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Oral presentation

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-gamma-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-gamma 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-gamma increased. Neither IFN-gamma 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.