CHARACTERISTICS OF NEW CASES OF INFILTRATIVE PULMONARY TUBERCULOSIS IN PATIENTS HAVING HIV INFECTION WITH MULTIDRUG RESISTANCE OF THE PATHOGEN ACCORDING TO MULTI-LAYER SPIRAL COMPUTED TOMOGRAPHY

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ABSTRACT

Background. *Identification of the characteristics of the pulmonary tuberculosis process using multi-layer spiral computed tomography (MSCT) in patients with tuberculosis and HIV infection is important in the diagnosis of tuberculosis, determining the dissemination of the process and its dynamics during treatment.*

The aim. *To determine the initial characteristics and dynamics of infiltrative tuberculosis according to MSCT in patients with and without HIV infection, with and without multidrug resistance (MDR) of Mycobacterium tuberculosis who were treated in a hospital.*

Materials and methods. *126 patients aged 19–59 years with tuberculosis, combined with HIV infection and without HIV infection were examined. For statistical processing, we used MS Excel (Microsoft Corp., USA) software package.*

Results. *Patients with tuberculosis and HIV infection in comparison with patients with tuberculosis and without HIV had more expressed intoxication syndrome and respiratory impairement in the clinical picture ($p < 0.00001$). Patients with coinfection were more likely to suffer from alcohol ($p < 0.05$) and drug addiction ($p < 0.001$).*

According to MSCT, the pathological process in HIV-positive patients with pulmonary tuberculosis was more disseminated ($p < 0.05$), included severe intrathoracic lymphadenopathy ($p < 0.0001$), more common pleural lesions ($p < 0.005$), less common destructive changes (cavities) ($p < 0.001$) and outcomes in form of fibro-cavernous tuberculosis ($p < 0.01$). Process regression was slower in patients with tuberculosis and HIV ($p < 0.005$).

According to MSCT, extensive lung damage, intrathoracic lymphadenopathy were more often found in patients with MDR in coinfection ($p < 0.05$). Cavities and fibro-cavernous tuberculosis outcomes were more common in patients with tuberculosis without HIV infection and with MDR ($p < 0.05$).

Conclusion. *MSCT provides detailed information about the pathological process in the lungs and its dynamics under the treatment of tuberculosis and HIV infection.*

Key words: *infiltrative tuberculosis, tuberculosis combined with HIV infection, computed tomography, multidrug resistance of Mycobacterium tuberculosis*

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ХАРАКТЕРИСТИКА ВПЕРВЫЕ ВЫЯВЛЕННОГО ИНФИЛЬТРАТИВНОГО ТУБЕРКУЛЁЗА ЛЁГКИХ У БОЛЬНЫХ С ВИЧ-ИНФЕКЦИЕЙ С МНОЖЕСТВЕННОЙ ЛЕКАРСТВЕННОЙ УСТОЙЧИВОСТЬЮ ВОЗБУДИТЕЛЯ ПО ДАННЫМ МУЛЬТИСПИРАЛЬНОЙ КОМПЬЮТЕРНОЙ ТОМОГРАФИИ

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РЕЗЮМЕ

Обоснование. *Выявление характеристик туберкулёзного лёгочного процесса методом мультиспиральной компьютерной томографии (МСКТ) у пациентов с туберкулёзом и ВИЧ-инфекцией является важным в диагностике туберкулёза, определении распространённости процесса и его динамики на фоне лечения.*

Цель исследования. *Определить исходную характеристику и динамику инфильтративного туберкулёза по данным МСКТ у пациентов с ВИЧ-инфекцией и без ВИЧ-инфекции с множественной лекарственной устойчивостью (МЛУ) и без МЛУ микобактерий туберкулёза, получавших лечение в стационаре.*

Методы. *Обследованы 126 пациентов 19–59 лет с туберкулёзом, сочетанным с ВИЧ-инфекцией, и без ВИЧ-инфекции. Для статистической обработки использовался пакет прикладных программ MS Excel (Microsoft Corp., США).*

