Background

Coinfection with the hepatitis C virus (HCV) in HIV+ patients has become a major problem. In Western Europe and the U.S.A approximately 30% of HIV+ patients are positive for HCV. Despite their impaired immune system, about 20% of HCV co-infected patients are able to spontaneously eliminate HCV. Previously we showed that natural killer cells are able to inhibit the HCV replication in the early stage of infection favoring spontaneous clearance. CD3+CD56+ NK-like T cells represent a T cell subpopulation that also expresses natural killer cell receptors and shares properties from both cell types. In this study, we investigated phenotype and function of CD3+CD56+ NK-like T cells in acute hepatitis C in HIV-positive individuals.

Methods

36 HIV+ patients with acute hepatitis C were enrolled into this study, including 13 patients with self-limited course of infection and 23 patients that subsequently developed chronic hepatitis C. Furthermore, 8 HIV+ mono-infected patients as well 12 HIV-/HCV+ healthy individuals were analyzed. CD3+CD56+ NK-like T cells were characterized phenotypically by FACS analysis. IFN-γ secretion, degranulation (CD107a) and inhibition of HCV replication was studied using HCV replicon containing HuH7.a2 cells as targets.

Table 1: Patient Characteristics

<table>
<thead>
<tr>
<th>HIV Status</th>
<th>HIV/aHCV</th>
<th>Genotype</th>
<th>Age (years)</th>
<th>Gender</th>
<th>ALT U/L</th>
<th>HCV RNA (x 10^4 IU/mL)</th>
<th>CD3+CD56+ NK-like T cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV(-)/HCV(-)</td>
<td>-</td>
<td>2</td>
<td>40</td>
<td>2</td>
<td>50</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>HIV+</td>
<td>HIV/aHCV</td>
<td>25</td>
<td>30</td>
<td>40</td>
<td>30</td>
<td>30</td>
<td>30</td>
</tr>
</tbody>
</table>

Results

A) B) C) D)

Figure 1. Frequency of CD3(+)CD56(+) NK-like T cells in acute HCV infection

Analyzing the frequency of circulating NK-like T cells we did not observe any significant difference between the study groups (Figure 1A). Furthermore, when patients with acute hepatitis C were analyzed separately, no statistically significant differences were observed in acute hepatitis C as compared to healthy individuals (Figure 1B). Interestingly, we found that in the group of HIV+ patients with acute hepatitis C a high expression of CD62L was associated with spontaneous clearance of HCV (Figure 1C). In addition, we observed a high capacity to block viral replication, confirming results reported to play an important role (Figure 1D).

Figure 2. Expression of C-type lectin receptors on CD3(+)CD56(+) NK-like T cells

Regarding surface expression of the maturation markers CD161, CD27 and CD127 on CD3(+)CD56+ NK-like T cells we found HIV+ patients in the acute phase of infection to display a significantly lower expression of all NK-like T cells positive for CD161, CD27 and CD127 respectively than healthy individuals. However, only expression of CD161 was observed significantly different between HIV mono-infected patients and HIV+ patients with acute hepatitis C.

A) B) C) D)

Figure 3. Frequency of CD3(+)CD56(+) NK-like T cells

Conclusions

Taken together, our data indicate that CD3(+)CD56(+) NK-like T cells are able to block HCV replication in an IFN-γ dependent manner but are functionally impaired in HIV+ patients with acute hepatitis C.