LEPROSY AND HIV CO-INFECTION

A prospective study at ALERT, in Ethiopia

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LSHTM/ ALERT
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HIV and Leprosy

HIV causes loss of effective cell mediated immunity and affects CD4+ function

Associated with opportunistic infections including mycobacteria *M. Tuberculosis* and *M. avium-intracellularare*

What would the effect of HIV infection be on leprosy?

Early predictions
- Increased case rate
- More lepromatous disease
- Worse response to MDT
- Fewer immune complications
Findings so far

• Being HIV+ve does not increase the risk of developing leprosy
• HIV infection does not preclude the usual range of immune responses to *M. leprae* as seen in skin biopsies
• HIV infected patients do not seem to have more lepromatous disease (FioCruz 2008)
• No evidence of higher relapse rates
  – But MDT regimens have very low relapse rates (<1% per)
  - Current MDT regimens appear adequate
• No data on adverse drug reaction profiles for co-infected patients taking leprosy MDT
• Leprosy /HIV patients appear to be at higher risk of reactions
An prospective study to get a clearer picture

• Descriptive data on skin lesions

• Descriptive data of nerve function

• Frequency of leprosy reactions

• Descriptive data on leprosy as IRIS

• Comparison of histopathological/immunological features
ETHIOPIA - Statistics

- Leprosy: 4187 new cases in 2007
- Adult HIV prevalence in 2005 → 2012:
  - 3.5% average → 1.5%
  - 11.7% urban → 4.3%
    (UNAIDS)
- HIV prevalence in leprosy patients:
  3.2% (1988) to 6.5% (1992) (Frommel)
Patient selection

• Entry criteria
  Individuals newly diagnosed or within 6 months of diagnosis with any type of leprosy, using the standardised WHO definitions (16-65 years old and be able to give informed consent).

• Exclusion criteria
  Patients who do not give consent; not willing to return for follow-up.
Two groups

Group 1: Leprosy patients with HIV co-infection

1. Patients known to be HIV positive who develop leprosy

2. Patients who are newly diagnosed, or within 6 months of diagnosis with leprosy and have HIV testing for some reason

3. Patients on HAART presenting with IRIS

4. Patients in the ALERT cohort: HIV patients on HAART, regularly examined for evidence of leprosy

Group 2: Leprosy patients HIV negative matched for leprosy type/age/sex
EVERY NEW LEPROSY PATIENT GETS AN HIV TEST!
(68-88% with PCT)

Clinical assessment
• Structured history – HIV/ Leprosy/ general
• Co-morbidities (TB, OI...)
• Medication history
• General clinical examination
• Skin examination
• Nerve function

Investigations
• HIV test
• CD4 count and viral load – 6 monthly and at time of leprosy reaction
• Skin smears
• Skin punch biopsy
• Skin biopsy for histopathology samples
• Blood sample - immunology study
RESULTS

• Enrolment period: 3rd Dec 2009 – to 15th Mar 2013
• 46 patients recruited
• 26 HIV positive
• 20 HIV negative (only 9 HIV negative patients came for >6months FU)
• (excluded 10 pts with leprosy for a long time)
## Baseline characteristics

<table>
<thead>
<tr>
<th>PARTICIPANTS with newly diagnosed leprosy</th>
<th>HIV positive</th>
<th>HIV negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of patients</td>
<td>26</td>
<td>20</td>
</tr>
<tr>
<td>Sex distribution</td>
<td>14 males, 12 females</td>
<td>14 males, 6 females</td>
</tr>
<tr>
<td>Median age (years)</td>
<td>35</td>
<td>30</td>
</tr>
<tr>
<td>Average recruitment BI:</td>
<td>3.8</td>
<td>2.1</td>
</tr>
<tr>
<td>MDT status</td>
<td>20 pre MDT, 3 on MDT, 3 RELAPSE</td>
<td>20 PRE MDT</td>
</tr>
</tbody>
</table>
Clinical Ridley- Jopling classification

26 patients with HIV

- 14 LT
- 4 BB
- 2 LL
- 5 BL
- 1 Neural

20 patients without HIV

- 16 BT
- 4 BB
- 2 LL
- 1 Neural
Presentation of co-infected patients (26)

- 50% (13) were patients from the HIV clinic, referred for a dermatological complaint
- 27% (7) were patients attending for leprosy diagnosis and HIV screening turned out to be positive (2 knew)
- 11% (3) present with IRIS
- 11% (3) OTHER – eye clinic, surgical clinic, relapse
TIMING OF DIAGNOSIS

- HIV first 65%
- Leprosy first (R) 8%
- HIV and leprosy at same time 27%

0-36 MONTHS

MEAN CD4 AT LEPROSY DIAGNOSIS: 264 (16-615)
NO CORRELATION WITH LEPROSY SIGNS, OR REACTION

13 PATIENTS (OF 16) WITH KNOWN HIV WERE ON HAART

60% HAD HISTORY OF OPPORTUNISTIC INFECTIONS (8 TB)
### Reactions

<table>
<thead>
<tr>
<th>Reaction status at diagnosis</th>
<th>Number</th>
<th>Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>RR</td>
<td>16</td>
<td>12 S, 3 mod, 1mild</td>
</tr>
<tr>
<td>ENL</td>
<td>4</td>
<td>2mod, 2 severe</td>
</tr>
<tr>
<td>Neuritis</td>
<td>3</td>
<td>3 severe</td>
</tr>
<tr>
<td>NO</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

**Reaction flare up**

Flare up rate of RR and ENL was high with 90% of patients having more than 3 flare ups in the 2 years.

- ENL AT 4/12 MDT
- RR AT 8/12 MDT
- 1 NO REACTION IN 3 YRS
Treatment of reactions

- Standard prednisolone regimens used for both RR and ENL according to severity
- Patients with lower CD4 had more recurrences and more resistance to prednisolone.
- No adverse reactions to treatment seen in this group
Leprosy as IRIS

Case definition
Leprosy and/or T1R or ENL within 6/12 of starting HAART

- Advanced HIV infection
- Low CD4 before starting HAART
- Increase in CD4 after HAART
- Viral load falling

3 leprosy IRIS cases

- 4 years on ART, stopped, very sick 3/12 later. Re-started ART and TB Tx: 2/12 later numerous inflammed lesion and neuritis (CD4 19 to 120)
- Hypopigmented lesions 4/12 into ART; 1/12 later severe RR (CD4 11 to 121)
- ENL 2/12 into ART (CD4 98 to 230)
HIV/Leprosy Summary

• HIV infection does not appear to impair local immune response to *M. leprae*
• Patients may present with typical leprosy lesions
• Higher risk of Type 1 reactions, and recurrences
• Presentation as IRD
• Treat with MDT
• Long immuno-suppression may be needed
Limitations of Study:

• Small number of patients.
• Potential loss to follow up.
• TIMING OF INFECTIONS!
APPROVALS AND ACKNOWLEDGMENTS

The study was approved by:
Ethics Committee of the LSHTM
ALERT and AHRI Ethical Review Committee
National Ethics Review Committee of Ethiopia

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