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Incidence of tuberculosis and mycobacteriosis among HIV-infected patients — clinical and epidemiological analysis of patients from north-eastern Poland

Zachorowania na gruźlicę i mykobakteriozy wśród zakażonych HIV — analiza kliniczno-epidemiologiczna pacjentów z regionu północno-wschodniego Polski

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Abstract

Introduction: According to WHO data, among patients infected with HIV, tuberculosis occurs in about 30% of patients and causes approximately 25% of deaths due to AIDS worldwide. The incidence rate of tuberculosis in the Polish population was 22.2/100,000 in 2011, while the average in European Union countries in 2011 was 14/100,000. Since 1985 to 30 April 2013 HIV infection in Poland was confirmed in 16,588 patients, while the number of reported tuberculosis cases in HIV-infected individuals in 2011 was 26. The aim of this study was to assess the prevalence and clinical course of tuberculosis and mycobacterial disease in HIV-infected patients treated in the Department of Infectious Diseases and Hepatology in Białystok.

Material and methods: We analysed documentation of 577 HIV-infected patients, their demographic data, epidemiological status, degree of immunosuppression (T CD4 and CD8 numbers) and stage of HIV infection.

Results: Complete follow-up was possible in 389 patients, of whom 265 (68%) were male. Tuberculosis (TB) was diagnosed in 41 patients (10.5%) and mycobacteriosis in 4 patients (1.03%). In 19 patients (42%) HIV and TB or mycobacteriosis were diagnosed simultaneously. The median CD4 T lymphocyte count was lower in patients with a simultaneous diagnosis of HIV and tuberculosis or mycobacteriosis compared to the group in whom TB/mycobacteriosis was diagnosed later. The number of CD4 T-cells less than 50 cells/μL was found in 63.2% (12/19) of patients when HIV and TB or mycobacteriosis were diagnosed simultaneously and in 38.5% (10/26) of patients who were diagnosed with TB or mycobacteriosis later than the HIV infection ($p = 0.14$). The median HIV viral load in patients in whom HIV infection and tuberculosis or mycobacteriosis were diagnosed at the same time was higher than in other patients and this difference was statistically significant. Pulmonary tuberculosis was the most common form of clinical disease and accounted for 60% of all cases. Among the analysed cases with HIV and tuberculosis or mycobacteriosis coinfection, tuberculosis or mycobacteriosis was the cause of death in 8 patients, and 9 died of other causes.

Conclusion: In our material of 389 HIV-infected patients, tuberculosis was diagnosed in 41 (10.5%) and mycobacterial diseases in 4 (1.03%). In 42% of co-infected patients (HIV+TB or mycobacteriosis) the diagnosis of both diseases was made at the same time. In these patients, a deep deficit of cellular immunity (CD4 $<$ 50 cells/μL) was observed more frequently than in patients diagnosed with TB or mycobacteriosis in the later course of HIV. HIV RNA viral load was significantly higher in the group diagnosed simultaneously than in the remaining patients with HIV and TB or mycobacteriosis coinfection.

Key words: co-infection, HIV, tuberculosis, mycobacteriosis, epidemiology

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Streszczenie

Wstęp: Zgodnie z danymi WHO wśród pacjentów zakażonych HIV, gruźlica występuje u około 30% pacjentów i jest przyczyną około 25% zgonów z powodu AIDS na świecie. Zapadalność na gruźlicę wśród populacji polskiej w 2011 roku wynosiła 22,2/100 000, natomiast średnia zapadalności w krajach Unii Europejskiej w 2011 roku — 14/100 000. W Polsce, od 1985 roku do 30 kwietnia 2013 roku potwierdzono 16 588 zakażeń HIV, natomiast liczba zgłoszonych w 2011 roku przypadków gruźlicy u zakażonych HIV wynosiła 26 przypadków. Celem pracy była ocena częstości i objawów klinicznych gruźlicy i mykobakterioz w materiale chorych zakażonych HIV, hospitalizowanych w Klinice Chorób Zakaźnych i Hepatologii Uniwersytetu Medycznego w Białymstoku.

