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Epidemiology, Clinical Course, Diagnosis and Treatment of Generalized Tuberculosis in Modern Circumstances. Literature Review

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ABSTRACT

The article reviews the scientific works of 90 sources. The results of the analyzes showed that scientific work on generalized forms of tuberculosis is rare. Generalized forms of tuberculosis are a formidable complication and serious condition and require the search for new diagnostic methods and complex treatment.

KEY WORDS: generalized tuberculosis, epidemiology, diagnosis, treatment, prognosis.

Generalized tuberculosis is a common form of the disease, peculiar in its pathogenesis and clinical manifestations, involving two or more organs in the pathological process; the emergence and course is associated with the spread of Mycobacterium tuberculosis by the hematogenous route [41, 43].

Generalized tuberculosis is registered as respiratory tuberculosis if there is a lesion of the respiratory system of the body. Official statistics do not provide data on the primary detection of all extra pulmonary localizations of tuberculosis [4].

EPIDEMIOLOGICAL FEATURES

In the last decade, there has been an increase in the incidence of both nonspecific inflammatory pulmonary diseases and tuberculosis and lung cancer [3,27,69,73.]. To prevent the spread of pulmonary tuberculosis, timely and reliable diagnosis of this disease is of great importance [77,44].

Socio-economic changes in Russia have led to a significant deterioration in the epidemiological situation of tuberculosis, aggravation of its characteristics and course [89]: cases of acutely progressive and generalized tuberculosis have increased significantly, which in Russia began to be observed in about 15% of newly diagnosed patients [88]. Late diagnosis of these cases leads to a high mortality rate of 78%, including 70% within the first year after the detection of the disease [90]. One of the factors in the increase in the number of severe processes with a progressive course, acute onset, massive bacterial excretion and low etiotropic therapy efficiency is an increase in the proportion of drug-resistant strains of mycobacterium tuberculosis, especially with multidrug resistance and super-resistance [37,59].

In patients with generalized forms of tuberculosis, as a rule, the respiratory organs are also affected - in 91.4% of cases [9]. In this case, the lymph nodes inside the chest are very often involved. Thus, there is evidence that in HIV-infected patients, tuberculosis of the intrathoracic lymph nodes occurs in 31.6% of patients versus 7.7% of those without HIV infection [24].

Tuberculosis of the abdominal organs develops mainly in patients with a widespread destructive process in the lungs (caseous pneumonia - 45.5%, disseminated tuberculosis - 20.5%, fibro-cavernous - 20.5%) [87].

The most common extra pulmonary forms of abdominal tuberculosis are lesions of the

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stomach and duodenum (erosion, ulcers), lesions of the large and small intestines (colonoscopy reveals erosion and ulcers in the ascending and cecum, inflammatory infiltration of the Bauhinia flap into the superficial ulceration). resembles ulcerative colitis and Crohn's disease [6]. Spleen, liver are also involved, interintestinal abscesses, peritonitis, lymphadenopathy of intra-abdominal lymph nodes occur. Ultrasound examination reveals: ascites, enlargement of mesenteric lymph nodes, hypoechoic areas in the liver and spleen, local wall infiltration, inflammatory infiltration of the mesenteric root of the small intestine [67].

Among hospitalized patients, pulmonary tuberculosis was combined with tuberculosis of the abdominal organs in 1.95% of cases. There was a tendency towards an increase in tuberculosis of the abdominal cavity organs from 1.6% in 2006 to 2.4% in 2008. The combined damage to the lungs and abdominal organs in 61.4% of cases is characterized by a pronounced intoxication syndrome and local symptoms of damage to the respiratory and gastrointestinal tract. In the structure of the forms of tuberculosis of the abdominal cavity organs, necrotizing ulcerative tuberculosis of the intestine (2/3) prevailed, which was complicated by peritonitis in 36.4% of cases [87].

