

Essay

The interaction of HIV and tuberculosis

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Tuberculosis (TB) is frequently observed in HIV-infected patients living in sub-Saharan Africa. HIV-TB co-infection poses many problems with regard to diagnosis, treatment, drug resistance, and burdens on the health systems of developing African countries. The aetiological agent of TB, *Mycobacterium tuberculosis*, interacts with HIV through a number of mechanisms that support disease progression to both acquired immune deficiency syndrome and full-blown TB in co-infected patients. This essay provides a brief summary of the interactions between HIV and TB, outlining the clinical significance of co-infection, as well as cellular interactions between HIV and *M. tuberculosis*.

Keywords: HIV, Tuberculosis, Co-infection.

The incidence of Tuberculosis (TB) in sub-Saharan Africa is on the increase and can be mainly attributed to HIV infection (El-Sony, 2006). Tuberculosis is now the most common co-infection that occurs with HIV disease and is a major factor responsible for the increased morbidity and mortality rates in HIV-infected individuals (Toosi et al., 2004). This association is of global concern and in populations where HIV-TB co-infection is prevalent there are massive burdens on health care systems (Devi et al., 2003; Kassu et al., 2007). The health and survival of HIV-negative individuals in the same community may also be threatened due to the increased burden of HIV-associated TB (Corbett et al., 2003).

There is an increased risk to disease progression from both pathogens in individuals who are concurrently infected with MTB and HIV (Bal et al., 2004). Mycobacterial infection in HIV-positive individuals is chronic and has a long-term impact on viral activity (Toosi et al., 2004). Tuberculosis accelerates the course of HIV infection through various mechanisms (Goldfield and Ellner, 2007). *M. tuberculosis* infection results in cytokine dysregulation and significantly increases the levels of secreted cytokines such as TNF- α and MCP-1 in infected

cells, thereby promoting HIV replication and genetic diversity (Bal et al., 2004). The T-lymphocyte turnover rate is also hastened by these cytokine perturbations (Siawaya et al., 2007). Latent HIV within T-lymphocytes may be activated through the interactions of these cells with MTB-infected phagocytes. Dually infected phagocytes have also been demonstrated to transmit HIV to T-lymphocytes (Toosi et al., 2004).

Conversely, HIV alters the course of TB. The non-cytopathic nature of HIV in phagocytic cells enables these cells to produce a prolonged milieu of cytokine factors, including IFN- γ and IL-6, which are conducive to both disease pathologies (Bal et al., 2004). Co-infection with HIV inhibits cell-mediated responses to MTB through interruption of IL-2 signaling (Lawn et al., 2001). Under these conditions the risk of acquiring MTB infections from the environment, progression to disease, or re-activation of a latent TB infection may occur rapidly (Glassroth, 2005; Swaminathan, 2004). The deleterious effects of HIV infection in CD4⁺ T-lymphocytes impair immune function, resulting in a failure to contain mycobacterial infection and restrict the replication of the microbe (Lawn, 2005). This has significance with regards to dissemination of MTB (Swaminathan, 2004). Immune reconstitution syndrome occurs after the commencement of HAART, at a stage when the MTB specific immune response is partially restored (Frothingham et al., 2005; Goldfield and Ellner, 2007; Lawn, 2005). Co-infection with HIV and TB presents various diagnostic challenges (Kassu et al., 2007). An atypical presentation may be observed due to HIV-induced immunodeficiency, mycobacterial dissemi-

Abbreviations: TB, Tuberculosis; HIV, Human Immunodeficiency Virus; MTB, *Mycobacterium tuberculosis*; TNF- α , Tumor necrosis factor- α ; MCP-1, Monocyte chemoattractant protein-1; IFN- γ , Interferon- γ ; IL-2, Interleukin-2; IL-6, Interleukin-6; HAART, Highly Active Antiretroviral Therapy; XDR-TB, Extensively Drug Resistant Tuberculosis.

nation and the lack of self-limiting tissue damage in the host (Lawn, 2005). In such cases where chest X-rays and smear results are of limited value, molecular techniques such as the nucleic acid amplification tests should be used to assist in the diagnosis of HIV-TB co-infection.

These tests provide a rapid, sensitive, and specific method for detecting both HIV and MTB at the gene level and can also be used to detect drug resistance in HIV and TB isolates (Cohen et al., 1998; Hoffman et al., 2007; Minh et al., 2000). The clinical management and survival of co-infected patients can be improved through accurate and early diagnosis (Uma Devi et al., 2003).

In most cases treatment of co-infected individuals with antiretrovirals and anti-TB drugs decreases viral load, increases CD4⁺ T-lymphocyte counts, and improves survival. Adverse effects to therapy have been reported in some instances (Goldfield and Ellner, 2007). Drug resistant forms of TB may arise from unfavourable pharmacokinetic interactions between anti-TB and antiretroviral drugs (Siawaya et al., 2007). A recent study in the Tugela Ferry district of KwaZulu Natal in South Africa reported an outbreak of XDR-TB. All patients with XDR-TB were found to have HIV co-infection. Survival rates in these individuals were also shown to be poor (Gandhi et al., 2006). Reliable markers for TB treatment responses will significantly improve patient management, the development of new drugs, and will allow for timely treatment interventions in HIV-positive individuals (Siawaya et al., 2007). Both HIV and TB are prevalent amongst populations in developing countries. Better education and infection control, as well as improving living conditions in these areas are necessary to combat these diseases (Fätkenheuer et al., 1999).

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