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RENTHENOLOGICAL CHARACTERISTICS OF HIV-INFECTION COMBINED WITH TUBERCULOSIS. MAIN CAUSES OF MORTALITY

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The purpose of the work is to analyze the X-ray and some laboratory changes of the groups of patients with HIV-infection combined with tuberculosis (TB) and TB mono-infection, as well as to determine the main causes of the mortality of such patients.

Patients and methods. We examined 351 patients, in particular 217 HIV/TB-related infections and 134 cases of tuberculosis only. The HIV/TB group was divided into 3 subgroups depending on the time of TB attachment to HIV infection.

Results. The most striking clinical symptomatology is typical for HIV/TB infected patients, compared to patients with TB alone. Persons with associated HIV/TB infection also differed from patients with TB only with a lack of changes in the X-ray of the thoracic cavity.

Drug resistance to one anti-TB drug is significantly more commonly found in the group with the associated infection. The same pattern is noted for subgroup 1 and 3 of HIV/TB.

The percentage of mortality from infiltrative TB for all those who died from the primary TB for associated HIV/TB infection is significantly higher than for patients with TB alone. With focal TB, caseous pneumonia, disseminated, generalized and extrapulmonary TB there is a tendency towards higher mortality in case of concomitant HIV infection. Probably this is due to the prescription of TB and a fairly large affection of the pulmonary tissue. In general, patients with HIV/TB died significantly more often than patients with TB mono-infection.

Conclusions. Individuals with associated HIV/TB infection differed from patients with TB only with brighter clinical symptoms, a significantly greater absence of changes in the X-ray of the chest cavity, drug resistance to one anti-TB drug and significantly higher mortality.

Key words: HIV infection; tuberculosis; X-ray characteristics; mortality.

HIV infection is a powerful factor contributing to the development of an active form of tuberculosis in the carriers of latent infection and increases the likelihood of

the development of tuberculosis relapses [1, 2]. The timeliness of the detection of tuberculosis as a secondary disease in the late stages of HIV infection is of particular importance, since in the conditions of immunodeficiency, delaying with the onset of treatment quickly leads to the generalization of the tuberculous process and the death of the patient, especially in the late stages of HIV infection, often there is the abacus of sputum and atypism of X-ray picture [3].

The purpose of the work – to analyze the X-ray and some laboratory changes of the groups of patients with HIV-infection combined with TB (TB) and TB mono-infection, as well as to determine the main causes of the mortality of such patients.

Patients and methods

Under observation there were 351 persons – 280 (79.8 %) men and 71 (20.2 %) women aged 23 to 60 years. The average age was (38.8 ± 1.2) years.

All patients were subjected to a comprehensive laboratory examination and divided into such groups.

I. Non-HIV-infected (immunocompetent) people with active first-time TB – 76 patients (TB group).

II. Uninfected HIV (immunocompetent) persons with chronic tuberculosis – 58 patients.

III. HIV-infected with active for the first time detected tuberculosis – 155 patients (HIV/TB group). Within the HIV/TB group, 3 subgroups were identified depending on the time of TB attachment to HIV infection:

Subgroup 1 – HIV-infected, in which TB was detected at different stages of HIV infection (primary illness) – 72 patients;

Subgroup 2 – persons in whom for several years prior to the registered HIV infection and the time of hypothetical infection (according to the epidemiological history) TB was diagnosed, that is, the primary disease was TB – 26 people;

Subgroup 3 – HIV-infected, in which the disease was recorded at about one time and it was impossible to find out which ailment was the primary one – 57 people.

IV. HIV-infected with chronic tuberculosis – 62 patients.

Comprehensive examination included the collection of complaints, anamnesis of life and disease, an epidemiological history, objective examination, X-ray methods of investigation, bacterial isolation by simple microscopy and through cultures.

Statistical processing of the obtained results of research was carried out with the help of the software complex Windows, Word and Excel; STATISTICA 6.0 using the method of variation statistics with validity determination using Student's criterion, and with the number of observations less than 20, the non-parametric Wilcoxon method for independent aggregates was used, or the dispersion analysis of Kraskale-Wallis [4]. U-Mann-Whitney Criteria was used to compare two independent groups. Differences were considered statistically significant at $P < 0.05$. For the correlation analysis, the Spirman rank method was used [7].

