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VIRAL OPPORTUNISTIC INFECTIONS IN PATIENTS WITH HIV-INFECTION

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Investigational results of frequency of determination of serological markers of viral infections among HIV-infected/AIDS persons on HAART are represented. The correlation of number of CD4-lymphocytes with presence of markers of active replication agents of viral co-infections such as herpes viruses (CMV, HSV1/2, EBV) and hepatitis B and C viruses in HIV-infected patients' samples of plasma has been carried out.

Key words: *HIV-infection/AIDS, viral co-infections, treatment.*

It is known that the growth of immunodeficiency in persons with HIV infection, accompanied by the development of secondary diseases of infectious and noninfectious origin. Among them a special place is occupied by opportunistic infections with pathogens which include CMV, HSV1/2 and EBV. In addition, HIV-positive individuals are at high risk of hepatitis B and C, because their agents have common ways of HIV-transmission. Recently, viral hepatitis is regarded as one of the main causes of death of HIV-infected persons [1].

Viral co-infections can significantly influence the course of HIV infection. Thus, the clinical forms of infection caused by herpes virus group, commonly found in patients with HIV infection in the third clinical stage, have a more aggressive nature with frequent relapses and generalized symptoms in these patients, which complicates the course of underlying disease. Herpes infection of nature is one of the main factors that determine the decline in cellular immunity and increase mortality of HIV-infected persons [2].

Influence of hepatitis B virus and C in the course of HIV infection to date is not fully understood. The conflicting results have been received in studying this question by different groups of researchers [3, 4]. Thus, some authors claim that hepatitis C does not affect the course of HIV infection and the effectiveness of highly active antiretroviral therapy (HAART) [5]. However, many studies have shown that in co-infection HIV-infection / hepatitis C in response to HAART have shown inadequate increase of CD4-lymphocytes, it increases the risk of AIDS mortality and HIV infection [6]. In addition, hepatitis C can enhance the hepatotoxicity caused by drugs to treat HIV infection [7].

Questions about the impact of viral hepatitis B on the course of HIV infection also remains poorly understood. Increased replicative activity of HIV and HBV co-infection for many researchers is questionable, while the relationship of hepatitis B with increasing degree of hepatotoxicity if HAART is more likely [8, 9]. However, in the early 90-ies have been shown that HBV regulatory proteins can enhance replication of HIV by binding to specific sites in the region of the genome of HIV LTR [10]. That is, the problem spread hepatitis B and C among persons with HIV infection, and their influence on the disease and the effectiveness of HAART requires further study.

The purpose of the study was to set the range of co-infections of viral origin in patients with HIV infection and to investigate the impact of these infections on the development of HIV by the number of CD4 lymphocytes.

Patients and methods

The study involved 127 patients with HIV infection who were on ambulatory treatment during 2007-2009 in a Chernivtsi Regional AIDS Center. Among these patients were 66 men and 61 women aged 19 to 44 years. Among examined there were 35 (27.6 %) patients with clinical stage I, 60 (47.2 %) – II, 22 (17.3 %) – III, 10 (7,9 %) – IV clinical stage.

In establishing the diagnosis took into account clinical and epidemiological data and results of laboratory research methods: serological and immunological (including determination of CD4-lymphocytes). The level of CD4+ T lymphocytes was studied after the disappearance of symptoms of acute infectious disease (after 4 weeks at least).

In serum samples of all patients with HIV infection by ELISA have been found markers of viral hepatitis B (HBsAg, IgM + G to HBcAg) and viral hepatitisC (IgG to the Core-, NS3-, NS4-, NS5-antigens), CMV (IgM and IgG), HSV1/2 (IgM

and IgG) and EBV (IgM and IgG to EBV capsid antigen). For studies were used test systems of НВО «Діагностичні системи» (Росія), АТЗТ НВК «Діапроф-мед» (Україна) and «DiaSorin» (Italy). In order to study replicating active forms of virus hepatitis B and C, in plasma samples of individuals, in which were found serological markers of infection by polymerase chain reaction (PCR), have determined the presence of HCV RNA and DNA of HBV. Data on the number of CD4-lymphocytes obtained from the charts of patients.

HAART was prescribed to patients in II and III clinical stages of HIV infection in the presence of CD4 less than 200 in 1 mm^3 of blood, and all patients in clinical stage IV regardless of lymphocyte count after they sign the "informed consent about the conduct of antiretroviral therapy for HIV infection" [11]. Therefore, HAART was given to 34 patients aged 21 to 44 years with HIV who were infected by parenteral and sexual transmission. Scheme of HAART for all HIV-infected individuals consisted of three antiretroviral drugs first line (zidovudine + lamivudine + efavir). All patients were on HAART for at least 3 months.

The results were treated statistically.

Results and discussion

It was found that all patients had antibodies of IgG to certain pathogens co-infections of viral origin.

Thus, in samples of blood serum of all patients found IgG to capsid antigen of EBV, to HSV1/2 and to CMV in 119 (93.7 %) and 113 (89.0 %) patients, respectively. IgM to EBV was found in 6 persons (4.7 %) to HSV1/2 – 10 (7.9 %) to CMV – in 21 HIV-infected persons(16.5 %). Thus, in 29.1% patients have been seen activation of chronic infections caused by CMV, HSV1/2 or EBV.

