ORIGINAL ARTICLE

Immune Reconstitution Tuberculosis in HIV Patients after Antiretroviral Therapy

Rajasekaran S, Vijila, Ravichandran N

Abstract

Free antiretroviral therapy is being given to eligible people living with HIV in India since April 2004. Govt. Hospital of Thoracic Medicine, Tambaram Sanatorium, Chennai is one of the largest centers managing HIV/AIDS patients with antiretroviral therapy in India.This study finds out the incidence of tuberculosis as the manifestation of 'Immune Reconstitution Syndrome (IRS)' after the initiation of Antiretroviral therapy in patients with HIV/AIDS. All the patients, placed under ART, were followed up for the occurrence of tuberculosis from April 2004 to December 2005 at GHTM, Tambaram Sanatorium, Chennai. 2330 HIV patients were initiated antiretroviral therapy till December 2005 and of whom 1409 (61%) were already treated for tuberculosis. 302 (12.9%) had IRS and 81 (3.5%) had tuberculosis, as the component of IRS. Occurrence of tuberculosis as IRS manifestation is significantly high after antiretroviral therapy. This results in starting or restarting anti tuberculosis treatment with the changed or modified antiretroviral therapy in a large number of patients, escalating treatment cost.

Key words

HIV, Tuberculosis, Immune Reconstitution Syndrome

Introduction

Immune Reconstitution Syndrome, occurring in persons with HIV after initiation of Anti Retroviral Therapy (ART), was recognised in mid-1997 (1) and early 1998 (2) by two groups of physicians, while describing atypical manifestations of CMV retinitis and MAC disease with abscess formation. More and more people are being initiated on ART under the National AIDS Control Programme in India. With a high prevalence in Indian population, Tuberculosis as a manifestation of Immune Reconstitution Syndrome is most likely to occur frequently among HIV patients after ART.

Material and Methods

Government Hospital of Thoracic Medicine, Tambaram Sanatorium (GHTM - Tambaram) is participating in the National free ART programme, ever since its inception, April 2004. All the HIV patients were screened for co-existing opportunistic infections, Tuberculosis, Immunological status and their eligibility and preparedness to be placed under Anti Retroviral Therapy.

All these patients were specifically screened for the possible presence or absence of tuberculosis by sputum smear microscopy for AFB, Chest radiography, ultra sonogram of abdomen. Examination of all the specimens of patients-FNAC of lymph nodes, Bronchial aspirate, pleural, pericardial and ascitic fluid and CSF for M. tuberculosis was performed in selected patients.

All those HIV patients initiated on ART (Zidovudine or Stavudine + Lamivudine + Nevirapine) were followed up every month. Occurrence of tuberculosis was detected, either as a part of Immune restoration or otherwise and treated accordingly.

From Govt. Hospital of Thoracic Medicine, Tambaram Sanatorium, Chennai-600 047.
Correspondence to : Dr. S. Rajasekaran, Superintendent, Govt. Hospital of Thoracic Medicine, Tambaram Sanatorium, Chennai-600 047.

Results

GHTM, Tambaram enrolled 2330 eligible and prepared HIV patients on ART from April 1, 2004 to December 2005. Majority (82.1%) was in the age group of 15 to 44 years in the male dominated (59%) study population (Table 1).

Immune Reconstitution Syndrome was found to occur for various opportunistic infections in 302 patients (13%). 94 patients (4.03%) were found to develop or being detected to have Tuberculosis after starting ART in them. As both early as well as late phase of Immune Restoration activity paving way for Immune Reactivation of TB occurs within 6 months, 81 patients (35%) were considered emerging with Immune Reconstitution Tuberculosis (Table 2).

Extra-pulmonary tuberculosis was found to be dominant proportion (61.7%) of Immune Reconstitution TB (IR-TB) in the study population (Table 3). Both the intra-thoracic and extra thoracic lymph nodal tuberculosis found to occur in 37% patients. Of the 31 patients developed pulmonary TB, 10 were found to be expectorating AFB in their sputa.

While 93% of IR-TB patients had base level CD4 count less than <200 cells/ mL of blood, 42% had fewer than 50 CD4 cells (Table 4). All those developed IR-TB, were treated with anti-inflammatory drugs, including steroid for a brief period and placed under Rifampicin containing Anti-TB treatment.

As Rifampicin has greater suppressive action on the blood level of Nevirapine, it was replaced by another potent antiretroviral agent, Efavirenz.