Materiał i metody: Analizowano dokumentację 577 chorych zakażonych HIV. Analizowano dane demograficzne, epidemiologiczne, stan układu immunologicznego w zakresie limfocytów T CD4 i CD8, fazę zakażenia HIV.

Wyniki: Pełna obserwacja możliwa była u 389 pacjentów, z których 265 (68%) to mężczyźni. Gruźlicę rozpoznano u 41 pacjentów (10,5%), mykobakteriozy u 4 pacjentów (1,03%). U 19 pacjentów (42%) rozpoznanie gruźlicy lub mykobakteriozy było równoczasowe z diagnozą HIV. Mediana liczby limfocytów T CD4 była niższa u pacjentów z równoczesnym rozpoznaniem gruźlicy i zakażenia HIV w porównaniu do grupy, u której gruźlicę rozpoznano później. Liczbę limfocytów T CD4 niższą niż 50 kom./μl stwierdzono u 63,2% (12/19) pacjentów, u których zakażenie HIV i gruźlicę (albo mykobakteriozę) rozpoznano równocześnie oraz u 38,5% (10/26) pacjentów, u których te choroby rozpoznano w późniejszym czasie ($p = 0,14$). Mediana wiremii HIV u pacjentów, u których zakażenie HIV i gruźlicę lub mykobakteriozę zdiagnozowano równocześnie, była wyższa niż u pozostałych pacjentów i różnica ta była istotna statystycznie. Gruźlica płuc była najczęstszą postacią kliniczną choroby i stanowiła 60% wszystkich przypadków. Wśród analizowanych przypadków pacjentów z współwystępowaniem gruźlicy lub mykobakteriozy i HIV, gruźlica/mykobakterioza była przyczyną zgonu 8 pacjentów, natomiast 9 zmarło z innych przyczyn.

Wnioski: W badanej populacji pacjentów gruźlicę rozpoznano u 41 pacjentów (10,5%), a mykobakteriozę u 4/389 pacjentów (1,03%). W 42% przypadków wśród badanych osób rozpoznanie zakażenia HIV i gruźlicy nastąpiło równoczasowo. W tej grupie chorych częściej obserwowano głęboki deficyt odporności komórkowej (limfocyty T CD4 < 50 kom./μl), a wiremia HIV RNA była istotnie wyższa niż w grupie chorych z HIV, u których gruźlicę lub mykobakteriozę rozpoznano później.

Słowa kluczowe: współwystępowanie, HIV, gruźlica, prątki atypowe, mykobakterioza, epidemiologia

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Introduction

According to the World Health Organization, 8.7 million cases of tuberculosis (TB) and 1.4 million deaths due to tuberculosis were registered in 2011. Tuberculosis is the second, in respect of frequency, cause of death due to infectious diseases in the general population, and it is listed among the top ten causes of deaths worldwide. 1/3 of the worldwide population (the general population and patients infected with human immunodeficiency virus) is infected with tubercle bacilli with no symptoms of the disease (the so-called latent tuberculosis). Whereas, HIV-infected patients, due to immunodeficiency (mainly decreased cellular immunity), are about 21–34 times more prone to develop active TB in comparison with the general population. In 2011, 1.1 million new TB cases among HIV-infected patients were registered worldwide, which accounts for 13% of all TB incidence in the general population. On a global scale, since 2004, the mortality rate due to TB among HIV-infected patients has decreased by approximately 25%, but it still remains the cause of one out of four deaths due to acquired immunodeficiency syndrome (AIDS). More than 70% of cases of HIV and TB coinfection occur in Africa [1, 2].

A total of 8,478 cases of TB were diagnosed in the Polish population in 2011, and the incidence rate was 22.2/100,000; new cases amounted to 19.7/100,000 and recurrences to — 2.5/100,000. In 2012, 7542 cases of TB were diagnosed, the incidence rate decreased to 19.6/100,000, new cases amounted to 17.3/10,000 and recurrences to 2.3/100,000 [3]. In European countries in 2011, 71,031 cases of tuberculosis were diagnosed, and the mean TB incidence was 14/100,000 [4].

