International Journal of Health Systems and Medical Science

ISSN: 2833-7433
Volume 2 | No 5 | May-2023

Causal Relationship of Immuno-Microbiological Parameters in Tuberculosis With Multiple and Broad Drug Resistance .

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Abstract: Tuberculosis continues to be one of the most common infections in the world and poses a huge threat to public health. The disease is still a complex socio-economic, medical and biological problem. In recent years, tuberculosis has become characterized by a high tendency to progression, rapid development of cavities, and polyresistance of Mycobacterium tuberculosis (MBT) to anti-tuberculosis drugs.

Key words and expressions: helminth, enterobiosis, allergy, diagnostics, hygiene

Introduction

Relevance of the problem. Tuberculosis continues to be one of the most common infections in the world and poses a huge threat to public health. The disease is still a complex socio-economic, medical and biological problem. In recent years, tuberculosis has become characterized by a high tendency to progression, rapid development of cavities, and polyresistance of Mycobacterium tuberculosis (MBT) to anti-tuberculosis drugs. The emergence of drug resistance in MBT is one of the main causes of chemotherapy failures, which leads to chronization of the process and an increase in mortality [Strelis A. K., 1999J. The increase in drug resistance of the Office in recent years is an unfavorable prognostic sign of epidemiological distress. In addition, the MBT resistance to antitubercular chemotherapeuticagents detected in first-time TB patients indicates that exogenous infection is now becoming increasingly important in the occurrence of the disease. Multiple drug resistance (MDR) of the Office is becoming a threatening problem in phthisiology. According to WHO, the MDR incidence rate of more than 3% in a particular territory allows us to assess it as a "hot spot". Meanwhile, in Russia, primary MDR in different regions ranges from 8.3% to 34.6% among newly diagnosed bacterial excretors [Shilova M. V., 2005; BaranovA.A 2006] Drug resistance occurs when antitubercular drugs are used improperly, as a result of their incorrect administration by health care workers, poor quality of medicines, or premature termination of treatment by patients.

Multidrug-resistant tuberculosis (MDR-TB) is a form of tuberculosis caused by a bacterium that does not respond to isoniazid and rifampicin, two of the most effective first — line anti-TB drugs. MDR-TB can be treated and treated with second-line medications. However, such treatment options require long-term use of expensive and toxic drugs.

In some cases, broader drug resistance may develop. Tuberculosis caused by a bacterium that does not respond to the most effective second-line anti-TB drugs can limit patients ' treatment options to a very large extent.

Multidrug-resistant tuberculosis (MDR-TB) continues to pose a critical situation and a threat to health security. In 2021, only one in three patients with drug-resistant tuberculosis was able to receive assistance. According to the WHO guidelines, the detection of MDR/RU-TB requires bacteriological confirmation of tuberculosis and drug resistance testing using molecular rapid tests or culture methods.

In 2022, the new WHO guidelines prioritize a 6-month treatment regimen for BPLM/BPL as the preferred course of treatment for patients who meet the relevant criteria. The shorter duration of the course, the lower number of medications taken by the patient, and the high efficiency of this new treatment regimen can help reduce the burden on health systems and manage valuable resources in order to further expand the coverage of diagnostic and treatment services for all those in need. In the past, the duration of MDR-TB treatment was at least 9 months and up to 20 months. WHO recommends increasing access to oral-only treatment regimens.

To date, the factors and causes contributing to an increase in drug resistance of the causative agent of tuberculosis, the clinical, radiological and microbiological characteristics of patients with MDR-tuberculosis of the lungs remain poorly understood [Sokolova G. B. etal., 2006]. It has been established that drug resistance of the pathogen develops as a result of one or several spontaneous mutations in independent genes of mycobacteria, which, as a rule, are formed нодunder the influence of inadequate drug therapy [Rattan A. et al., 1998; Tungusova O. S., Maryandyshev A. O., 2001; Krasnov V. A., Ursov I. G., 2004]. Despite the key role of mycobacteria and their biological properties in determining the nature of the course of tuberculosis, an important role in the development of the disease is also assigned to the mechanisms of immune dysregulation [Mayansky A. II., 2002; Mishin V. Yu. etal., 2002]. The fact that the degree of immunological reactivity disorders closely correlates with the clinical and radiological manifestations of tuberculosis infection and reflects the severity of the disease course is proven to date. Moreover, changes in the immune status of patients with pulmonary tuberculosis are associated with a decrease in the effectiveness of therapeutic measures [Gergert V. Ya. etal., 1995; Mishin V. Yu.etal., 2002]. It is possible that the appearance, or rather the multiplication of drug-resistant forms of MBT in the course of standard chemotherapy, is a consequence of the weakening of the body's immune surveillance.

