ORIGINAL STUDY

DIAGNOSTIC FEATURES OF TUBERCULOSIS IN HIV ROMANIAN PATIENTS-SHORT REPORT

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ABSTRACT

The prevalence of tuberculosis (TB) in Romania has been declining during the last ten years, but it is still the highest within European Union. Methods: Demographic data, diagnostic criteria and therapeutic outcomes are retrospectively assessed in 65 new TB cases with concomitant HIV/AIDS, who were diagnosed in Galati County during 2005-2011. Results: In the sample analysed, the incidence of new TB cases was 22.18%. Tuberculosis was the first HIV event in 26% patients with new HIV diagnostic. The main characteristics of HIV-TB co-infected patients were the prevalent male sex, rural living area, nosocomial paediatric HIV transmission, young median age 21 [15;62] and median CD4 count 129/µL [4; 847] at the time of TB diagnostic. The site of TB was 31% pulmonary, 29% extra-pulmonary and 40% disseminated. Etiological diagnostic was sustained by bacteriology (52.3%) and/or histology (17%). TB cured in 69.4% of cases, relapsed in 8.3% and was a cause of death in 22.2%. The risk of death is higher when severe immunodepression, hepatitis B co-infection and deferred antiretroviral to the end of tuberculosis intensive treatment phase. Conclusion: Higher efficiency of TB diagnostic and treatment programmes, as well as earlier HIV recognition is necessary in order to improve the European TB and HIV indicators of Romania.

KEYWORDS: *HIV, AIDS, death, relapse, Romani.*

1. Introduction

The main targets of World Health Organization in the Global Plan to stop tuberculosis for 2015 are to reduce the incidence of tuberculosis thorough early diagnostic, improve treatment quality and prevent the spread of the disease. The surveillance of TB in Europe report points the declining trend of 15,2% rates of infection since 2005. Although the number of cases of tuberculosis has been dropping in Romania, the prevalence rate of 98.2/100000 in 2010 is the highest in the European Union [1].

If HIV infectionis associated, the worldwide risk of tuberculosis is 20-30 higher [2]. HIV-tuberculosis co-infection is the cause of 400,000 deaths per year all over the world and represents a quarter of HIV related mortality [2]. According to CDC classification of clinical HIV infection, tuberculosis is a marker of acquired immunodeficiency syndrome (AIDS) [3].The National TB Control Programme in Romania recommends the screening for human immunodeficiency virus (HIV) inall the patients with TB diagnostic [4].Clinical and histological aspects of

HIV-tuberculosis co-infection are influenced by the severity of immunsupression [5]. Atypical clinical presentation of tuberculosis are frequently present in HIV patients with CD4 lymphocytes level less than 350/μl, while patients over 350/μl have similar manifestations with non-HIV patients. Extrapulmonary tuberculosis is more likely related to advanced immunosupression with a CD4 count under 200/μl[5].

HIV- tuberculosis co-infection is a continuous challenge in an attempt to provide the antiretroviral treatment initiation at the right moment, to obtain the immune recovery needed to cure optimally the coexisting TB ,and taking into account the length the TB treatment, drugs toxicity or drugs-drugs interactions[6-8].

The objectives of this study are to compare the clinical characteristics and outcome of new tuberculosis cases in patients' depending on concomitant or previous HIV diagnostic.

2. Material and Methods

We retrospectively studied 65 patients with HIV infection recorded in the Infectious Diseases Clinic Galati – Romania. Including criteria were age over 15 and notification of new TB diagnostic since January 2005 through December 2011. Tuberculosis was considered based on clinical, epidemiological, bacteriological or imaging criteria of the National TB Control Programme [9]. Patients were included if they had either confirmed TB diagnostic by positive smear, culture, histology or clinically defined features of TB when other diagnostics were ruled out. Tuberculosis was classified as pulmonary or extra-pulmonary localized. Disseminated tuberculosis was considered if more than 2 organs were involved.

