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Severe acute retroviral syndrome and immune reconstitution syndrome as risk factors for malignancies in HIV-infected subjects

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Malignancies are unfortunately common in HIV-infected patients, even in the era of effective antiretroviral treatment (ART).

At the same time, some immunological abnormalities can be risk factors for oncogenesis and lymphomagenesis. In patients with secondary immunodeficiency states (non HIV), e.g. after bone marrow transplantation or long-time steroid therapy, low cytotoxic-T-cell responses to oncogenic viruses can provocate their oncogenesis. It was shown, that low cytotoxic CD8-T-cellresponses in acute SIV infection determine severity of symptoms and more progressive course of disease. Low CTL responses may be particularly due to acquisition by CD8 T-cells the phenotype characteristics of CD8 T-regulatory cells. In the same time, such switching to regulatory phenotype may be due to proinflammatory microenvironment, e.g. like in patients with autoimmune diseases.

In patients with HIV/AIDS there are some clinical and immunological risk factors for oncological complications, for example immune reconstitution syndrome is a probable risk factor for NHL.

There are data that severe acute retroviral syndrome (or severe acute simian immunodeficiency virus infection) as a factor for more aggressive course of HIV or SIV infection correspondingly.

Hypothesis

1) Severe acute retroviral syndrome and/or immune reconstitution syndrome are the risk factors for oncological complications in HIV-infected subjects.

2) Low cytotoxic CD8 T-cell responses to HIV-infected cells and acquisition by CD8 T-cells the phenotype characteristics of CD8 T-regulatory cells can determine the severity of symptoms in primary HIV-infection.

The *aim* is 1) to estimate the rate of oncological complications in HIV-infected subjects in correspondence with severity of acute retroviral syndrome and immune reconstitution syndrome; and 2) to examine phenotypic characteristics of HIV-specific CD8 T-cells and regulatory CD8 T-cells in patients with primary HIV-infection.

Materials and methods. We propose both retrospective and prospective analyses of clinical data of HIV-infected patients with malignancies. The retrospective analyses will include evaluation of severity of acute HIV diseases and immune reconstitution syndrome using to medical charts in patients with documented malignancies.

The prospective analyses will include phenotypic characterization of HIV-specific CD8 T-cells and regulatory CD8 T-cells in patients with different course of acute HIV-infection.

Enrolment patients will be at St.-Petersburg AIDS Center and Botkin Infectious Diseases Hospital.

Proposed results. Evaluation of variety of severity of acute retroviral syndrome and immune reconstitution syndrome in comparison with defining immunological features will enable to estimate its association with oncogenesis.

Determination of phenotypic characteristics of HIV-specific CD8 T-cells and regulatory CD8 T-cells in primary HIV infection will enable to define immunological features in different variants of acute retroviral syndrome.

Brain Lesions in HIV-infected patients with Highly Active Antiretoviral Therapy: clinical and radiological comparisons

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Background and Purpose: The wide use of highly active antiretroviral therapy (HAART) significantly alters the structure of secondary manifestations of HIV-infection, including neurocognitive impairments and opportunistic infections resulting in brain lesions. The purpose of our study is to characterize the radiological semiotics of brain lesions of HIV patients having different immune status and viral load upon HAART.

Material and methods: Study group comprised 110 HIV patients. HIV infection was confirmed with standard laboratory tests. All patients were tested for CD4-cell counts and viral loads and subjected to brain MRI. The received data include duration, route of infection, disease stage and phase, clinical information about opportunistic infections, start date of HAART intake and its duration, CD4 counts, viral load, results of laboratory tests for opportunistic infections. Subgroups were defined according to

HAART regimens, immunosuppression levels, and opportunistic infection-caused brain lesions. The results were treated using statistical procedures available in MS Excel.

