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MODERN DIAGNOSIS AND CLINICAL COURSE OF RESISTANT FORMS OF PULMONARY TUBERCULOSIS IN UZBEKISTAN

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Abstract
A survey of 244 patients from the southern regions of the Republic of Uzbekistan was carried out in the period from 2016 to 2020. The age of patients ranged from 18 to 86 years; the average age was 52 years; men were 2.2 times more than women.
Bacterioscopy examination revealed MBT in 154 (63.1%) cases, and 90 (36.9%) cases of MBT were not detected. Growing of pathological material was carried out on the solid medium of Levenshtein-Jensen - in 229 (93.9%) patients and in 206 (89.9%) cases, growth of colonies of Mycobacterium tuberculosis was noted. And the liquid medium BACTEC MGite 960 - in 15 (6.1%) cases and 11 (73.3%) cases, a positive result was obtained. PCR diagnostics was carried out in the Gene / Xpert device - in 244 (100%) patients and 237 (97.1%) cases, DNA of mycobacterium tuberculosis was detected, and in the HAINtest device - in 164 (67.2%) cases and 100% of cases positive result.

Keywords: *resistant form of tuberculosis, pulmonary tuberculosis, clinical course, diagnosis, treatment*

Introduction:

According to WHO experts, drug-resistant tuberculosis is; a case of pulmonary tuberculosis with isolation of MBT resistant to one or more anti-tuberculosis drugs [3,4,5,10].
The worldwide spread of multidrug-resistant tuberculosis (MDR-TB) is a major obstacle to TB control and achievement of targets set by the World Health Assembly and one of the United Nations Sustainable Development Goals [1,3,9,12,13].
For modern phthisiology, an even more serious problem is the drug resistance of the causative agent of tuberculosis, since it is one of the factors that reduce the effectiveness of treatment. Since 1999, since the statistical recording of data on multidrug resistance (MDR) of Mycobacterium tuberculosis (MBT) to anti-tuberculosis drugs in patients with tuberculosis, the incidence rate of tuberculosis with MDR MBT in the Russian Federation has increased by 2.4 times - from 1.7 (1999) to 4.1 per 100,000 populations in 2012. The number of TB patients with MDR MBT among all registered patients increased by 8.6 times over the last period from 1.9% to

16.3%. This significantly reduces the results of treatment and increases mortality [3,4,5,14].

The study of the structure of MBT DR in young patients showed a decrease in monoresistance by 1.8 times, an increase in MDR by 1.7 times, multiresistance did not change significantly. Among the main drugs, drug resistance increased significantly to isoniazid and rifampicin, and significantly decreased to ethambutol. Among the reserve drugs, a significant increase in resistance to protionamide was noted. [3,6,7,11].

The low level of effectiveness in the treatment of TB patients is due to the lack of timely diagnosis and control of chemotherapy, as well as effective modern drugs. The analysis suggests that the timely administration of an adequate chemotherapy regimen to patients with MDR pulmonary tuberculosis contributes to the achievement of treatment effectiveness in a shorter time in terms of sputum smear negativity and sputum smear conversion in 77.8% and 78%, respectively, as well as the outcome of the course of treatment - "cure" in 26% [3,8].

Materials and Methods of Research:

The work is based on examination data of 244 patients from the southern regions of the Republic of Uzbekistan who received treatment in the centers of phthisiology and pulmonology in the Bukhara region - 148 (60.7%), Navoi region - 30 (12.3%), Kashkadarya region - 32 (13 .1%) and Surkhandarya region - 34 (13.9%) cases in the period from 2016 to 2020.

