A Paradoxical Treatment of Mycobacterial Immune Reconstitution Inflammatory Syndrome

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Introduction

Immune reconstitution inflammatory syndrome (IRIS):
- A collection of inflammatory disorders in HIV-infected patients with severe lymphopenia after the initiation of antiretroviral therapy (ART).
- IRIS can cause significant morbidity and mortality.
- Corticosteroids are the mainstay of therapy in managing severe IRIS.

Tumor Necrosis Factor (TNF):
- Critical in the defense against mycobacterial infections.
- Inhibition of TNF has been shown to lead to the increased incidence of active TB.

Infliximab:
- A chimeric anti-TNF monoclonal antibody. Here we report the use of infliximab in HIV-infected patients with mycobacterial IRIS unresponsive to prednisone or corticosteroid treatment.

Methods

- The three patients were participants of a completed observational study evaluating predictors of IRIS
  NCT00286767: study of HIV-infected, ART-naive patients with CD4+ T cells <100 cells/µL, patients were followed for up to 96 weeks after ART-initiation
- CD4 T cell counts and HIV-RNA were measured at week(s) 0, 2, 4, 8, 12, 24, 36 and 48.
- Cryopreserved peripheral blood mononuclear cells from each patients were thawed, rested for 2hrs., and stimulated for 6hrs with heat-killed MAC or PPD in the presence of anti-CD49d, brefeldin and monensin at 37°C and 5% CO2.
- After stimulation, cells were stained with fluorescent conjugated antibodies to intracellular cytokines and detected using an LSR II flow cytometer.
- Plasma inflammatory markers including CRP, IL-6, IFNy, and TNF were measured using a multi-array electrochemiluminescence assay.
- Data were analyzed using FlowJo version 9.7.6.

Case Reports

<table>
<thead>
<tr>
<th>Patient</th>
<th>Description</th>
<th>ART</th>
<th>Unmasking MAC-IRIS</th>
<th>Infliximab</th>
<th>Paradoxical TB-IRIS</th>
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</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>31 years old African American male diagnosed with Pneumocystis pneumonia (PCP).</td>
<td>Emtricitabine 200mg daily.</td>
<td>Presented with R cervical lymphadenopathy 4 weeks after the initiation of ART.</td>
<td>Tapering of prednisone was unsuccessful with worsening of lymphadenopathy.</td>
<td>On tapering of prednisone developed chylothorax likely due to obstruction of thoracic duct by lymphadenopathy.</td>
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<tr>
<td>Patient 2</td>
<td>41 years old male from Honduras presented with R knee pain and swelling.</td>
<td>Emtricitabine 200mg daily.</td>
<td>Presented with R cervical lymphadenopathy 4 weeks after the initiation of ART.</td>
<td>Infliximab was given every 2 weeks for a total of 3 infusions.</td>
<td>No clinical improvement with prednisone tapering was successful.</td>
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<tr>
<td>Patient 3</td>
<td>42 years old male from Cameroon presented with cervical and axillary lymphadenopathy.</td>
<td>Emtricitabine 200mg daily.</td>
<td>Presented with painful cervical and axillary lymphadenopathy and fever a week after the initiation of ART.</td>
<td>Unmasking MAC-IRIS.</td>
<td>Paradoxical TB-IRIS.</td>
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Figure 1: CT scan of the neck showing lymphadenopathy occurring the right internal jugular vein in patient 1 (a) before and (b) after infliximab infusion. Chest X-ray showing right pleural effusion in patient 2 (c) and over 2L of fluid drained from chylothorax (d).

Conclusions

- Infliximab use was associated with clinical improvement in three steroid-unresponsive mycobacterial IRIS patients.
- No obvious adverse impact on immune recovery and virologic control was observed in these patients.
- The use of TNF inhibitor in treating severe mycobacterial IRIS could merit further assessment in clinical trials.

Acknowledgement

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