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The Relationship of Tuberculosis and Pneumonia in Children, Clinical Characteristics

Nabieva Zumrat Tukhtaevna

Bukhara State Medical Institute

Annotation: Every year three million people die from tuberculosis in the world, and eight million more get sick. Over the past few years, domestic doctors have recorded an explosion of this disease in our camp. Every year, the number of patients increases by 25-30% and, most worryingly, children and adolescents often become victims. Last year, the incidence of tuberculosis was 10.2 per 100 thousand boys and girls. For comparison, in developed countries it ranges from 2.5 to 5.3 . In a number of regions, this indicator, alas, corresponds to the incidence in developing countries of Asia and Africa - 65-70 per 100 thousand children. [2]

Keywords: tuberculosis, nonspecific lung diseases, treatment, diagnosis.

A third of the world's population is infected with tuberculosis of the elderly. If a person is infected and has not been given preventive treatment, he is at risk of getting sick throughout his later life.Tuberculosis, as an infectious and socially significant disease, continues to be one of the serious health problems in Uzbekistan [1]. Every year three million people die from tuberculosis in the world, and eight million more get sick. Over the past few years, domestic doctors have recorded an explosion of this disease in our camp. Every year, the number of patient's increases by 25-30% and, most worryingly, children and adolescents often become victims. Last year, the incidence of tuberculosis was 10.2 per 100 thousand boys and girls. For comparison, in developed countries it ranges from 2.5 to 5.3. In a number of regions, this indicator, alas, corresponds to the incidence in developing countries of Asia and Africa - 65-70 per 100 thousand children.[2] The epidemiological well-being of tuberculosis implies the need to improve the methods of prevention, diagnosis and treatment of this disease. The presence of pulmonary tuberculosis creates a number of prerequisites for the occurrence of concomitant diseases of the respiratory system: the duration of the inflammatory process in the respiratory system with corresponding morphological and functional consequences, drug aggression [3, 4]. At the same time, often the symptoms of a non-specific lung disease (NZL) that is, non-tuberculosis, are regarded as a manifestation (complication) of the course of the main tuberculosis process and maneuvers are carried out to modify the main (basic) chemotherapy of tuberculosis. At the same time, a lot has been saved up There are facts indicating that co-existing NSL significantly aggravate the course of the tuberculosis process, modify its clinical manifestations and negatively affect the final result of treatment. The most studied aspect of this problem is the diseases occurring with bronchial obstruction: chronic obstructive pulmonary disease (COPD), chronic bronchitis, as well as pneumonia, lung tumors. Sometimes practical phthisiologists lack the knowledge and technological equipment for their temporary diagnosis and adequate therapy of NSL. To a certain extent, this is facilitated by interdepartmental barriers separating 2 specialties: phthisiology and pulmonology. The purpose of this study was to determine the frequency of the presence of NSL in patients with pulmonary tuberculosis (TL), to assess the possibilities of their diagnosis and treatment [1,3].