The age of the patients varied from 18 to 86 years, the mean age was 52.1±2.9 years. Table 2.1 shows that men were 2.2 times more than women, the number of patients aged 19-59 years - 65.2% (working age), 60-69 years - 18.4%; over 70 years old - 16.4%. It should be noted that the most common incidence occurred after forty years - 75.4% of patients and the peak age period was from 50 to 59 years in 23.4% of cases. Sick rural population was observed - in 185 (75.8%), urban population - in 56 (23.0%) and homeless people - in 3 (1.2%) cases. The analysis noted that the disease was 3.3 times more common in rural populations. Of the 244 cases - in 73 (29.9) patients, the profession was an employee, 13 (5.3%) - agricultural workers, 4 (1.6%) - students, in a single (0.4%) case - a physician, and more often in total, people without a certain job, who are more likely not to undergo a preventive medical examination - in 153 (62.8%) cases.

The localization of the tuberculous process in most patients was observed on both lungs - in 89 (36.5%), in 86 (35.2%) - damage to the right lung and less cases of the left lung - in 69 (28.3%) patients. Table 2 shows that frequent localization of

tuberculous lesions of the lung was noted in the upper lobe of the lungs - in 169 (69.3%), less often in the lower lobe of the lung - in 24 (9.8%) patients. It should be noted that a total lesion of one lung was observed in 51 (20.9%) cases, and a total lesion of both lungs - in 29 (11.9%) patients in whom the clinical manifestation of the disease was severe. Out of 244 patients, in 151 (61.9%) patients, the disease was detected for the first time, and in 93 (38.1%) - again, i.e. they have previously received treatment. It should be noted that 21 (8.6%) patients were previously prisoners.

Out of 244 patients, generalized forms of tuberculosis occurred in 11 (4.5±2.5%) cases, of which mild tuberculosis with tuberculous pleurisy - in 7 (2.9±1.1%) cases, the organs of the genitourinary system were determined - in 2 (0.8±0.2%) and with tuberculous spondylitis - in 2 (0.8±0.2%) patients.

Results and Discussion

All patients underwent bacteriological examination of sputum, and in 100% of cases the clinical diagnosis was verified bacteriologically.

In 74 (30.3±2.7%) patients, the disease developed slowly over more than 1 year, with a characteristic progression of general malaise, rare rises in temperature to subfebrile, sometimes accompanied by a dry cough. Subacute course of the disease with progression within 1 year, weight loss, subfebrile temperature, dry cough and sweating in the evenings was observed in 24 (9.4±1.8%) patients, in 26 (10.6±1.9%) cases, the duration of the above symptoms is up to 6 months, it should be noted that in 120 (47.6±2.4%) patients it was up to 3 months - the clinical course of the disease was acute, with a temperature rise of more than 38.0 ° C, with intoxication, weight loss more than 10% of the total, with a strong growing dry or wet cough with sputum and with a deterioration in the general condition of patients.

The duration of complaints of patients before establishing the final diagnosis ranged from 1 month to 10 years, on average 6.3±1.7 months.

The general condition of the patients upon admission to the clinic was as follows: relatively satisfactory - 11 (4.5%) cases, moderately severe - 217 (88.9%), and with a serious condition - 16 (6.6%) cases. Consciousness of patients was normal - in 240 (98.4%) cases, and soporous state - in 4 (1.6%) cases.

The general weakness of patients is most often observed - 99.6%, sweating - 90.2%, cough with sputum - 89.3%, weight loss - 77.9% of cases, and in rare cases dry cough - 3.7% and an increase in body temperature above 380 - 6.2% of patients (who are infected with a mixed flora of MBT + normal microflora or complicated by caseous pneumonia).

The patients were examined by all general clinical methods: anthropometric, palpation, percussion, auscultation of organs and instrumental methods.

Examination revealed chest pain in 115 (47.1±3.2%) patients, changes in chest configuration in 57 (23.4±2.7%) patients, pectoral muscle atrophy in 30 (12.3 ±2.1%) and expansion of the intercostal space - 42 (17.2±2.4%) cases.

