Возможности хирургического лечения у больных при сочетанной патологии ВИЧ/туберкулез

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ДЛЯ КОРРЕСПОНДЕНЦИИ

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Цель – определить эффективность хирургического лечения у больных с коморбидной патологией ВИЧ/туберкулез.

Материал и методы. Доля операций у больных ВИЧ-инфекцией составила 4,4% (25 операций) из 572 радикальных резекции легких, выполненных по поводу туберкулеза легких. Для оценки эффективности хирургических методов было сформировано 2 группы сравнения: 1-я группа – 23 прооперированных пациента, 2-я группа – 25 пациентов без хирургического лечения.

Результаты. При определении вида и объема оперативных вмешательств у больных ВИЧ-инфекцией предпочтение отдавалось малотравматичным операциям, хирургическое лечение назначалось планово, с участием в лечении врача-инфекциониста, после проведения курса антиретровирусной терапии в предоперационном периоде и достижения количества CD4⁺-Т-лимфоцитов >200 кл/мкл. Проведенные операции были эффективными в 100% случаев, послеоперационные осложнения и летальность отсутствовали. В резецированном участке легкого у всех обнаружены микобактерии туберкулеза, почти половина – множественная (МЛУ) и широкая лекарственная устойчивость (ШЛУ). Послеоперационная летальность отсутствовала. В 1-й группе спустя 2 года после операции сняты с учета почти 70%, в группе без операции только 4% ($p=0,00001$).

Заключение. При сравнительном анализе выявлено, что применение хирургического пособия сокращает сроки лечения и повышает его эффективность.

Финансирование. Исследование не имело спонсорской поддержки.

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Possibilities of surgical treatment of patients coinfecting with HIV/tuberculosis

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Aim – to determine the effectiveness of surgical treatment in patients with HIV/tuberculosis comorbid pathology.

Material and methods. The percentage of operations in patients with HIV-infection was 4.4% (25 operations) out of 572 radical lung resections performed for pulmonary tuberculosis. To assess the effectiveness of the surgical methods, 2 comparison groups were formed: the 1st – a group of 23 operated patients, the 2nd – a group of 25 patients without surgical treatment.

Results. When determining the type and volume of surgical intervention in patients with HIV-infection, low-traumatic operations were preferable. Surgical treatment was prescribed as planned, with the participation of an infectious disease doctor in treatment, after a course of antiretroviral therapy had been carried out in the preoperative period and a CD4⁺-T-lymphocyte count of >200 cells/ μ L had been achieved. The operations performed were 100% effective, there were no postoperative complications and mortality. MBT was found in all situations in the resected area of the lung. Half of the identified mycobacteria was multidrug and broadly resistant. There was no postoperative mortality. In the 1st group, 2 years after surgery, almost 70% were removed from the register. In the group without surgery, 2 years after therapy, only 4% were removed from the register ($p=0.00001$).

Conclusion. A comparative analysis revealed that surgical treatment reduces duration of treatment and increases effectiveness.

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HIV-infection is a factor that has a negative impact on the epidemiology of tuberculosis. According to the World Health Organization (WHO) and other sources since 2006 and at present, the number of cases of tuberculosis with concurrent HIV-infection has increased by 2.9 times [1, 2]. This is due to the fact that the possibility of tuberculosis contraction in HIV-positive individuals is 100 times higher than in HIV-negative people [3, 4]. Increasing number of comorbid TB diseases/HIV is associated with high mortality [5–11]. The disease affects mainly people of young and working-age [5, 10, 11]. The search for optimal methods of treatment is an actual problem [12, 13]. Surgical treatment is one of the methods in complex treatment that allows increasing the effectiveness of treatment [14–17]. The surgical methods of treatment effectiveness for patients with tuberculosis combined with HIV-infection is still to be studied [18, 19].

Material and methods

In 2016–2017, 572 radical lung resections were performed for pulmonary tuberculosis, while the proportion of operations in patients with HIV-infection was 4.4% (25 cases). There was held an analysis of surgeries in patients with pulmonary tuberculosis combined with HIV-infection. To assess the effectiveness of the inclusion of surgical methods in treatment, two comparison groups of patients were formed: 1 – group of 23 patients who were operated, 2 – group of 25 patients without surgical treatment. Efficacy was evaluated by the criterion of deregistration after recovery.