Over the past 20 years, the incidence of respiratory tuberculosis has increased significantly, while the incidence of extra pulmonary tuberculosis has decreased from 3.3 per 100 thousand population in 1992 to 2.5 per 100 thousand population in 2010 [46]. This is explained by the fact that extra pulmonary forms are much more difficult to detect due to the complexity of using radiation and laboratory diagnostic methods. The availability of medical care is also important [4].

Spinal lesions with various forms of active tuberculosis of the respiratory organs were often encountered - in 91 (77.1%) and with lesions of other organs and systems were diagnosed - in 27 (22.9%) patients. Tuberculosis of the genitourinary organs - 10 (8.5%), tuberculosis of peripheral lymph nodes - in 10 (8.5%), exudative pleurisy - in 7 (5.9%) and a single case (0.8%) observed tuberculosis of the eyes, at the same time - in 12 (10.2%) cases, multiple organ tuberculosis or tuberculosis lesions of the skeletal system with tuberculosis of the spine or other organs [57].

PATHOGENESIS AND PATHOMORPHOLOGY OF GENERALIZED TUBERCULOSIS

Untimely diagnosis of tuberculosis is due to both subjective and objective factors, in particular: insufficient phthisiatricians alertness of general practitioners, the peculiarity of the pathomorphosis of tuberculosis, the presence of background diseases, and difficulties in the interpretation of morphological studies [15,60].

The pathogenesis of generalized tuberculosis is primarily associated with the presence of bacteremia. More often it occurs with primary tuberculosis during the period of dispersion of mycobacterium in the body. In secondary forms of the disease, mycobacterium enter the bloodstream from insufficiently healed or aggravated foci in the lungs, lymph nodes, bones, kidneys and other organs [41,43].

The onset of bacteremia is largely promoted by hyper sensitization of the body due to a bacterial or viral infection, allergic disorders, vitamin deficiency, impaired protein and other types of metabolism, specific superinfection with prolonged and massive contact with bacteriophages, as well as an immunodeficiency state and impaired phagocytes function of macrophages. Most often, generalization of the process occurs in hematogenous forms of tuberculosis - disseminated and miliary tuberculosis, which are the result of immune deficiency [42,43].

Morphological signs of abdominal tuberculosis: serous or serous-hemorrhagic ascitic fluid in the abdominal cavity, millet eruptions on the peritoneum, liver capsule, spleen, enlargement of

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mesenteric lymph nodes, often adhesive process. Complications requiring surgical interventions: perforation of tuberculosis ulcers, abdominal abscesses [46,66,67.].

Reliable endoscopic signs of abdominal tuberculosis are: the presence of millet eruptions on the parietal and visceral peritoneum, fibrinous overlays on the intestinal loops and on the peritoneum, injections of organ vessels. Recently, the course of tuberculosis polyserositis has changed [75]. Tuberculosis pericarditis often occurs. Modern pericarditis is characterized by such signs as: torpid development without an acute onset, a tendency to chronic course, lack of direct evidence of a tuberculosis process, morphological changes with a significant thickening of the pericardial layers. Tuberculosis meningitis is one of the most severe forms of extra pulmonary tuberculosis [23]. In HIV-infected patients, tuberculosis meningitis occurs in the last stages of immunosuppression, when the CD4 + level is below 100 cells / μl. Mortality in this group reaches 36.8-98% [67].

FEATURES CLINICAL COURSE

Generalized tuberculosis can occur with a predominance of pronounced phenomena of general intoxication (hectic temperature, headache, darkened consciousness, sometimes delirium, there may be roseolous skin rashes, severe tachycardia) or symptoms of respiratory failure (severe shortness of breath - up to 50-60 respiratory movements per minute , cyanosis) against the background of intoxication. In addition, meningitis, meningoencephalitis may be noted as a manifestation of generalized tuberculosis or meninges, that is, mild meninges signs due to edema of the meninges as a manifestation of general intoxication [41,85].

