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HIV and tuberculosis co-infection at the Tuberculosis and Respiratory Diseases Diagnostic Center at the Provincial Hospital of Tiznit, Morocco

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Abstract

Background: Tuberculosis continues to be a public health priority, especially with the emergence of HIV. Our objective is to describe the epidemiological, clinical, para-clinical, therapeutic and evolutionary aspects of TB/HIV co-infection.

Materials and methods: A retrospective study was conducted through the analysis of data from 216 tuberculosis patients admitted to the Tuberculosis and Respiratory Diseases Diagnostic Centre in Tiznit (Morocco), from June 2018 to June 2020. Cases of TB-HIV co-infection will be identified, and the result will be studied.

Results: The data of 216 patients were collected from the Diagnostic Centre for Tuberculosis and Respiratory Diseases of Tiznit and among them 22 cases of co-infections were recorded. The average age of our patients is 40 years, and the sex ratio H / F is 2.6. 41% of co-infected patients were smokers. AIDS was the revealing mode of BK infection in 77.2% of the patients. Eighteen patients (81.8%) had an isolated pulmonary localization, 13.6% had an isolated extrapulmonary localization and 4.5% had a mixed localization. Node location was the most common extrapulmonary involvement (66.6%).

Clinically, the cough-fever-weight loss triad was found in 80% of cases. Chest X-rays were abnormal in 86.3% of co-infected patients. The search for Koch bacillus in the sputum was positive in 40.9% of the patients. The Xpert gene was present in 90.9% of cases and found Mycobacterium tuberculosis and sensitive to rifampicin. The treatment included antibacillary drugs according to the appropriate protocol, with an overall duration of 6 to 9 months. The antiretroviral treatment was a combination of two nucleoside and one non-nucleoside analogue. The outcome was favourable in 18 cases (81.8%), death occurred in 4 cases (18.1%), drug toxicity in 36.3% of cases, including hepatotoxicity (50%) mainly related to anti-tuberculosis drugs.

Conclusion: TB-HIV co-infection is a lethal association, hence the interest in setting up a joint collaboration between the national tuberculosis control programme and the AIDS control programme in order to implement strategies for screening, diagnosis, prevention and management of co-infected patients.

Keywords: *tuberculosis; HIV; co-infection; treatment*

Introduction

Tuberculosis is the ninth leading cause of death worldwide and the leading cause of death due to a single infectious agent [1]. As early as 1986, there was a resurgence of tuberculosis, which is largely linked to the human immunodeficiency virus (HIV) pandemic. However, tuberculosis is the leading cause of death among people living with HIV [2].

People infected with TB and HIV are 20 to 30 times more likely to develop active TB than those who are not. Tuberculosis and HIV form a lethal association, each accelerating the progression of the other [2]. The interactions between TB and HIV are multiple and are changing the epidemiology, clinical presentation and management of these diseases [3].

The excess mortality in HIV-positive tuberculosis patients is due to the evolution of the HIV infection itself, the emergence of multi-resistant strains, and even drug intolerances that lead to the discontinuation of treatment [2].

However, the management of HIV/TB co-infection poses several problems, including the increased toxicity of anti-tuberculosis drugs, the possible occurrence of interactions between anti-tuberculosis and antiretroviral treatments, the risk of resistant tuberculosis and the risk of inflammatory immune reconstitution syndrome (IRIS) [3].

In the aim to understand the tuberculosis and HIV co-infection, we conducted a retrospective study to analyze the clinical, epidemiological, therapeutic and evolutionary aspects of tuberculosis in HIV infected patients.

Material and methods

The study was conducted on the Diagnosis Center of Tuberculosis and Respiratory Diseases at Tiznit city, Agadir, Morocco. All patients who are co-infected with TB and HIV between June 2018 and June 2020 were recruited in the study and provided written informed consent. All included patients were treated by the same medical staff. For each included patient, socio-demographic factors, clinical manifestations, biological parameters and diagnosis procedures were noted. Chest X-ray was performed in all patients.

All patients and side effects of antibacillary drugs according to the guidelines of the national program in Morocco [4].

