Immune Reconstitution Inflammatory Syndrome (IRIS) in HIV-schistosomiasis co-infected patients undergoing anti-retroviral treatment

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HIV and schistosomiasis

• In sub-Saharan Africa the prevalence of helminths is overwhelming and Spread of HIV/AIDS is still alarming

• Helminths are reported to have influence on the pathogenesis of HIV-1

• Mwinzi et al., 2004 reported pathology associated with S. mansoni in HIV-1 patients leading to reduced CD4+ T cells
Immune Reconstitution Inflammatory Syndrome (IRIS)

- IRIS occurs during HAART-associated immune recovery, caused by pathogen-specific immune responses to pre-existing or latent infections
- Shelburne et al., 2005 reported that 10-40% of patients who start HAART developed IRIS
- Three (3) cases of Schistosoma-related IRIS reported so far
Objectives

• To develop a case definition for Schistosoma-associated IRIS
• To determine the prevalence for Schistosoma–associated IRIS
**Study design**

**Informed consent and recruitment**

**Parasitological screening and VCT + clinical screening**

- Time 0:
  - 2 weeks
  - Eosinophil count, IgE, liver function tests and parasite screening, CRP and neopterin
  - CD4 counts and HAART decision

- 1 month:
  - 1st IRIS event or 7 months

- 3 months:
  - CD4 and Vit D, viral load

- 12 months:
  - Eosinophil count, IgE, liver function tests and parasite screening, CRP and neopterin; Vit D, CD4 and viral load
Methodology

HIV infected

Test for Schisto
Either –ve or +ve; CD4 count

If positive: treat with PZQ

CD4< 350
Plan to start HAART

Ultrasound and lab + stool

F/up at 2wks: lab+stool

F/up at 1 month: lab +stool

F/up at 3 months: lab + stool, ultrasound

F/up at 6 months; one year: lab + stool, ultrasound

If Schisto-complaints (diarrhea, skin problems, abdominal distention, liver test elevation etc):
Extra F/up visit, extra Lab, Extra stool, extra Ultrasound

CD4>350
Not starting HAART

F/up at 6 months: Lab, stool

Follow up at 12 months: lab + stool
<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>S. mansoni</strong></td>
<td>541</td>
<td>68.8</td>
</tr>
<tr>
<td><strong>HIV (HAART)</strong></td>
<td>126</td>
<td>23.29</td>
</tr>
<tr>
<td>Male</td>
<td>50 (24-62 yrs)</td>
<td>43.48</td>
</tr>
<tr>
<td>Female</td>
<td>65 (22-63 yrs)</td>
<td>56.52</td>
</tr>
<tr>
<td><strong>Hookworm</strong></td>
<td>2</td>
<td>1.74</td>
</tr>
<tr>
<td><strong>Ascaris</strong></td>
<td>0</td>
<td>N.A</td>
</tr>
<tr>
<td><strong>Trichuris</strong></td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td><strong>malaria</strong></td>
<td>0</td>
<td>N.A</td>
</tr>
<tr>
<td><strong>T.B</strong></td>
<td>0</td>
<td>N.A</td>
</tr>
<tr>
<td><strong>co-infection (with more than 1 other)</strong></td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>
## Results (1)

Prevalence (n) of schistosomiasis, HIV, and IRIS at each follow-up

<table>
<thead>
<tr>
<th>Follow-up</th>
<th>HIV+(%)</th>
<th>S. Mansoni (n)</th>
<th>+ve</th>
<th>IRIS (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>100</td>
<td>93 (75%)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2 weeks</td>
<td>100</td>
<td>30 (23.8%)</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>1 month</td>
<td>100</td>
<td>34 (27%)</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>3 month</td>
<td>100</td>
<td>43 (34%)</td>
<td>12</td>
<td></td>
</tr>
</tbody>
</table>
Format for Case definition

**Sm treatment status**

- Sm diagnosed and treated before ART initiation
- Not treated for Sm, diagnosed to be negative

**Outcome**

- Paradoxical Rxn within 3 months
- Active Sm egg release on ART

**Case definition**

- Paradoxical Schistosoma associated IRIS
- HAART associated schistosomiasis (could be unmasking schistosoma-IRIS)

Schematic presentation of the possible forms of schistosoma associated IRIS.
Adapted from Graeme Meintjes et al Lancet Infect Dis 2008
# Results (2) Case study 1

<table>
<thead>
<tr>
<th>Follow-up</th>
<th>S.m +/-</th>
<th>CD4</th>
<th>Viral load copies</th>
<th>Clinical manif.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>+ (treat)</td>
<td>76</td>
<td>5.65</td>
<td>-</td>
</tr>
<tr>
<td>2 weeks</td>
<td>-ve</td>
<td>72</td>
<td>3.37</td>
<td>2, 3, 4, 5 &amp; 6</td>
</tr>
<tr>
<td>1 month</td>
<td>+ve</td>
<td>72</td>
<td>&lt;</td>
<td>2, 3, 4, 5, 6, 7, 8</td>
</tr>
<tr>
<td>3 month</td>
<td>+ve</td>
<td>243</td>
<td>&lt;</td>
<td>1, 2, 3, 4, 5, 6, 8</td>
</tr>
</tbody>
</table>

1-Emergence of hepato-splenomegaly and vein enlargement, 2-Increased CD4, 3-Reduced viral load, 4-bloody/watery diarrhea, 5-skin rashes, 6-abdominal pain 7 – abdominal distention, 8 – starts excreting eggs

**Case of Paradoxical IRIS : n = 21**
## Results (3) Case study 2

<table>
<thead>
<tr>
<th>Follow-up</th>
<th>S. m +/-</th>
<th>CD4</th>
<th>Viral load copies</th>
<th>Clinical manif.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>-ve</td>
<td>186</td>
<td>5.78</td>
<td>-</td>
</tr>
<tr>
<td>2 weeks</td>
<td>-ve</td>
<td>240</td>
<td>2.91</td>
<td>2, 3, 4, 5, 6</td>
</tr>
<tr>
<td>1 month</td>
<td>-ve</td>
<td>267</td>
<td>&lt;</td>
<td>2, 3, 4, 5, 6</td>
</tr>
<tr>
<td>3 month</td>
<td>+ve</td>
<td>279</td>
<td>&lt;</td>
<td>2, 3, 4, 5, 6, 8</td>
</tr>
</tbody>
</table>

1-Emergence of hepato-splenomegaly and vein enlargement, 2-Increased CD4, 3-Reduced viral load, 4-bloody/watery diarrhea, 5-skin rashes, 6-abdominal pain 7 – abdominal distention, 8 – starts excreting eggs

**Case of Unmasking** IRIS n= 9
CD4 and EPG at baseline

\[ P = 0.017 \]
Results (4)

Preliminary/proposed case definition specific for \textit{Schistosoma}-associated IRIS

Criteria for suspected cases:
- An initial presence of schistosomiasis or re-emergence of schistosomiasis and a combination of the following: Bloody/watery diarrhea, skin rashes, abdominal pains, skin lesions, abdominal distention.
- Adequate adherence to ART

Criteria for confirmed cases:
- Radiological examinations showing worsening or emergence of hepato-splenomegaly, portal vein enlargement
- Increase in CD4+ lymphocyte count and significant reduction in viral load count, adequate adherence to ART
- Exclusion of other conditions that could explain the clinical manifestations of the patient
Conclusions

- Some patients (23.8%) with HIV and schistosomiasis co-infection develop *Schistosoma* associated IRIS upon HAART.

- Low CD4 and egg counts at the start of HAART seems the main predictors of *Schistosoma* associated IRIS.
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