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PREDICTION OF LIVER FIBROSIS IN CHRONIC VIRAL HEPATITIS C IN HIV-INFECTED

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Abstract
Liver lesions in children with HIV infection remain a pressing problem due to the frequency of their occurrence and the diverse etiology of the diseases. HIV is considered the cause of many hepatobiliary disorders; hepatotropic effects can be exerted by: chronic viral hepatitis B and C, opportunistic infections, in addition, there is a direct effect of the human immunodeficiency virus and the hepatotoxic effect of antiretroviral therapy (ART) drugs.

Keywords: HIV, infection, viral hepatitis, treatment, liver

Introduction

Despite significant advances in diagnosis, prevention and treatment, HIV infection and parenteral viral hepatitis are socially significant diseases that influence, among other things, the demographic situation in the country [1-3]. The relevance is determined by the wide distribution of these infections, the variety of clinical forms, the significant frequency of adverse outcomes, as well as the commonality of epidemiological, social and economic factors [4-6].
Viral hepatitis C is a global health problem; 71 million people worldwide have CHC; more than one million new cases and 1.34 million deaths from this infection are recorded annually [7-9]. This is more than the human immunodeficiency virus (HIV/AIDS)-related mortality rate of 1 million [11–13]. CHC is becoming a significant cause of morbidity and mortality among people living with HIV [25]. This also applies to pediatric patients, given the perinatal route of transmission of pathogens. Mothers co-infected with hepatitis C virus

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and HIV are the main source of HIV/HCV in infancy and childhood [14]. In the case of coinfection of HIV with the hepatitis C virus (HCV) in the mother, the frequency of perinatal transmission of HCV increases from 6 to 20%, as a result, the child can be infected with two viruses simultaneously [15-19]. Most children with HCV in Russia are infected vertically from infected mothers [20-23].

In children, fibrosis progresses at a slow rate, so there are few established reliable risk factors for disease progression [26-29]. The development of progressive liver disease in these patients occurs infrequently until the duration of infection exceeds 30 years [30].

However, during HIV infection, the phenomenon of aggressive fibrogenesis of the liver occurs, so the study of fibrotic processes in the liver and the rate of their progression in children is relevant, and the possibilities of their scientific and practical implementation are of undoubted interest.

Research methods

Laboratory research methods. Among the patients examined, the main method of detecting HIV infection (in children over 18 months old) was testing using enzyme-linked immunosorbent assay (ELISA) or chemiluminescence immunoassay (CHLA). Testing for HIV using the AIDS ELISA method is carried out on an automatic enzyme immunoassay analyzer "ELISYS" model "ELISYS QUATRO" (Human GmbH, Germany) (photometric method), as well as on a photometer for microplates "Mark" version "iMark" (BioRad Laboratories , Inc., USA) (photometric method). Testing for HIV using the CHLA method is carried out on an immunochemical modular analyzer for in vitro diagnostics “ARCHITECT i2000 sr mobdule” (Abbott, USA) (chemiluminescence method). To confirm a positive ELISA result, the immunoblotting (IB) method is used. This method allows you to detect antibodies to HIV-1 or HIV-2 in the test sample of blood serum (plasma) due to interaction with HIV 1 antigens (env1: gp160, 120, 41; pol: p 31, 51; gag: p 24, 17), or HIV 2 (env 2: gp 36, 105), applied to the test strip, and thus confirm the seropositivity of the sample or identify possible nonspecific reactions. The IB method is based on the method of indirect enzyme immunoassay, which makes it possible to determine the spectrum of antibodies

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to HIV proteins. All children underwent a clinical blood test, the level of erythrocytes, leukocytes, platelets, hemoglobin, hematocrit, differentiation of leukocyte populations and a number of other indicators were determined. During the study, the following biochemical blood parameters were determined: ALT, AST, total bilirubin and its fractions, gammaglutamyl transpeptidase, alkaline phosphatase, total cholesterol, glucose, urea, creatinine, total protein, albumin.