Markers of viral hepatitis was found in 71 of 127 patients (55.9 %). This test for the presence of HBsAg was positive in 11 persons (8.7 %), the IgM + G to HBcAg – in 30 (23.6 %) and IgG to HCV found in 41 patients (32.3 %). It should be noted that in most cases, serum samples, anti-HCV-positive patients had a complete set of the spectrum of antibodies to antigens of HCV (IgG class antibodies to the Core-, NS3-, NS4-, NS5-antigens). This usually correlates with active replication of virus of hepatitis C. Draws attention to the fact that in 12.6 % of patients of this group was diagnosed mixed-hepatitis (hepatitis C + hepatitis B).

Analysis of the frequency of detection of serological markers of co-infection viral genesis according to route of HIV infection showed that markers of hepatitis B often found in HIV persons with sexual mechanism of transmission and markers of hepatitis C and mixed-hepatitis – in HIV infected persons with parenteral mechanism of transmission probably. This can be explained by the fact that the risk of sexual transmission of hepatitis B virus is much higher than for hepatitis C virus [3]. Among 56 patients in whom were not identified markers of viral hepatitis, most (85.7 %) – were probably infected with HIV through sexual contact. Activation markers of herpetic infections established among various ways of HIV infection about the same frequency.

We found a lot of serological markers of hepatitis B and C in patients with HIV infection. Therefore, to establish the presence or absence of active replication agents of viral hepatitis in plasma anti-HCV-and anti-HBV-positive persons by PCR detected HCV nucleic acids and HBV. Found RNA of HCV in samples of plasma 36 (87.8 %) of 41 patients. PCR results confirm the high rate of frequency activation of pathogen hepatitis C, obtained through ELISA.

DNA of HBV in plasma samples of HBsAg-positive and/or anti-AHD-positive persons not revealed. This may be due to the fact that in the majority of patients "lamivudine" (3TS) included in the scheme of HAART, which is included in the scheme of first line therapy for HIV infection, and is used for treatment of hepatitis C. On the basis of the results we can argue that the scheme HAART mentioned above quite effectively inhibits replication of HBV. The literature describes the phenomenon of suppression of replication HBV in patients with acute or chronic hepatitis C [12]. The aboved conclusion is come, and other researchers [13].

To analyze the impact of viral co-infections on the level of CD4 lymphocytes in HIV-infected persons, all patients of the study group were divided into 6 subgroups: the first subgroup – patients who had no serological markers of viral co-infections in a phase of reactivation, second subgroup – those who had markers of hepatitis C virus, the third subgroup – patients who have markers of hepatitis B virus, the fourth subgroup – patients who have markers of mixed infections HCV + HBV; fifth subgroup – people who had antibodies class IgM to herpes virus group, the sixth subgroup – patients who have markers of viral hepatitis, and herpetic infections in the acute stage. It appeared that there was no statistically significant difference between the average performance level of CD4-lymphocyte count for all subgroups of patients.

That is, for patients who entered to the studied group was not established according to the level of CD4-lymphocytes on the presence of co-infections of viral origin. It should be noted that at this stage of the study were taken into account co-infection of viral

origin during active replication of pathogens other than hepatitis B, for which there were cases of activation among patients in the study.

Conclusions

1. Analysis of co-infections of viral origin in HIV-infected individuals showed a wide distribution of the parenteral viral hepatitis and chronic infections of HSV1/2, CMV and EBV. Found that in 55.9 % of patients with HIV infection had markers of hepatitis B and C. It is established that serological markers of hepatitis C and mixed-hepatitis (HCV + HBV) often detected in HIV positive patients with parenteral mechanism of transmission of HIV and hepatitis B markers – mainly in HIV positive patients with sexual mechanism of transmission of HIV.

2. It is shown that in patients taking HAART, the replication of HBV was suppressed quite effectively. However, the development of HIV replication promotes active HCV.

3. The activation of chronic infections caused by CMV, HSV1/2 and EBV was found in patients in 29.1 %.

4. Mean number of CD4-lymphocytes in HIV-infected people who had markers of viral co-infections, little different from the level of CD4-lymphocytes of patients in whom these markers were not found. This may indicate the effectiveness of antiretroviral therapy, which was used in patients with AIDS.

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ВІРУСНІ ОПОРТУНІСТИЧНІ ІНФЕКЦІЇ У ХВОРИХ НА ВІЛ-ІНФЕКЦІЮ

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РЕЗЮМЕ. Представлено результати дослідження частоти виявлення серологічних маркерів ко-інфекцій вірусного генезу в осіб, хворих на ВІЛ-інфекцію/СНІД, які перебувають на антиретровірусній терапії (АРТ). Досліджено взаємозв'язок між кількістю CD4-лімфоцитів і наявністю маркерів активної реплікації збудників ко-інфекцій, спричинених вірусами групи герпесу (цитомегаловірусом, вірусом простого герпесу 1 та 2 типів, вірусом Епштейна-Барр), а також вірусами гепатитів В і С, у плазмі ВІЛ-інфікованих пацієнтів.

Ключові слова: *ВІЛ-інфекція/СНІД, вірусні ко-інфекції, лікування.*

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