HIV Viral Escape in Central Nervous System: A Retrospective Cohort

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Abstract

Introduction: Combination antiretroviral therapy (cART) effectively reduces HIV replication in plasma and cerebrospinal fluid. CSF HIV escape is defined by viral replication in CNS despite virologic suppression in plasma or by higher viral load in CSF than in plasma. The aim of this study was to characterize the patients who met criteria of CNS HIV escape during a 4-year period in a Portuguese hospital. Human immunodeficiency virus (HIV) enters the central nervous system (CNS) early during the course of infection, establishing a unique viral reservoir in this compartment. Combination antiretroviral therapy (cART) has changed the HIV epidemic, since it effectively reduces viral load in blood and cerebrospinal fluid (CSF) to undetectable levels by current commercially available assays.

Background: Nonetheless, HIV may continue to replicate at low levels in CNS despite virologic suppression in peripheral blood, leading to viral CNS compartmentalization both with or without neurologic symptoms. This clinical entity is termed CNS HIV escape and is defined in current guidelines either by detectable HIV viral load in CSF but undetectable in plasma or by higher HIV viral load in CSF than in plasma. Although asymptomatic in most cases, CSF/plasma discordance can be neurologically symptomatic, and even cases of severe neurologic impairment have been reported. Moreover, neuroimaging features that might be helpful in the recognition of neurosymptomatic escape have been described .

Method:- From a total of 42 lumbar punctures performed with CSF HIV viral load request, from November 2014 to September 2018 in Hospital Professor Doutor Fernando Fonseca, Amadora, Portugal, we retrospectively identified patients with HIV-1 infection who presented with detectable HIV RNA in CSF samples. We selected patients who were over 17 years old and were on cART for more than 6 months and we compiled patients who met criteria of CNS viral escape as defined below (n=12). Nineteen patients were excluded as had undetectable CSF HIV viral load and the remaining (n=11) have not met the criteria below nor were on antiretroviral therapy for at least 6 months. We defined CNS HIV escape according to European AIDS Clinical Society (EACS) current guidelines: HIV viral load detectable in CSF (>20 copies/mL) but undetectable in plasma

Results: Between November 2014 and September 2018, HIV viral load in CSF was measured in 42 adult patients with chronic HIV infection at our institution. Twelve of these patients (29%) met the criteria for CNS viral escape, all of which were on cART for more than 6 months. As summarized, the population comprised 9 men and 3 women with a mean age of 42 years (± 8). Half of the patients were from sub-Saharan Africa, while the others were of Portuguese origin. The mean duration of HIV-1 infection was 9 years (± 8) and most patients had experienced advanced immune suppression in the past (median nadir CD4+ T-cell count was 47 cells/µL (12-92) and 92% of patients had stage 3 infection according to the Centers for Disease Control and Prevention (CDC) case definition 6), with diverse AIDS defining conditions, which had occurred at a median of 2 years (2-6) before the event. Four (4) patients had chronic co-infection with hepatitis viruses (Two (2) patients with hepatitis B virus and Two (2) patients with hepatitis C virus). Patients had been on cART for a mean duration of 6 years (± 4), and most of them had experienced previous multiple cART regimens. The current cART regimen consisted of two nucleoside analogue reverse transcriptase inhibitors (NRTIs) plus a protease inhibitor (PI) boosted with ritonavir in 9 patients; two NRTIs plus an integrase inhibitor (II) in 2 patients; and NRTI plus a ritonavirboosted PI plus a non-nucleoside reverse transcriptase inhibitor (NNRTI) in one patient. The most common ritonavir-boosted PI was darunavir (800 mg QD) (6 patients), followed by atazanavir (2), lopinavir (1) and saquinavir (1). Both patients whose regimen included an Integrase strand transfer inhibitor (INSTI) were on dolutegravir. Mean CNS penetrationeffectiveness (CPE)7 score for current regimen was 7(± 1). Periods of non-adherence to cART were reported in patients' medical records in three cases and one patient had experienced treatment failure.

Biography

Bárbara Flor-De-Lima is currently working in a Infectious Diseases Department, Hospital Professor Doutor Fernando Fonseca, Amadora, Portugal

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