Results

The gender and age characteristics of patients, social aspects and the method of detecting pulmonary tuberculosis in the comparison groups were studied. In the 1st group, there were 11 men (47.8%), 12 women (52.2%). In the 2nd group, there were 12 (52.2%) men and 11 (42%) women, respectively ($\chi^2=0.08$; $p=0.7817$). The average age of the 1st group was 32.6 ± 1.52 [95%; confidence interval (CI) 25.48–35.79] and the 2nd group was 33.16 ± 1.36 [95%; CI 30.34; 35.98] ($U=280.5$; $p=0.893$). In terms of social characteristics and the methods of detecting pulmonary tuberculosis, the comparison groups did not have significant differences. In both groups, most patients were unemployed, 15 (65.2%) patients in 1st group, and 15 (60.0%) patients in 2nd group. A history of drug abuse was observed in 8 (34.8%) patients in the 1st group and in 10 (40.0%) patients in the 2nd group. 5 (21.7%) patients in 1st group and 5 (20.0%) patients in 2nd group stayed in a correctional labor institution. The groups are comparable for comparative analysis.

In the 1st group, tuberculosis was detected using annual large picture frame photoroentgenography 9 (39.1%), during examination at the AIDS center 6 (26.1%), during complaints in the general medical network 5 (21.7%), during examination at a tuberculosis dispensary as contact 3 (13.0%).

In the 2nd group, tuberculosis was detected using annual large picture frame photoroentgenography 8 (32.0%), during examination at the AIDS center 7 (28.0%), during complaints in the general medical network 6 (24.0%), during examination at a tuberculosis dispensary as contact 4 (16.0%).

Table 1. Clinical forms of tuberculosis in patients of the studied groups

Clinical forms of tuberculosis	1 st group (n=23) ABS (%)	2 nd group (n=25) ABS (%)	Pirson criterion χ^2 (p)	Pirson criterion with Yates's correction χ^2 (p)
Tuberculoma pulmonum	19 (82.6)	19 (76.0)	0.32 (0.5733)	0.04 (0.8356)
Cavernous pulmonary tuberculosis	1 (4.4)	2 (8.0)	0.27 (0.6015)	0.01 (0.9405)
Fibrous-cavernous pulmonary tuberculosis	3 (13)	4 (16.0)	0.08 (0.7719)	0.01 (0.9050)
Destruction of lung tissue	16 (69.6)	16 (64.0)	0.17 (0.6828)	0.01 (0.9186)
Bacterioexcretion, discovered by:				
Microscopy	11 (47.8)	12 (48.0)	0.0001 (0.9904)	0.08 (0.7817)
Molecular-genetic methods	8 (34.8)	8 (32.0)	0.04 (0.8381)	0.01 (0.9186)
Inoculation of medium	4 (17.4)	6 (24.0)	0.32 (0.5733)	0.04 (0.8356)
DST (Multidrug resistance and extensive drug resistance*)	6 (26.1)	7 (28.0)	0.02 (0.8816)	0.03 (0.8602)
Total number of patients	11 (47.8)	9 (36.0)	0.69 (0.4064)	0.29 (0.5911)
	23 (100)	25 (100)		

Note. ABS – absolute; DST – drug susceptibility testing. * – including DST analyzes obtained from surgical material.

The main method for detecting tuberculosis in both groups was annual large picture frame photo-roentgenography.

In most cases, 11 (47.2%) patients in 1st group and 14 (56.0%) patients in 2nd group, HIV-infection was diagnosed before pulmonary tuberculosis. The index did not have significant differences between groups, but in the first group there were more patients and amounted to 56% $\chi^2=0.32$ ($p=0.57$).

HIV-infection was detected during examination for tuberculosis in 8 (34.8%) patients from the 1st group and 7 (28.0%) patients in the 2nd group, all these patients were tested for HIV for the first time $\chi^2=0.26$ ($p=0.6125$). Much less often patients were already registered with a phthisiatrician with a diagnosis of pulmonary tuberculosis, in the 1st group there were 4 (17.4%) people and in the 2nd group – 4 (16.0%) people $\chi^2=0.02$ ($p=0.8972$).

CD4-lymphocyte count was determined in all patients at the time of admission. In the 1st group 459.09 ± 46.41 [95% CI 362.84; 555.33], in the 2nd – 429.64 ± 47.07 [95% CI 332.49; 526.79] ($p=0.476$).

14 (60.9%) patients received antiretroviral therapy before surgery. Before the operation, the level of CD4⁺-T-lymphocytes averaged 459.09 ± 46.41 cells/ml.

The characteristics of the clinical forms of tuberculosis in the groups had no significant differences.