Table 1

Age and Sex distribution of the study population

Age Group	Male	Female	Total	%
Upto 14	105	98	203	8.7
15-29	15	342	494	21.2
30-44	957	463	1420	60.9
> 44	155	58	213	9.2
Total	1369	961	2330	100
%	59	41		

Table 2

Time of TB detection after ART

Months	Patients detected with TB	Immune reconstitution TB	%
Upto 3	60	60	3.5
4-6	21	21	
> 6	13	--	
Total	94	81	

Table 3

Immune Reconstitution TB : Manifestations

TB Manifestations	Patients	%
Pulmonary TB	31	38.3
Intra-Thoracic Lyphnodes	23	28.4
Extra-Thoracic Lyphnodes	7	8.6
TB Abdomen	7	8.6
TB Pleural Effusion	7	8.6
TB Meningitis	5	6.1
TB Spine	1	1.2
TOTAL	81	99.8

Table 4

Immune Reconstitution TB and Base level CD4 Cells

Base Level CD4 Cell	IR-TB	%
Upto 50	34	42.0
51-100	21	25.9
101-150	15	18.5
151-200	5	6.2
> 200	6	7.4
TOTAL	81	100

Discussion

Immune Reconstitution Tuberculosis assumes greater importance in Indian scenario, as Government of India is determined to scale up Antiretroviral therapy for thousands of eligible AIDS patients. With the increasing HIV-TB co-infection prevalence, identification of the

clinical condition IR-TB at the earliest and institution of appropriate treatment are essential.

While the Immune Reconstitution syndrome was observed for all kinds of opportunistic infections to the extent of 13%, IR-TB was found to be the cause in 3.5% of 2330 patients studied. An earlier Indian study in a smaller group of 144 HIV patients on ART observed the incidence of Immune Reconstitution Syndrome (TB) to be 15.2 cases per 100 patients years (3). The implication of Antiretroviral programmes in countries with high TB prevalence needs prospective investigation of a larger cohort (4).

GHTM, Tambaram is on the right stage to provide the necessary insight of a large group of HIV patients on ART with 97% of patients reporting with more than 95% of treatment adherence.

Disseminated TB was the predominated manifestation of IR-TB in this study as well as reported in western world (5). The major impact of IR-TB in the programme setting is, apart from the increased pill burden for the patients-taking treatment for HIV and TB, the escalating Efavirenz containing ART treatment cost.

Acknowledgement

The wholehearted assistance provided by the entire ART team, doctors, nurses, counsellors, pharmacists and data entry operators is gratefully acknowledged.

References

1. Jacobson MA, Zegans M, Pavan PR *et al*. Cytomegalovirus retinitis after initiation of HAART. *Lancet* 1997 ; 349 : 1443-45.
2. Race EM, Adelson-Mitty J, Kriegel GR *et al*. Focal mycobacterial lymphadenitis following initiation of protease-inhibitor therapy in patients with advanced HIV-1 disease. *Lancet* 1998 ; 351 : 252.
3. Kumarasamy N, Chaguturu S, Mayer KH *et al.* Incidence of Immune Reconstitution Syndrome in HIV-Tuberculosis co-infected patients after initiation of generic antiretroviral therapy in India. *J AIDS* 2004 ; 37 : 1574-76.
4. Breen RA, Smith CJ, Cropley I, Johnson MA, Lipman MC. Does Immune reconstitution syndrome promote active tuberculosis in patients receiving highly active antiretroviral therapy? *AIDS* 2005 ; 19 : 1201-06.
5. Michailidis C, Pozniak AL, Mandalia S, Basnayake S, Nelson MR, Gazzard BG. Clinical Characteristics of IRIS Syndrome in patients with HIV and Tuberculosis. *Antivir Ther* 2005 ; 10 : 417-22

GUIDELINES FOR ARTICLES TO BE SUBMITTED UNDER EACH CATEGORY TO *"JK SCIENCE"* JOURNAL OF MEDICAL EDUCATION & RESEARCH

Article Type	Summary: No. of Words	Key Words: No. of Words	Text : No. of Words	Sub-Headings	Tables: Max. No.	Figures: Max. No.	No. of References
ED	NR	NR	600-800	NR	NR	NR	£ 10
RA	NR	NR	3000	Variable	2	2	30-35
OA	200	3-5	2000	Standard	4	2	20-25
SC	100	3-5	1200	Standard	2	1	10-15
CR	< 50	3-5	600-800	Standard	1	3	< 10
DR	NR	NR	1000	NR	1	1	< 10

ED = Editorial RA = Review Article; OA = Original Article; SC = Short Research Communication; CR = Case Report; DR = Drug Review; NR = Not Required