

Oral presentation

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Phenotypic characterization of HIV-specific CD8 T cells during acute infant HIV infection

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Objective

Infants infected with HIV-1 fail to contain viral replication as efficiently as adults. In the absence of antiretroviral therapy (ART), opportunistic infections are common and mortality rates range between 10–45% in HIV-infected infants. To understand better the factors underlying rapid infant HIV-1 progression, we examined HIV-specific CD8 T cells during the acute and chronic phases of infection.

Methods

HIV-infected pregnant Kenyan women were recruited from 1999–2003. Other than antenatal prophylaxis, neither women nor infants received ART. Serial blood specimens were obtained at delivery and months 1, 3, and quarterly thereafter until death or two years. IFN- γ -producing CD8 T cells were quantified with ELISpot assays using HLA-matched HIV-1 peptides as antigens. In a subset of 7 infants, HIV-specific CD8 T cells were quantified using class I HLA tetramers. Cellular phenotype was described using multicolour flow cytometry; PBMC were stained with tetramers and antibodies to cellular proteins.

Results

ELISpot assays were performed in 67 infants who acquired HIV-1 before 1 month of age. HIV-specific IFN- γ release was detected 39% of infants at 1 month of age, and 58% at 3 months. The magnitude of responses to individual peptides was low, but within the range observed in

adults (median 230 HIVSFC/million PBMC, range 50–2040 HIVSFC/million PBMC). High frequencies of HIV-specific CD8 T cells were detected during acute infection using tetramers (median 0.67%, range 0.045–3.8%). Over time, the frequency of cells identified by tetramer staining declined and the frequency of cells producing IFN- γ increased. Neither IFN- γ production nor frequencies of tetramer-stained cells correlated with HIV-1 viral load. During acute HIV-1 infection, the phenotype of infant HIV-specific CD8 T cells was similar to that observed in adults; HIV-specific CD8 were activated, CD27+CD28-, CD45RA-, CD95+ and contained low levels of perforin. Similar to adults, during chronic infection infant HIV-specific cells transitioned to a resting phenotype and increased expression of CD57, suggesting the accumulation of senescent cells. In contrast to adults, the majority of infant HIV-specific CD8 cells expressed CD95 during chronic infection, suggesting ongoing susceptibility to apoptosis. Also unlike adults, perforin declined to very low or undetectable levels HIV-specific CD8 cells, suggesting low cytotoxic potential.

Conclusion

The relatively poor control over HIV-1 viral replication during infancy may be explained by differences in T cell functionality between infants and adults, which may include higher susceptibility to Fas-mediated apoptosis and low cytotoxic potential.