According to the forms of the tuberculous process, the patients were diagnosed with: tuberculoma in the 1st group – 19 (82.6%), in the 2nd group – 19 (76.0%), fibrous-cavernous pulmonary tuberculosis 3 (13%) and 4 (16.0), $\chi^2=0.08$ ($p=0.7719$), cavernous tuberculosis 1 (4.4%) and 2 (8.0%) $\chi^2=0.27$ ($p=0.6015$) (see Table 1).

Pulmonary tuberculoma was detected to be the main form $\chi^2=0.32$ ($p=0.5733$). According to the characteristics of the prevalence of the tuberculous process, decay cavities in the operated lung among all patients were $\chi^2=0.17$ ($p=0.6828$) equally in the majority of those observed in the groups. Fibrous-cavernous pulmonary tuberculosis was limited in volume of the lesion within one lobe of the lung. This allowed them to apply surgical treatment, there were a minimum number of such patients.

After the operation, a macroscopic examination of the surgical material was carried out; the presence of a cavity of destruction in tuberculoma (or tuberculomas) was observed in 12 of 19 cases (63.1%). At the time of registration, mycobacterium tuberculosis (MBT+) was detected in 11 (47.8%) patients in the 1st group and 12 (48.0%) in the 2nd group, $\chi^2=0.0001$ ($p=0.9904$). At the same time, in all these cases, mycobacteria in sputum were detected by bacterioscopy, molecular-genetic methods (GeneXpert MTB/RIF), on liquid nutrient media with

Table 2. Concomitant diseases and addictions in patients in comparison groups

Concomitant diseases	1 st group (n=23) ABS (%)	2 nd group (n=25) ABS (%)	Pirson criterion χ^2 (p)	Pirson criterion with Yates's correction χ^2 (p)
Chronic bronchitis	2 (8.7)	3 (12.0)	0.14 (0.7081)	0.01 (0.9215)
Diabetes mellitus	0 (0)	0 (0)	–	–
Chronic viral hepatitis type B	0 (0)	1 (4.0)	0.94 (0.3324)	0.0001 (0.9664)
Chronic viral hepatitis type C	15 (65.2)	15 (60.0)	0.14 (0.7091)	0.01 (0.9405)
Alcoholism	6 (26.1)	6 (24.0)	0.03 (0.8675)	0.03 (0.8675)
Drug addiction	5 (21.7)	7 (28.0)	0.25 (0.6168)	0.03 (0.8675)
Total number of patients	23 (100)	25 (100)	–	–

automatic registration BACTEC MGIT and inoculation on a standard Lowenstein-Jensen medium. Among patients with a positive MBT test, a drug susceptibility test (DST) of mycobacterium tuberculosis (MBT) was performed. Multidrug resistance or extensive drug resistance was detected in 11 (47.8%) patients of the 1st group and 9 (36.0%) of the 2nd group $\chi^2=0.69$ ($p=0.4064$).

There were no significant differences in the groups in terms of clinical forms of pulmonary tuberculosis, bacterial excretion and results of drug sensitivity.

All patients before the operation received specific anti-tuberculosis therapy according to standard antibacterial chemotherapy regimens. The decision to prescribe surgical treatment was made after the completion of the intensive phase of chemotherapy; patients with multidrug resistance and extensive drug resistance took specific antibacterial drugs for at least 6 months before surgery.

When analyzing opportunistic pathology (see Table 2), one of the most frequently diagnosed diseases was chronic viral hepatitis type C ($n=15$; 65.2% in the 1st group and $n=15$; 60.0% in the 2nd group) $\chi^2=0.14$ ($p=0.7091$). Chronic viral hepatitis type B was not detected in patients of the 1st group, in the 2nd group it was detected in 1 (4.0%) patient $\chi^2=0.94$ ($p=0.3324$). Chronic bronchitis was in 2 (8.7%) patients in the 1st group and in 3 (12.0%) patients in the 2nd group $\chi^2=0.14$ ($p=0.7081$). Alcoholism in the 1st group was observed in 6 (26.1%) patients, in the 2nd group it was also observed in 6 (24.0%) patients $\chi^2=0.03$ ($p=0.8675$). There were 5 (21.7%) active drug addicts in the 1st group, in the 2nd – 7 (28.0%). $\chi^2=0.25$ ($p=0.6168$). There were no differences in concomitant and opportunistic diseases in the groups, all diseases are associated with social factors, which in most cases determine the presence of HIV-infection.

The structure of the performed radical operations in the first group of patients is shown in Table 3.