Statistical research methods

Statistical processing of the research materials was carried out using parametric and nonparametric analysis methods. Accumulation, adjustment, systematization of initial information and visualization of the results obtained were carried out in Microsoft Office Excel spreadsheets. Statistical analysis was carried out using the IBM SPSS Statistics version 26 (USA) application package. To check whether the distribution of the characteristic corresponds to the normal law, the Shapiro-Wilk test was used. In the case of describing quantitative indicators with a normal distribution, arithmetic means (M) and standard deviations (SD) were calculated. Sets of quantitative indicators whose distribution differed from normal were described using the values of the median (Me), first and third quartiles (Q1; Q3). Nominal data were described with absolute values and percentages. Differences between the assessed groups were considered statistically significant at $p<0.05$.
To compare quantitative indicators in two independent study groups, the Student's test was used (if the distribution of characteristics corresponded to the normal law) and the Mann-Whitney test (otherwise). Comparison of three groups for quantitative indicators, the distribution of which differed from normal, was performed using the Kruskal-Wallis test. Group medians were compared using the independent samples median test (Median Test).

Results

According to the regional registry, as of March 30, 2023, 784 patients with chronic hepatitis C were registered in the Bukhara region. Moreover, only 389 people had a diagnosis of CHC confirmed by RNA PCR for hepatitis C, of which 86 were children and adolescents under 17 years of age inclusive. The absolute

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majority are men, who accounted for 63.7%, women – 36.3%, respectively. For the period from 2014 to 2022. In AIDS, 22 children with coinfection with HIV and HCV were observed. In addition, information about patients with CHC is entered into the monitoring system for patients with viral hepatitis C "Register of Patients with Viral Hepatitis C". In 90-95% of cases, CHC in early childhood occurs in anicteric, subclinical and inapparent forms with a high frequency of chronicity. According to all researchers, the frequency of chronic HCV infection is high, from 40-56% to 81% or more [7, 12]. In childhood, chronicity most often forms as a primary chronic process during vertical infection of the child from the mother. 118 Between 1% and 4% of children with CHC are at risk of developing cirrhosis, while fibrosis and severe inflammation may occur in 15% with CHC [36, 35]. Advanced stages of liver fibrosis in children with CHC develop in the presence of concomitant pathology (hematological diseases, obesity, oncopathology, co-infection with HIV, HBV) [11, 27]. In HIV infection, the phenomenon of aggressive liver fibrogenesis occurs, so the study of fibrotic processes in the liver and the rate of their progression in children is extremely relevant. Despite the high reliability of the results, liver puncture biopsy has a number of limitations in pediatric practice and the risk of complications, especially in patients with severe liver damage accompanied by hemostasis disorders [11, 35]. In recent years, the search for non-invasive methods for diagnosing fibrosis has been carried out in several directions. Despite the fact that at the present stage much attention is paid to reducing the rate of progression of HIV infection and CHC, and non-invasive methods for diagnosing fibrosis are being actively developed, many unresolved issues remain.

Conclusions

In the structure of liver lesions in HIV-infected children of the Bukhara region, CHC predominated (64.6%). Less common were CMV hepatitis (12.3%) and hepatotoxic effects of ART (23.1%), which were characterized by the absence of signs of fibrosis in the liver tissue.

The epidemiological features of HIV/HCV co-infection in children were the perinatal route of infection - 90.5%, the predominance of genotype 1 of the

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hepatitis C virus - 57.1%. Clinical and laboratory features of CHC were characterized by the presence of asthenovegetative syndrome (85.7%), hepato-(28.6%) and splenomegaly (57.4%), and undulating hyperenzymemia. Every fifth coinfected child had high levels of HCV RNA. Among concomitant diseases, half of the patients had lesions of the nervous system, and a quarter had cognitive and intellectual-mnestic disorders.

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