

The impact of HIV-1 infection and exposure on natural killer (NK) cell phenotype in Kenyan infants during the first year of life.

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Abstract

Natural killer (NK) cells play an important role in the containment of HIV replication during primary infection, though their functions are impaired during chronic HIV infection. Infants experience more rapid HIV disease progression than adults, but contributions of infant NK cells to containing HIV infection are unknown. The aim of this study was to determine the impact of HIV infection on infant NK cell phenotype by evaluating samples and data from a cohort study of women and their infants, conducted in Nairobi, Kenya between 1999 and 2003. The percentage and phenotype of NK cells was evaluated longitudinally by multi-parameter flow cytometry over the first year of life in HIV-infected (HIV+, $n = 16$), HIV-exposed uninfected (HIV-EU, $n = 6$), and healthy unexposed controls (HIV-, $n = 4$). At birth, NK subset distributions based on expression of CD56 and CD16 did not differ between HIV+, HIV-EU, or HIV- infants. However, HIV infection was associated with a subsequent decline in NK cells as a percentage of total lymphocytes ($p < 0.001$), and an expanding proportion of CD56-CD16+ NK cells ($p < 0.001$). Activated CD38(bright)CD69+ NK cells were more frequent in the HIV+ infants, followed by HIV-EU and HIV- infants, in both CD56(dim) ($p = 0.005$) and CD56(bright) compartments ($p = 0.03$). HIV infection and exposure was also associated with a significant decline in the percentage of perforin-expressing NK cells in the CD56(dim) compartment over the first year of life, with HIV+ infants losing approximately 2.5% ($p < 0.001$) and HIV-EU infants losing 3.0% ($p = 0.01$) of perforin+ cells per month. Thus, infant HIV infection is associated with alterations in NK cell subsets, activation, and cytolytic potential that could contribute to their poor control over HIV infection. Furthermore, exposure to HIV infection in infants who escaped infection is also associated with alterations in NK cells that may contribute to the reduced ability to fight infections that is observed in HIV-EU infants.