

## The First Report of HIV-1 Group O Infection in Canada

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### Abstract

We report here the first case of HIV-1 group O infection in Canada. The patient presented with a progressive decline in CD4<sup>+</sup> T lymphocyte count despite an undetectable plasma viral load, due to an inability to detect group O infection by standard techniques. This in turn resulted in a delay in initiation of treatment.

**Keywords:** HIV-1 group O; Viral load; Genetic variability

### Case Report

A male patient originally from Cameroon was diagnosed with HIV infection in September 2009. His female partner was HIV negative and the patient was asymptomatic. Infection is thought to have been through heterosexual relations.

Biological data showed negative serology for hepatitis A and C viruses, syphilis (VDRL) and HTLV, and there was evidence of cured hepatitis B with no detection of HbS antigen and positive antibodies for HbC and Hbs. He also had positive IgG for CMV, VZV and Rubella. However, there was no evidence of active tuberculosis and the patient had a negative PPD reaction and a normal chest-Xray.

His CD4<sup>+</sup> T lymphocyte count was 219 cells per mm<sup>3</sup> (8%) and his HIV viral load (VL) was undetectable, as measured by b-DNA-technique. The patient refused all treatment including primary PCP-prophylaxis and was G6PD normal.

A plasma virological sample was sent for sequencing but routine tests designed for HIV-1 group M failed to detect HIV nucleic acid. Specific primers for HIV-1 group O (HIV-O) were then used and the virus was amplified and sequenced. Genotyping revealed HIV-O clade A and resistance genotyping showed polymorphisms in antiretroviral (ARV)-target regions and the following resistance-associated mutations: A98G, K103R, V106I, E138A, V179E, Y181C (RT), Q58E, I62V, I64V, H69R, K70E, A71V, L89I (PR) and L68I, I72V, L74I, T124A, S153A, G163Q, T206S (IN).

Using usual algorithms for interpretation of resistance (HIValg), it was determined that the virus was susceptible to NRTIs, PIs except tipranavir (low level resistance) and Integrase inhibitors (INIs), and displayed resistance to NNRTIs.

During follow-up, the CD4<sup>+</sup> T lymphocyte count decreased from 219 to 144 (6%) while VL remained undetectable by the b-DNA technique. In August 2011, the CD4<sup>+</sup> T lymphocyte count was 141 (6%) and his VL was 205, 082 copies per ml by the Abbott RealTime technique. The patient agreed to be treated with tenofovir/

emtricitabine/lopinavir/r and trimethoprim-sulfamethoxazole but unfortunately never returned to the clinic.

### Discussion

HIV-O is a rare variant of HIV-1 that is prevalent in Cameroon, where it represents 1% of HIV/AIDS cases. In France, the « RES-O » survey identified 141 such patients in 2014. In fact, the first report of such a case was in 1992, and the cases in France represent the largest number of confirmed HIV-O infections outside of Cameroon [1]. A few sporadic cases have also been reported in other African countries and the United States. However, none had been reported in Canada until now, despite an increasing proportion of non-B subtype infections from 2003 that are strongly associated with heterosexual activity involving immigrants from endemic countries (Canadian HIV strain and drug resistance surveillance program, Public Health Agency of Canada report, 2011).

Our study highlights the poor performance of certain tests for VL measurement. The patient displayed a decrease in CD4<sup>+</sup> T count, suggesting disease progression in the absence of treatment, despite an “undetectable viral load”. It has already been reported that some commercial tests, e.g. b-DNA, are not adept at HIV-O detection; group O viruses were also inefficiently detected by each of the Monitor v1.5, Cobas Taqman HIV-1 v1. (Roche), and VERSANT 3.0 assays [2,3]. In contrast, specific techniques that target the LTR or IN regions of HIV group O have been developed in France [4,5] and quantification of HIV-O is also available with the RealTime HIV-1 (Abbott) and Cobas Taqman HIV-1 assay, (version 2) (Roche) [6]. In our case, the patient’s “undetectable VL” was due to use of the b-DNA technique.

In 1994, concerns were raised about the possible lack of sensitivity of commercial serological tests for detection of HIV-O variants, because these tests are based on group M antigens. Although the addition of antigens specific to group O in the testing and introduction of fourth generation ELISA tests represents an improvement, recent publications have shown that the risk of false negative diagnosis of HIV-O still exists, regardless of the method used (ELISA or rapid diagnostic test) [7].

HIV-O genotyping requires specific primers for amplification and sequencing of antiretroviral (ARV)-target regions [1] and these are unavailable in routine laboratories. Furthermore, no specific genotypic resistance algorithm exists for HIV-O and few studies have attempted to establish correlations between the genotype and phenotype of HIV-O isolates or the subsequent emergence of resistance and clinical responsiveness to ARVs [1]. It is well established that first-line ARV regimens for HIV-O could include two NRTIs plus a PI or two NRTIs plus an integrase inhibitor [8] but that NNRTIs are inactive against the RT of HIV-O [9].

Furthermore, we recently showed that HIV-1 group O variants display higher susceptibility to raltegravir *in vitro* than does HIV-1 group M [10]; these findings are consistent with the excellent virological responses that have been achieved in HIV-O-infected patients treated with raltegravir based-regimens [8].

In conclusion, the methods used to measure HIV viral load should take account of HIV-1 group O. Although genotyping for HIV-O may only be available in specialized laboratories, the increased numbers of non-B and recombinant HIV infections in Canada should alert clinicians as to the risk of underestimating the possibility of group O infection [11]. Interpretations of group O genotypes for resistance may be complicated by the presence of multiple polymorphisms in such variants. Our case also highlights the problem of loss to follow up of HIV-infected individuals in Canada and should encourage vigilance among physicians. We are unaware of the current whereabouts of this patient or his health status. It is possible that an earlier definitive diagnosis and rapid initiation of therapy might have motivated this patient to continue to be followed at our clinic.

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