Case Report

No cure of HIV infection in a child despite early treatment and apparent viral clearance

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A woman at 41 weeks’ gestation presented to our hospital in December, 2009, in labour. She had a history of intravenous drug use, and was unaware of her HIV status. Rapid HIV-1 testing was positive and she had high viral load. A small-for-gestational-age boy was delivered vaginally, in good condition. 12 h after his birth virological analyses, comprising HIV 1-2 antibody western blot (gag, pol, env) and HIV-1 antigen p24, were positive, and his HIV-RNA viral load was 152 560 copies per mL. We started prophylaxis with zidovudine and nevirapine within 12 h of birth, but at day 4 his viral load was 13330 copies per mL. After checking for possible viral resistance we started triple antiretroviral therapy with ritonavir boosted lopinavir, zidovudine, and lamivudine. Plasma viral load was 3971 copies per mL at day 15, 49 copies per mL after 3 months, and below assay detection at 6 months. Viral load remained undetectable and CD4 T cells were higher than normal range (appendix).

At 3 years of age, tests for HIV antibodies, DNA, p24, RNA, and repeated viral cultures were negative. In view of these results and recent reports of apparent cure of HIV infection, and in agreement with the mother, we stopped antiretroviral therapy (ART). At this time we examined peripheral blood mononuclear cells (PBMCs) for immune response. Even with the apparent clearance of HIV, we saw increased numbers of activated CD4 and CD8 T cells (CD25+, HLA-DR14+, CD69+), alterations of the T-cell differentiation pathway with reduced naive and central memory, increased effector memory, and terminally differentiated CD4 and CD8 T cells. On stimulation of PBMCs with HIV (AT-2), we saw increased proportions of HIV-specific, perforin-producing and granzyme-producing cytotoxic T lymphocytes, and interferon α and tumour necrosis factor α-secreting CD4 and CD14+ cells (appendix). Concentrations of mRNA (real time PCR) and protein (cytometric analysis) confirmed these results [A: correct? Please note we use the active form]. 1 week after stopping treatment, the patient’s viral load was undetectable and antigen and antibody tests were negative; however, viral load rebounded (36 840 copies per mL) within 2 weeks. We restarted treatment with the same drug combination, and 10 days later viral load was 346 copies per mL, but tests for HIV DNA, antigens and antibodies, and Western Blot became positive. Viraemia was suppressed below detectability by month 3 of therapy.

Reports of two recent cases had raised hopes of a cure from HIV infection. The so-called Berlin patient had an apparent cure after an allogeneic haemopoietic stem cell transplant from a donor with the CCR5-Δ32 mutation, which is protective against HIV infection.1 The so-called Mississippi child was believed to be cured thanks to early initiation of ART.2 This report raised the possibility of achieving a cure without procedures such as bone marrow transplant with CCR5-Δ32 cells. However, recent evidence of viral rebound in the Mississippi child shattered this hope.

In our patient, even with apparent clearance of the virus, HIV was not eradicated. Analysis of immune responses carried out when all signs of infection were absent showed immune changes similar to those seen in people infected with HIV.3-4 The presence of immune activation, impairments in the memory-naïve differentiation pathway, and HIV-specific cytolytic T lymphocytes suggested ongoing viral replication. These findings differentiate the case from the Mississippi child and the Berlin patient, in whom HIV-specific T lymphocyte-mediated immune responses and immune activation were not detected5 or were absent.1 In our patient early in-utero infection, low birth weight, and high viral load at birth may have precluded longlasting viral remission.

The availability of many classes of potent antiretroviral drugs has substantially decreased HIV morbidity and mortality, but these drugs cannot eradicate the virus because they do not eliminate viral reservoirs. The search for an HIV cure continues.

Contributors VG and GVZ managed the patient and wrote the report. DT and MB did immunological analyses and NZ and MRG did virologic analyses. MC designed the study and wrote the report. Consent to publication was obtained.

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References