Results

The data of 216 tuberculosis patients were collected at the Diagnostic Center of Tuberculosis and Respiratory Diseases Tiznit province. Among the patients under study, 22 are co-infected with tuberculosis and HIV. Moreover, these data were collected over a period of 2 years (June 2018 to June 2020). The average age of patients

with HIV/tuberculosis co-infection was 40 years with extremes ranging from 23 to 85 years. There were 16 males (72.7%) and 6 females (27.2%) with a sex ratio of 2.6, with a male predominance.

In our series, 59% (13) of the studied cases were single, followed by married patients at (06) 27.2%. Of all cases, 72.7% of the patients were of urban origin, while only six were of rural origin.

In addition, 41% of co-infected patients were smokers and 4.5% were cannabis dependent. Also, more than half of the studied cases were not addicted to any toxic substance.

The history of pulmonary tuberculosis was found in 2 of our patients (9%), treated according to the 2RHZE/4RH regimen and whose evolution was unfavourable, while the notion of tuberculosis contagion was found in only 3 cases.

In our series, AIDS was the revealing mode of BK infection in 17 cases (77.2%), while only 5 cases (22.7%) were known to be BK positive from 5 months to one year.

Symptomatologically, 90.9% of our patients had general signs, such as chills (5%), fever (86%), night sweats (30%), weight loss (80%), asthenia (70%) and anorexia (73%). Respiratory signs were present in 18 patients, i.e., 81.8% of the cases, with dry cough (28%), productive cough (60%) of which 30% were purulent, and rarely haemoptysis (5%), half of our patients (50%) presented at least one extra-respiratory sign (skin signs, digestive signs, adenopathy, and neurological signs) (Table 1).

Clinical manifestations	Number of cases	Percentage
General signs	20	90,9%
Respiratory signs	18	81,8%
Extra Respiratory Signs	11	50%

Table 1: Clinical manifestations in co-infected patients.

There are three types of tuberculosis localizations: an isolated pulmonary localization in 18 cases (81.8%), an isolated extra-pulmonary localization in 3 cases (13.6%) and a mixed localization in 01 case (4.5%).

Nodal location was the most frequently found extra-pulmonary involvement (66.6%), followed by pleural location (33.3%).

The Hemogram was carried out in all our patients, proving abnormal in 20 cases (90.9%). The CRP performed in 18 cases (81.8%) was always high with an average of 51.9 mg/l, a maximum value of 150 mg/l and a minimum value of 15 mg/l. The sedimentation rate was achieved in only 4 patients (18.1%), it was normal in 1 case and accelerated in 3 cases, with an average of 120 mm during the first hour.

Sputum testing for ASPB was performed in 22 cases, and was positive in 9 cases, i.e. (40.9%).

However, culture was performed in only 2 cases, returning positive in one and negative in the other.

In our study, the Xpert MTB/RIF test was performed in 20 of our patients, or 90.9% returning positive in the cases studied without any resistance to rifampicin. The Xpert MTB/RIF result confirmed the direct microscopic examination result in 9 patients, while it returned positive in 13 patients with negative microscopy.

Two patients underwent lymph node biopsy; cytopuncture was suggestive of tuberculosis in both cases.

Chest X-ray was performed in all our patients, finding abnormalities in 19 cases, i.e. (86.3%), alveolar syndrome, interstitial syndrome, cavitary syndrome, nodular opacities, and pleurisy.

In our series, all our patients were put under antibacillary treatment according to the recommendations of the national program of fighting against tuberculosis according to different protocols distributed as follows:

- The 2RHZE/4RH regimen was recommended in 21 of our patients (95.4%).

- The 2RHZE/7RH regimen was recommended in 1 patient (4.5%) with multifocal tuberculosis.

In general, the tolerance of the antibacillary drugs was good. 08 patients (36.3%) had side effects. The main side effects observed were hepatic cytolysis in 04 cases, hepatic cholestasis in 03 cases and digestive intolerance in 01 case.

The management of side effects generally consisted of stopping the treatment and then gradually reintroducing it after improvement of symptoms and correction of abnormalities.

The evolution was favourable in 18 cases, i.e. (81.8%), death occurred in 4 cases, i.e. (18.1%). The causes of death were: Tuberculosis and HIV infection, severe sepsis and cardiorespiratory arrest.

