sCD163, T Cell Activation, and HIV Progression in Perinatally-Infected HIV+ Children

Introduction

CD163 is a hemoglobin scavenger receptor expressed primarily on monocytes and macrophages that endocytoses haptoglobin-hemoglobin complexes. It also plays a role in erythroblast adhesion and immune sensing of bacteria. When exposed to pro-inflammatory stimuli such as lipopolysaccharide (LPS), Fcγ receptor crosslinking, or oxidative stress, CD163 sheds via proteinase-mediated cleavage as soluble CD163 (sCD163). Thus, plasma levels of sCD163 reflect non-specific monocyte and macrophage activation.

In HIV infection, chronic inflammation in the innate and adaptive immune systems is associated with disease progression. HIV+ adults have high plasma sCD163 levels that persist despite antiretroviral treatment (ART). Elevated plasma sCD163 levels in HIV+ adults have been linked to non-AIDS morbidities including cardiovascular disease and neurocognitive dysfunction. Moreover, sCD163 predicts all-cause mortality in adults. With each milligram per liter increase in plasma sCD163 levels, the incidence of death increases by 6%.

In children, persistent inflammation during development leads to additional long-term comorbidities such as cognitive developmental delay and early onset cardiovascular disease. There is limited data on plasma sCD163 levels in children. We investigated plasma sCD163 levels in HIV+ children and their correlations with HIV disease progression, T cell activation and intestinal mucosal damage.

Methods

We studied a Kenyan cohort of 77 perinatally-infected HIV+ children, comprising 44 untreated (ART-) and 33 on antiretroviral therapy (ART+), and 45 HIV- children. We evaluated plasma sCD163 levels in HIV+ children and their correlations with HIV disease progression, T cell activation and intestinal mucosal damage.

Results

Treatment naive HIV+ children have higher levels of plasma sCD163 compared to HIV- and ART+ children. Within one year of antiretroviral therapy, plasma sCD163 levels normalize to levels similar to HIV- children. sCD163 correlates with HIV disease progression, marked by increasing viral load and T cell activation and decreasing %CD4 and CD4:CD8 ratios in children. Compromised gut barriers and microbial translocation may trigger monocyte activation and sCD163 release, as sCD163 directly associates with IFN-γ. Thus sCD163 is linked to inflammation in the innate and adaptive immune systems. Interestingly, sCD163 plasma levels correlated directly with %CD4 and inversely with IL-2 in memory CD4 T cells, suggesting sCD163 may potentiate activated CD4 T cell proliferation and have a potential inhibitory role on homeostatic CD4 T cell proliferation. In summary, high plasma sCD163 levels in HIV+ children are associated with HIV disease progression, T cell activation, and gut mucosal disruption, and may serve as a biomarker of advancing HIV status.

Conclusions

References


Table 1: Subject Characteristics

<table>
<thead>
<tr>
<th>HIV-</th>
<th>HIV- ART-</th>
<th>HIV+ ART+</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>45</td>
<td>44</td>
<td>33</td>
</tr>
<tr>
<td>Age</td>
<td>12 (10-16)</td>
<td>11 (9-14)</td>
<td>12 (8-13)</td>
</tr>
<tr>
<td>Female</td>
<td>18 (40%)</td>
<td>25 (57%)</td>
<td>20 (60%)</td>
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<tr>
<td>%CD4</td>
<td>38 (33-42)</td>
<td>24 (13-28)</td>
<td>32 (26-40)</td>
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<td>HIV log copies/mL</td>
<td>4.8 (4.2-5.2)</td>
<td>2 (2.0-2.0)</td>
<td>p=0.0004*</td>
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</tbody>
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*Median values with upper and lower quartile range.

Fig. 1: High plasma sCD163 levels in untreated HIV+ children normalize with treatment

Fig. 2: Elevated plasma sCD163 levels correlate with HIV disease progression

Fig. 3: Plasma sCD163 levels correlate with T cell activation and gut mucosal disruption

Fig. 4: Plasma sCD163 levels and CD4 T cell proliferation

References