Association of HIV diversity and survival in HIV-infected Ugandan infants

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BACKGROUND

In resource-limited settings, many HIV-infected children die before two years of age. In this study, we analyzed the association between HIV diversity and survival in HIV-infected infants. HIV diversity is usually evaluated by sequencing individual viral variants. We developed a rapid high resolution melting (HRM) assay that can be used to assess HIV diversity without sequencing. In the HRM assay, regions of the HIV genome are amplified in the presence of a fluorescent dye. The resulting HIV amplicons are then warmed over a range of temperatures, and an HRM score is determined by analysis of the resulting melting curve (Figure 1).

RESULTS

Analysis of HIV diversity in infants

HRM scores for samples from 6-8 week-old infants were higher than those obtained using plasmid controls. Twenty-one of the 31 infants were alive at 12 months and had samples available for testing from 12 or 18 months of age. Higher HRM scores were associated with older age (beta=0.47, P=0.006; for Gag2; beta=0.47, P=0.006; for Pol; beta=0.24, P=0.016; where beta is the estimated mean increase in the HRM score associated with one year increase of age).

The HRM assay is highly reproducible, and HRM scores are significantly associated with sequence-based measures of HIV diversity [1]. In this study, we used the HRM assay to measure the level of diversity in three regions of the HIV genome, and examined the relationship between HIV diversity and infant survival.

METHODS

Study samples

Samples were obtained from 31 Ugandan infants in the HIVNET 012 clinical trial who were HIV-infected by 6-8 weeks of age. Most of these infants received single dose nevirapine (sdNVP) for prevention of HIV mother-to-child transmission [2]. The plasma samples tested in this study were collected at 6-8 weeks, 12 months, and 18 months of age.

In a multivariate hazard model that included HIV viral load at 14 weeks of age and HRM score, higher HRM scores (for Gag2, mean of Gag1 and Gag2, and the mean of Gag1, Gag2, and Pol) were associated with death (Table 2).

Table 2. Logistic regression analysis of HRM scores and infant survival

The X axis shows the time since birth in days (infant age); the Y axis shows the survival probability. The number of infants still alive in each group (≤ Q3, >Q3) at each time point is shown below each graph.