

## Clinical and morphological changes in the liver in patients with pulmonary tuberculosis.

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**Annotation:** The aim of this study is to obtain information about the clinical and morphological changes in the liver in patients with pulmonary tuberculosis.

**Key words:** hepatitis C, disseminated pulmonary tuberculosis, HIV infection, liver pathology.

### Introduction.

Liver damage in opportunistic diseases against the background of HIV infection largely determines the prognosis, effectiveness of therapy and outcome of the disease. The etiology of liver damage in HIV infection is diverse, but viral hepatitis and tuberculosis are currently coming to the fore, often in the form of combined pathology. The association of HIV infection with tuberculosis and viral hepatitis leads to rapid progression of both tuberculosis infection and liver cirrhosis and accelerates the development of AIDS [1, 2]. In 2012, there were more than 10 thousand patients with HIV infection in Krasnodar Krai, 2/3 of whom were diagnosed with tuberculosis. From 1991 to 2004, the number of patients with tuberculosis combined with HIV infection in the region increased by 65.2 times. Diagnosis of tuberculosis in patients with HIV infection causes serious difficulties, which is associated with the peculiarities of the course of tuberculosis at different stages of HIV infection. Among those who died from HIV infection in 2006, tuberculosis was the cause of death in 59% of cases [3, 4]. In subsequent years, the mortality rate from HIV-associated tuberculosis decreased from 24.1 (2007) to 10.2 (2011) per 1000 patients with HIV infection [3]. A significant number of tuberculosis patients die annually from non-tuberculous diseases and other external causes. Among all patients who died from tuberculosis in the Russian Federation in 2009, 43.7% were patients whose death occurred from other causes - 13.8 thousand patients [2]. Among the causes leading to death are liver damage, primarily cirrhosis resulting from hepatitis C. Thus, chronic hepatitis C is registered in every fourth patient with tuberculosis [1, 6, 8]. In recent years, Russia has maintained an unfavorable epidemiological situation with regard to both viral hepatitis and tuberculosis; this trend can also be observed in the Krasnodar Territory [1, 2, 4, 5]. The incidence of hepatitis C in the Krasnodar Territory increased from 57.12 to 94.8 per 100 thousand in 2007-2011, i.e. by 1.7 times [2]. At the same time, there was an increase in mortality among the working-age population from non-alcoholic liver fibrosis and cirrhosis: by 50.5% in 2000-2005, to 23.8 per 100 thousand; in 2011, this figure was 20.1 per 100 thousand [2]. It is known that tuberculosis at the stage of secondary diseases of HIV infection is manifested by a progressive course, has a tendency to generalization, often with multiple extrapulmonary localizations, including liver damage [3, For correspondence: Irina Yurievna Babaeva, Prof., Department of Infectious Diseases and Phthisiopulmonology, State Budgetary Educational Institution of Higher Professional Education, Kuban State Medical University, Ministry of Health of the Russian Federation, e-mail: irenb74@mail.ru 6, 7]. In the domestic literature, the issues of analyzing pathomorphological changes in secondary diseases in patients with HIV infection have not been

given sufficient attention. At the same time, correct assessment of the degree of liver damage in patients with HIV infection, tuberculosis and hepatitis C can significantly affect the choice of treatment tactics. In connection with the above, we considered it necessary to summarize our experience gained in pathomorphological studies that were performed on autopsy material from patients with tuberculosis, hepatitis C and HIV infection. The aim of the study was to establish the features of the course and morphological manifestations of tissue reactions in the liver in patients with chronic hepatitis C and disseminated pulmonary tuberculosis against the background of HIV infection. Materials and methods. Pathomorphological studies were performed on autopsy material from 11 patients treated at the Municipal Health Institution AIDS Center (Sochi) in 1993-2004 for tuberculosis combined with HIV infection and hepatitis C. The comparison group consisted of three patients with HIV infection and hepatitis C and one patient with generalized hematogenous tuberculosis with chronic hepatitis C. Autopsy protocols of the deceased, pathological diagnoses and conclusions were studied. From the archival autopsy material, after fixation in 10% formalin and embedding in paraffin, serial histological preparations were made with subsequent staining with hematoxylin and eosin and picro-fuchsin and fuchselin. Pathohistological analysis of the preparations was performed using a Zeiss light microscope ( $\cdot 100$ ,  $\cdot 200$ ,  $\cdot 400$ ,  $\cdot 600$ ). The patients were tested for the presence of viral hepatitis markers; in all cases, serological markers of HCV (IgG anti-HCV, antibodies to non-structural proteins NS3, NS4, NS5) were registered. The diagnosis of HIV infection was confirmed by ELISA and immunoblot. The diagnosis of tuberculosis was based on a triple microbiological examination of sputum for the presence of *Mycobacterium tuberculosis* using fluorescence microscopy, quantitative assessment of the massiveness of bacterial excretion and bacteriological examination by sowing on dense nutrient media and Finn-2 medium. Results and discussion Histopathological features of HIV infection and hepatitis C without tuberculosis were used as a comparison group. Three autopsy observations were studied. The main pathological diagnosis in all cases was: HIV infection, while at the late (4B-5) stage of HIV infection, aplasia of the lymphoid elements is observed and diffuse plasmatization persists. Conclusion Having studied the morphological state of the liver in the combination of tuberculosis with HIV infection and hepatitis C, we noted changes of varying severity depending on the stages of the combined pathology. At the early (2B) stage of HIV infection, in the presence of tuberculosis in patients, rapid progression of hepatitis C to the stage of liver cirrhosis is possible, which becomes the main cause of death. Tuberculosis can be represented by localized forms. For late (4B-5) stages of HIV infection, the development of generalized forms of tuberculosis with damage to various organs and systems is characteristic. In this case, morphological changes in the liver can be of varying severity. Typical are severe circulatory disorders in the organ, sometimes incompatible with life, pronounced dystrophic and necrotic changes in the liver parenchyma, inflammatory reactions caused by both generalized tuberculosis and hepatitis C. Hematogenous generalization of disseminated pulmonary tuberculosis against the background of HIV infection leads to the acute formation of confluent caseous-necrotic foci in all organs and tissues, including the liver. It has been established that with acute progression of disseminated pulmonary tuberculosis with generalization, a monocytoid reaction and lymphopenia occur, while at the late (4B-5) stage of HIV infection, aplasia of the elements of the lymphoid series is noted and diffuse plasmatization persists. A correlation has been revealed between the severity of the process and the degree of expression of exudative changes. Such a morphological picture greatly complicates the comprehensive treatment of the patient. One generalized tuberculosis with liver involvement can be the cause of the above-described picture, and its combination with HIV infection and hepatitis C reduces the chances of a favorable outcome of the disease. Thus, the identified pathomorphological

changes in the liver in patients with combined manifestations of HIV infection, tuberculosis and hepatitis C can become decisive in the outcome of the disease and should be taken into account when choosing a scheme of etiotropic and pathogenetic treatment, as well as determining the stages of therapy.

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