Результаты. *У пациентов с туберкулёзом и ВИЧ-инфекцией в сравнении с пациентами с туберкулёзом без ВИЧ в клинической картине чаще были выражены синдром интоксикации и нарушение функции внешнего дыхания ($p < 0,00001$). Лица с коинфекцией чаще страдали алкогольной ($p < 0,05$) и наркотической зависимостью ($p < 0,001$). Патологический процесс по данным МСКТ у ВИЧ-позитивных пациентов с туберкулёзом лёгких имел большую распространённость ($p < 0,05$), выраженную внутригрудную лимфоаденопатию ($p < 0,0001$), чаще встречалось поражение плевры ($p < 0,005$), реже выявлялись деструктивные изменения ($p < 0,001$) и исходы в фиброзно-кавернозный туберкулёз ($p < 0,01$). Регрессия процесса была замедлена у пациентов с туберкулёзом и ВИЧ ($p < 0,005$). По данным МСКТ распространённое поражение лёгких, внутригрудная лимфоаденопатия чаще регистрировалось у пациентов с МЛУ при коинфекции ($p < 0,05$). Деструктивные изменения и исход в фиброзно-кавернозный туберкулёз чаще наблюдались у пациентов с туберкулёзом без ВИЧ-инфекции с МЛУ ($p < 0,05$).*

Заключение. *МСКТ даёт детальную информацию о патологическом процессе в лёгких и о его динамике под действием лечения при туберкулёзе и ВИЧ-инфекции.*

Ключевые слова: *инфильтративный туберкулёз, туберкулёз в сочетании с ВИЧ-инфекцией, компьютерная томография, множественная лекарственная устойчивость микобактерий туберкулёза*

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In the Russian Federation, there is a tendency to increase the proportion of HIV-infected patients among patients with newly diagnosed tuberculosis, it has a negative impact on the epidemiological process of these infections [1].

Despite the considerable variety of anti-tuberculosis drugs for treating for tuberculosis patients [2], the efficacy of treatment of coinfected patients is significantly lower than of HIV-negative tuberculosis patients [3]. The problem of multidrug resistance (MDR) to anti-TB drugs is also an ongoing issue. In patients with a combination of tuberculosis and HIV infection, MDR is detected much more frequently, cure is more difficult to achieve, and at the same time, a full range of new highly effective antituberculosis drugs is available [4–6].

Patients with co-infection of pulmonary tuberculosis and HIV infection have higher rates of drug resistance and therefore increased mortality according to J.W Wilson et al [7].

The main contribution to the determination of the localization, prevalence, and activity of the tuberculosis process is made by methods of radiation diagnostics: radiography, multi-layer spiral computed tomography (MSCT). MSCT method significantly complements traditional X-ray examination when assessing morphological changes in patients with pulmonary tuberculosis, and in the group of persons with tuberculosis and HIV co-infection in the presence of immunosuppression significantly increases the efficiency of X-ray examination [8].

Consequently, detection of characteristics of tuberculous pulmonary process by MSCT among tuberculosis patients, and especially in patients with tuberculosis combined with HIV infection, is important in primary diagnosis of tuberculosis, determination of process prevalence and its dynamics against the background of specific treatment. A detailed study of the radial semiotics of tuberculosis in co-infected patients, including in their dynamics, will help to improve treatment approaches and contribute to the prevention of relapses.

THE AIM OF THE STUDY

To determine the initial characteristics and dynamics of infiltrative tuberculosis according to multi-layer spiral computed tomography in patients with and without HIV infection, with and without multidrug-resistant *Mycobacterium tuberculosis* treated in hospital.

MATERIALS AND METHODS

Inclusion criteria: microbiologically confirmed infiltrative tuberculosis as the most frequent clinical form of tuberculosis; three MSCT studies of the chest organs – on admission, after 2 and 6 months of treatment.

A total of 126 patients aged 19 to 59 years with newly diagnosed infiltrative tuberculosis were examined: 68 (44 males and 24 females) with isolated pulmonary tuberculosis (TB) and 58 (45 males and 13 females) with TB and HIV co-infection (TB/HIV). The mean age of patients in the TB/HIV group was 32.9 ± 0.9 years and in the TB group 35.9 ± 1.1 years. In the TB/HIV group, all patients had stage 4B of HIV infection, with $CD4^+$-lymphocyte counts ranging from 90 to 420 cells/μL.

Among 68 patients in the group with newly diagnosed infiltrative TB without HIV infection, MDR was detected in 23 (33.8 %), and among 58 patients with TB/HIV coinfection, MDR was detected in 44 (75.8 %; $p < 0.01$).

All patients received inpatient treatment in pulmonary tuberculosis departments and the department for tuberculosis patients with HIV infection of the Irkutsk Regional Clinical Tuberculosis Hospital.