Palpation revealed an increase in voice trembling in 70 (28.7±2.9%) cases, a decrease in voice trembling in 129 (52.7±3.2%) and the rest - in 45 (18.4±2.5%) cases no change was found. Percussion of the lungs revealed dullness of lung sound in 208 (85.2±2.3%) patients, box sound in 12 (4.9±1.4%) and lung sound in 27 (11.1±2.0%) patients. %) cases. Auscultation of the lungs plays an important role in the detection of pulmonary diseases. During auscultation of the lungs, weakened vesicular breathing was observed in 211 (86.5 ± 2.2%) patients, bronchial breathing - in 12 (4.9 ± 1.4%) patients, breathing was not auscultated - in 4 (1.6 ± 0 .8%) and vesicular respiration - in 21 (8.6±1.8%) cases.

Pathological symptoms, anatomical features of the lungs and chest organs, ways and place of pleurisy distribution were carefully examined. A 6-minute walk test was carried out - this is the most common exercise test in the world used to determine the functional status of patients with respiratory pathology, assess the prognosis of the disease and the effectiveness of therapy. This test is highly sensitive to changes in its methodology, therefore it is recommended to strictly comply with the technical requirements developed jointly by the European Respiratory Society and the American Thoracic Society: patients who have overcome more than 551 m - FC 0, 426-550 m - FC I, 301-425 m - FC II , 151-300 m - FC III and those who covered a distance of less than 150 m - FC IV on the recommendation of the New York Heart Association (NYHA - New York Heart Association).

Concomitant diseases occurred in 223 (91.4%) cases: chronic obstructive pulmonary disease (COPD) and chronic bronchitis - in 18 (8.1%) cases, anemia - in 51 (22.9%) cases, cardiovascular diseases - in 51 (22.9%), diseases of the hepatobiliary system - in 32 (14.3%), genitourinary system - in 14 (6.3%), diabetes mellitus - in 41 (18.4%), mental illness - in 6 (2.7%), AIDS - in 5 (2.2%) and MDR TB + diabetes mellitus + hepatitis - in 5 (2.2%) patients. Anemia in many cases met with other diseases. In 85 (34.8%) patients, there were more than 2 types of concomitant diseases with pulmonary tuberculosis.

When analyzing, noted that drug-resistant pulmonary tuberculosis often develops in people living with chronic diseases, weakened immune systems or with underlying diseases. The disease was most often detected in patients with concomitant diseases of the cardiovascular, hematopoietic, hepatobiliary systems

and diabetes mellitus. The clinical course was severe and the treatment of patients in this category was quite complicated.

All patients underwent complex diagnostic, clinical, laboratory and instrumental research methods. Complete blood count, biochemical blood tests, coagulogram, urinalysis, ECG, ultrasound of internal organs: liver, kidneys, pancreas, pelvic organs, retroperitoneal space, and X-ray examination of chest organs were performed in all patients.

In patients with pulmonary tuberculosis, a decrease in hemoglobin was often found - in 67.2% of cases; acceleration of ESR - in 55.3%; leukocytosis - in 49.6%; increased liver enzymes and bilirubin - in 38.1%; violation of the filtration functions of the tubules of the kidneys - in 9.8% of patients and it should be noted that leukocyturia - in 87.7%; erythrocyturia - 26.6%; proteinuria - 23.3% of cases.

Also, the patients underwent microscopy of sputum, surgical material, pleural fluid - they were studied by the molecular genetic PCR method on the Gene / Xpert and HAINtest apparatus, as well as seeding methods in solid and liquid medium.

In 216 (88.5%) cases, a bacterioscopy method for diagnosing tuberculosis was performed - a study of a smear after processing and staining according to the Ziehl-Nelsen method.

Bacterioscopy examination revealed MBT in 154 (63.1%) cases, and 90 (36.9%) cases of MBT were not detected.

Sowing of pathological material was carried out on the solid medium of Levenshtein-Jensen - in 229 (93.9%) patients and in 206 (89.9%) cases, growth of colonies of Mycobacterium tuberculosis was noted. And the liquid medium BACTEC MGite 960 - in 15 (6.1%) cases and 11 (73.3%) cases, a positive result was obtained.