Results: The average age of HIV patients was 36±13 years, the average duration of infection 8±8 years. In total 91 patients received HAART without consideration of breaks and duration of therapy. The mean blood CD4 cell count and viral load were 270 mL^{-1} and 224837RNA copies per 1 mL, respectively. 65 patients were found to have MRI-visualized brain lesions corresponding to HIV-associated encephalopathy and 38 patients showed opportunistic brain lesions. No HAART was associated with more severe brain lesions, including gliosis, demyelination, granulematous inflammation. The prevalence of such opportunistic infections as toxoplasmosis and cryptococcosis was high.

Conclusions: Structural changes in the brain visualized with MRI are frequent manifestations of opportunistic infections in HIV patients. The course, localization and severity of the changes depend on immunosuppression and viral load. The early start of HAART may contribute to prevention of the brain involvement in HIV. Clinical and radiological comparisons of HIV patients suggest that MRI is indispensable for clinic-diagnostic examination of HIV patients.

Cytomedalovirus as an atherosclerosis progression factor in HIV-infected and HIV-uninfected patients

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Background: due to wide-spreading of combination antiretroviral therapy (cART), life expectancy of HIV-infected patients is steadily increasing, and the major causes of death in HIV-infected patients are non-AIDS related. One of the leading causes of death in these patients is now the early development of cardiovascular disease (Miller et al., 2014). High risk of development of cardiovascular diseases in HIV-infected patients is associated with chronic immune activation, which could lead to atherosclerosis progression (Nou et al., 2016). The cause of this immune activation remain unclear. It is possible, that other virus co-infection could trigger such activation. Cytomegalovirus infection (CMV) is one of the most common infections among HIV-infected patients. CMV is associated with the chronic immune and inflammatory diseases, with development and progression of atherosclerosis and high risk of complications, such as acute myocardial infarction (Nieto et al., 1996, Blum et al., 1998, Gattone et al., 2001). The study, performed in our laboratory, had shown a positive correlation between CMV replication and acute coronary syndrome. However, the causal relationship of these facts has not been proven. Suppressed HIV infection followed, however, CMV infection, represents a native model for studying the connection between cardiovascular disease and CMV.

Objective: to determine the influence of cytomegalovirus infection on the progression of atherosclerosis in HIV-infected patients.

Materials and methods: 1. Materials: blood and atherosclerotic plaques samples of HIV-infected patients after a long period of successful therapy. Samples will be obtained from the Moscow AIDS center. *2. Methods:* real-time PCR, flow cytometry, electron microscopy will be used in this study for DNA, RNA and CMV proteins detection in blood plasma, red blood cells and vascular walls, affected with atherosclerosis.

Expected results: a study of HIV-infected patients allows to identify cohorts of CMV-negative individuals, and individuals with high and low CMV level. The majority of HIV-infected patients are people of middle and young age, so we could exclude the age as a risk factor of atherosclerosis, what is impossible in general population. Our research data, submitted for publication, suggests an important role of CMV in the development of atherosclerosis in HIV-negative patients with atherosclerosis. The study of this effect in HIV-infected patients, where the processes of atherosclerotic changes are significantly accelerated, will allow to determine the connection between CMV and cardiovascular diseases.

Conclusion: the successfully treated HIV infection, nevertheless leading to the early development of cardiovascular diseases, is a promising model to elucidate the role of CMV in this process. The results of this study may lead to new treatment strategies as in HIV-infected patients, as in the general population.

Cognitive impairment and its correlations with mental disorders in HIV-infected patients with early syphilis

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The objective of the study was to determine the correlations between cognitive impairment in HIV-infected patients with early syphilis and mental disorders.

Method. 65 HIV-infected patients with early syphilis were examined by a clinical method. Cognitive impairment was assessed by means of BNCE test.

Results. The sample included 45 men (average age 32,09±9,83) and 20 women (average age 31,7±5,97). Mental disorders were identified in most patients (83%). We revealed a high incidence of addictions (46,2%). Opiate dependence (F11, ICD-10) was established in 18,5% of patients. The dependence on multiple drug use (F19; including opiate dependence in all cases) was revealed in 13,8% of patients. The dependence on stimulants (F15) and the dependence on alcohol (F10) were found in 4,6% and 32,3% of pati-