(36.85%), and the relapsecourse in 36 cases (63.16%). A comparative assessment of the severity of the disease shows that HI has been more often detected in HIV-infected patients at stages 2B and 3B, which means that the number of patients with a progressive course of HIV infection has prevailed. HI coupled with HIV with damage to skin and mucous membranes has been characterized not only by more abundant and widespread elements of the vesicular rash, but also by its slowed regression, lasting more than 1 month (from 6 to 8 weeks).

The results of the research have shown that with herpetic infection of HIV-infected children, severe immunosuppression is observed. The number of leukocytes in children under 6 years of age during the onset of relapse has been characterized by moderate leukopenia (5.0±1.76 *) (p <0.05) with relative lymphocytosis (64.9±1.40) (p <0.01) preserved in remission (61.4±1.82) (p <0.05). The subpopulation composition in children from 1 year to 6 years with RHI during the period of exacerbation has been characterized by a pronounced decrease in the relative (22.6±1.35) and absolute (0.74±0.15) levels of CD4,% cells compared with the control group (37.7±1.47) (1.47±0.06) (p <0.001). In the group of children from 6 years to 15 years, there has also been a significant decrease in the relative content of SD4,% cells during periods of exacerbation (23.4±2.51) (p <0.001) and remission (27.3±3.09) (p <0.01). The humoral immunity has been characterized by an increase in the values of all classes of immunoglobulins. The IgM level mg/μl in children from 1 year to 6 years has increased during the period of exacerbation of the disease (1.5±0.68) (p <0.05), and in remission (1.5±0.19).

Clinical case: Boy,GiyasovKomil, 3 years. Diagnosis at admission: Herpetic infection, HIV infection, stage 3 (persistent generalized lymphadenopathy, persistent hepatosplenomegaly, recurrent aphthous stomatitis, enlargement of the parotid salivary glands, recurrent upper respiratory tract infections, persistent fever, persistent diarrhea, ıpersistent oral candidiasis, severe recurrent bacterial pneumonia, HIV-associated encephalopathy). Coexistingdiagnosis: congenital heart disease (ventricular septal defect), Sturge-Weber phacomatosis, mild anemia (hemoglobin level - 98 g/l). A child has had multiple developmental stigmas. Immunological parameters: CD4 level - 23.6 cells/μl. Virological research method have not been available. ART initiated, scheme: lamivudine, zidovudine, nevirapine. In 2 months after the beginning of therapy, its clinical, immunological (CD4 - 27.7 cells/μl), virological (viral load has not been determined) effectiveness has been noted. The hemoglobin level has been 14 g/l, that caused the replacement of the medication.

Thus, the occurring immunological changes in herpes infection in HIV-infected children have disclosed signs of combined immune deficiency. The data presented in the research indicate that, with herpetic infection in HIV-infected children, the cellular and humoral immunity systems are suppressed and unbalanced. However, there is a functional inadequacy of the body's natural resistance system. The emerging immunological shifts of herpes infection in HIV-infected children indicate severe immunosuppression - leukopenia, lymphocytosis, a significant 1.3 times decrease in the content of CD3-, CD4-, cells, an increase in the levels of all classes of immunoglobulins in the period of exacerbation of the disease, signs of combined immune deficiency have been revealed. The data presented in the research indicate that, with a herpetic infection in HIV-infected children, the cellular and humoral immunity systems are suppressed and unbalanced. However, there is a functional inadequacy of the body's natural resistance system

Thus, the action of such unfavorable factors as an early age at the time of infection, coexisting diseases with the formation of complications, with the progression of immunodeficiency has worsened the course of the disease in infected children, and led to a severe recurrent course of herpes infection in HIV-infected people. Against the background of secondary immunodeficiency due to HIV, HI becomes generalized with multiple lesions of the internal organs and central nervous system.

Conclusion

It has been established that herpetic infection in HIV-infected children especially of the young age, has a course of severe and continuously recurring forms.

It has been found that the prevailing form of recurrence of herpes infection in HIV-infected children is herpes of skin (52.64%). Against the background of progression of immunodeficiency, a worsening of the course of the disease has been noted, the frequency, severity and complication of herpetic infections and their relapses increase, becoming generalized with multiple lesions of the internal organs and central nervous system.

It has been established that with herpes infection in HIV-infected children, severe immunosuppression is observed - leukopenia, lymphocytosis, a significant 1.3 times decrease in the content of CD3-, CD4-cells, an increase in the levels of all classes of immunoglobulins in the period of exacerbation of the disease.

Ethical Clearance: No ethical approval is needed.

Source of Funding: Self

Conflict of Interest: Nil

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