Results and Discussion

We have analyzed X-ray data in patients with pulmonary TB. It was found that there was no change in the combination of HIV and TB in chest X-ray of chest cavity (13.4 ± 3.2 %) than in patients with TB alone (0.0 ± 0.0 %) ($P < 0.05$). No patient was diagnosed with TB (patients of subgroup 2) in HIV-infected patients, who had been diagnosed with TB for several years prior to HIV, did not register changes in the X-ray image. In subgroups 1 (primary HIV) and 3 of patients in whom the two diseases were first detected at the same time, there were no X-ray manifestations of the disease in (16.7 ± 5.1) and (13.3 ± 5.1) % respectively (in both cases $P < 0.01$).

Common lesions of lungs in three or more particles are almost identical in patients with TB in combination with HIV infection – (55.4 ± 4.7) % and without it – (56.9 ± 3.5) %. There were also no significant differences between the groups of HIV/TB patients.

Destructive changes in the lungs are more commonly detected in immunocompetent patients with TB – (43.1 ± 3.5) % compared to HIV-infected patients – (31.3 ± 4.4) % ($P < 0.05$). This difference in the rates is obviously due to the heterogeneity of the population of HIV/TB patients: yes, the frequency of destruction was less in subgroup 1 – (27.8 ± 6.1) % compared with the group of TB monoinfection ($P < 0.05$).

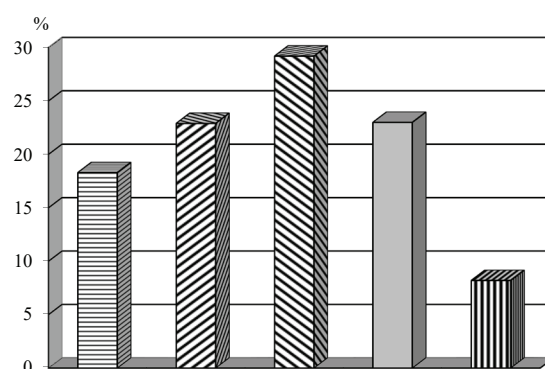
Results of the bacterial isolation study were analyzed. It was found that the number of positive results was not significantly different between HIV/TB-associated groups and TB monoinfection.

When comparing drug resistance to one anti-TB drug, significant differences were observed between the HIV/TB group – (15.5 ± 3.9) %, subgroups 1 and 3, where the scores were higher (17.9 ± 6.1) and (17.1 ± 6.4) % respectively, compared to patients with TB alone (4.5 ± 2.0) % ($P < 0.05$). There were no significant differences

in the frequency of multidrug resistance and multivariate drug resistance.

The data we received differs from the results of other studies. So, Dhungana G.P. (2015), as well as Gordin F.M. and Matts J.P. (2016) showed that there is no difference between the prevalence of drug resistance of mycobacterium tuberculosis to one or more drugs in HIV-positive and HIV-negative patients [5]. The work of other researchers concerned the differences in drug resistance within a group of HIV-infected patients. Yes, Panteleev A.M. and co-authors (2007) showed that in 62.9 % of HIV-infected patients, polyresistance was observed, mono-resistance was observed only in 7.6 % of cases. Indigenous researchers have shown that the effectiveness of treatment of individualized antimycobacterial regimens (AMTCs) is inadequate, even among patients with multidrug-resistant TB: «effective treatment» was achieved in 64.0-41.8 % of patients, respectively, which does not reach the WHO target (85 %). Such results indicate the need to improve anti-mycobacterial therapy due to its reduction and addition to the existing regime of another bactericidal anti-TB drug [6].

