HIV Long-term non-progression and Immune Reconstitution Syndrome: Epidemiology informing immunopathogenesis

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Professor Easterbrook is a Professor of HIV/GU Medicine and consultant physician in infectious diseases at Kings College London, where she has led the department of HIV and Genitourinary Medicine for ten years. Her HIV research programme encompasses epidemiology, clinical trials as well as collaborative pathogenesis work on the mechanisms of resistance to HIV, based on a national cohort of HIV infected long-term non-progressors. Recent research has focussed on the HIV epidemic in the African and Caribbean communities in the UK, HIV Immune Reconstitution Syndrome and operational challenges to the global rollout of antiretroviral therapy. She is principal investigator of several key epidemiological studies in the UK and sub-Saharan Africa, and also directs the HIV Clinical Trials Unit at Kings College Hospital, London. She was recently Head of Research at the Infectious Diseases Institute, Makerere University, Kampala on a one year Wellcome Trust sabbatical award, and was appointed in August 2009 as International Associate Director for Global Health at the UK Royal College of Physicians.

Abstract

Long term-non-progression:
Despite varying rates of disease progression, the majority of HIV-infected individuals eventually progress to AIDS in the absence of antiretroviral therapy (ART). However, approximately 2% of HIV infected individuals maintain long-term stability in their CD4 count (>500 cells) and are referred to as long-term non-progressors (LTNPs). A further subset (0.5 -1%) also achieve impressive viral control (viral load <500 or even <50 copies/ml) in the absence of ART and are termed Elite controllers. An understanding of the mechanisms for LTNP and natural viral control may yield critical insights for prophylactic and therapeutic antiviral interventions. The heterogeneous mechanisms that contribute to this phenotype will be reviewed briefly, including host genetic factors, innate and adaptive immune responses, and attenuated viral infection.

HIV Immune Reconstitution Syndrome:
Between 10% and 40% of patients who start ART experience a syndrome characterized by an excessive inflammatory response and a paradoxical deterioration in clinical status. This phenomenon is thought to be due to an ART-associated recovery of pathogen-specific immune responses to pre-existing or latent infections, and has been termed immune reconstitution inflammatory syndrome (IRIS). While the clinical features of IRIS are well-documented, a better understanding of the immunopathogenesis is needed to develop strategies to prevent and treat IRIS. I will show data from clinico-pathological assessment of patients with IRIS that mechanisms differ according to the type of pathogen, and whether the immune response is against viable or non-viable organisms.