Discussion

Tuberculosis and HIV infection affect a young population, which is reported in many studies [5]. In sub-Saharan Africa the average age of HIV/TB co-infection is 39 years in 2017 [6]. And it is 33 years in Asia [7], which is consistent with the results of our study where the average age was 40 years.

The gender distribution depends on the epidemiological profile of HIV infection in each country. In Asia it is mainly men who are affected with a sex ratio of 5.06 [7]. The same applies to our series with a sex ratio of 2.6.

In sub-Saharan Africa it is mainly women who are affected with a sex ratio of 0.8 [6].

In our series, 59% of the subjects were single, followed by married subjects at 27.2%. Of all cases, 72.7% of the patients were of urban origin, while only six were of rural origin. However, in an Asian study of 340 co-infected subjects, it was concluded that nearly 50% of the patients were married and more than half lived in an urban area [7].

41% of the patients in our series were smokers, which is consistent with the study by Perriot and colleagues and confirms that smoking is a risk factor for tuberculosis infection [8]. Among the opportunistic pathogens linked to HIV infection, M. tuberculosis occurs relatively early, a fact that our series confirms; at the time of diagnosis of tuberculosis, more than 77.2% of patients were HIV positive.

The most frequent location of tuberculosis differs from one study to another and (Table 2) represents a comparison between the different international series.

Location / Series	Pulmonary tuberculosis	Extra-pulmonary tuberculosis	Multifocal tuberculosis
Asia [6]	67,6%	14,7%	17,6%
Morocco (Casablanca) [8]	30,4%	69,6%	--
Our series, Morocco (Tiznit)	**81,8%**	**13,6%**	**4,5%**
Sub-Saharan Africa [5]	30 %	50 %	20%

Table 2: Comparison between the different international series concerning the location of Bk infection

The fact that bacilloscopy was positive in only 40.9% of co-infected persons was a limitation of the direct examination. The sputum examination after Ziehl-Neelsen staining, although considered a reference technique among direct examinations, is less sensitive than culture on the one hand, and on the other hand, bacilloscopy positivity

is less frequent in HIV-infected patients with a CD4 count below 200/mm^3 [10].

The use of molecular biology (Xpert MTB/Rif) in the diagnosis of pulmonary and extrapulmonary tuberculosis has been evaluated in several studies with variable results [11-15]. The results of our study revealed that for all samples included, Xpert MTB/Rif was positive, making real-time PCR a more powerful tool than microscopy in the diagnosis of tuberculosis, a conclusion that is shared by Tortoli and Iram *et al.* [12,16].

HIV co-infection significantly reduced the sensitivity of microscopy but did not significantly affect the performance of the Xpert MTB/RIF test [17].

In our study, patients were treated with a combination of four antibacillaries according to the appropriate therapeutic regimen, the total duration of treatment ranged from 6 to 9 months, and only 81.8% were on antiretroviral therapy.

The side effects of anti-TB drugs are more frequent and severe in HIV-infected patients treated for TB disease [18]. These effects are observed in 20 to 40% of HIV-infected patients and occur within the first 2 months of treatment [19]. In our study, 8 patients (36.3%) experienced side effects.

The treatment of tuberculosis is standardised, but the decision to treat is inseparable from the evaluation of possible side effects that justify the pre-treatment assessment.

In a study in France, on a group of 64 patients after an average follow-up of 26 months, 84% of the patients completed the treatment with only 5% of relapses and 1.5% of deaths attributable to tuberculosis [20]. On the other hand, in our series the mortality rate remains high at 18.1%, the same as in the study by El Kettani and colleagues (21.7%) [9].

Conclusion

Tuberculosis is the most common opportunistic infection and the leading cause of death in patients with HIV infection. In Morocco, the prevalence of HIV infection remains low. However, tuberculosis is endemic. The interaction between these two infections worsens the vital prognosis and increases the mortality rate in co-infected patients.

Early detection of HIV, rapid initiation of antiretroviral treatment and routine cotrimoxazole prophylaxis in all people living with HIV with TB, as well as preventive treatment with isoniazid are essential elements in improving the management of TB-HIV co-infection.

In Morocco, there is a need for joint collaboration between the national tuberculosis control programme and the national AIDS control programme in order to implement strategies for screening, diagnosis, prevention and management of co-infected patients.

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