Retrovirology

Poster presentation

P07-11 LB. Impact of highly active antiretroviral therapy on cell-free and cell-associated HIV-1 in cervicovaginal secretions and blood

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from AIDS Vaccine 2009
Paris, France. 19-22 October 2009

Published: 22 October 2009

Retrovirology 2009, **6**(Suppl 3):P397 doi:10.1186/1742-4690-6-S3-P397

This abstract is available from: http://www.retrovirology.com/content/6/S3/P397

Background

Heterosexual contact is a major route for HIV-1 transmission and cervicovaginal secretions (CVS) contain both cell-associated and cell-free virus. Nevertheless, these different forms of HIV-1 and their involvement in sexual transmission have been poorly characterized.

Methods

CVS and blood were sampled in 80 HIV-1 infected women. Cells phenotype was analyzed by flow cytometry and levels of spontaneous HIV-1-antigen secreting $CD4^+$ T cells were evaluated by ELIspot assay. Cell-free virus was quantified in CVS and paired plasma while cell-associated virus was assayed in cell-culture supernatants.

Results

Cell-free HIV-1 RNA was frequently detected in CVS from patients viremic for HIV RNA in plasma but was unusual in aviremic patients (75% versus 16%, and mean = 5921 copies/ml versus 2696 copies/ml, respectively, $P < 0.001$). Levels of HIV-1 RNA were positively correlated in CVS and plasma ($\rho = 0.7$, $P < 0.001$). CVS contains low T lymphocytes quantities (mean = 120 $CD4^+$ cells/ml and 133 $CD8^+$ cells/ml) and CVS-derived $CD4^+$ T cells are mostly memory and activated lymphocytes ($CD45RA^-$, $HLA\text{-}DR^+$, $CD38^+$, $CD69^+$). Those cells were strikingly different from blood $CD4^+$ T cells with a phenotype exhibiting a mucosal profile with higher expression of CD103 combined with lower expression of CCR7. Cell-associated HIV-1 RNA was detectable in only 3/51 CVS including 2 from viremic patients, whereas 28/51 plasma cell-culture supernatants were positive. Levels of cell-associated HIV-1 RNA were higher in blood samples of viremic individuals than in undetectable subjects ($P = 0.01$).

Conclusion

Therapy reduces viral production and shedding in genital and blood compartments but cell-free HIV-1 remains detectable in some aviremic patients. Level of genital cell-free HIV-1 RNA is influenced by systemic viral replication in contrast to genital cell-associated HIV-1, which may be influenced by local factors. The little amount of $CD4^+$ T cells observed in CVS suggests that sexual transmission occurs independently of HIV-1-infected cells located in CVS but involve intraepithelial cell-associated HIV-1 or cell-free virus.