Molecular genetic method - PCR (polymerase chain reaction) diagnostics was carried out in the Gene / Xpert apparatus - in 244 (100%) patients and 237 (97.1%) cases, DNA of mycobacterium tuberculosis was detected, and in the HAINtest apparatus - in 164 (67, 2%) of cases and 100% of cases received a positive result. Aim to detect MTB complex + rifampicin resistance and MDR-TB detection and no separate detection step required, allows multiplexing, internal control can confirm negative results, high resolution, high specificity, very good reproducibility.

In 11 (4.5%) cases, postoperative pathological material was examined microscopically on BC using the Ziehl-Nelsen method and bacteriological seeding - MGite BAKTEK 960 on liquid and solid Levenshtein-Jensen medium, with the determination of MBT sensitivity to antibiotics or genetic-molecular - PCR diagnostics.

Plain radiography of the chest before the hospital stage was carried out in 244 (100%) patients in the frontal projection in standard laying.

In 239 (97.9%) cases, pulmonary tuberculosis was established by X-ray methods, and in 2.1% of cases, pulmonary tuberculosis was excluded when interpreting the diagnosis.

In 230 (94.3%) cases, X-ray examination revealed X-ray symptoms, as they occur with pulmonary tuberculosis.

At each month, a control radiography was performed to determine the effectiveness of the treatment. Table 2.7 shows that the radiological symptom "Periscisuritis" was often encountered - in 74.6% of cases.

Computed tomography (CT or MSCT) was performed in 31 (12.7%) patients on a Somatomspira l HP spiral tomography, the thickness of the tomographic slice was from 2 to 5 mm for diagnostic purposes.

It should be noted that the analysis 6.5 ± 1.7% of cases with CT examination of pulmonary tuberculosis is excluded, this does not belittle the value of this modern method of radiation diagnostics, while the correct interpretation of the data is a particularly important diagnostic step. CT scan is more appropriate and informative for diagnosing pulmonary tuberculosis and evaluating the effectiveness of the treatment.

Bronchoscopy was performed in 14 (5.7%) patients who had difficulty in diagnosing and verifying the diagnosis. Out of 14, 7 (50%) patients had pulmonary tuberculosis confirmed, and 2 (14.3%) had oncopathology and 5 (35.7%) cases had another pathology. In 7 (50%) patients in whom tuberculosis was not detected by the bronchoscopy method, subsequent studies by the bacteriological method in the sputum revealed a stable form of MBT.

Ultrasound examination (ultrasound) of the internal organs and the pleural cavity was performed in 214 (87.7%) patients, of which 122 (57.0%) cases revealed various pathologies of the internal organs: chronic hepatitis - in 11.1% of cases, chronic cholecystitis - in 20.1%, chronic pancreatitis - 13.5%, chronic inflammatory disease of the urogenital organs - in 5.7% and exudative pleurisy - 1.2% of cases.

In 11 (4.5%) cases, during histological examination of postoperative material, 100% of cases revealed pulmonary tuberculosis and carried out pathological material (pus, exudate, pathological fluids ...) PCR diagnostics and bacteriological examination.

R21qPatients who were found to have a stable form of pulmonary tuberculosis underwent complex treatment according to the standard with pathogenesis therapy and strict adherence to a healthy lifestyle.

When analyzing table 11, it is noted that patients entered the phthisiatric clinic in 88.9% of cases in the late phases of the disease, which the general condition of these patients was severe. In 6 (2.5%) patients, the process was in the resorption phase with

an improved condition, which revealed a stable form after some time of anti-tuberculosis therapy with the first line of an anti-tuberculosis drug.

Conclusions

1. Resistant forms of pulmonary tuberculosis have a variety of clinical symptoms, which makes timely diagnosis difficult.
2. X-ray and CT scan diagnostics are informative diagnostic methods, and bacteriological verification of the form of Mycobacterium tuberculosis has a particularly important role in the diagnosis and adequate treatment of patients in this category.

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