

MYCOBACTEREMIA IN TUBERCULOSIS PATIENTS WITH HIV INFECTION*

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Summary:

Background: Mycobacteremia in HIV positive tuberculosis patients is associated with extra-pulmonary tuberculosis and disseminated tuberculosis.

Objective: To study the occurrence of mycobacteremia among HIV-infected patients with tuberculosis (both pulmonary and extra-pulmonary forms) using radiometric BACTEC method.

Methods: HIV positive patients admitted to the Government Hospital of Thoracic Medicine with a clinical diagnosis of tuberculosis were screened. HIV serology was reconfirmed using ELISA (two different tests) at Tuberculosis Research Centre. Five ml of venous blood was collected on the day of admission to the ward before start of anti-tuberculosis therapy.

Results: Of the 105 patients screened, 85 were found to be eligible for analysis. Patients were aged between 20-40 years, with a male preponderance (5:1). Pulmonary tuberculosis was the predominant form of tuberculosis (85%), while 15 % had associated extra-pulmonary involvement. Eight-four percent of the patients had CD4 counts of less than 200 cells/mm³, with 42% being below 50 cells/mm³. Four of the 85 patients were blood culture positive; three were identified as *M.tuberculosis* and one as *Mycobacterium phlei*.

Conclusions: Mycobacteremia was detected in 4% of HIV positive patients with tuberculosis. All of them were immunosuppressed with CD4 counts of <50 cells/m³. More work needs to be done in India to understand the risk factors and outcome of patients with mycobacteremia.

Key Words: Mycobacteremia; Tuberculosis; TB/HIV

INTRODUCTION

Mycobacteremia has been described in febrile HIV-positive individuals with all forms of tuberculosis as varying from 10-64%, depending on the clinical presentation. Both tuberculosis and HIV pose major public health problems in India. Estimated 2 million new cases of tuberculosis and 5,00,000 deaths occur every year in this country. About 40% of the adult population is infected with *M.tuberculosis* and the incidence of smear positive disease is 2-4/100,000¹. The first HIV positive person in India was located in Chennai in 1986 and since then the epidemic has grown rapidly. It is estimated that there were 3.86 million HIV-positive persons in India at the end of 2001 and that the prevalence in the adult population was about 0.6%. The six high prevalence states where the prevalence in ante-natal women is over 1% include Tamil Nadu, Karnataka,

Andhra Pradesh, Maharashtra, Nagaland and Manipur².

Pulmonary tuberculosis is still the most common form of tuberculosis, even among HIV positive persons, though extra-pulmonary tuberculosis and disseminated tuberculosis have become more common than before. Mycobacteremia is a key event in the pathogenesis of tuberculosis but is usually not detected in immunocompetent individuals³. The reported prevalence of mycobacteremia in HIV+ persons with tuberculosis ranges from 10 to 64%⁴. It has been recognized as an important cause of pyrexia of unknown origin (PUO) in HIV-infected patients⁵. The frequency of mycobacteremia has not been studied well in India. This study was designed to look for mycobacteremia in patients with HIV and tuberculosis admitted to a tertiary care centre.

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MATERIAL AND METHODS

This prospective study was conducted between June and November 2001 at the Government Hospital for Thoracic Medicine Tambaram. One hundred and five consecutive patients admitted with a clinical diagnosis of tuberculosis were recruited; a detailed history was taken and physical examination was done. Blood was examined by culture and for CD4 counts. Five ml of blood was inoculated into a BACTEC bottle (BACTEC 13A, Becton Dickinson) and processed for isolation of mycobacteria using BACTEC 460 TB system. Positive BACTEC cultures were confirmed for the presence of acid-fast bacilli by fluorescence microscopy and sub-cultured further on conventional (LJ) medium. The CD4 lymphocyte count was measured by flow cytometry by standard techniques using Becton Dickinson FACScan.

RESULTS

Patients were aged between 20-40 years, with a male preponderance (5:1). In all, 85 tuberculosis patients were confirmed to have HIV infection by positive results on 3 ELISA tests. Of the HIV positive patients, 85% had presented with symptoms suggestive of pulmonary tuberculosis, while 15% had associated extra-pulmonary involvement along with pulmonary disease. The predominant clinical features were fever (75%), cough (69%) and weight loss (50%). Almost 95% had a history of high-risk sexual behavior and 44%

of these patients were being simultaneously treated for some type of sexually transmitted disease or HIV associated symptoms like chronic diarrhoea (31%), oral thrush (21%) and lymphadenopathy (19%). The radiographic features included extensive bilateral parenchymal infiltrates (in 80%), the rest showing atypical features like lower lobe infiltrates, pleural involvement and hilar adenopathy.

The CD4 counts of the HIV positive patients ranged between 32 and 750 cells/mm³ (mean 125 cells/mm³); 84% of the patients had CD4 counts of <200 cells/mm³ and 42% had a CD4 count of <50 cells/mm³, indicating that most patients had profound immunosuppression at the time of investigation for symptomatic HIV/TB disease. CD4 counts were available for 10 of 20 HIV seronegative pulmonary tuberculosis patients and the mean was 932 cells/mm³ (range 770 to 1100 cells/mm³).