According to our study, the mortality among the first-ever detected patients with TB monoinfection and combined HIV/TB infection significantly differed (8.2 ± 2.4) and (23.0 ± 2.9) % respectively ($P < 0.001$), which is also reflected in the latest epidemiological information bulletin «HIV-infection in Ukraine». In HIV/TB subgroups 1, 2 and 3, the mortality rate was significantly higher (18.3 ± 4.3), (22.9 ± 5.0), and (29.2 ± 5.6) %, respectively, compared with patients only with TB ($P < 0.05-0.001$, Fig. 1).



HIV/TB				TB-mono-infection, n=134
1 subgroup, n=82	2 subgroup, n=70	3 subgroup, n=65	In general, n=217	
18,3±4,3 ⁵	22,9±5,0 ⁵	29,2±5,6 ⁵	23,0±2,9 ⁵	8,2±2,4 ¹⁻⁴

Fig. 1. Mortality in the studied groups of patients. Note. The number in degree indicates the subgroup with which there is a significant difference ($P < 0.05-0.001$).

The causes of death of HIV/TB patients for the forms of TB were analyzed (Table 1). For infiltrative TB, the percentage of mortality was statistically significantly higher in the HIV/TB group and in subgroups 2 and 3 than in patients with TB alone ($P < 0.01$). There were no deaths from focal TB, caseous pneumonia, generalized and extrapulmonary TB in case of TB mono-infection. Concomitant

HIV infection in all of these forms of TB resulted in isolated cases of death of patients: 3 cases of caseous pneumonia, 2 with generalized and 2 with extra-pulmonary TB. The trend towards higher mortality in HIV infection is noticeable, but due to the limited number of observations, it can not be established that the difference between the groups being compared is significant.

Table 1

Causes of death of patients depending on the form of tuberculosis

The form of TB	HIV/TB								TB-mono-infection	
	1 subgroup		2 subgroup		3 subgroup		In general		abs. number	M %± m %
	abs. number	M %± m %	abs. number	M %± m %	abs. number	M %± m %	abs. number	M %± m %		
Focal TB	1 (n=9)	11,1± 10,5	0 (n=11)	0,0± 0,0	0 (n=8)	0,0± 0,0	1 (n=28)	3,6± 3,5	0 (n=17)	0,0± 0,0
Infiltrative TB	8 (n=37)	21,6± 6,8	10 (n=31)	32,3± 8,45	11 (n=35)	31,4± 7,85	29 (n=103)	28,2± 4,45	5 (n=48)	10,4± 4,42-4
Caseous pneumonia	1 (n=6)	16,7± 15,2	1 (n=3)	33,3± 27,2	1 (n=7)	14,3± 13,2	3 (n=16)	18,8± 9,8	0 (n=1)	0,0± 0,0
FCT	0 (n=1)	0,0± 0,0	1 (n=14)	7,1± 6,9	0 (n=1)	0,0± 0,0	1 (n=16)	6,3± 6,1	1 (n=3)	33,3± 27,2
Disseminated TB	6 (n=18)	33,3± 11,1	0 (n=5)	0,0± 0,0	2 (n=6)	33,3± 19,2	8 (n=29)	27,6± 8,3	1 (n=4)	25,0± 21,7
Generalized TB	0 (n=5)	0,0± 0,0	1 (n=2)		1 (n=1)		2 (n=8)	25,0± 15,3	0 (n=1)	0,0± 0,0
Non-pulmonary TB	1 (n=6)	16,7± 15,2	0 (n=3)	0,0± 0,0	1 (n=7)	14,3± 13,2	2 (n=16)	12,5± 8,3	0 (n=52)	0,0± 0,0
In general	17 (n=82)	20,7± 4,55	13 (n=70)	18,6± 4,75	16 (n=65)	24,6± 5,35	46 (n=217)	21,2± 2,85	7 (n=134)	5,2± 1,91-4

Note. The number in degree indicates the subgroup with which there is a significant difference ($P < 0.05-0.001$).

The same argument applies to patients with other forms of TB, although the tendency towards higher mortality of patients with FCT without concomitant HIV infection draws attention. Probably this is due to the prescription of TB and a fairly large affection of the pulmonary tissue.