In Poland, since the introduction of HIV diagnostic tests in 1985 until April 30th 2013, 16,588 cases of HIV infection were diagnosed. The number of new cases is not decreasing and a growing number of sexually (hetero- and homosexual) transmitted HIV infections is observed [5–7]. During this period, there were 2908 cases of AIDS registered in Poland and 1207 cases of death due to this disease [8]. According to the data of the National Institute of Public Health, the following number of new cases of HIV/AIDS were diagnosed: in 2008 — 958/207 in 2009 — 716/127, in 2010 — 747/173, in 2011 — 1188/241.

According to the European Centre for Disease Prevention and Control (ECDC), there were 27 cases of the coincidence of HIV and TB in 2009 in Poland, 22 — in 2010 and 26 in 2011.

In European Union countries (the European Economic Area) 1334 cases of HIV infection in patients with TB were reported in 2009, 1055 — in 2010, and 1003 in 2011 [4]. The last report on HIV/TB coincidence by the ECDC did not take into account several countries, including Poland, due to a lack of data concerning the number of performed tests checking HIV infection in TB patients. According to the ECDC and the WHO, the number of HIV-infected people and the number of TB and HIV coinfections worldwide is underestimated [2, 4]. Even more than 50% of people are not aware of being infected with HIV [9, 10]. According to the WHO, only 40% of TB patients worldwide underwent testing directed at HIV infection; this proportion was even lower in European countries, and in 2009 it amounted to 23.9%. However, it should be emphasized that since 2004 the number of performed tests directed at HIV infection in TB patients has increased worldwide more than ten times [2]. In Europe in 2011, 53.6% of TB patients underwent testing directed at HIV infection [4].

In Poland, specialized extensive medical care of HIV-infected patients with coexisting TB or mycobacteriosis is provided in 17 centres localized in 14 cities, in cooperation with the agenda of the Ministry of Health — the National AIDS Centre.

The aim of the present study was a retrospective, clinical and epidemiological analysis of the incidence of TB and mycobacteriosis in patients with confirmed retroviral infection, treated at the Department of Infectious Diseases and Hepatology of the Medical University of Białystok, coming from the Podlasie, Warmia and Mazury regions.

Material and methods

Medical documentation of 577 HIV-infected patients from the period from 1989 to 2011 was analysed. Diagnosis of HIV was based on showing the presence of anti-HIV antibodies in two screening enzyme-linked immunosorbent assays (ELISA), confirmed by western blot method. Tuberculosis and mycobacteriosis were diagnosed based on clinical symptoms, microbiological examinations, results of direct smears, cultures on solid and fluid media, histological and radiological examinations (X-rays, MRI — magnetic resonance imaging, CT — computed tomography, ultrasonography). The following factors were analysed: age of patients, sex, route of HIV transmission, T CD4 lymphocytes count and HIV viral load at the time of diagnosis of HIV and TB or mycobacteriosis, the date of diagnosis of HIV and TB/mycobacteriosis infection, and the time that passed between diagnosis of the two diseases. In statistical analysis the Mann-Whitney U test, Fisher's exact test and t-Student test were used. The Statistica program was used to conduct statistical tests.

Results

From the group of 577 HIV-infected patients, data concerning infective complications were registered in 389 patients. 265 (68%) out of them were males from 18 to 67 years of age, and 124 (32%) were females from 18 to 64 years of age. The remaining 188 patients, who were seen during single visits, were not included in the analysis. 75 deaths (13%) were registered in the whole group (n = 577) during the study period.

Patients who probably had been infected with HIV through intravenous drug use (IVDU) accounted for 55% (214/389), through heterosexual relations — 12.5% (49/389) and homosexual relations — 10% (39/389), in 22.5% of patients (87/389) the route of transmission was not established (Table 1).

Tuberculosis was diagnosed in 41 out of 389 patients (10.5%), and mycobacteriosis in 4 patients (1.03%). The mycobacteria species indentification revealed in 1 patient — *Mycobacterium avium complex (MAC)* aetiology, in 2 patients — *Mycobacterium kansasii*, and in 1 patient the species was not identified.