Every year, 10 million new cases of active tuberculosis are detected in the world, of which approximately 10% occur in children under the age of 15, which leads to approximately 80,000 deaths [2]. The proportion of children with latent tuberculosis infection (LT) who subsequently develop tuberculosis is significantly higher than among adults[15].The goals of the World Health Organization (WHO) tuberculosis control strategy will not be achieved without addressing the issue of diagnosis and treatment of LT.This stimulates the development of new diagnostic tests with a high prognostic indicator – an indication of the likelihood of developing the disease among those infected with mycobacterium tuberculosis (MBT) [22, 25]. Preventive treatment of people at risk of developing LTI into a disease is a key component of the WHO document on the tuberculosis eradication strategy "END–TB strategy" 2016-2035[4]. Tuberculin tests are based on the determination of delayed-type hypersensitivity resulting from infection with MBT, non-tuberculosis mycobacteria or immunization with BCG vaccine [2, 3, and 21]. Most of the antigens contained in tuberculin are present in the vaccine strain M. bovis BCG and in non-tuberculosis mycobacteria [9].The Mantoux test has a fairly high sensitivity (the frequency of positive reactions in tuberculosis) [19], while the specificity (the frequency of negative reactions in the absence of tuberculosis) varies depending on the number of false positive results caused by BCG vaccination or sensitization with non-tuberculosis mycobacteria [7]. In modern conditions, the Mantoux test with 2 TE PPD-L (intradermal injection of tuberculin) is mainly used to detect tuberculosis infection in the world. In Russia in recent years, this test has been used as the first stage for the detection of tuberculosis infection in children under 7 years of age, as well as in the selection of children for BCG revaccination at 6-7 years of age according to the orders of the Ministry of Health of Russia [4, 5].Sequencing of the M. tuberculosis genome has had an undeniable impact on understanding the biology of this pathogen [2]. Comparative studies of the M. bovis and M. bovis BCG genomes and comparative analysis of M. tuberculosis H37Rv and M. bovis BCG [3, 4] led to the identification of the RD1 zone present in all M. tuberculosis strains and pathogenic M. strains. bovis, but absent in all M. bovis BCG vaccine strains and most mycobacteria of the external environment. Two of the most fully described antigens suitable for diagnostic purposes (ESAT-6 and CFP-10) are encoded in the RD1 zone. In Russia, in the laboratory of Biotechnology of the Research Institute of Molecular Medicine (Moscow), it was developed for intradermal test preparation diaskintest, which is a tuberculosis recombinant allergen (ATP), which includes a hybrid recombinant protein ESAT-6 – CFP-10, produced by Echerichia coli BL21 (DE3)/pCFP-ESAT [1]. According to the results of clinical trials, which showed high sensitivity and specificity, especially in children [3], ATP (diaskintest drug) it was registered in 2008 and has been introduced into healthcare practice since 2009 [7]. The reviews of the WHO Tuberculosis eradication strategy (END TB strategy) [4] identified priority tasks, including the development of biomarkers for the detection and diagnosis of tuberculosis and LT in children, including systematic screening. A biomarker should have a low cost to detect tuberculosis at the primary care level. It is emphasized that the diagnosis of tuberculosis in children in the world needs to be improved – its funding is extremely inadequate, since it is believed that childhood tuberculosis has a limited impact on the morbidity of the population due to low contagiousness. However, interest in the diagnosis of tuberculosis in children is gaining momentum, including in terms of studying new biomarkers of tuberculosis infection [6]. Currently, in Russia, children from the first year of life to the age of 7 are subject to annual tuberculin diagnostics using a Mantoux test according to the order of the Ministry of Health of Russia No. 124n [5]. The same order regulates the screening for tuberculosis in children from 8 to 17 years old only with the help of a skin test with ATP. Since this order makes it possible to use a sample with ATP in medical organizations of primary health care, this allows the use of this sample in the presence of indications and in children under 7 years of age, in particular in the differential diagnosis of post-vaccination and infectious allergies. Until 2020, the following approach to grouping dispensary observation of children with an increase in the reaction to the Mantoux test was maintained: the transition of a negative reaction to a positive one ("turn" of the sample) is regarded as primary infection of MBT, and children were observed in the VIA group of dispensary observation (GDN). But if there was already a positive reaction earlier, regarded as a post-vaccination allergy, and the size of the reaction (papule) to the sample increased by 6 mm, then this is also considered an infection of MBT, children are subject to observation in the VIB GDN, and if the size of the papule reaches 17 mm – in the VIB

GDN.Since 2020, according to the order of the Ministry of Health of the Russian Federation No. 127n [6], the dispensary grouping has been changed, all children with an altered reaction to skin tests are observed in the VIA GDN. In case of a positive reaction to the test with ATP, children are referred to a phthisiologist for an in–depth examination – they perform computed tomography (CT) of the chest organs (OGC), if necessary - bacteriological and molecular genetic examination for MBT. Objective: to evaluate the effectiveness of mass screening for the detection of tuberculosis infection in children aged 1 to 7 years in Moscow in different periods