Table 3. Types of surgical interventions in operated patients ($n=23$)

Types of surgical interventions	ABS (%)
Segmental atypical lung resections	15 (65.2)
Polysegmental resections	5 (21.7)
Bilateral segmental atypical lung resections	2 (8.7)
Lobectomy	1 (4.3)
Total	23 (100)

Note. ABS – absolute.

Patients underwent the following operations: lung resection (within 1–2 segments) – 15 (65.2%) people; polysegmental lung resection – 5 (21.7%) people; lobectomy – 1 (4.3%) person; bilateral resection (within 1–2 segments on each side) – 2 (8.7%) patients. A total of 23 operations were performed. In patients with a diagnosis of fibrocavernous tuberculosis (3 people), the following operations were performed: 1 lobectomy, 1 polysegmental resection, 1 lung resection within 1–2 segments. A patient with cavernous pulmonary tuberculosis (1 person) underwent polysegmental resection. Major surgeries (combined resection of the lung, bilobektomiya, pneumonectomy) in this group of patients were not performed. Intraoperative and postoperative complications were absent, all patients were discharged in satisfactory condition. Postoperative wounds healed by primary intention, there was no slow expansion of the lung and residual cavities. The operations were effective in all patients. The average hospital stay for HIV-infected patients was 52 ± 1.1 bed days and did not have statistically significant differences from the indicator among all operated patients. 5 (21.7%) patients who underwent a long stage of preoperative chemotherapy stayed in hospital for more than 70 days. Postoperative complications among all operated patients in 2016–2017 were <1%. Postoperative mortality in 2016–2017 was absent.

After 2 years (≈ 24 months) of observation, an analysis of the effectiveness of treatment of patients in the comparison groups was performed (see Table 4).

Table 4. Treatment results after 2 years (≈ 24 months)

Treatment result	1 st group ($n=23$) ABS (%)	2 nd group ($n=25$) ABS (%)	Pirson criterion χ^2 (p)	Pirson criterion with Yates's correction χ^2 (p)
Removed from dispensary registration with recovery	16 (69.6)	1 (4.0)	22.51 (0.00001)	19.74 (0.00001)
Transferred to the third group of dispensary registration and continues to be registered in the dispensary	4 (17.4)	9 (36.0)	0.10 (0.7471)	0.0001 (0.9697)
Reactivation or progression of the tuberculous process	1 (4.3)	3 (12.0)	0.92 (0.3379)	0.19 (0.6631)
Removed from the dispensary registration for other reasons	1 (4.3)	2 (8.0)	0.27 (0.6015)	0.01 (0.9405)
Death of a patient from HIV-infection	1 (4.3)	3 (12.0)	0.92 (0.3379)	0.19 (0.6631)
Total number of patients	23 (100)	25 (100)	–	–

In the 1st group, 16 (69.6%) patients were removed from the dispensary registration with recovery, $\chi^2=22.51$ ($p=0.00001$), which is significantly more often compared with non-operated patients. 4 (17.4%) patients were transferred to the 3rd group of dispensary registration and continue to be registered, reactivation of the tuberculous process in the postoperative period was observed in 1 (4.3%) patient, death as a result of progression of HIV-infection was also observed in 1 (4.3%) patient.

The results of treatment of patients in the 2nd group differed significantly: 1 (4.0%) patient was removed from the dispensary registration with recovery, 9 (36.0%) patients were transferred to the 3rd group of dispensary registration and continue to be registered, progression of the tuberculous process was observed in 3 (12.0%) patients, death due to progression of HIV-infection was observed in 3 (12.0%) patients. 7 (28.0%) patients continue to be in the former dispensary registration group, in the 1st group there were no such patients $\chi^2=7.54$ ($p=0.0060$).

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Conclusion

Surgical treatment was prescribed as planned, with the participation of an infectious disease doctor in treatment, after a course of antiretroviral therapy was carried out in the preoperative period and a CD4⁺-T- lymphocyte count of >200 cells/ μ L was achieved. When determining the type and volume of surgical intervention in patients with HIV-infection, preference was given to low-traumatic operations. The operations performed were 100% effective, there were no postoperative complications and mortality.

MBT was found in all situations in the resected area of the lung. Half of the identified mycobacteria had multidrug and extensive drug resistance. There was no postoperative mortality. CD4-lymphocyte counts in all operated patients were >400 cells/ μ L. All patients received antiretroviral therapy before surgery and completed the main course of chemotherapy.

During treatment of patients with comorbidity of HIV-infection and tuberculosis, the use of surgical methods of treatment has shown its effectiveness.

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