Males predominated among patients coinfected with HIV and TB — 34/41 (75.6%) (Table 1).

Table 1.Characteristics of the study population

Tabela 1. Charakterystyka badanej populacji

Number of analysed patients — n (%)		389 (100%)
Sex n (%)	Female	124 (32%)
	Male	265 (68%)
Route of HIV transmission n (%)	Homosexual	39 (10%)
	Heterosexual	49 (12.5%)
	IVDU*	214 (55%)
	Uknown	87 (22.5%)
Patients co-infected with HIV and tuberculosis — n (%)		41 (10.5%)
Sex n (%)	Female	7 (15.6%)
	Male	34 (75.6%)
Patients co-infected with HIV and mycobacteriosis — n (%)		4 (1.03%)
Sex n	Female	1
	Male	3

*intra venous drug use

Table 2. Characteristics of patients co-infected with HIV and tuberculosis or mycobacteriosis

Tabela 2. Charakterystyka pacjentów z współwystępowaniem HIV i gruźlicy lub mykobakteriozy

Age at diagnosis HIV (years)		28 (17–51)	
Route of HIV transmission n (%)	Homosexual	4 (8.9%)	
	Heterosexual	5 (11.1%)	
	IVDU[#]	27 (60%)	
	Uknown	9 (20%)	
Age at diagnosis Tbc or mycobacteriosis (years)		31.5 (19-52)	
	Simultaneous with HIV	31 (24-49)	p = 0.89
	Later than HIV	32 (19-52)	
Diagnosis TB n (%)	Simultaneous with HIV	16 (39%)	
	Later than HIV	25 (61%)	
Diagnosis of mycobacteriosis n	Simultaneous with HIV	3	
	Later than HIV	1	
Lymphocytes T CD4 (cells/μL)[€]	Mycobacteriosis + HIV	45 (19–203)	p = 0.57
	Tuberculosis + HIV	53 (3–993)	
Lymphocytes T CD4 (cells/μL)[€] TB/Mycobacteriosis	Simultaneous with HIV	44.5 (3–993)	p = 0.26
	Later than HIV	68 (4–391)	
HIV viral load (log 10 copies/mL)*	Mycobacteriosis + HIV	5,08 (SD = 1,22)	p = 0.64
	Tuberculosis + HIV	4,88 (SD = 0,56)	
HIV viral load (log 10 copies/mL)* TB/Mycobacteriosis	Simultaneous with HIV	5.23 (SD = 0,56)	p = 0.04
	Later than HIV	4.18 (SD = 1,41)	

[#]intra venous drug use; [€]median (range); *mean (standard deviation SD)

16/41 (39%) patients were diagnosed simultaneously with TB and HIV/AIDS. Among patients with mycobacteriosis, the two diseases were diagnosed simultaneously in 3/4 patients (Table 2). In the remaining patients, TB or mycobacteriosis were diagnosed on average 5.7 years after the diagnosis of HIV. At the moment of diagnosis of TB or mycobacteriosis, 16 (36.6%) patients were actively drug or/and alcohol dependent.

The median T CD4 lymphocyte count in the group with diagnosed TB was 53 cells/μL, whereas in the group with diagnosed mycobacteriosis it was 45 cells/μL (p = 0.57). The median T CD4 lymphocyte count was lower in patients with simultaneous diagnosis of HIV and TB/mycobacteriosis (44.5 cells/μL) compared to those in whom TB or mycobacteriosis was diagnosed later (68.0 cells/μL), but the difference was not statistically significant (p = 0.26) (Table 2). T CD4 lymphocyte count was found to be lower than 200 cells/μL in 73.7% (14/19) of patients in whom coinfection with HIV and TB/mycobacteriosis were diagnosed simultaneously, and in 80.8% (21/26) of patients, who had previously diagnosed HIV and TB or mycobacteriosis was diagnosed later (p = 0.72) (Fig. 1). With the cut off point at the level of 50 cells/μL, these proportions amounted to 63.2% (12/19) and 38.5% (10/26) (p = 0.14), respectively (Table 3). The mean HIV viral load during diagnosis of TB was 4.88 log 10 copies/mL, and during diagnosis of mycobacteriosis it was 5.08 log 10 copies/mL (p = 0.64). The mean HIV viral load in patients who had HIV infection and TB diagnosed simultaneously amounted to 5.23 log 10 copies/mL (n = 9), whereas in the remaining patients it was 4.18 log 10 copies/mL (n = 15); the difference was statistically significant (p = 0.04) (Table 2).

