Local T-cell response to HSV-2 reactivation in treated HIV-1

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MATERIALS AND METHODS

Study participants. Healthy, HIV-2-negative adults enrolled in a natural history biopsy protocol at the University of Washington Virology Research Clinic in Seattle, WA. The University of Washington Human Subjects Review Committee reviewed and provided the protocol and all patients provided written consent. HIV viral load and CD4+ T cell count were measured at the time of enrollment. Biopsies were obtained at the time of an HIV-2 lesion, at the time of healing and in that same location 2, 4, and 8 weeks later. The biopsy tissue specimen was kept frozen in optimal cutting temperature compound (Tissue-Tek. Sakura Firefly USA, Inc., Torrance, California) and stored at -80°C.

Statistical analyses. All statistics were performed using STATA (Statacorp, College Station, TX). Time course data were compared using two-tailed, unpaired t-tests without assumption of equal variances. Linear regression was performed to observe the relationship between peripheral and tissue T cells.

RESULTS

Clinical and virologic characteristics of 10 HIV+ and 15 HIV-study participants

**HIV**-gull quantitative PCR performed from biopsy tissue, listed as positive (+), negative (-), or not performed (0). In time sequence (Lesion, Healing, 2wk, 4wk, 8wk, and Control). Only 3 of 10 HIV- participants had biopsied performed at the 4-week time point. 10 HIV+ and 10 HIV- participants were chosen from subjects enrolled in a natural history biopsy protocol at the University of Washington Virology Research Clinic in Seattle, WA (Table 1). The mean time to healing was significantly longer in the HIV+ participants (mean 11.7 ± 7.8 days, p = 0.005 N = 15). Five of 8 HIV+ compared to 1 of 6 HIV- participants had a positive HSV PCR from tissue at 8 weeks.

CONCLUSIONS

There was greater time to healing and increased frequency of shedding in the HIV+ individuals compared to the HIV uninfected.

HIV-infected individuals had more frequent reactivation of HSV by PCR of tissue biopsies.

A less robust CD4+ T cell response was seen in biopsies HSV-2 reactivation in treated HIV+ participants than in HIV- participants from the initial response to 2 weeks after healing.

This CD4+ cell discrepancy was also seen in the CD4+ cells of the DEJ, though the significance of this is unknown.

A small difference was also seen in presence of CD8+ T cells in biopsies of healed lesions in HIV+ individuals and in the DEJ of the lesions. It is unclear whether CD4+ T cells play a role in the recruitment of CD8+ T cells to the DEJ, though there is some suggestion that this is possible.

The number of CD4+ T cells in the lesion in the HIV+ individuals corresponded with the number of CD4+ T cells in the lesion, however this relationship did not hold true at other Biopoints.

Decreased presence of CD4+ T cells may be a contributor to increased time to healing as well as increased frequency of reactivation in HIV-infected individuals.

HSV shedding as detected by PCR from biopsies is discordant from apparent immune control of overt disease.

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