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HIV-I virological remission for more than 11 years after interruption of early initiated antiretroviral therapy in a perinatally-infected child

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Background: Durable HIV-I remission after interruption of combined antiretroviral therapy (cART) has been reported in some adults who started cART during primary HIV-I infection. The in utero HIV-I-infected «Mississippi child», exhibited transient viral control after interrupting very early-initiated cART. However viremia rebounded 27 months later, leaving unclear the possibility of obtaining long-term post-treatment remission in vertically-infected children. Here we report the case of a perinatally-HIV-I-infected adolescent who shows unprecedented virological remission more than 11 years after cART discontinuation.

Methods: HIV-RNA and CD4+ T-cell counts have been monitored since birth. Ultrasensitive HIV-RNA, PBMC-associated HIV-DNA, flow-cytometry-assessed frequency of HIV-specific CD8+ T-cells, CD8+ T-cell mediated HIV-suppression, reactivation of the CD4+ T-cell reservoir were evaluated after 10 and 11 years of control off therapy. Plasma concentrations of antiretrovirals were determined by tandem mass spectrometry.

Results: One infant born from a woman with uncontrolled HIV-I viremia received zidovudine-based prophylaxis during 6 weeks. HIV-RNA and DNA were not detected 3 and 14 days after birth. HIV-DNA was detected at 4 weeks of age. HIV-RNA reached a peak of 2.1x10⁶ copies/ml at 3 months of age when cART (zidovudine, lamivudine, didanosine, ritonavir) was initiated. HIV-RNA was undetectable one month later and remained below assay-detection limits while on cART, except at 15 and 21 months of age. Between 5.8 and 6.8 years of age cART was discontinued by the family. HIV-RNA was undetectable at 6.8 years of age and cART was not resumed. HIV-RNA has remained < 50 copies/ml through 18.3 years of age, except for one blip (515 copies/ml). CD4+ T-cell counts remained stable. After 11 years of control off therapy (confirmed by undetectable plasma concentrations of antiretrovirals), HIV-RNA was below 4 copies/ml and HIV-DNA was 2.2 Log copies/10⁶ PBMC. Low levels of HIV-RNA and p24 were detected upon activation of CD4+ T-cells with PHA. HLA genotype showed homozygosity at several loci (A*2301-;B*1503/4101;C*0210/0802;DRB1*1101-;DQB1*0602-). HIV-specific CD8+ T-cell responses and T-cell activation were very weak. HIV-I western blot was positive with absence of antibodies against gp110 and p18.

Conclusions: This case provides first-time evidence that very long-term HIV-I remission is possible in perinatally-infected-early-treated children, with similar characteristics as reported in adult post-treatment controllers.

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