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Prevalence of latent TB infection in HIV infected persons in the Sylvanus Olympio teaching hospital of Lomé

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ABSTRACT

Objective: Determine the prevalence of latent TB infection in HIV-infected people.
Method: Using a cross-sectional study on HIV-infected persons monitored in the Department of Lung and Infectious Diseases of CHU Sylvanus Olympio of Lomé from August 10, 2010 to November 10, 2010. All patients are receiving anti-retroviral therapy and have no clinical or radiological symptoms of TB, and had never received tuberculin skin test (TST) in the last 3 months. The CD4 rate of all patients was more than 200 cells/μl. The diagnosis of latent TB infection is based on the measurement of at least 5 mm of skin induration, 72 h after a subcutaneous injection of 5 IU of purified tuberculin.
Results: One hundred and fifty four persons were included in the study, of which 107 were female and 47 were male. The median age was 40 years old. Eleven patients were exposed to a risk of TB and only 70.7% of patients had a BCG scar. A suspicion of former TB was found in 18.8% of patients and approximately 45% of patients were very immunocompromised with a CD4 rate between 200 and 350; 117 patients had a positive TST. This represents an overall prevalence of 76% of latent TB infection.
Conclusion: The prevalence of latent TB infection obtained with the TST is high in this study. A similar study using the interferon-gamma release assay, which is more specific, would be more helpful to obtain more reliable epidemiological data on patient outcomes and to determine the appropriateness of the use of chemoprophylaxis with isoniazid.

Introduction

Latent TB infection is an infection without clinical, bacteriological and radiological signs. This is typically a person who has a positive tuberculin skin test (TST) with normal chest radiograph [1]. The diagnosis of latent tuberculosis (TB) remains unclear. The main problem with the test is its low specificity. The interpretation must consider the possibility of false positives [2]. These are mainly due to former vaccination with BCG or infection with non-tuberculosis mycobacteria. The TST should be performed with the intention of detecting and treating latent tuberculosis. Mass screening is not recommended. In fact, the positive predictive value of the TST is even lower if the prevalence of TB infection in the tested group is low, hence the need to test only risk cases. In Africa, HIV infection is the greatest risk factor to developing TB [3–5]. However, despite the fact that TB/HIV co-infection is increasing more and more, no chemoprophylaxis of latent TB infection with isoniazid among people with TST of more than 5 mm is not yet applied. This first study of its kind in Togo aims to provide preliminary data on the prevalence of latent TB infection in people with HIV to be a basis for target strategy. Moreover, this

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study was initiated because of the lack of data on the prevalence of latent TB infection among HIV-infected persons.

Methods

This is a cross-sectional study on a group of HIV-infected persons monitored in the Ambulatory Treatment Center (ATC) of the Department of Respiratory and Infectious Diseases at the Sylvanus Olympio University Hospital (CHU SO) of Lomé between the period August 10, 2010 to November 10, 2010. All patients are adults and aged at least 18 years and are receiving antiretroviral therapy. All patients have not developed any clinical or radiological symptoms of TB and have never received a TST in the 3 months prior to the study period. In addition, no patient received immunosuppressive therapy, and the CD4 count of all patients was more than 200 cells/μl. The TST consisted of the subcutaneous administration of five international units of purified tuberculin. The measurement of the induration was made 72 h after the injection. The test is considered positive if the induration measurement is over 5 mm. A chest radiograph was performed on all patients who were exposed to a risk of TB or had been declared cured of a former case of TB. The exposition of a risk of TB, the appreciation of TB history of vaccination by the BCG scar, and the CD4 count were the main studied parameters.

The statistical analysis was performed with SPSS software and the chi-2 test has allowed comparing qualitative variables. A p value less than 0.05 was considered statistically significant.

Results

A total of 154 people were included in the study. More than 60.4% of patients were aged between 25 and 44 years with a female predominance (sex ratio 0.44). A total of 11 patients were exposed to a risk of TB and only 70.7% of patients had a BCG scar. A suspicion of former TB was found in 18.8% of patients and approximately 45% of patients were very immuno-compromised with a CD4 count between 200 and 350 cells/μl (Table 1).

A total of 117 patients had a positive TST. This represents an overall prevalence of 76% of latent TB infection (Table 2).

Table 1 – General characteristics of the population at baseline.

