Letter

Multiclass primary antiretroviral drug resistance in a patient presenting HIV-1/2 dual infection

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Introduction

HIV-2 infection is mainly concentrated in West African countries with an estimated number of 1 to 2 million infections [1,2]. As a result of socioeconomic links to West African countries and human migration, HIV-2 infection is also found in European countries. For instance, HIV-2 is responsible for 4.5% of AIDS cases in Portugal [3] and has been associated with 1.8% of new HIV infections documented in France between 2003 to 2006 [4].

HIV-2 is known for intrinsic resistance to non-nucleoside reverse transcriptase inhibitors (NNRTIs), therefore, best treatment options for treatment-naive patients rely on boosted protease inhibitor (PI) regimens [5,6]. Based on in vitro PI sensitivity data, two effective treatment combinations consist of tenofovir/emtricitabine plus lopinavir/ritonavir or zidovudine/lamivudine plus darunavir/ritonavir [7]. However, a high frequency of K65R and Q151M mutations have been reported in patients receiving nucleoside reverse transcriptase inhibitors (NRTIs) as well as multiclass drug resistance emergence in a cohort from Senegal [8,9]. By contrast, emerging data from HIV-2 integrase sequences coming from treatment-naive patients show no major mutations to integrase inhibitors, providing an opportunity for treatment of HIV-2-infected patients [10].

Key mutation sites conferring resistance to drug classes are not fully shared by HIV-1 and HIV-2 viruses due to genome differences; therefore, the global spread of an HIV-2 epidemic can lead to a greater frequency of HIV-1/2 dual infections with complex drug resistance challenges for antiretroviral treatment options.

Case report

The case of a 23-year-old heterosexual man, born in Côte d’Ivoire, in good health until October 2010 when he complained of persistent diarrhoea, fatigue and weight loss, is reported. In March 2011 he decided to move to Switzerland for appropriate medical care. He denied a previous HIV test, exposure to antiretroviral drugs, intravenous drug use or having had a blood transfusion.

Immunovirological assessment

The positive antibody result of a fourth generation HIV screening test (HIV Ag/Ab Combo Assay, COBAS ELECSYS HIV combi PT, Roche Diagnostics, Rotkreuz, Switzerland) was followed by an immunodot directed against HIV-1- and HIV-2-specific antigens revealing a strong positive antibody response (3+) in all bands (INNO-LIA HIV 1/2 Score; Innogenetics NV, Ghent, Belgium). The patient’s CD4+ T-cell counts were 408 cell/mm3 (25.4%) as determined by multiparameter flow cytometry.

HIV-1/2 reverse transcriptase activity was 4.351 nU/ml equivalent to 82.902 copies/ml total viraemia, measured by product-enhanced reverse transcriptase assay [11]. At the same time point, HIV-1 viral load was 21.000 copies/ml (COBAS AmpliPrep/COBAS TaqMan version 1.0; Roche Diagnostics), demonstrating a major role of HIV-2 contribution to total viraemia.

Genotypic analysis

Results of both viruses’ genotypic analyses are summarized in Table 1. Briefly, HIV-1 analysis was performed with Virco algorithm (VirtualPhenotype™, Virco TYPE HIV-1 Assay Virco Laboratory, Mechelen, Belgium) as part of the routine HIV assessment from the Centre Hospitalier Universitaire Vaudois (Lausanne, Switzerland). Related drug resistance mutations were assigned according to the IAS–USA 2011 consensus. HIV-2 genotypic analysis was done at the virology laboratory of the University Hospital of Bordeaux (Bordeaux, France) using primers previously described for amplification of reverse transcriptase and protease regions [12]. The obtained fragments were sequenced on both strands using the ABI BDV3.1 on an automated Applied Biosystems 3500XL.
Table 1. Primary drug resistance mutations and related polymorphisms present in a dual HIV-1/2-infected individual

<table>
<thead>
<tr>
<th>Viral clade</th>
<th>NRTI mutations</th>
<th>NNRTI mutations</th>
<th>PI mutations</th>
<th>Integrate mutations</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-1</td>
<td>M184V</td>
<td>V90wt/I</td>
<td>V111, K201, M36I, 69K, 89I</td>
<td>None</td>
</tr>
<tr>
<td>CRF02_AG</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>A</td>
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Bold in nucleoside reverse transcriptase inhibitor (NRTI) mutations column represents major drug resistance mutations. CRF, HIV-1 circulating recombinant form; NNRTI, non-nucleoside reverse transcriptase inhibitor; N/A, not available; PI, protease inhibitors.

Discussion

To the best of our knowledge, this is the first report of multiclass primary drug resistance in the context of HIV-1/2 dual infection. This case underlines the pitfall of dual HIV infection with two different patterns of resistance to NRTIs as demonstrated in the genotypic resistance tests performed on both viruses. Surprisingly, mutation M184V is traced in this patient after several months of treatment-naive HIV-1 infection, NRTI mutation M184V becomes quickly undetectable when transmitted as primary resistance in treatment-naive patients. However, we ignore if a different kinetic applies for resistant viral populations in the context of HIV-1/2 coinfection. Furthermore, this report underscores the limitations of current treatment options in the context of circulating HIV-1/2 dual infections, despite the irrefutable progress achieved in HIV-1 treatment. In addition, it highlights the pertinence of guiding HIV-1/2 dual infection treatment choice on genotypic analysis of both viruses. In conclusion, it brings awareness of the need of new drugs to treat multiclass-resistant HIV-1/2 infections.

Disclosure statement

The authors declare no competing interests.

References