Based on the conducted studies of dapa medical and social characteristics, the leading clinical syndromes of widespread destructive MDR tuberculosis of the lungs identified for the first time are identified, which determine the features of the disease and facilitate its timely diagnosis. The obtained new data of a fundamental nature on the mechanisms of metabolic imbalance and dysfunction of phagocytic blood cells in patients with MDR and drug-sensitive pulmonary tuberculosis, recorded both before and during specific therapy, expand the existing understanding of the immunopathogenesis of tuberculosis infection. They can serve as a basis for further study of the mechanisms of changes in the parameters of the immune status in pulmonary tuberculosis, as well as the effect of anti-tuberculosis therapy on the state of immunological reactivity. The results of the study theoretically substantiate the need to include in the standard treatment program of patients with pulmonary tuberculosis immunomodulatory agents for the prevention and correction of immunodeficiency conditions caused by the influence of not only the pathogen, but also anti-tuberculosis drugs. Immunological parameters were determined that allow predicting drug resistance of the pathogen (production of nitric oxide мононуклеарамиby peripheral blood mononuclear cells) and a favorable outcome of the disease (the value of spontaneous and stimulated HCT test) in patients with pulmonary tuberculosis with multiple resistance to antitubercular drug with high accuracy. The course of multiple drug-resistant and drug-sensitive pulmonary tuberculosis is characterized by similar changes in the general status of the disease, unidirectional violations of clinical and immunological indicators, the degree of significance of which is determined by the course variant and clinical form of the disease. At the same time, the severity of the course of the pathological process, clinical manifestations of the disease and dysfunction of a non-specific link of immunity are more pronounced in fibro-cavernous multiple drug-resistant pulmonary tuberculosis than in its infiltrative and disseminated forms. Drug-resistant pulmonary tuberculosis is characterized by rapid (in every second patient within 1 year) development of a widespread specific process in the lungs, a wide range of complications and concomitant pathology, which in 57.5% of cases leads to disability of group II. With the same prevalence of the pathological process in the lung tissue, multiple drug-resistant pulmonary tuberculosis is accompanied by more pronounced violations of the function of external respiration, slow normalization of the objective status of patients, massive bacterial

excretion, and longer periods of sputum negation and abacillation during therapy than drug-sensitive pulmonary tuberculosis.Dysfunction of the non-specific immune system in multidrug-resistant pulmonary tuberculosis is caused by inhibition of the anti-infective effect of the immune system. neutrophil potential, receptor-expressing function, and metabolic depletion of phagocytes against the background of an increase in their absorption, enzymatic activity, and the content of nonenzymatic cationic proteins in neutrophils. At the same time, the level of nitric oxide production by peripheral blood mononuclear cells in patients with multiple drug-resistant pulmonary tuberculosis remains within the normal range in infiltrative, decreases in dissociated, and, on the contrary, increases in fibro-cavernous forms of infection.

The differential indicator дизрегуляцииof cell dysregulation of nonspecific resistance in tuberculosis infection and chronic obstructive pulmonary disease in the acute stage is the activity of alkaline phosphatase in neutrophils and basal production of nitric oxide by mononuclear blood leukocytes. At the same time, the level of stimulated nitric oxide production makes it possible to predict the drug resistance of mycobacteria to antitubercular drugs, and the value of the HCT test indicates the positive dynamics of the X-ray picture during antitubercular therapy in patients with multiple drug-resistant pulmonary tuberculosis.

Standard antituberculous chemotherapy is accompanied by a tendency to normalize the total number of white blood cells and the white blood cell formula, the content of glycogen in monocytes and neutrophils, and lysosomes in neutrophils, which proves the determining role of the pathogen in the formation of immune disorders in pulmonary tuberculosis. The immunotoxic effect of antituberculous drugs is indicated by the inhibition of the number of SPL - and Rsu-prsepting neutrophils and monocytes, the secretion of nitric oxide (more pronounced in drug-resistant pulmonary tuberculosis) and the reserve reactivity of neutrophils during treatment.