All patients were examined with general clinical and biochemical methods of examination. Microbiological examination methods included molecular-genetic (GeneXpert) with determination of rifampicin resistance, luminescence microscopy, cultures performed on dense and liquid nutrient media. All patients underwent chest MSCT before the initiation of treatment, and in 2 and 6 months of treatment. Human immunodeficiency virus RNA and $CD4^+$ lymphocyte count were obtained in HIV co-infected patients.

In order to identify statistically significant differences, MS Excel application package (Microsoft Corp., USA) was used, the mean (M), standard error of the mean (m) were calculated, and the χ^2 method with Yates correction was applied. The specified critical significance level was $p < 0.05$.

The work was carried out in accordance with the principles of the World Medical Association Declaration of Helsinki. Study protocol was approved by the Committee on Ethics of Scientific Research of the Irkutsk State Medical Academy of Postgraduate Education, a branch of the Russian Medical Academy of Continuing Professional Education of the Ministry of Health of the Russian Federation (Protocol No. 10 dated December 24, 2021).

RESULTS AND DISCUSSION

Infiltrative tuberculosis was diagnosed at preventive fluorographic examination in 41 (60.3 %) tuberculosis patients without HIV infection and 25 (43.0 %) with HIV infection ($p > 0.05$).

During clinical examination, 19 (28.0 %) tuberculosis patients and 6 (10.0 %) coinfected patients had no complaints ($\chi^2 = 2.95$; $p < 0.05$). Moderately severe symptoms of intoxication and a small, low-productive cough were statistically significantly more common in the TB group of patients: 34 (50.0 %) versus 6 (10.0 %) patients in the TB/HIV group ($\chi^2 = 13.4$; $p < 0.0005$). A severe intoxication syndrome, fever, cough, and dyspnoea were only observed in 15 (22.0 %) patients with infiltrative tuberculosis and in the vast majority, 46 (79.0 %), of patients with infiltrative tuberculosis combined with HIV infection ($\chi^2 = 24.2$; $p < 0.00001$).

The social profile of the studied patients is shown in detail in Table 1.

Table 1 indicates that drug and alcohol addiction were statistically significantly more common in the TB/HIV co-infected group of patients. No statistically significant difference was observed between the compared groups in the presence of nicotine addiction, whether or not there is official employment, and time spent in detention facilities.

X-ray examinations play an important role in detecting pathological changes in patients with pulmonary tuberculosis. The radiologist's opinion is considered to be the basis for the formation of a clinical diagnosis according to the current clinical classification. Classical radiological characteristics of tuberculosis in co-infected patients are more common in the early stages of HIV infection. Against the background of severe immunodeficiency, radiological symptoms often begin to acquire an atypical character. In this case, MSCT becomes the main method for detection and evaluation of lung changes against the background of tuberculosis infection. The semiotics of infiltrative tuberculosis according to MSCT is presented in Tables 2–4.

The localisation of the tuberculosis process was «classical» in almost 90 % of the patients in both groups, with lesions in the apical (S1), posterior (S2) and upper basal (S6) segments of the lungs. However, a more prevalent tuberculosis process (involvement of three or more lung segments) was statistically significantly more frequently diagnosed in the TB/HIV group – 70.6 % (41/58) versus 35.3 % (24/68) in the TB group ($\chi^2 = 8.47$; $p < 0.05$).

TABLE 1

CHARACTERISTICS OF THE SOCIAL PROFILE OF PATIENTS IN THE TB AND TB/HIV STUDY GROUPS

Social characteristics	TB group ($n = 68$)		TB/HIV group ($n = 58$)		p
	abs.	%	abs.	%	
Alcohol addiction	19	27.8	30	51.7	$p < 0.05$*; $\chi^2 = 4.21$
Drug addiction	3	4.4	22	37.9	$p < 0.001$*; $\chi^2 = 10.7$
Smoking (more than 10 cigarette per day)	15	22.0	23	40.0	$p > 0.05$
Lack of legal job	43	63.2	42	72.4	$p > 0.05$
Stay in corrective-labour institutions	9	13.2	9	15.5	$p > 0.05$

Note. * – hereinafter differences are statistically significant.