Positive results of direct smears were obtained in 15 (33%) patients: the presence of acid-fast bacilli in sputum was found in 12 patients, in urine — in 2 patients, and in direct smears of lymph node biopsy specimen — in 1 patient. Acid-fast bacilli were cultured from clinical material in 30 (67%) patients, from sputum — in 26 patients, from urine — in 2 patients, and from cerebrospinal fluid and pleural fluid — in one patient each. Tuberculosis was diagnosed with the help of histopathological examination of peripheral lymph nodes in 6 patients (in 2 patients at autopsy), and in one patient — based on the result of a positive genetic study (Table 4). The most frequent clinical

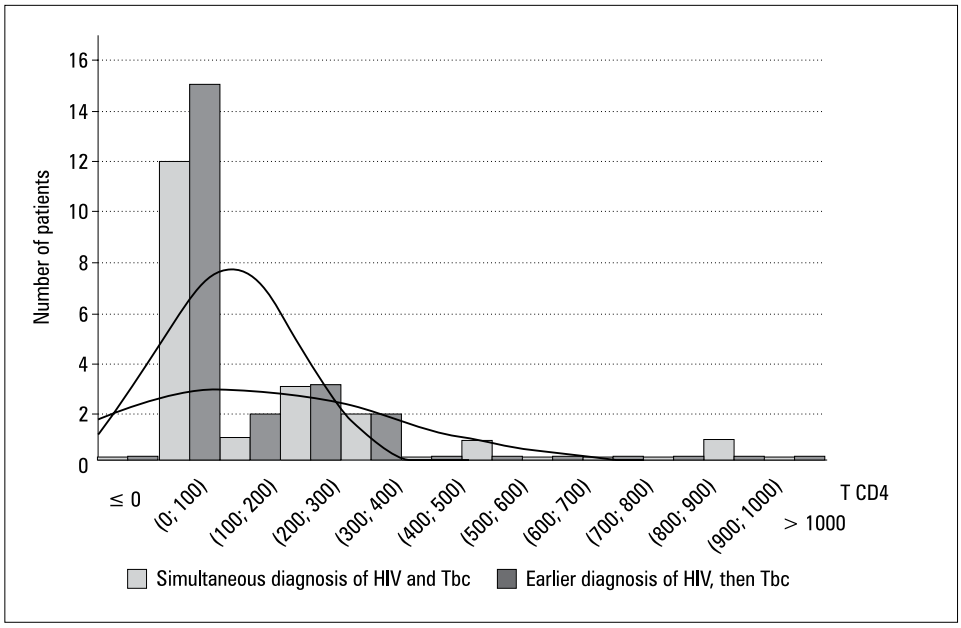

Figure 1. Number of observed cases of TB depending on the number of T CD4 lymphocytes during diagnosis

Rycina 1. Liczba obserwowanych przypadków Tbc w zależności od liczby limfocytów T CD4 podczas rozpoznania

Table 3. Number of CD 4 T — cells at diagnosis of tuberculosis or mycobacteriosis

Tabela 3. Liczba limfocytów T CD 4 w chwili rozpoznania gruźlicy lub mykobakteriozy

Lymphocytes T CD4+ (cells/μL)	Cases of mycobacteriosis		Cases of tuberculosis				p	
	Simultaneous with HIV diagnosis n = 3	After prior HIV diagnosis n = 1	Simultaneous with HIV diagnosis n (%) = 16 (40)		After prior HIV diagnosis n (%) = 25 (56)			
< 50	1	1	11 (69)	12 (75)	9 (36)	20 (8)	0.14	0.72
50–200	1	–	1		11(4)			
200–500	1	–	2		5 (20)			
> 500	–	–	2		0			