WHO estimates that there were 558,000 new cases of tuberculosis with resistance to rifampicin — the most effective first-line drug, of which 82% were multidrug-resistant.

The эпиднадзоруEuropean Tuberculosis Surveillance and Monitoring Report 2019, presented jointly by the WHO Regional Office for Europe and the European Center for Disease Prevention and Control of the World Health Organization, shows that over the past five years, Europe has seen a 10% annual decline in tuberculosis deaths, the fastest in the world.

However, multidrug-resistant tuberculosis poses a threat to the populations of European countries, which bear about 23 % of the total global burden of multidrug-resistant tuberculosis .The epidemic situation of tuberculosis in the world at the beginning of the XXI century remains tense: according to the World Health Organization (N=73) on the problems of multiple and broad-spectrum tuberculosis (MDR) in 2017, 10.4 million people fell ill with tuberculosis in the world, including 580 thousand patients, which accounted for 5.6% of their total number, tuberculosis with multiple drug-resistant pathogen (N=73) on the problems of tuberculosis with multiple and broad drug-resistant XDR-TB) [1,2]. The spread of MDR-TB in the WHO European region has led to a slowdown in the rate of decline in the incidence of tuberculosis: in 2011-2014, from 5.4% to 4.3) fortуберкулеза с множественной и широкой multipleand broad-spectrum tuberculosis, and in 2014-2016 to 3) for multiple and broad-spectrum tuberculosis,3) for multiple and broad-spectrum tuberculosis lekar% [2,3) on the problems of tuberculosis with multiple and broad lekar, 4, 5]. In 2016, every 5th case of MDR-TB in the world was registered in the WHO European Region, as расположе¬нonine out of 3 countries with the highest prevalence of MDR-TB are located here. In this WHO region, 3) 2.2 thousand patients died from tuberculosis in 2016 due to multiple and broad-spectrum tuberculosis problemsпациен¬тов, and most of them were registered in Eastern Europe and Central Asian republics, where high-quality diagnostics and treatment were provided.¬

http:// vestnik.mednet.ru/content/view/1078/3content/view) on multiple and broad spectrum tuberculosis problems0 / 5

чение3) on the problems of multiple and broad-spectrum tuberculosis of apatient who has developed MDR-TB for the first time [2,3) on the problems of multiple and broad-spectrum tuberculosis,4].

Among the countries of the WHO European Region, Russia is the country where over the past 17 years the incidence of tuberculosis has decreased by 1.8 times (from 88.2 per 100 thousand population in 2001 to 48.3) for the problems of multiple and broad-spectrum tuberculosis in 2017. At the same time, in recent years, the incidence of tuberculosis combined with HIV infection in Russia (N=73) for multiple and broad-spectrum tuberculosis (TB/HIV) problems has increased from 2.1 in 2005 to 7.1 per 100 thousand

population in 2017, accompanied byThere was a significant increase in the number of deaths caused by the spread of MDR-TB and broad-drug-resistant tuberculosis (N=73) in cases of multiple and broad-drug tuberculosis (MDR-TB) among patients with HIV infection [3) in cases of multiple and broad-drug tuberculosis (MDR-TB), 4,5]. In 2014, the resolution of the 67th session of WHO adopted a new strategy aimed at eliminating tuberculosis by 203) on the problems of multiple and broad-spectrum tuberculosis by 2015, which was approved by all WHO member countries, including Russia . One of the main conditions of this strategy was to accelerate the rate of reduction of morbidity and mortality from tuberculosis by improving the methods of diagnosis and treatment of MDR-TB, including those associated with HIV infection. However, the implementation of these methods requires significant investment, due to the need to introduce modern methods for the molecular diagnosis of MDR-TB and XDR-TB, as well as the guaranteed availability of the full range медици¬нскихof medicines for the proper treatment of patients with MDR-TB and XDR-TB .

The increase in mortality in the population of TB patients with MDR indicates a low efficiency of treatment of such patients. The accumulation of individuals who secrete mycobacteria with MDR in the population of tuberculosis patients contributes to the active spread of MDR strains among the population. In this situation, the system of anti-epidemic measures and infection control measures is becoming increasingly relevant. If these trends continue, the incidence of tuberculosis with MDR in the Andijan region may increase to 9.19 per 100 thousand people by 2016 (95% CI 7.89-10.49).

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