TABLE 2

LOCALISATION AND PREVALENCE OF INFILTRATIVE PULMONARY TUBERCULOSIS ACCORDING TO MSCT IN TB AND TB/HIV GROUPS

Indicators		TB group ($n = 68$)		TB/HIV group ($n = 58$)		p
		abs.	%	abs.	%	
Localization of the pathological process	Typical (S1, S2, S6)	59	86.8	50	86.2	$p > 0.05$
	Atypical (segments of the lower lobe)	9	13.2	8	13.8	$p > 0.05$
The prevalence of the pathological process	1 segment	9	13.2	5	8.6	$p > 0.05$
	2 segments	35	51.4	12	20.7	$p < 0.001$*
	3 segments	20	29.4	20	34.5	$p > 0.05$
	4 segments	4	5.9	14	24.1	$p < 0.005$*
	5 segments	0	0	7	12.0	$p < 0.005$*

TABLE 3

INTRATHORACIC LYMPH NODE ENLARGEMENT BY MSCT IN TB AND TB/HIV GROUPS

The number of groups of enlarged lymph nodes of the mediastinum	TB group (n = 68)		TB/HIV group (n = 58)		p
	abs.	%	abs.	%	
1 group	6	31.5	7	17.9	$p > 0.05$
2 groups	11	57.8	23	58.9	$p > 0.05$
3 or more groups	2	10.5	9	23.0	$p > 0.05$
Total	19	27.9	39	67.2	$p < 0.0001$*

TABLE 4

RADIOLOGICAL SEMIOTICS OF INFILTRATIVE TUBERCULOSIS ACCORDING TO MSCT IN TB AND TB/HIV GROUPS

Indicators	TB group (n = 68)		TB/HIV group (n = 58)		p
	abs.	%	abs.	%	
Thickening of pulmonary pleurae	8	11.7	18	31.0	$p < 0.01$*; $\chi^2 = 7.097$
Pleural fluid	6	8.8	17	29.3	$p < 0.01$*; $\chi^2 = 8.804$
Decay cavity	31	45.6	10	17.2	$p < 0.001$*; $\chi^2 = 5.8$

Patients with a TB/HIV combination have a high incidence of intrathoracic lymphadenopathies with escalating immunodeficiency. The lymph nodes of the following groups are most commonly enlarged: paratracheal, tracheobronchial, bifurcation and bronchopulmonary. Multi-layer spiral computed tomography is a reliable method for detecting the condition of mediastinal lymph nodes. MSCT method enables not only to detect lymph node enlargement (short diameter – more than 10 mm) and their number, but also to assess the structure of lymph nodes, changes in their contours, the perinodular and mediastinal fibre condition. Generally, lymph nodes of mediastinum and lung roots have spindle or oval shape, therefore, it is appropriate to measure the short and long diameters during MSCT, which will coincide only in case of rounded shape of the lymph node.

In our study, enlargement of intrathoracic lymph nodes (ITLNs) was statistically significantly more common in the group of HIV positive patients with infiltrative tuberculosis. No statistically significant difference was observed in the number of affected groups of the ITLNs in patients with infiltrative pulmonary tuberculosis depending on the HIV infection status.

Pathological changes of the pleura in tuberculous lung disease occur in 30 to 50 % of cases as indicated in the literature. Pleural lesions were detected statistically significantly more often in the presence of immunodeficiency in our study. The existence of pleural fluid was also more common in the group of patients with tuberculosis and HIV co-infection.

Destructive processes of lung tissue in HIV-positive patients from the TB/HIV group were diagnosed statistically significantly less frequently than in the group of patients with isolated tuberculosis. The outcome to fibrotic cavernous tuberculosis was also diagnosed statistically significantly more often in the TB group, in 29.4 % (20/68) versus 10.3 % (6/58) in the TB/HIV group ($\chi^2 = 6.949$; $p < 0.008$).

The X-ray dynamics of pathological tuberculosis process in the lungs was assessed according to MSCT after 2 and 6 months of treatment. The data is presented in tables 5 and 6.

According to the data of multi-layer spiral computed tomography, as evident from Tables 5 and 6, against the background of the ongoing treatment, positive dynamics after 2 and 6 months of treatment was registered statistically significantly more often in patients with isolated tuberculosis. After 2 months, almost 60.0 % of patients in both groups had no dynamics on the background of the conducted treatment. After six months, no significant change was observed in every second patient in the TB/HIV group and in 36.7 % (25/68) of the TB group.

Negative dynamics after 2 months was registered in every third patient in the group with TB and HIV co-infection. The negative results obtained in the TB/HIV group require further, more detailed study of this issue.