In general, patients with HIV/TB dying significantly more often than those with TB mono-infection – (21.2±2.8) vs. (5.2±1.9) % ($P < 0.001$). The same pattern applies to all HIV/TB subgroups, as compared to TB patients: (20.7±4.5) % in those who have been diagnosed with TB in the context of primary HIV infection (subgroup 1) (18,6±4.7) % of patients who had HIV infection (subgroup 2) and

(24.6±5.3) % of HIV-infected patients in whom primary illnesses were reported to be approximately at one time (subgroup 3) ($P < 0.001$).

Conclusions

1. In a group with a combined HIV/TB infection, drug resistance to one of the anti-TB drugs was noted.
2. Persons with associated HIV/TB infection differed from patients with TB only with brighter clinical symptoms, significantly fewer changes in the X-ray of the chest cavity and significantly higher mortality.
3. The group of patients with combined HIV/TB infection was markedly higher in fatality.

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РЕНТГЕНОЛОГІЧНІ ХАРАКТЕРИСТИКИ ВІЛ-ІНФЕКЦІЇ, ПОЄДНАНОЇ З ТУБЕРКУЛЬОЗОМ. ОСНОВНІ ПРИЧИНИ СМЕРТНОСТІ

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РЕЗЮМЕ. Мета роботи – проаналізувати рентгенологічні та деякі лабораторні зміни груп хворих на ВІЛ-інфекцію в поєднанні з туберкульозом (ВІЛ/ТБ) та при туберкульозі як моноінфекції, а також визначити основні причини смертності таких пацієнтів.

Пацієнти і методи. Обстежено 351 пацієнта, зокрема 217 з поєднаною інфекцією ВІЛ/ТБ та 134 випадки туберкульозу. Групу ВІЛ/ТБ розділили на 3 підгрупи залежно від часу приєднання туберкульозу до ВІЛ-інфекції.

1-а підгрупа – ВІЛ-інфіковані, в яких на різних стадіях ВІЛ-інфекції (первинне захворювання) був виявлений ТБ – 72 пацієнти;

2-а підгрупа – особи, в яких протягом декількох років до зареєстрованої ВІЛ-інфекції і часу гіпотетичного зараження (за епідеміологічним анамнезом) був діагностований ТБ, тобто первинним захворюванням був ТБ – 26 людей;

3-я підгрупа – ВІЛ-інфіковані, в яких захворювання були зареєстровані приблизно в один час і з'ясувати, яка недуга виявилася первинною, було неможливо – 57 осіб.

Результати. Найяскравіша клінічна симптоматика характерна для хворих з ко-інфекцією ВІЛ/ТБ, порівняно з пацієнтами, які хворіють лише на туберкульоз. Особи з асоційованою ВІЛ/туберкульозною інфекцією також відрізнялися від хворих на туберкульоз тим, що у них зміни на рентгенограмі грудної порожнини були незначні.

Резистентність до одного з протитуберкульозних препаратів значно частіше реєструється у групі із супутньою інфекцією. Така ж картина відзначена для 1-ї та 3-ї підгруп ВІЛ/ТБ.

Рівень смертності від інфільтративного туберкульозу при асоційованій ВІЛ/туберкульозній інфекції значно вищий, ніж серед пацієнтів, що страждають лише на туберкульоз. При вогнищевому туберкульозі, казеозній пневмонії, дисемінованій, генералізованій та позалегеновій формах туберкульозу спостерігається тенденція до збільшення смертності у разі супутньої ВІЛ-інфекції. Ймовірно, це пов'язано із значним ураженням легеневої тканини. Загалом хворі з ко-інфекцією ВІЛ/ТБ помирають значно частіше, ніж пацієнти з туберкульозною моноінфекцією.

Висновки. Пацієнти з поєднаною патологією ВІЛ/ТБ відрізнялися від хворих лише на туберкульоз яскравішими клінічними симптомами, достовірно частішими змінами при рентгенографії органів грудної порожнини, медикаментозною стійкістю до одного з протитуберкульозних препаратів та значно вищою летальністю.

Ключові слова: ВІЛ-інфекція, туберкульоз, рентгенологічні зміни, смертність.

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Конфлікту інтересів немає.

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