Parameters	Value/number	Proportion
Epidemiological characteristics		
Total	154	100%
Median age in years (range)	40 (18–64)	–
Sex M/F	107/47	–
Suspicion of contagion	11	7.14
BCG scar	109	70.7
History of tuberculosis	29	18.8
Immunological characteristics		
CD4 count between 200 and 350 cells/μl	69	44.8
CD4 count $\geqslant$350 cells/μl	85	55.2

Table 2 – Characteristics of the population according to the tuberculin skin test (TST).

Parameters	Value/number	Proportion
Positive TST with BCG scar	83/109	76.1
Positive TST without BCG scar	34/45	75.6
Positive TST with suspicion of contagion of TB	26/29	89.7
Positive TST without suspicion ofcontagion of TB	91/125	72.8
Positive TST with CD4 rate <350 cells/μl	54/69	78.3
Positive TST with CD4 rate >350 cells/μl	63/85	74.1

p(BCG) = 0.938; p(contagion TB) = 0.556; p(CD4) = 0.443.

Discussion

The diagnosis of latent TB infection based on the delayed hypersensitivity test is based on a specific cell-mediated response [6,7].

Thus, according to international recommendations, the test is considered positive when the skin reaction is at least 5 mm for those HIV infected [8]. But, in HIV-uninfected people, the TST becomes significant in the case of phlyctenular reaction, or if the induration reaches 15 mm within a population with low-risk factors of TB [2]. Nowadays, the TST remains – despite its lack of specificity – the cheapest and most widely used test in the diagnosis of latent TB infection. However, the interferon-gamma release assay (IGRA), which is more specific to measure cell-mediated responses, is available today on the market. The major advantage of the IGRA test is its increased specificity in the diagnosis of latent TB infection among populations vaccinated with BCG. This situation applies to immunocompetent adults with a positive TST in the context of very low risk of TB infection [9]. The prevalence of latent TB infection is high in this study (76%). This situation is found in most studies in developing countries where the prevalence can reach 90% of subjects living with HIV. However, in developed countries, the prevalence is relatively low [10,11]. The reasons for this disparity would be linked to the prevalence of TB in these different regions of the world. In fact, most of the new cases of TB and HIV diagnosed each year are found in the third world. In this study, the prevalence is probably exaggerated because the vast majority of patients who have been vaccinated and who still bear the scars of BCG may have a positive TST. This is due to the fact that even though the previous vaccination of this population was done 20 years before, it can still provide antibodies. However, the results of the study showed no significant difference between people vaccinated with BCG scar and unvaccinated ones (Table 2; $p = 0.938$). The TB immunity with BCG is known to decrease with age [12,13]. Similarly, the suspicion of contagion of TB had no impact on the positivity of the TST ($p = 0.556$). In fact, this element was very subjective and difficult to measure. In addition, false skin positive reactions can also come from atypical mycobacteria. The diagnosis may

have been provided by the IGRA, but its high cost is the main factor of inaccessibility.

The immune status assessed according to CD4 rate has not had a significant impact on the result of the TST, whether it be patients whose CD4 count was between 200 and 350 cells/μl or those whose CD4 rates was above 350 cells/μl ($p = 0.443$). Indeed, patients were excluded from the study whose CD4 rate was under 200 cells/μl because the progression to end-stage of HIV can promote reactivation of latent TB bacilli contrasting with the frequent energy of TB which can be observed with these patients. Thus, both the TST and the IGRA would not be good tests for assessing latent TB infection in those immuno-compromised by HIV [14]. It is also for this reason that the tuberculin skin induration of 5 mm is sufficient to diagnose latent TB in those HIV infected regardless of the CD4 rate. But, in people free from any risk factors, the TST reaction becomes significant when the measure of the induration is at least 15 mm in diameter [2].

No patient received treatment for latent TB. Indeed, although international guidelines recommend starting treatment of latent TB infection in high-risk persons, in Togo, the national strategy has not yet integrated it. The reasons are the difficulties of getting patients to accept taking medication for a period of 6 months while they are fully asymptomatic. This would decrease observance of the treatment which, in turn, would cause the emergence of multi-resistant mycobacteria of which treatment is difficult and too expensive.

Conclusion

The latent TB infection is a poorly elucidated problem in Togo where TB and HIV are endemic. The results obtained in this study show the extent of what could be done in order to find solutions to reduce the incidence of TB disease. The TST, although somewhat unspecific, can represent an excellent screening test in developing countries with limited resources; although IGRA is more specific to the latent TB diagnosis, it is also very expensive.

Conflict of interest

The authors declare that they have no conflict of interest.

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