The duration of complaints of patients before the diagnosis was from 4-5 months to 3.6 years, on average - 7.2 months. In the clinical course, symptoms of spondylitis prevailed, but along with this, there was a cough - dry or with sputum, pronounced intoxication syndrome, in 14 (5.1%) - hemoptysis, in 4 (1.5%) patients with periodic short-term attacks of suffocation. With tuberculosis of the genitourinary system (MPS) + tuberculosis spondylitis (TS), which was diagnosed in 8 (2.9%) patients, there were complaints of frequent urination, pain in the kidney area, burning, discoloration of urine (red), etc. Osteoarticular tuberculosis + TS - multiple organ tuberculosis was found in 12 (4.3%) patients, of whom hip joint lesion was detected - in 4 (1.5%), knee joints - in 3 (1.1%), trochanteritis - in 1 (0.4%), wrist joint - in 1 (0.4%), sterna tuberculosis - in 1 (0.4%) and rib lesion in 2 (0.7%) cases, respectively. In the clinical course, in this category of patients, pronounced pain prevailed, which intensified with slight movement. Peripheral lymph node tuberculosis (TPL) + TS was found in 7 (2.5%) patients, while the patients did not feel much anxiety. Exudative pleurisy + TS was observed in 7 (2.5%) patients who complained of lack of air, chest pain and a rare dry cough. In 6 (2.2%) patients, tuberculosis lesions of three human systems and organs were diagnosed. Fibrous cavernous tuberculosis (FCT) of the lungs + TMS + TS occurred in 2 (0.7%) patients who had a varied clinical picture. This category of patients showed clinical symptoms of the corresponding three organs and systems, where the pathological process was localized. TPL + focal pulmonary tuberculosis + TS occurred in 3 (1.1%) patients, in which the following clinical signs were characteristic: an enlarged palpable lymph node, cough, sputum production and clinical symptoms of tuberculosis spondylitis. A patient with focal pulmonary tuberculosis + eye tuberculosis + TS occurred in a single case, while eye tuberculosis was established after 4.5 months from the start of special therapy, in the form of retinal detachment in the upper outer part of the right eye, which manifested itself as visual impairment in this area [57].

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The portrait of a patient with generalized tuberculosis in combination with HIV infection is presented mainly by a young man with signs of social maladjustment. The duration of HIV infection before tuberculosis was detected in these patients averaged 7.2 ± 1.4 years. Among concomitant diseases, chronic viral hepatitis C, drug and alcohol addiction prevailed. In 2/3 of patients, tuberculosis was detected for the first time when contacting the general medical network. Common processes (disseminated pulmonary tuberculosis) prevailed, almost half of the patients had tuberculosis of the genitourinary system, one third of the patients had tuberculosis meningitis, tuberculosis spondylitis, and intestinal tuberculosis. One third of the patients were in serious condition, the same number of patients showed a change in consciousness. Half of the patients were diagnosed with leukopenia, a third with lymphopenia. Bacterial excretion was detected in less than half of the patients, including 40% of the MBT were not isolated from sputum, while a quarter of the patients had drug resistance, of which 33.3% and 10% had multiple and extensive drug resistance, respectively. Disintegration of lung tissue and intrathoracic lymphadenopathy had almost half of the patients. In the majority of patients, tuberculosis appeared against the background of HIV infection in an extended stage with a decrease in the absolute level of CD4-lymphocytes, in 66.7% of patients - below 0.2 × 10/9 L [43].

DIAGNOSTICS

The difficulty of establishing a diagnosis in many patients was due to a polymorphic, partly atypical clinical picture of the course of tuberculosis infection, which developed against the background of prolonged, uncontrolled intake of nonspecific anti-inflammatory drugs [15,57,60].

The main methods of diagnostics and monitoring of pulmonary tuberculosis, used at present, are general clinical, radiation, laboratory, microbiological, molecular genetic, histological. Each of these methods has its drawbacks and cannot be considered absolute [49,69]. The clinical symptomatology of infectious pulmonary diseases is determined by the presence of intoxication and pulmonary syndromes, which do not have specific characteristics and therefore cannot be used as a reliable diagnosis of pulmonary tuberculosis [34,19,69,70].

