FUNCTIONAL CURE AND SEROREVERSION AFTER ADVANCED HIV DISEASE FOLLOWING 7 YEARS OF ANTIRETROVIRAL TREATMENT INTERRUPTION.

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BACKGROUND

Early antiretroviral (ARV) treatment during acute HIV infection can lead to functional cure in a subset of patients called post-treatment controllers. However, there are few reports of functional cure after discontinuation of ARV therapy in patients with chronic HIV-infection. Some authors call these patients "secondary controllers." We report a 51-year old woman diagnosed with advanced AIDS who has no detectable HIV-1 RNA levels after 7 years off-therapy.

CASE REPORT

The patient was hospitalized in 1996 with diagnosis of AIDS wasting syndrome and probable toxoplasma encephalitis. Two positive HIV-1 ELISA tests and a positive Western Blot (WB) confirmed the HIV-1 diagnosis. She was treated with pyrimetamin, clindamycin and leucovorin and started ARV therapy with zidovudine, didanosine and nevirapine soon after diagnosis. Pre-treatment HIV-1 RNA levels and CD4+ T-cell counts are not available. After two weeks on ARV therapy, CD4+ T-cell count and HIV-1 RNA levels were 164 cells/µl and 2,200 copies/mL (RT-PCR), respectively. She recovered without neurologic sequela. After one year on treatment, she developed virologic failure with HIV-1 RNA levels 36,000 copies/mL (Nasba HIV-1) and CD4+ T-cell count 490 (32%) cells/µl. ARV therapy was changed to stavudine, lamivudine and indinavir in November 1997 achieving and maintaining virological suppression since then except for a blip (54 copies/mL) in August 2000. Indinavir was switched to abacavir in November 2000 as simplification. ARV therapy was interrupted in 2007 due to dyslipidemia and lipodystrophy. After that, the HIV-1 RNA levels remained below limit of detection to the time of this report.

METHODS

CD4+T cell count was measured by flow citometry and HIV-1 RNA levels were assessed by Roche® Standard or Ultrasensitive RT-PCR Amplicor -automated Cobas- until March 2010, and by Cobas/Ampliprep, thereafter. HIV-1 viral load was also measured by bDNA CHIRON HIV-1 RNA 3.0.

Through 2013 proviral HIV-1 DNA in PBMCs was performed by RealTime PCR targeting the HIV-1 *pol* gene and nested PCR targeting *gag, pol* and *env* genes. The presence of CCR5 Δ32 deletion was studied by PCR.
HLA class I-typing for the B locus was performed by Luminex.
Antibodies against HIV 1 and 2 were re-tested by Quimioluminiscence and HIV-1 Western blot.

RESULTS

CD4+T cell count and HIV-1 RNA levels over time are shown in Figure 1. Since discontinuation of ARV therapy, HIV-1 RNA levels remained below the limit of detection and the CD4+T cell count was stable between 568 and 885 cells/µl. Current CD4/CD8 T-cell ratio is 1.4.

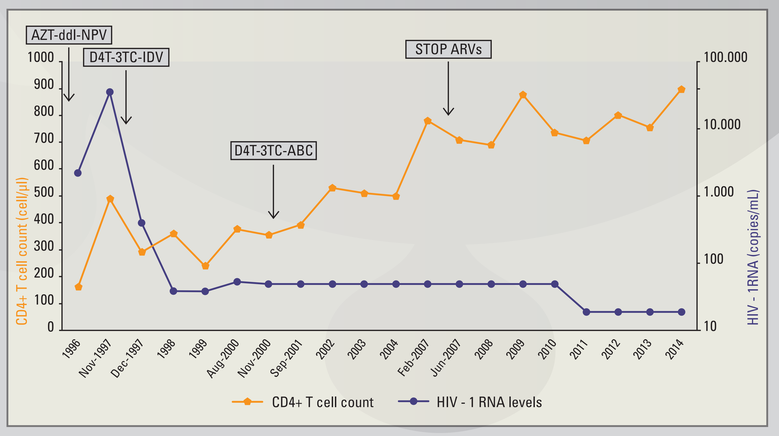

Figure 1. CD4+T cell count and HIV-1 RNA levels over time.

Proviral HIV-1 DNA was not detected in PBMCs. No CCR5 Δ32 deletion was detected. HLA-B was 41;58. HIV-1 and 2 antibodies and WB were tested, resulting non-reactive in two separate occasions (Table 1).

Test	Result
Proviral HIV-1 DNA	Negative
CCR5	Wild type
HLA B	B41;B58
HIV 1 and 2 Antibodies	Negative
HIV Western blot	Negative

Table 1. Laboratory test results.

DISCUSSION

This is a case of functional cure that also seroreverted after initial diagnosis of advanced AIDS. In accordance with some other reports of "secondary controllers," it suggests that post-treatment control could be achieved following chronic HIV-1 infection in some patients with advanced AIDS who lack the protective HLA-B alleles or the CCR5 Δ32 deletion. Further studies will be performed to assess T cell viral reservoirs and immunological response to HIV-1 in this patient.

LITERATURE CITED

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