HIV-2 - a diagnostic and therapeutic dilemma: Implications for practice

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Case report

Case Report: 42-year old male presented with a positive HIV ELISA detected through migration screening in Australia. He was originally from South Asian background and revealed no significant sexual risk factors. He denied history of injecting drug use or blood transfusion. He was a heavy alcohol user but never used recreational drugs. He had a minor surgical procedure done with traditional practitioner that involved bleeding but no other history of blood exposure.

His regular female partner, who is also South Asian, tested negative for HIV. His ELISA was reactive for HIV1/2 and HIV-1 Western Blot was indeterminate but his HIV-2 Western blot was reactive. (Fig .1)

Human Immunodeficiency Virus (type-1 and 2) Antibody/Antigen Tests

Architect Ag/Ab rpt	**Reactive**	*
Genscreen Ab	**Reactive**	*

Antibodies to Human Immunodeficiency Virus (type-1) DETECTED by ELISA.

Human Immunodeficiency Virus (type-1) p24 Antigen

p24 ELISA	Negative

Human Immunodeficiency Virus (type-1) Western Blot	
Biorad LAV HIV-1 blot	
p18	No Band
p24	**3+**
p34	**3+**
p40	**3+**
gp41-45	**Trace**
p53	No Band
p55	**3+**
p68	**1+**
gp120	No Band
gp160	No Band

Human Immunodeficiency Virus (type-2) Western Blot	
p16	3+
p26	3+
p34	3+
gp36	3+
p56	3+
p68	3+
gp105/125	3+
gp140	3+

Figure 1. HIV-1 and HIV-2 Western Blot results

Clinical examination was unremarkable except bilateral enlarged parotids. His CD4 T-cell count was 832 (42%) cells/mm^{3}and did not have any other significant laboratory abnormality except for mildly elevated liver enzymes. His Thyroid function tests were normal and other autoimmune profile as normal. He had latent TB with no evidence of active TB.

Further tests were performed at the Victorian Infectious Diseases Research Laboratory (VIDRL). HIV-1 DNA PCR was negative. HIV-2 RNA virus load was also performed on ABI PRISM® 7500 using real time TaqMan® Assays. This target amplifies a 157bp segment of the *gag* region. The HIV-2 RNA was undetectable. (standard growth curve shown in Fig. 2 but does not have curve for our patient as he was undetectable)

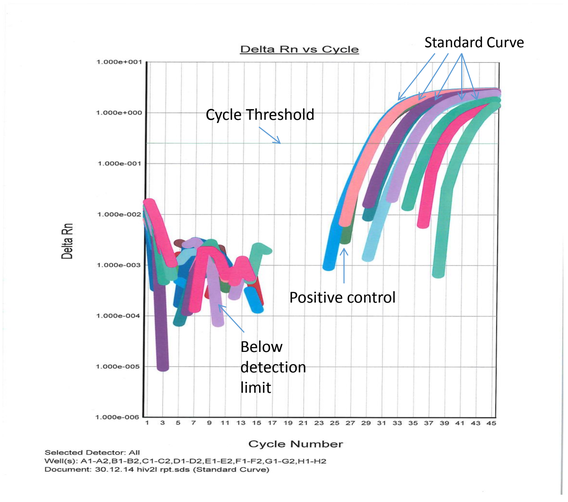

Figure 2. Standard growth curve on the ABI for a HIV-2 amplification

Patient advised of his HIV-2 status and advised safe sex with regular follow up for HIV-2 viral load and CD4 counts.

Discussion and implications for practice

HIV-2 was first identified in 1986 as a cause of AIDS in West Africa and phylogenetically clusters with Simian Immunodeficiency virus from sooty mangabeys.

Data on the prevalence and incidence rates of HIV-2 are limited with an estimated 1 to 2 million people in West Africa infected with HIV-2.
HIV-1 has spread globally, whereas HIV-2 has mostly remained limited to West Africa, where it is endemic Guinea Bissau, Ivory Coast, Senegal, Burkina Faso, the Guinea, Ghana and Gambia. It is also reported from Europe (mainly Portugal), USA and India.

The transmission rate for HIV-2 compared to HIV-1 is very low both by sexual route (5 to 10 fold) and mother to child transmission (20 to 30 fold). Several studies confirm that rates of perinatal transmission of HIV-2 are low with and without interventions (0%–4%), which may be a result of reduced plasma viral loads and less cervical viral shedding, compared with that seen in HIV-1-infected women.

Category	HIV-1	HIV-2
Viral replication	High	Low
Transmission fitness	100-fold more	Less
Viral replication	High viral RNA load	Lower viral RNA load
Viral load in semen	High	Low
Viral set point	Higher	Lower
Co-receptor usage	CCR5 and CXCR4	CCR1,2,3,5;CXCR4,6
CD4 counts	Lower at undetectable viral load	Higher at undetectable viral load

Table 1: HIV-1 and HIV-2 comparison

Replication rates for HIV-2 are about 100-fold lower than those for HIV-1 and this results in markedly lower plasma viral loads. Around 80% of the HIV-2-infected patients behave like long-term non-progressors. HIV-2 disease progression can be differentiated based on HIV-2 viral load as follows:
Low or undetectable viral loads: mortality rates similar to general population - low rates of T-cell turnover (both CD4+ and CD8+) and minimal immune activation.
'High' HIV-2 viral loads, (>10, 000 copies/mL): mortality rates similar to those for HIV-1 infected individuals at much higher viral loads.

Development of HIV-2 viral load assays has been challenging with no commercially available assay, leaving in-house assays or unvalidated derivatives of commercial kits as the only testing option. Plasma RNA values can vary widely between laboratories due to limitations in terms of their sensitivity, accuracy and coverage of HIV-2 genetic diversity. There is need to standardize, validate, and commercialize simple, low-cost HIV-2 viral load assays.

Prior acquisition of HIV-2 improves AIDS-free survival with subsequent HIV-1 infection. There are limited data on management strategies and no RCTs addressing the question of when to start ART or the choice of initial or second-line therapy for HIV-2 infection have been completed. Additionally, HIV-2 is intrinsically resistant to NNRTI and to enfuvirtide (T20) and some protease inhibitors are not effective, limiting the treatment options. The specific mutations encountered following failed antiretroviral therapy in HIV-2- infected patients have similarities to those seen in HIV-1- infected patients.

References:

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Key messages

- Clinicians should be cognisant of unrecognised dual infected HIV1/HIV-2 patients who acquired HIV in areas of high HIV-2 endemicity and were diagnosed prior to the introduction of universal HIV-2 testing.
- HIV-2 is associated with very low or undetectable levels of HIV-2 in plasma.
- Asia Pacific regional interest group may stimulate further research in HIV-2 and associated challenging issues related to diagnosis, monitoring and treatment.

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