Table 4.Performed tests in the diagnosis of tuberculosis or mycobacteriosis

Tabela 4. Badania wykonane w procesie diagnostycznym gruźlicy lub mykobakteriozy

Type of test performed		Result	
		Positive, n	Negative, n
Direct smears		15	30
Clinical specimens culture media (tubercle bacilli): (atypical mycobacterial bacilli)		(26) : (4)	15
Histopathology		6	
PCR		1	–
Radiology examination	Chest X-ray	33	4
	USG	3	–
	MRI	4	–
	CT	9	–

PCR — polymerase chain reaction; RTG — chest X-ray; CT — computed tomography; MRI — magnetic resonance imaging; USG — ultrasonography

form of TB was pulmonary disease, which was diagnosed in 27 patients (60%). Among 18 patients with extrapleural forms, disseminated TB was diagnosed in 15 patients (36.6%), lymphatic TB — in 2 (4.9%) patients, and pleural TB — in 1 patient. Four cases of disseminated TB were confirmed during postmortem pathomorphological examination of various tissues. Mantoux test was performed in 9 patients, and a positive reaction (> 6 mm) was obtained in 3 cases.

Mycobacteriosis was diagnosed in 4 patients based on symptoms of the disease, X-ray examination and confirmed presence of atypical mycobacteria in biological material. In one case it was the species *Mycobacterium kansasii*, in two cases it was MAC, and in one patient the species was not established and the strain was recognized as mycobacteria other than tuberculosis (MOTT). In this group of patients two persons had the pleural form of the disease, and two had disseminated.

About three weeks after the beginning of antiretroviral treatment, TB symptoms appeared in 2 patients without prior diagnosis of TB, and intensification of symptoms in patients with already diagnosed TB was observed in 7 patients. Based on clinical manifestation and additional examinations, in these 9 patients, immune reconstitution syndrome was recognized. Among the analysed patients with HIV and TB or mycobacteriosis coinfection, the direct cause of death in 6 patients was TB, mycobacteriosis — in 2, and 9 patients died of other reasons.

Discussion

As one of the diseases which most frequently accompany HIV infection, TB is used as an AIDS indicator [11]. It is considered that 1/3 of the general population worldwide is infected with TB, and intravital risk of active TB is 5–10% [11–13]. European epidemiologic studies show an increased risk of TB in HIV-infected male patients, drug-addicts, alcoholics, patients with low T CD4 lymphocytes count, high HIV viral load, and of Eastern European origin, which is in accordance with the results of the present study [13].

In Poland the death rate due to TB amounted to 1.7/100,000 in 2011, and it is approximately twice as high as the death rate in older countries of the European Union; however, since 1995 it has shown a downward tendency [2–4]. In Poland in 2010 the proportion of deaths due to TB was 0.2% of all deaths due to other reasons, and 26.7% of all deaths due to infectious diseases. Mortality due to TB in the Polish population in 2009 was 743 (9.02%) deaths of all 8236 TB cases, in 2010 it was 575 (7.66%) of 7,509, and in 2011 it was 640 (7.55%) of 8478 [14]. In the present study, of the 75 deaths in the observed population, 6 (8%) were caused by TB and 2 (2.7%) by mycobacteriosis. In the group of patients with HIV and TB, mortality due to TB was 14.6% (6/41). Two out of four patients with diagnosed mycobacteriosis died.

One of the reasons for the high mortality due to TB or mycobacteriosis in the study group was the fact that in many patients HIV infection was recognised at late stage, simultaneously with TB or mycobacteriosis. At the late stage of HIV infection, a deep suppression of the immune system and high values of HIV viral load are observed, which is combined with a poor prognosis. In patients, who had HIV infection diagnosed at the late stage of the disease (late presenters), reconstruction of the immune system during antiretroviral treatment is slow, despite the increasing absolute number of lymphocytes, their function is disturbed, and prognosis as to long survival is bad. According to the reports, antiretroviral treatment of HIV-infected patients significantly decreases mortality due to TB in the case of coincidence of the two diseases. In some cases, despite the applied antiretroviral treatment, the patient's poor compliance with the treatment is directly responsible for ineffective therapy, and indirectly — for high mortality in this group [15]. Furthermore, in the analysed group of patients with TB or mycobacteriosis, 16 (36.6%) patients were actively drug or/and alcohol dependent, which made the treatment considerably more difficult, and to some extent, was the cause of therapy failure.