The following data were studied based on medical records: age, sex, living rural or urban area, educational level, smoking behavior, tuberculosis siteand CD4 cell countper μL at the time of tuberculosis diagnostic. Patients were divided into two groups, depending on HIV-TB sequence: group 1 with concomitant diagnostic and group 2 with HIV/AIDS and with TB later development .Treatment consisted of a hospitalized intensive phase and an ambulatory phase under the supervision of a nurse and was represented by the standardized first line regimen [9]. . We considered nonadherent the patients missing the drugs for more than two consecutive weekly visits, according nurse's report on TB adherence. The outcomes of TB treatment were recovery, relapse and death.

Collected data were statistical analyzedusingMicrosoft EXCEL - Statistical Analysis Tool Pack software. Patients' characteristics were described by medians and frequencies (%). Numerical variables were analyzed by two-sample t-tests andcategorical variables were compared with Fisher's exact test. The factors associated with concomitant or later TB diagnostic inHIV patients were assessed by binary logistic regression, considering significant level a p value of <0.05.

3. Results

At the end of 2011 there were recorded 293 HIV infected patients in Infectious Diseases Daily Clinic Galati. From 2005 to 2011, we notified 22.18% (65/293) new cases of tuberculosis among HIV patients, Furthermore, 26% of the newly HIV diagnosed patients experienced tuberculosis as the first opportunistic event.

The diagnostic of tuberculosis was confirmed by classical bacteriological exam in 52.3% and/or histological criteria in 17%. The prevalent characteristics among the patients with tuberculosis are young age under 25 (73.8%), male sex (61.5%), low formal education (58.5%) and advanced immunossupression with CD4 lymphocytes level

under 350/uL (83.1%). Median age on tuberculosis diagnosis was 21 [15; 62] years. At the moment of TB diagnostic, 37% (24/65) patients were under ART, 23% (15/65) deferred ART until complete TB treatment, 40% (26/65) initiated ART together with TB treatment and experienced immune reconstruction inflammatory syndrome (IRIS) in 9% (6/65).

Table I. *Characteristics of HIV patients with Concomitant (group 1) or subsequent (group 2) new TB diagnostic*

	Group1(N=30)	Group 2 (N=35)	OR	CI 95%	p
Age TB >25	15	3	10.66	3.06; 37.11	<0.001
Age HIV <14	8	27	30	8.82; 94.54	<0.001
Sex male	22	18	2.59	0.92; 7.30	0.059
Rural living area	14	18	1.32	0.545; 3.21	0.446
Formal education >8 years	19	8	5.82	2.04; 16.06	0.002
Smokers	18	15	2	0.74; 5.35	0.129
CD4<200	23	22	2.39	0.88; 6.47	0.049
CD4<350	28	26	4.28	1.06; 22.06	0.040
HBV co-infection	6	13	2.36	0.77; 7.19	0.213
Periferic adenitis	18	10	3.75	1.35; 10.35	0.020
Extrapulmonary or disseminated TB	21	24	1.06	0.37; 3.07	0.558
Bacteriologic notification	21	22	1.37	0.48; 3.89	0.336
Outcome					
Death	8	7	1.46	0.44; 4.77	0.629
Recovery	18	23			
Relapse	4	5	1.02	0.23; 4.36	0.366

Table II. *Localization of tuberculosis in HIV patients (N=65)*

Anatomic Sites of TB	No patients
Pulmonary involvement	
Miliary	11
Primary tuberculosis	3
Secondary tuberculosis	44
Extra-pulmonary involvement	
Meningoencefalitis	5
Osteoartritis (Spondyles L1-2)	1
Kidney	1
Lymphadenopathy	
periferical	28
abdominal	5
mediastinal	28
Serositis	
pleural effusion	22
poliserositis	3

The outcome within the first year of tuberculosis diagnostic was recovery 63%, relapse 9% and death 23% [Table I].