Most patients turn to doctors of the general medical network when signs of any disease appear, both general and symptoms from certain organs and systems, including tuberculosis. For the timely diagnosis of tuberculosis, an effective search is required in the form of constructive interaction between general medical doctors, therapists, surgical specialists, and morphologists [15,57,60].

Since the discovery of X-rays by V. X-rays, the X-ray method has been one of the main in the diagnosis of respiratory tuberculosis. Improvement of X-ray technology in recent years has made it possible to more accurately diagnose pulmonary tuberculosis, as well as to effectively control its treatment [56.]. Nevertheless, according to some authors, in connection with the clinical pathomorphosis of pulmonary tuberculosis, a frequent cause of diagnostic errors and difficulties in treatment is the erasure of differences in the clinical and radiological manifestations of respiratory diseases [21,61,69,82]. Accordingly, the role of such modern high-resolution X-ray diagnostic methods such as digital tomosynthesis and multislice computed tomography, which significantly increase the information content of the revealed changes in the lungs, is increasing [54, 55, 68, 29].

For more than a hundred recent years, the detailed symptoms of tuberculosis lesion of the lungs, depending on the form and course of the disease, have been developed and are constantly being improved, algorithms for differential diagnosis have been developed [39]. Modern X-ray

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methods make it possible to identify and detail structural changes in the affected organ, establish the localization, length, complications of the tuberculosis process [26]. The use of computer programs for transforming an image obtained in the course of ray studies is promising [62, 64]. However, the determined X-ray signs cannot be pathological only for pulmonary tuberculosis. According to the radiological data, it is impossible to make a final conclusion about the genesis of morphological changes [38]. As a result, X-ray techniques need to be confirmed by other methods.

Determinations of the presence of Mycobacterium TB in a patient's body are based mainly on the detection of specific antibodies. Historically, the first method is tuberculin diagnosis, which consists in detecting antibodies fixed on cells (lymphocytes, monocytes) when they interact with tuberculin. Currently, the intradermal test (Mantoux test) is widely used. This test retained its diagnostic value only among pediatric and adolescent patients, when its result is one of the diagnostic criteria [63]. In addition, tests with subcutaneous administration of tuberculin are of some auxiliary value in the diagnosis of tuberculosis, when they are guided by a characteristic general, local and focal reaction (Koch's test). "Diaskintest" is a new method for diagnosing tuberculosis disease and the state of infection, which is based on determining the reaction of the examined person's body to specific proteins that are found only in virulent strains of mycobacterium tuberculosis [47]. A positive Mantoux test result means that the person being examined has either been exposed to a tuberculosis infection, or has recently received BCG vaccination, or is infected with non-pathogenic mycobacterium that cannot cause disease and do not require any treatment [11.]. Unlike the Mantoux test, a positive Diaskintest result indicates with a high degree of accuracy that the person being examined is either infected with tuberculosis at the moment or is already sick with it [69].

Recently, a new method for diagnosing latent tuberculosis, QuantiFERON TB-2G, has appeared, which is devoid of the drawbacks of a skin test [78]. It is based on the in vitro detection of interferon gamma production by the patient's blood lymphocytes. Antigens ESAT-6 and CFP-10 M. tuberculosis are used as inducers of interferon synthesis during its implementation. These antigens are expressed by M. tuberculosis, M. bovis, M. africanum, but they are absent in the BCG vaccine strain and most non-tuberculosis mycobacterium, including M. avium, M. intracellulare. Thus, a high specificity of the test readings is achieved [17]. Increasing the sensitivity of the test and the objectivity of its readings is achieved by automating the detection of interferon. Tests conducted by Japanese specialists from the Tuberculosis Research Institute have shown that the specificity and sensitivity of the QuantiFERON TB-2G test are 98.1 and 89.0%, respectively [30]. Immunological diagnosis of tuberculosis is very promising [12]. However, to date, not a single serological test has been developed that has such a high sensitivity that it could replace the currently used methods of diagnosing tuberculosis [5, 69].

