Case report

Triple infection with HIV-1, HTLV-1 and *Strongyloides stercoralis*, rendering CD4+ T-cell counts a misleading entity

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We report the case of a Gabonese HIV-patient who presented with haemoptysis, weight loss, fulminant diarrhoea and subsequent ileus and elevated CD4+ T-cell counts. He was diagnosed with *Strongyloides stercoralis* and human T-lymphotrophic virus type-1 infection. After treatment of the strongyloides hyperinfection syndrome, his CD4+ T-cell counts dropped greatly. The initially elevated CD4+ T-cell counts were misleading to the clinicians with regard to decision-making on antiretroviral therapy initiation.

Introduction

This case report describes the case of a 35-year-old HIV-1-infected man presenting to the HIV clinic in Lambaréné, Gabon. He was antiretroviral therapy (ART)-naive and his immunological status appeared to be good, with a CD4+ T-cell nadir of 1,500 cells/µl. He developed a severe illness with haemoptysis, diarrhoea and subsequent ileus and was diagnosed with *Strongyloides* hyperinfection syndrome and human T-lymphotrophic virus type 1 (HTLV-1). His CD4+ T-cell count dropped greatly after treatment of the hyperinfection syndrome, suggesting a more advanced clinical stage of the HIV-1 infection than previously estimated. We believe this report of a triple infection displays complex immunological interplay between HIV-1, HTLV-1 and *Strongyloides stercoralis*, rendering CD4+ T-cell counts to a less useful tool.

Case details

An HIV-1-positive, ART-naive, 35-year-old male presented in June 2012 to the HIV clinic in Lambaréné, Gabon, with haemoptysis, persisting after treatment with broad-spectrum antibiotics. Initially he had no constitutional symptoms. The chest X-ray showed no abnormalities and sputum microscopy was negative for acid fast bacilli. CD4+ T-cell counts were remarkably high, with repeated values around 1,500 cells/µl. The full blood count yielded a mild microcytic anaemia with a haemoglobin of 10.4 g/dl without further abnormalities. There was no history of opportunistic diseases and his high CD4+ T-cell counts suggested he was in a pre-clinical stage with no reason to initiate ART.

Following routine periodic treatment for intestinal parasites with a single dose of albendazole 400 mg ('deworming'), the patient reacted with fulminant watery diarrhoea and vomiting, with weight loss of over 10% of his initial body weight. He developed a paralytic ileus which resolved spontaneously in due course. He remained afebrile throughout. Larvae of *S. stercoralis* were identified in the sputum, and many larvae were also found in the faeces (see Figure 1). The patient was treated with a curative dose of ivermectin 200 µg/kg body weight/day for five days, thus accounting for his state of immune-suppression and hyperinfection (whereas in otherwise uncomplicated infection a single-day treatment is considered adequate in the majority of cases) after which his clinical status improved greatly; the ileus resolved, he could eat normally again and gained weight. However, his CD4+

Figure 1. Larvae in a native stool sample of the patient on direct microscopy

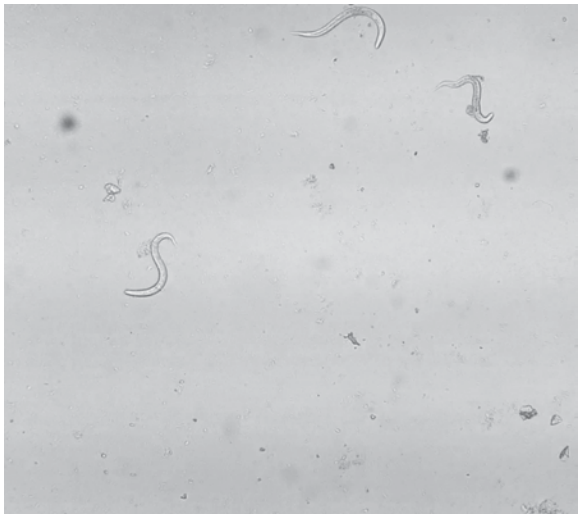

Image seen with ×400 magnification on light microscopy.

T-cell count decreased rapidly to 100 cells/μl, as confirmed by repeated measurements, and serology turned out positive for HTLV-1 (antibodies and western blot). The patient started ART and is doing well up to the time of writing.