According to the WHO, multi-drug resistant TB strains (MDR-TB) are the cause of active TB in approximately 3.7% of new TB cases and in about 20% of previously treated cases. It is estimated that approximately 60% of all MDR-TB cases are registered in India, China and the Russian Federation. Due to its close location to Poland, it is worrying that the proportion of MDR-TB in Belarus amounts to 32.3%. Extensively, drug resistant TB (XDR-TB) was already identified in over 84 countries worldwide, and it is estimated that among MDR-TB strains, its proportion reaches approximately 9% [2, 12, 16]. According to epidemiological data, the prevalence of MDR-TB in Poland is low. 32 cases of TB caused by MDR-TB, including 1 case of XDR-TB were found in 2010. 109 cases of drug-resistant TB caused by strains resistant to at least 1 tuberculostatic drug, and 36 MDR-TB cases, were registered in 2011. It accounted, re-

Figure 2. Spleen mycobacteriosis (autopsy specimen). The picture shows multiple nodules crumbling whitish cream-colour (picture taken by the author)

Rycina 2. Mykobakterioza śledziony (materiał sekcyjny). Na zdjęciu widoczne mnogie rozpadające się guzki barwy białawo kremowej (zdjęcie wykonane przez autora)

Figure 3. Intra-abdominal lymph nodes mycobacteriosis (autopsy specimen). The picture shows significantly enlarged intra-abdominal lymph nodes packages (picture taken by the author)

Rycina 3. Mykobakterioza węzłów chłonnych wewnątrzbrzusznych (materiał sekcyjny). Na zdjęciu widoczne znacznie powiększone pakiety wewnątrzbrzusznych węzłów chłonnych (zdjęcie wykonane przez autora)

spectively, for 1.3% and 0.4% of all reported TB cases in 2011 [3, 17, 18]. We did not find MDR-TB cases in the present study but, according to the literature, the number of registered cases increases together with longstanding observation [19]. In Poland drug-sensitivity is examined in all patients in whom tuberculous bacilli are cultured. The methodology of the examination and problems connected with the culture of bacillus, i.e. a very long cell cycle (cell division every 24 h) often complicates and delays the introduction of the proper treatment. Moreover, the clinical course of TB or mycobacteriosis in patients with a deep immunodeficiency often has an atypical character. The above-mentioned difficulties may result in delayed treatment and inappropriate choice of tuberculostatic drugs, which may lead to ineffective therapy and development of acquired drug-resistance [20].

Due to a lack of obligation to report mycobacteriosis cases to the register, data concerning the prevalence of the disease in Poland are underestimated. According to American statistical data, the incidence of mycobacteriosis worldwide ranges from 1 to 1.8 per 100,000 persons [21]. Patients with acquired or congenital immunodeficiency syndromes, and, among them, the population of HIV-infected patients, are the high risk group for mycobacteriosis and for death due to the disease [22, 23]. In the present study, two out of four cases of diagnosed mycobacteriosis ended with death. In one case mycobacteriosis of *Mycobacterium kansasii* aetiology was diagnosed in a Vietnamese citizen, in whom HIV infection was diagnosed at the same time (the so-called late presenter). Laboratory investigations showed a deep deficit in immunity — the number of T CD4 lymphocytes was 19 cells/μL. Mycobacteriosis in this patient is typical of HIV-infected patients with a considerable deficit in immunity. At the level of T CD4$<$50 cells/μL mycobacteriosis should be taken into account in differential diagnosis of opportunistic infections.

