

An elite controller in pregnancy – Towards a definition of recovery, though not cure?

Archuleta S^{1,2}, Tang JWT³, Lee CK³, Huan PT³, Barkham T⁴, Oon L⁵, Koay ESC³

¹Division of Infectious Diseases, University Medicine Cluster, National University Hospital; ²Department of Medicine, Yong Loo Lin School of Medicine, National University of Singapore; ³Molecular Diagnosis Centre, Department of Laboratory Medicine, National University Hospital; ⁴Department of Microbiology and Infectious Diseases, Tan Tock Seng Hospital; ⁵Department of Pathology, Singapore General Hospital Singapore

CASE

An otherwise healthy, asymptomatic, 22-year-old pregnant Indian woman presenting for her routine antenatal screen at 12 weeks gestation was found to be positive for HIV antibodies (Abbott Architect HIV Ag/Ab Combo). Her CD4 count was 551 cells/ μ l and her HIV RNA viral load was undetectable (<40 copies/ml, Abbott Real-Time HIV-1 RNA). Her previous medical history included mild-intermittent asthma and genital warts.

Further confirmatory testing showed the following positive bands on her Western blot assay (Genelabs, MP Diagnostics HIV Blot 2.2): p24, gp41, gp120, gp160, confirming a positive HIV status. Further supplementary testing demonstrated the presence of anti-HIV antibodies only and no p24 Ag (VIDAS DUO ULTRA HIV5/P24II, Biomerieux) and a proviral HIV DNA assay was negative on whole blood (Roche Amplicor HIV-1 DNA Test v 1.5). Since these results were surprising, we also checked the woman's CCR5delta32 status using an in-house assay, which showed that she was wild-type for this allele, i.e. the CCR5delta32 mutation was not present (**Figure**).

Despite the absence of detectable HIV-1 RNA in this woman, she was given the recommended therapy for a newly diagnosed HIV patient in pregnancy, consisting of zidovudine, lamivudine and ritonavir-boosted lopinavir combination therapy (from gestational week 16) and she later delivered a full-term, healthy baby, by Cesarean section. She abstained from breast-feeding as advised.

There was no evidence of HIV infection in the infant at least 12 months after delivery during the post-natal period of monitoring with HIV-1 RNA viral load, HIV-1 DNA PCR and anti-HIV/p24Ag serological testing.

Throughout her pregnancy and beyond, the woman's white cell markers remained within normal limits (**Table**).

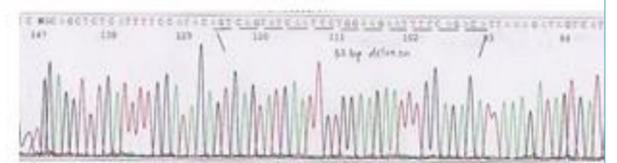
Test Name	Reference Range	Units	14/10/2009	11/05/2011
CD4 / CD8 Ratio	0.50 - 2.50		0.67	0.8
CD4 %	25 - 50	%	30	34
CD4 Absolute Count	280 - 1430	cells/ μ l	551	851
CD8 %	13 - 40	%	45	42
CD8 Absolute Count	165 - 1045	cells/ μ l	826	1060

CCR5delta32 testing

- Gel Electrophoresis: Amplicons were run on a 3% agarose gel. The primers flanking the 32 base-pair deletion were used to obtain the wild-type (183 bp) and deleted fragments (151 bp).
- Absence of 151 bp bands indicate wild-type CCR5 locus (on human chr 3p21) in this patient, confirmed on sequencing.



Methods based on Liu et al. Cell 1996;86:367-77.



DISCUSSION

An elite controller has been defined as having “persistently undetectable plasma RNA for 15-20 years, with stable CD4 counts, without therapy” (Saksena et al. AIDS Review 2007;9:195-207). Low or undetectable levels of proviral HIV DNA are also a feature. This case does not meet the definition quite yet because 15-20 years have not passed, and additional tests need to be performed to check if other markers found in other elite controllers are also present (Miura et al. J Virol 2009;83:3407-12). Only one convincing case of HIV clearance has been documented – an HIV-1 infected patient who underwent stem-cell transplantation for acute myeloid leukemia from a donor homozygous for the CCR5delta32 mutation (Allers et al. Blood 2011;117:2791-9). Yet, such cases raise interesting questions as to what might be the criteria for defining HIV clearance and recovery.

For comparison, consider infection by another virus, varicella zoster (VZV) which is the cause of chickenpox and shingles. Whilst most people recover from the primary infection, the virus is never cleared from the body since the virus remains latent in dorsal root ganglia for life. It can reactivate occasionally to cause shingles. HIV has not been present in the human population for the duration of a typical human lifespan just yet, but when it has, it will be interesting to see whether in some of these elite controllers HIV mimics VZV – mostly quiescent, but with the occasional flare, during which the host immune response, perhaps combined with prompt therapy, can bring it under control once again.

Correspondence:

Dr. Sophia Archuleta
Division of Infectious Diseases, University Medicine Cluster
1E Kent Ridge Road, NUHS Tower Block, Level 10, Singapore 119228
Email: sophia@nus.edu.sg