Discussion

S. stercoralis is an intestinal nematode that is common in (sub-)tropical areas [1]. Transmission of this geohelminth is favoured by humidity. The life cycle of *S. stercoralis* consists of two stages; one as an independent organism living in soil, and the other as a parasite living in humans, after the infective filariform larvae penetrate the skin of the host. Once entered, the larvae spread haematogenously and migrate through the lungs to the intestines, where mostly rhabditiform larvae reside. The rhabditiform larvae are excreted with stool and can survive long periods in the soil. Sometimes, rhabditiform larvae can transform within the intestine to filariform larvae, facilitating auto-infection of the host by penetration through the intestinal mucosa [1].

Infection with *S. stercoralis* is mostly asymptomatic, but a hyperinfection syndrome can occur in patients with impaired cell-mediated immunity due to, for example, corticosteroid therapy [1,2]. Although initially predicted as an opportunistic infection in HIV-patients, evidence is accumulating that, in contrast to HTLV-1, HIV-infection does not lead to disseminated strongyloidiasis [3]. HIV-infection leads to a loss of T-helper 1 immune activity, but there may be little change in T-helper 2-mediated immunity [4]. This might elucidate why HIV-infection is not a direct risk factor for hyperinfection with *S. stercoralis*.

Severe strongyloidiasis has been associated with infection by HTLV-1 [5]. HTLV-1 preferably infects T-cells, inducing spontaneous proliferation of these cells and increased production of the T-helper 1 cytokines interferon-γ and tumour necrosis factor-α [6]. By decreasing the production of T-helper 2-related cytokines like interleukin (IL)-4, IL-5 and IL-13, the virus may inhibit the immune response to *S. stercoralis*, facilitating hyperinfection [7]. Moreover, HTLV-1 is known to infect dendritic cells [8], which may hamper the immune response to other antigens.

In the case presented here, infection with HTLV-1 might have caused a defective dendritic cell function, as well as a temporary increase in the number of T-helper 1 $CD4^+$ cells causing an ineffective immune response to *S. stercoralis*. This masked the severity of immunosuppression induced by HIV, and the high $CD4^+$ T-cell counts were misleading to the responsible clinicians.

Conclusion

Clinicians should consider the diagnosis of HTLV-1 in both HIV-infected and -uninfected patients from endemic areas with disseminated strongyloidiasis. In coinfected individuals, $CD4^+$ T-cell counts may be less helpful in decision making on ART initiation.

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Disclosure statement

The authors declare no competing interests.

References

1. Mejia R, Nutman TB. Screening, prevention, and treatment for hyperinfection syndrome and disseminated infections caused by *Strongyloides stercoralis*. *Curr Opin Infect Dis* 2012; **25:**458–463.
2. Fardet L, Genereau T, Poirot JL, Guidet B, Kettaneh A, Cabane J. Severe strongyloidiasis in corticosteroid-treated patients: case series and literature review. *J Infect* 2007; **54:**18–27.
3. Siegel MO, Simon GL. Is human immunodeficiency virus infection a risk factor for Strongyloides stercoralis hyperinfection and dissemination. *PLoS Negl Trop Dis* 2012 **6:**e1581.
4. Sindhu S, Toma E, Cordeiro P, Ahmad R, Morisset R, Menezes J. Relationship of *in vivo* and *ex vivo* levels of TH1 and TH2 cytokines with viremia in HAART patients with and without opportunistic infections. *J Med Virol* 2006; **78:**431–439.
5. Carvalho EM, Da Fonseca PA. Epidemiological and clinical interaction between HTLV-1 and Strongyloides stercoralis. *Parasite Immunol* 2004; **26:**487–497.

6. Porto AF, Neva FA, Bittencourt H, *et al*. HTLV-1 decreases Th2 type of immune response in patients with strongyloidiasis. *Parasite Immunol* 2001; **23:**503–507.
7. Montes M, Sanchez C, Verdonck K, *et al*. Regulatory T cell expansion in HTLV-1 and Stronyloidiasis co-infection is associated with reduced IL-5 responses to *Strongyloides stercoralis* antigen. *PLoS Negl Trop Dis* 2009; **3:**e456.
8. Jones KS, Petrow-Sadowski C, Huang YK, Bertolette DC, Ruscetti FW. Cell-free HTLV-1 infects dendritic cells leading to transmission and transformation of CD4+ T cells. *Nat Med* 2008; **14:**429–436.

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