For the timely diagnosis of tuberculosis of the abdominal organs, it is recommended to conduct a bacterioscopic examination of feces for MBT, occult blood, endoscopy, ultrasound and X-ray of the abdominal organs [87].

The central place in the systemic inflammatory response is the production of a wide range of proteins - acute phase reactants (POF) by the liver, the changes in the concentration of which increase to varying degrees. The level of a number of proteins increases significantly (C-reactive protein), moderately (haptoglobin, α1-acid glycoprotein, α1-protease inhibitor, fibrinogen), may remain within the reference range (ceruloplasmin, α2-macroglobulin) and require individual assessment, or may decrease (albumin, transferrin) [14]. The complexity of the analysis lies in the

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fact that they are characterized by polyfunctionality and they are all capable of influencing one or several links of the inflammatory process [45]. Haptoglobin, α1-acid glycoprotein and ceruloplasmin have antioxidant properties. Direct antibacterial effects have been shown for CP and hemopexin, which bind copper and gemstones, respectively [83]. The α1-protease inhibitor, α2-macroglobulin and α1-acid glycoprotein have antiprotease activity. Their important function is to inhibit the activity of elastase-like and chymotrypsin-like proteinases coming from granulocytes to inflammatory exudates and causing secondary tissue damage. The regulator of the inflammatory response is elastase, which in different situations can act as both a pro-inflammatory and an anti-inflammatory agent [30]. An important modulatory component of the systemic inflammatory response syndrome is adenosine, the extracellular accumulation of which leads to a decrease in the activity of immune cells and to the protection of tissues from damage. One of the possible ways to study this relationship between adenosine and the functional state of immune cells is to study the activity of adenosine deaminase, which regulates the level of adenosine, converting it into inosine [10, 14].

BACTERIOLOGICAL VERIFICATION METHODS

The development and implementation of promising technologies for the accelerated diagnosis of TB and the determination of the drug susceptibility of the pathogen are extremely important to ensure highly effective treatment based on the selection of personalized chemotherapy regimens. One of the most promising and demanded directions in the development of laboratory TB diagnostics, which is supported by WHO, the Global Laboratory Initiative and the European Laboratory Initiative, is the use of molecular genetic methods [74].

More than a century of experience of phthisiatricians all over the world has proved that the “gold” standard for diagnosing tuberculosis is the classic combination of microscopic and cultural methods for studying mycobacterium tuberculosis, which remain relevant today, despite the emergence of a large number of alternative methods. Bacterioscopic examination is the most accessible, fastest and cheapest method for detecting acid-fast mycobacterium [58]. However, the limits of the method, even with the use of the most advanced microscopic technology, including luminescence, make it possible to detect acid-fast mycobacterium when their content is not less than 10,000 microbial bodies in 1 ml of material. This amount of mycobacteria is found in sputum only in patients with common, progressive forms of tuberculosis [1]. With a slight severity of the tuberculosis process in the lungs, only 34% of patients manage to detect the pathogen during bacterioscopy of a smear from sputum, even after repeated repeated examinations. In the absence of visible changes on radiographs, the detection of mycobacteria in a sputum smear is unlikely. A nanoimmunofluorescence method has been developed for the rapid detection of tuberculosis bacteria in pathological material [52]. It is carried out using silicone nanoparticles with covalently immobilized protein A. In sensitivity, it is significantly superior to the fluorescent method for diagnosing tuberculosis. The use of an epifluorescent filter facilitates the recording of test results and reduces the time required for this [65].

