Reduced Peripheral α4β7+ CD4+ T Cells Correlate with Mucosal CD4+ T Cell Loss in Acute HIV Infection (AHI)

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ABSTRACT

Intestinal CD4+CCR5+ T cells are rapidly and profoundly depleted early during acute HIV infection (AHI) contributing to persistent systemic immune activation. The integrin homing receptor α4β7 is thought to play a major role in the propagation and dissemination of HIV+ T cells expressing high levels of α4β7+ T cells are CD4+CCR5+ and also express high levels of CCR5 and activation markers. Due to the difficulty monitoring intestinal CD4+ T cells we evaluated α4β7 as a predictive marker for the loss of intestinal CD4+CCR5+ T cells during early AHI.

Thirty-three subjects underwent phlebotomy and sigmoid biopsy at the time of AHI diagnosis. AHI was grouped using the fourth generation (4thG) immunoassay (IA) staging, with all stages being HIV RNA+ (Stage I: 4thGIA/3rdGIA; II: 4thGIA/3rdGIA; III: 4thGIA/3rdGIA). Of the 33 subjects 14 were 4thGI and 19 4thGIII. During 4thGI the frequency of mucosal CD4+CCR5+ T cells and peripheral β7+CD4+ T cells remained comparable to HIV-uninfected subjects, however with progression of 4thG stage a significant decrease in frequency was observed (Table 1). The frequency of peripheral β7+CD4+ T cells correlated inversely with plasma (r=-0.52, p<0.001) and sigmoid (r=-0.36, p=0.03) HIV RNA and directly (Table 1). The frequency of peripheral β7+CD4+ T cell subsets at the time of AHI diagnosis.

RESULTS

Frequency of peripheral CD4+β7+ T Cells Correlates Inversely with the Plasma and Colonic HIV RNA during AHI

QUESTION

Does the expression of α4β7 on peripheral CD4+ T cells predict the loss of mucosal CD4+CCR5+ T cells during early AHI?

CONCLUSION

• There is a significant loss of mucosal CD4+CCR5+ T cells observed during AHI from 4thGI to 4thGIII.

• The loss of mucosal CD4+CCR5+ T cells closely parallels the loss of CD4+β7+ CM T cells.

• Those results indicate that monitoring the expression of α4β7 on peripheral CD4+ T cells could be a useful surrogate marker to estimate CD4+CCR5+ T cell loss in the mucosa.

The views expressed are those of the authors and should not be construed to represent the positions of the U.S. Army or the Department of Defense.