In the Saratov region over the last five years (2015-2019). Monitoring of the tuberculosis incidence rate not only on the territory, but also in the groups of dispensary observation (IV and VI groups), as well as analysis of the data of group III (from 2020 – VIB accounting group) can improve the quality of anti-tuberculosis measures, paying special attention to the work with high-risk groups (children of the first 6 years life, adolescents, children from foci of tuberculosis infection). Bronchial asthma (BA) is a heterogeneous disease based on different biological mechanisms, including the action of different genes [3]. Genetic studies conducted in the last few decades have shown an association of AD with 100 genes, and this list continues to grow[1-3,]. The insufficiently studied genes include the EGFR gene. This gene is localized on the 7th chromosome at the 7p11.2 locus and encodes the transmembrane epidermal growth factor receptor (EGFR). EGFR is a transmembrane glycoprotein with a molecular weight of 170 kDa, with tyrosine kinase activity. EGFR belongs to the epidermal growth factor receptor family. The EGFR family consists of four transmembrane receptors: EGFR, ERBB2, ERBB3 and ERBB4. Growth factors and their transmembrane receptor kinases play an important role in cell proliferation, survival, adhesion, migration and differentiation. EGFR is expressed on the surface of both normal and transformed epithelial cells and is an important regulator of cell proliferation [8, 12,]. Single nucleotide polymorphism (ONP) rs2227983 in the form of replacement of nucleotide G with nucleotide A leads to the replacement of amino acids R [Arg] by K [Lys]. According to the dbSNP database, the frequency of genotypes of polymorphism rs2227983 of the EGFR gene in the Caucasian population: AA – 8.1%, AG – 40.5%, G – 51.4%. The EGFR gene is normally expressed in many types of tissues, interacts with many metabolites, including controls mitogenic signals entering cells [19]. A number of studies have shown the involvement of the EGFR protein in the development of certain inflammatory diseases, immune disorders, lung cancer and other organs [7]. A number of publications report on the possible role of the EGFR gene in the development of AD [2, 4, 5], on the association of the EGFR gene with remodeling and hyperreactivity of the respiratory tract in AD [2, 5, 15, 20]. The polymorphism A2073T of the EGFR gene in children with AD has been studied in Russia [2]. Predisposition to the development of AD was noted in homozygotes of the poT allele of the polymorphic variant 2073A>T of the EGFR gene [2]. At the same time, studies of the single nucleotide polymorphism (ONP) rs2227983 of the EGFR gene in AD have not been described. The aim of the study was to study the polymorphism rs2227983 of the EGFR gene in patients with allergic asthma and in healthy individuals. Peritonitis is still the main cause of mortality in patients with acute surgical pathology [9]. To study the pathogenetic mechanisms of various peritonitis, as well as to develop treatment methods, many experimental models of the purulent-inflammatory process in the abdominal cavity have been created [6, 9, 10], but there is no model for primary tuberculous inflammation of the peritoneum. According to E. E. Chepurnykh et al., all methods of obtaining experimental peritonitis can be conditionally divided into two groups: the introduction of foreign bodies or chemicals into the abdominal cavity and inoculation of solutions with a high titer of non-specific bacterial flora [10]. The disadvantages of such models include the use of anesthesia and the use of surgical techniques, the development of a local peritoneal process (intra-abdominal abscess), as well as the rapid death of animals against the background of developing abdominal sepsis [10, 20]. Modeling of tuberculous peritonitis (TP) has a number of objective difficulties, primarily due to the fact that during the development of the disease in vivo, mycobacterium tubercule (MBT) penetrates into the peritoneal leaves hematogenously, lymphogenously or contact from primary foci of infection (more often from the lungs), the process has a subacute or chronic course and –before and after the use of a skin test with ATP in primary health care institutions as an additional diagnostic method. Monitoring and analysis of epidemiological indicators of the incidence of tuberculosis in children and adolescents in the Saratov

region help to improve the work of medical organizations in the territory to carry out anti-tuberculosis work. The digital data embedded in the indicators clearly reflect the sections of anti-tuberculosis measures (early detection of tuberculosis and the formation of risk groups, immunoprophylaxis, work in the foci of tuberculosis infection), which is directly related in the future to the incidence, prevalence, mortality from tuberculosis. In recent years, there has been a decrease in the incidence of tuberculosis in children and adolescents in the Saratov region, which reflects the general trend towards improving the epidemic situation in the Russian Federation. In the Saratov region, tuberculosis mortality among the child population is not recorded from kidneys detected during autopsy. In a similar work by F. Namiotti and A. Baciocchi, published in the journal "La Riforma Medica" (1893), there is an indication of the development of isolated tuberculous omentitis. In later experiments M. B. Lurie (1929), K. Omachi (1953) and S. E. Woodruff (1958) lesions of serous leaflets were not observed in intraperitoneal infection with MBT culture of rabbits and rats [19]. TP refers to the so-called primary peritonitis and accounted for only 0.04-0.7% of all detected cases of tuberculosis until the 1990s. In the modern world, the number of patients with TP is increasing even in countries where tuberculosis was previously rare, and this is directly related to the growth of migration flows, the spread of diseases associated with immunodeficiency, including HIV infection, the use of glucocorticoids and TNF blockers, the prevalence of diabetes mellitus, peritoneal dialysis and fibrotic liver diseases [1, 3]. Peritoneum is the sixth most common extrapulmonary localization of tuberculosis in the USA, Canada and the EU, it occurs in 3.5% of cases of pulmonary tuberculosis and in 31-58% of cases of abdominal tuberculosis [23]. There are no such statistics for the Russian Federation.Thus, an attempt to create a TP model as close as possible to a human one remains relevant for use in the development of new diagnostic and treatment methods. The main conditions for modeling TP are reproducibility and uniformity of its development. Food regime.\

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