The culture method for detecting mycobacteria is more sensitive and has a number of advantages over the microscopy method [25]. It allows detecting mycobacterium TB in the presence of several dozen viable individuals of the pathogen in the pathological material under study. A very important advantage of the method is the possibility of obtaining a culture of the pathogen, which can be studied in detail, identified and studied in relation to drug sensitivity, virulence and other biological properties. There are real opportunities to improve the efficiency of

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classical methods of microbiological research by improving the methods of material preparation, the use of new dyes, modification of cultivation systems and registration of the growth of mycobacteria, for example, the use of automated systems such as VASTEC MGIT 960 [51]. Reproduction of tuberculous mycobacteria in liquid nutrient media occurs much faster than in solid media [69].

The use of the PCR method for the diagnosis of tuberculosis makes it possible, within 1 working day (2-3 hours), to establish the presence of MBT DNA in the diagnostic material. Preference is given to test systems with real-time result detection, which almost completely eliminate the risk of sample contamination with amplification products [13].

The most promising method for determining genotypic drug resistance is real-time multiplex PCR. The advantage of this method over the technologies described above is the absence of a hybridization stage and evaluation of the results in real time, which reduces the possibility of contamination. An example of such test systems is GeneXpert MTB / RIF (Ceiphid, USA). However, this test system determines resistance only to rifampicin (specificity 90%) and is characterized by a very high cost of analysis. Among the Russian PCR test systems for the determination of MDR, one can note the Amplitub-MDR-RV produced by CJSC Syntol (specificity for rifampicin and isoniazid is about 94%) [50, 79].

Direct methods for detecting MBT include methods for detecting specific fragments of the pathogen DNA chain in the test samples of diagnostic material. Among the molecular biological methods used for this, the most widespread method is the polymerase chain reaction, which is based on a multiple increase in the number of copies of a specific DNA region (the so-called directed DNA amplification) [2]. The method is especially relevant for tuberculosis, since it is effective against pathogens with high antigenic variability (including L-forms), the determination of which requires long-term cultivation or complex nutrient media, as well as against intracellular parasites and persistent microorganisms [84]. Along with this, PCR diagnostic methods are very promising for interspecies and strain identification of mycobacteria for differentiation of tuberculous and non-tuberculous mycobacteria (causative agents of mycobacteriosis), for rapid determination of drug resistance of mycobacteria [80].

The method of histological examination of tissue affected by a specific process is referred to as reliable methods for diagnosing tuberculosis. It allows the detection of granulation tissue and caseous necrosis, specific for tuberculosis, in biopsy material. This invasive method should be used in the most difficult cases of pulmonary tuberculosis diagnosis. However, the information content of histological examination is limited by the relative specificity of tuberculous granuloma [36]. Similar morphological changes occur in sarcoidosis and other granulomatous processes. In addition, in patients with immunodeficiency (AIDS, hemoblastosis, immunosuppressive therapy, cytostatic therapy), the formation of tubercles is impaired or they are not formed. Histological examination of biopsy material, bacteriological examination on solid and liquid nutrient media, including using the Bactec MGIT - 960 system and molecular genetic diagnostics (Geno Type MTBDR plus (Hein test) and Xpert MTB / R1F) are referred to as methods of diagnosis verification. Clinical anamnestic, Xpert MTB / R1F, X-ray, bacterioscopic, skin tests with tuberculin, Diaskintest, GUANTIFERON - TV GOLD methods are referred to as screening research methods [28]. Currently, bacterioscopic and bacteriological (and their modifications) research methods are still the "gold standard" in the diagnosis of pulmonary tuberculosis.

Modern methods of diagnosing pulmonary tuberculosis (PCR diagnostics, serological diagnostics) are being actively introduced into practical health care and are increasingly important

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in the diagnosis of tuberculosis, however, they must be confirmed by bacterioscopic and / or bacteriological research methods.

The morphological method for confirming tuberculous pathology is reliable, but in many cases it should be borne in mind that there are limitations to its use.

At present, despite the availability of a variety of modern methods for diagnosing tuberculosis, there is a need to develop and introduce new methods for rapid, high sensitivity and specificity diagnostics [69].