TABLE 5

DYNAMICS OF PULMONARY TUBERCULOSIS PROCESS AFTER 2 MONTHS OF TREATMENT ACCORDING TO MSCT DATA IN TB AND TB/HIV GROUPS

Dynamics according to MSCT	TB group ($n = 68$)		TB/HIV group ($n = 58$)		p
	abs.	%	abs.	%	
None	39	57.3	35	60.3	$p > 0.05$
Positive	23	33.8	6	10.3	$p < 0.005$*; $\chi^2 = 4.8$
Negative	6	8.8	17	29.3	$p < 0.005$*; $\chi^2 = 6.3$

TABLE 6

DYNAMICS OF PULMONARY TUBERCULOSIS PROCESS AFTER 6 MONTHS OF TREATMENT ACCORDING TO MSCT DATA IN TB AND TB/HIV GROUPS

Dynamics according to MSCT	TB group ($n = 68$)		TB/HIV group ($n = 58$)		p
	abs.	%	abs.	%	
None	25	36.7	29	50.0	$p > 0.05$
Positive	39	57.3	19	32.7	$p < 0.01$*; $\chi^2 = 4.1$
Negative	4	5.8	10	17.2	$p < 0.05$*; $\chi^2 = 3.8$

TABLE 7

RADIOLOGICAL SEMIOTICS OF INFILTRATIVE TUBERCULOSIS ACCORDING TO MSCT IN TB AND TB/HIV GROUPS IN MULTIDRUG-RESISTANT PATIENTS

Indicator	TB + MDR group ($n = 23$)		TB/HIV + MDR group ($n = 44$)		p
	abs.	%	abs.	%	
Atypical localization of the pathological process (lower lobe)	4	17.4	8	18.1	$p > 0.05$
A common process (lesion of 3 or more lung segments)	14	60.8	38	86.3	$p < 0.05$*; $\chi^2 = 4.278$
Intracoracic lymphadenopathy	9	39.1	32	72.7	$p < 0.01$*; $\chi^2 = 7.180$
Thickening of pulmonary pleurae	4	17.3	14	31.8	$p > 0.05$
Pleural fluid	3	13.0	13	29.5	$p > 0.05$
Decay cavity	10	43.4	8	18.1	$p < 0.05$*; $\chi^2 = 3.716$
Outcome in fibrocavitary tuberculosis	12	52.1	5	11.3	$p < 0.005$*; $\chi^2 = 11.218$

Drug-sensitive tuberculosis patients received inpatient treatment with chemotherapy regimen I or III if their TB was confirmed to have DNA with preserved sensitivity to rifampicin before the results of the drug sensitivity test. MDR-TB patients were treated with IV empirical (according to rifampicin-resistant molecular genetic methods) or test (according to culture results on liquid or dense nutrient media) chemotherapy regimens.

Radiation semiotics of drug-resistant patients with isolated infiltrative tuberculosis and those with co-infection of tuberculosis and HIV infection are presented in Table 7.

According to MSCT data, widespread lung damage (3 segments or more) and intrathoracic lymphoadenopathy were statistically significantly more often diagnosed in patients with MDR in the TB/HIV group. As opposed to this, destructive changes and outcome in fibrotic cavernous tuberculosis were statistically significantly more often diagnosed in multidrug-resistant patients in the group with isolated pulmonary tuberculosis. No statistically significant difference was observed in the localisation of the tuberculosis process and the presence of pathological changes in the pleura in drug-resistant patients with isolated infiltrative tuberculosis and in those co-infected with tuberculosis and HIV infection.

CONCLUSION

The data obtained indicate the need for further improvement of work on the early detection of tuberculosis in HIV-infected patients, the use of chest X-ray examinations and immunodiagnostics [7]. Radiological diagnostics in immunodeficient patients should be optimised, with a priority being assigned to thoracic MSCT. Particular attention should be provided to patients from risk groups (drug and alcohol addiction) for tuberculosis towards early detection and timely diagnosis. MSCT methods should be performed to assess the dynamics of the tuberculosis process against the background of treatment, as it is not possible to track the dynamics of specific changes in the lungs of immunodeficient individuals based on radiological examination, which may lead to unwarranted termination of treatment and early relapses of the disease.

Conflict of interest

The authors declare no conflict of interest in relation to this article.

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