Abstract: 89

HIV-1 subtypes

Sudden viral load increase as an indicator of HIV-1 superinfection in HAART-naive HIV-infected patients

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Introduction: HIV superinfection is defined as infection with a second HIV strain ≥1 month after primary infection and following seroconversion. Superinfection plays an important role in driving HIV genetic diversification through recombination and may modify the patient’s drug susceptibility profile. Studies investigating its true incidence in men who have sex with men (MSM) are limited. Our aim was to determine the occurrence of superinfection events among HAART-naive MSM who showed a sudden increase in plasma viral load during routine clinical monitoring.

Methods: The clinic database was screened for eligible patients. These were HAART-naive MSM who showed a viral load increase of ≥0.5 log10 cps/ml relative to either one previous measurement for patients with recent infection, or the mean of two previous consecutive measurements differing by <0.3 log10 cps/ml in patients with established (>6 months) infection. Pol gene sequences (RT aa 1-335; PR aa 1-99) were obtained from plasma RNA collected immediately before (=baseline) and immediately after (=follow-up) the viral load increase by population sequencing. In one patient clones were generated from plasma viral RNA at baseline and from CD4-derived proviral DNA after the increase. Sequence subtyping was carried out by phylogenetic analysis. Identification of genetically divergent sequence pairs was carried out using an HKY85 model in PAUP. Determination of potential recombinants was carried out using SimPlot distance plotting, Recombination Detection Program v3.41, and tree construction using sequence fragments.

Results: Among 138 eligible patients, 47 had stored baseline and follow-up samples available for analysis. Their median (range) age was 37 (24-57) years; the ethnicity was 91% white, 4% black-Caribbean, 2% black-African and 1% other; the median (range) viral load increase was 0.6 (0.5-1.5) log10 cps/ml. Among these, we identified 5 (10.6%) white patients aged 28-41 years that showed divergent pol sequences between baseline and follow-up samples. The median (range) viral load increase in these 5 patients was 1 (0.6-1.2) log10 cps/ml. One patient had seroconverted during the previous 6 months whereas the other 4 had established infection. All 5 patients showed infection with subtype B virus at baseline. At follow-up, 4 patients showed a divergent B subtype pol sequence whereas one had A1. Two B»B patients showed complete replacement of the baseline pol sequence with a highly divergent follow-up sequence. This was confirmed by clonal analysis of proviral DNA from CD4 cells in one case. In one patient the baseline RT sequence showed no major resistance mutations whereas the follow-up sequence showed V179D/G33E. In the second patient the baseline RT sequence showed M41L and T215S, whereas the follow-up sequence showed no evidence of resistance mutations. In the other two B»B patients there was evidence of recombination between the baseline and the follow-up sequence. Full genome analysis is ongoing to characterise the possible recombinants.

Conclusions: Evidence of possible superinfection can be detected in 10.6% of HAART-naive MSM that show a sudden increase in viral load during routine follow-up and are tested by widely available pol gene sequencing. In selected patients, repeating pol gene sequencing may be indicated prior to starting HAART.

No conflict of interest