STATE OF THE ART TREATMENT

The World Health Organization's (WHO) "Tuberculosis Control Strategy" aims to reduce the incidence of tuberculosis to less than 10 cases per 10 5 people per year by 2035. The main approach to achieving this goal is to strengthen efforts to find and treat people with active tuberculosis, conduct universal screening for those at high risk, and provide preventive therapy for those at risk of progression to active tuberculosis.

Standard controlled chemotherapy for tuberculosis is highly effective in treating tuberculosis caused by a susceptible pathogen [81,18].

Conducting a microbiological study of the drug susceptibility of Mycobacterium TB to the main and reserve anti-TB drugs is necessary in each case of isolating a culture of Mycobacterium TB. After receiving data from a microbiological study of the drug susceptibility of Mycobacterium TB, it is necessary to correct chemotherapy and prescribe individualized treatment regimens [53].

Treatment of MDR-TB patients is long-term with multicomponent chemotherapy regimens, often accompanied by adverse reactions to the drugs used and their combinations. This, especially in the absence of proper motivation and psychological support, increases the risk of withdrawal from treatment among patients, thereby increasing the likelihood of an unfavorable outcome [20, 31]. Even an improvement in the patient's condition and a decrease / disappearance of the symptoms of the disease can be the reason for the patient's premature termination of the chemotherapy course due to an incorrect assessment of his condition [76].

Several studies show that early sputum culture negative and conversion status at 6 months may serve as a predictive marker of treatment success in MDR-TB patients [40,48].

In organizing tuberculosis treatment, special attention should be paid to scrupulous implementation of standard chemotherapy regimens and solving the problem of treatment evasion. Further improvement of anti-epidemic measures among the migrant population is necessary [8].

According to domestic studies, almost 90% of patients with pulmonary tuberculosis develop at least one undesirable side reaction. The presence of side effects requiring a change in the scheme of specific therapy or its temporary cancellation is accompanied by treatment, according to various sources, from 60 to 80% of newly diagnosed patients [33,86,77]. As found, drug complications arising in the course of treatment of pulmonary tuberculosis seriously impede the formation of therapeutic cooperation of the patient [14], significantly reduce the clinical and economic efficiency of therapy [35,71,72,22], and are also associated with a high risk of treatment failure and mortality of patients [32].

Patients with an unfavorable psychological status should be classified as a potential risk group for the occurrence of side effects during chemotherapy. In the complex of basic therapeutic measures in such patients, the normalization of their psychophysiological state is shown, which

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will contribute to the implementation of the principle of continuity of chemotherapy as one of the factors of its effectiveness [86].

The use of radical-restorative operations of the spine in generalized forms of tuberculosis improves the general condition of the patient and has a significant role in the recovery of patients. Conducting 2-3 months of anti-tuberculosis therapy with pathogenetic therapy before the operation period with deep lung lesions with the release of mycobacteria is advisable and reduces complications during anesthesia and in the early operating period. Joint treatment of specialists and adequate therapy, taking into account the sensitivity of mycobacterium to anti-tuberculosis drugs, timely carrying out a radical-restorative operation to recover patients with generalized forms of tuberculosis [57].

The lethal outcome was stated in 23 patients (52.3%), which indicates the severity of the course of tuberculosis of the abdominal cavity organs in combination with pulmonary tuberculosis [87].

In the conditions of an unfavorable epidemiological situation for tuberculosis, which, along with an increase in the structure of the clinical forms of a specific process, is a manifestation of the modern pathomorphosis of this disease, acutely progressive forms of pulmonary tuberculosis have acquired particular importance, a clear knowledge of the diagnostic and treatment tactics of which is necessary for every doctor [37].

CONCLUSION

Thus, in the literature, there are not enough scientific works devoted to the problem of generalized forms of tuberculosis, but the problem is urgent and requires further research, with the search for new methods of diagnosis and improvement of modern methods of treatment. Rehabilitation methods and methods that improve the psychoemotional state of patients in this category have not been sufficiently studied and require further research.

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