Letter to the Editors

Challenges in HIV and visceral Leishmania co-infection: future research directions

Dear Sirs,

We would like to draw your attention to a recent article entitled ‘Clinical characteristics and treatment outcome of patients with visceral leishmaniasis (VL) and HIV co-infection in northwest Ethiopia’ (Hurissa et al. 2010). We commend the authors for bringing to attention such a significant public health problem and neglected disease. We share the concern of the authors about the limitations of retrospective data. But as stated in the article, the high rate of HIV/VL co-infection and its poor treatment outcomes need due attention. Thus, we would like to suggest future research directions.

Even at the diagnostic level, HIV/VL co-infection is challenging. As tissue aspiration for demonstration of the parasite is potentially associated with dangerous risks, diagnosis in district settings is often based on signs, symptoms and serology. However, the validity of rk-39 in northern Ethiopia has been questioned (Diro et al. 2007), and its usefulness would even be more doubtful in HIV co-infection (WHO 2007). Future research should focus on better diagnostic tests applicable in field conditions. Leucoconcentration is a simple technique, which can easily be performed at district clinics, is highly specific and has a good sensitivity in HIV patients (Izri et al. 1996). However, its value has not been explored in Africa.

Diagnosing HIV in patients with VL is equally problematic. False positivity rates of HIV rapid diagnostic tests of up to 60% have been reported in human African trypanosomiasis (Lejon et al. 2010), and several reports suggest that this could equally apply to VL-co-infection (Ribeiro et al. 1992). Research is needed to develop HIV testing algorithms specific for settings with high HIV–VL co-infection rates.

The treatment outcome of patients with HIV/VL is poor. Given the high toxicity of antimonials in co-infected patients (Laguna et al. 2003), clinical trials with less toxic but more expensive drugs such as liposomal amphotericin B could be a way forward. Whereas Hurissa et al. (2010) observed mortality rates of 24.5% for co-infected patients treated with antimonials vs. 3.8% for HIV-negative patients, the mortality rate among co-infected patients treated with liposomal amphotericin B was 7.7%. To what extent this also relates to a differential impact on HIV replication merits further research: whereas increased HIV-1 replication has been observed with antimonials (Barat et al. 2007), amphotericin B may inhibit HIV-1 replication (Waheed et al. 2008). Promising results have been reported with VL combination therapy in HIV-negative patients, but this remains unexplored for VL–HIV co-infection (van Griensven et al. 2010).

Monitoring patients on treatment is difficult. A lot of signs and symptoms, like splenomegaly and fever, can be caused by other opportunistic infections. Combined with the poor treatment response and high relapse rates, it often leads to numerous invasive diagnostic procedures. Moreover, the immune reconstitution inflammatory syndrome has been described in VL–HIV co-infection (Gelanew et al. 2010), which further complicates matters. There is an urgent need for surrogate markers that can be used to monitor response to VL treatment, especially in HIV patients.

Whereas earlier initiation of antiretroviral treatment (ART) improves outcomes for most opportunistic infections (Zolopa et al. 2009), there are virtually no data on patients with HIV–VL. As immune restoration is considered key for a successful VL treatment response, early initiation of ART might be important. On the other hand, drug interactions between antileishmanials and antiretrovirals have been hardly studied, particularly with the newer drugs like miltefosine. Moreover, early initiation could theoretically enhance the problem of IRIS. However, its relevance in VL–HIV infection is not well defined, as this has never been systematically and prospectively assessed, much less in areas with anthroponotic VL. Finally, several in vitro studies demonstrated the effect of HIV protease inhibitor drugs against different Leishmania species (Trudel et al. 2008). Could these drugs also be clinically superior to the other groups? As they are also renowned for their potential to interact with other drugs, this requires careful assessment.

To improve the care for HIV–VL co-infected patients in African settings, we will have to provide answers to diagnostic, treatment and monitoring questions. Hence, we need well designed research projects including clinical trials on new ways of treating HIV/VL co-infection.

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References