Tuberculosis was localized in 20 (31%) cases pulmonary only (P), 19 (29%) extra-pulmonary (EP) and 26 (40%) disseminated. Radiologic pulmonary

findings are frequently complex. There are recorded 29 (63%) infiltrates, 20 (43.5%) ulcerous, 17 (39%) nodules, 10 (22%) caseosis, 7 (15%) cavitary or 11 (24%) military lesions. The most common extensive pulmonary and extrapulmonary aspects are 22 (34%) pleural effusion, 28 (43%) mediastinal and 28 (43%) peripherical lymphadenopathy [Table II].

4.Discussions

Patients with concomitant new TB and HIV diagnostics are older, more formal educated and appear with lower CD4 count, compared to subsequent TB long after HIV diagnostic. Most of these patients come from Romanian HIV/AIDS paediatric cohort, nosocomially infected during early childhood, between 1987 and 1990.

Averageage of HIV- TB co-infected patientsin this study is lower than national average age of new TB cases without HIV coinfection: 24.1 versus 41.8 years. In Romania, tuberculosis is the most frequent HIV associated disease, being either an indication for HIV testing, or AIDS defining disease during the HIV follow-up [1,10]. The average yearly rate of TB on HIV positive patients in our clinic decreased from 10% in 2002 to 1% in 2008, but tends to relapse in 2011 to 3%. Meanwhile, the national notification rate of tuberculosis decreased from 137.7/100000 in 2002 to 98.2/100000 in 2010[1,9]. In the near future, regional economic crisis and poverty are expected to increase tuberculosis,first in vulnerable HIV/AIDS and then in the general population[12,13,14].

Peripheral lymph nodes and low CD4 count <350/uL are the most expected tuberculosis features when tuberculosis and HIV are concomitant diagnostic, in our study (Table I).

The rate of tuberculosis cases confirmed by culture is 52.3%is inferior to the indicators of the most UE countries, but similar to the Romanian national reported data 59.3% [1]. Positive cultures were achieved mostly in pulmonary involvement (p=0.013; OR=4.10; CI95%: 1.3-12.7).

Outcomes of tuberculosis treatment were 63%successful cure, 13.8% tuberculosis relapse and 23% death in the next year after TB notification.Treatment success rate was lower, comparative to the national indicator (85.4%) [1]. Adherence evaluationsat the end of TB treatment report 24% (12/50) nonadherent patients. Non-adherence is related with previous HIV to TB diagnostic (p=0.015; OR=3.77; CI95%: 1.27-11.1) and TB relapse outcome (p=0.003; OR=11; CI95%: 2.7-49.9).

Death rate 23% is considerablyhigh in our study. Comparative data from our HIV clinic predict higher mortality in TB co-infected patients thanwithout TB(OR=3.5; p=0.002; CI 95%: 1.70-7.18).The mortality risk is higher in patients with CD4 count under 200/μL(p=0,006; OR=13.33; CI95%:2.29-77.58),HBV co-infection(p=0.030; OR=4.25; CI95%: 1.21-14.86) and deferred to ART (p=0.024; OR=6.09; CI95%:1.32-28.00), but no significant correlation was found with sex, smoking, concomitent HIV- TB diagnostic or clinical presentation of tuberculosis.

The limitationsof the study are the missing data on TB-drug resistance. The microbiologic new diagnostic tools are not affordable in our clinic. Monitoring of CD4 count and HIV-viral load are not regularly available along the TB treatment for statistical evaluation of TB impact on HIV progress.

5. Conclusions

In conclusion, based on the data from the discussed analysis features and outcome of TB are similar in patients with concomitant and previous HIV diagnostic.Young age, frequent late presentation with tuberculosis as first AIDS opportunistic disease, high rate of extrapulmonary and disseminated TB forms are characteristics of TB-HIV co-infection in

our study. Co-infection tuberculosis and HIV is a risk factor of mortality. High mortality related to HIV-TB co-infection requires us to intensify the efforts for implementation of national preventing programmes for HIV and tuberculosis. Reasonable financing of curative health programmes are necessary toachieve newTB diagnostic techniques, HIV immunology and virology monitoring and adequate antiretroviral treatment supply.

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