The second case concerned a Polish citizen, who also had HIV infection diagnosed at the advanced stage of immunodeficiency syndrome (indicator of the disease — septicaemia of *Salmonella spp*. aetiology). Then, antiretroviral treatment was introduced immediately. The patient was hospitalized again about half a year later, with consciousness disturbances, periodically with psychotic symptoms, fever, cachexy, and accompanying persistent cough. The performed laboratory examinations showed a significantly lowered number of T CD4 lymphocytes — 26 cells/μL, HIV viral load was 550 copies/mL. Microbiological examinations showed the presence of acid-fast bacilli in direct smears from sputum, additionally, bacilli culture from urine and sputum were obtained. After about two months of hospitalization and therapy, the patient's condition had been gradually deteriorating, psychotic symptoms intensified and delusional symptoms appeared. MRI showed changes that could correspond to encephalitis connected with HIV infection. Despite the applied intensive symptomatic and antituberculous treatment, the patient died. Postmortem examination showed disseminated mycobacteriosis with affected lymph nodes of the abdominal cavity (Fig. 2), spleen (Fig. 3), lungs, li-

ver and kidneys, with no affected central nervous system. The result of microbiological examination of the patient's sputum, obtained after his death, showed the presence of MOTT with no identified species, resistant to rifampicin, isoniazid, ethambutol and sensitive to streptomycin.

The fatal course of the disease in the described patients had many explanations. The main reasons were probably diagnosis of HIV and mycobacteriosis at the very late stage of HIV disease, and the ineffectiveness of the applied antituberculous treatment. Due to the observed significant deterioration of the patients' condition after antiretroviral treatment, it may be presumed that the indirect cause of death was an accompanying immune reconstitution syndrome. There were also observed adverse events during the applied therapy.

According to experts' recommendations, HIV-infected patients with no symptoms of the disease and with the number of lymphocytes T CD4 < 50 cells/μL, should receive primary prevention against MAC in the form of azithromycin, clarithromycin or rifabutin, until the function of the immune system is improved. It is extremely important to exclude mycobacteriosis and TB prior to onset of prevention [11, 24].

In Poland, next to mycotic infections (mainly Candida spp.), TB is the most frequent opportunistic disease that accompanies HIV/AIDS. It was also found that disseminated forms of TB are more frequently observed in HIV-infected patients than in the general population [25, 26]. In the present study, patients with disseminated TB accounted for a significant proportion of all study subjects (36.6%).

A positive phenomenon, observed among the population not infected with HIV, is a slow decline in incidence and mortality rates (and total number of deaths) due to TB, and maintaining such a tendency in longstanding prognoses. Meanwhile, the TB incidence rate among HIV-infected patients has stayed at the same level with a minimal downward tendency, whereas according to longstanding observations, the total number of deaths due to HIV and TB coinfection is decreasing [2, 3].

It should be emphasized that each patient with diagnosed TB or mycobacteriosis should undergo testing directed at HIV infection, and HIV-infected patients should be diagnosed for the presence of TB or mycobacteriosis [11, 27]. According to a WHO report, in Poland in 2011 maximally 15% of patients with diagnosed TB underwent testing directed at HIV infection. Positive examples of activity directed at HIV recognition in TB patients can be seen in Russia, the USA and many African countries, where HIV serological status is investigated in 75% of TB patients. Globally, in 2011, among TB patients who underwent testing directed at HIV infection, the proportion of positive results amounted to 23%. The proportion of positive results was different for individual regions of the world and it fluctuated from 2.1% in Eastern Asia, through 3.5% in Central Asia and Western Europe, 6.8% in Eastern Europe to 46% in Sub-Saharan Africa [2].

Conclusions

In the studied population of HIV/AIDS patients, TB was diagnosed in 41 patients (10.5%) and mycobacteriosis in 4 patients (1.03%). In 42% of patients with coinfection, HIV and TB or mycobacteriosis were diagnosed simultaneously. A deep deficit in cellular immunity (CD4 < 50 cells/μL) was more frequently observed in this group of patients, and HIV RNA viral load was significantly higher than in the remaining groups.

Conflict of interest

The authors declare no conflict of interest.

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