Mycobacterium tuberculosis was isolated from the blood of three patients (3.5%) and *Mycobacterium phlei* from one (Table 1). The time taken for identification of mycobacteremia ranged from 22-43 days. All the three patients with *M. tuberculosis* bacteremia had CD4 counts of less than 50 cells/mm³. One of the *M. tuberculosis* isolates was observed to be multi-drug resistant. Considering only those patients who had CD4 counts <100/mm³, 3(10%) out of 30 had *M. tuberculosis* bacteremia.

Table 1: Prevalence of mycobacteremia in patients with tuberculosis with/without HIV sero-positivity

Category	CD4 Count (cells/mm ³)					Mycobacteremia found
	>500	200-500	100-200	<100	NA	
HIV Negative (N=20)	10	-	-	-	10	0/20
HIV Positive (N=85)	2	6	10	30	37	4/85*

NA = Not available

* 3 patients with *M. tuberculosis* and 1 with *M. phlei*

DISCUSSION

This study found the proportion of disseminated tuberculosis in Indian tuberculosis patients with HIV and tuberculosis to be 3.5%, with different levels of immunodeficiency. The proportion was somewhat lower than that reported by others¹⁻³ which could be because patients were not selected on the basis of CD4 counts or for investigation of PUO. Bacteremia due to mycobacteria has been reported in HIV/AIDS patients from developed as well as developing countries; *M. avium* is the most common agent found in studies from developed countries while *M. tuberculosis* is more common in patients from developing countries⁶. Further, the frequency of disseminated tuberculosis as evidenced by mycobacteremia increases as CD4 counts fall⁷. In our study, if only patients with CD4 counts of <100/ml are considered, the occurrence of mycobacteremia due to *M. tuberculosis* increases to 10 %. Occurrence of mycobacteremia is usually related to the form of tuberculosis, being 17% in extra-pulmonary tuberculosis and 43-83% in disseminated tuberculosis⁸. Usually, the diagnosis of disseminated tuberculosis is difficult but blood culture could help in diagnosing mycobacteremia in patients with low CD4 counts. In this study, 3 of the pulmonary tuberculosis patients were found to have disseminated tuberculosis based on mycobacteremia detected, *M. phlei*, which is a saprophyte, having never been reported to cause disease/infection, even in the HIV setting. More work needs to be done in India to determine the prevalence of non-tuberculous mycobacteremia in HIV positive patients. Research is also required to investigate their clinical course and outcome to determine if these patients need more aggressive therapy.

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REFERENCES

1. Dye C, Scheele S, Pathania V, Raviglione MC. Global burden of tuberculosis: estimated incidence, prevalence and mortality by country. *JAMA* 1999;282:677
2. National AIDS Control Organization, New Delhi, December 21001.
3. Von Reyn CF. The significance of bacteremic tuberculosis among persons with HIV infection in developing countries. *AIDS* 1999;13:2193
4. Robert W Shafer, Robert Goldberg, Marcellino Sierra and Aaron E Glatt. Frequency of *Mycobacterium tuberculosis* bacteremia in patients with tuberculosis in an area endemic for AIDS. *Am Rev Respir Dis* 1989;140:1611
5. Lennox Archibald, Meyno O den Dulk, Kisali J Pallangyo and L Barth Reller. Fatal *Mycobacterium tuberculosis* blood stream infections in febrile hospitalized adults in Dar es Salaam, Tanzania. *Clin Infect Dis* 1998;26:290
6. L Clifford McDonald, Lennox K Archibald, Sunthorn Rheanpumikankit, Somsit Tansuphaswadikul, Boonchuay Eampokalap, Okey Nwyananawu et al. Unrecognized *Mycobacterium tuberculosis* bacteremia among hospital inpatients in less developed countries. *Lancet* 1999;354:1159
7. Brenda E Jones, Summer MM Young, Diana Antoniskis, Paul T Davidson, Francoise Kramer and Peter F Barnes. Relationship of the manifestations of tuberculosis to CD4 cell counts in patients with human immunodeficiency virus infection. *Am Rev Respir Dis* 1993; 148:1292
8. Thomas W Barber, Donald E Craven and William R McCabe. Bacteremia due to *Mycobacterium tuberculosis* in patients with human immunodeficiency virus infection. *Medicine* 1990;69(6):375

GENERAL COUNSELLING FOR HIV

With the uprising HIV epidemic in the country, it has become imperative for every physician to acquire knowledge and skills for HIV counselling, comprising general, post-test and HIV-positive patient counselling.

- ❑ General counselling involves several aspects, namely, personal, phycho-social, professional and financial.
- ❑ For personal and psycho-social counselling, the physician must educate as well as assist a person to understand and accept the changes, if any, which are required to gain self-assurance, maintain quality of life, review future goals and plans, forge family acceptance/adjustments and decide on social/community relationships.
- ❑ For professional and financial counselling, the physician must practise how to educate in order to convince and assure, yet stop short of creating confusion and scare. If the information conveyed regarding the disease, its prevention as well as treatment, is adequate it will help in making a person take control of his situation and make his own decision instead of feeling helpless and dependent on others.
- ❑ Try to focus on what can be done and how, instead of what might inevitably happen. Discuss how much can be achieved with the financial and other resources available instead of technology that is available but is out of reach.
- ❑ Join hands in equipping the person to cope with the situation, convincing him/her that HIV infection does not always progress to AIDS, that AIDS is not necessarily fatal and that means for long term survival are available.
- ❑ Kindle hope that the system will support his efforts for long-term survival and that there is no need to feel lonely and let down.

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