

Case Report: *Strongyloides stercoralis* Hyperinfection in a Patient with HTLV-1: An Infection with Filariform and Rhabditiform Larvae, Eggs, and Free-Living Adult Females Output

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Abstract. *Strongyloides stercoralis* is the main etiological agent of human strongyloidiasis. Severe strongyloidiasis is commonly associated to alcoholism, corticosteroid use, and human T cell lymphotropic virus type 1 (HTLV-1) coinfection. Herein, we report a case of a 13-year-old boy coinfecting with *S. stercoralis* and HTLV-1, excreting several parasitic forms in the stool. The parasitological examination of his feces showed a large amount of filariform (about 3,000 larvae per gram of feces) and rhabditiform larvae (about 2,000 larvae per gram of feces). In addition, free-living adult females (about 50 parasites per gram of feces) and eggs (about 60 eggs per gram of feces) were detected. The main laboratory findings pointed to high immunoglobulin E (IgE) levels (228 UI/mL) and eosinophilia (11.6%). The patient was treated with three courses of ivermectin (200 µg/kg twice, 2 weeks apart), achieving the parasitological cure. An increase of about 19 times in interleucina (IL)-17 level was observed following the parasitological cure, in addition to a decrease in the white blood cell, eosinophil counts, and IgE levels. This is the first case report, to our knowledge, in which an *S. stercoralis* adult free-living female was described in human feces and where an increase in IL-17 levels after *Strongyloides* treatment in a HTLV-1 coinfecting individual was observed. This finding raises the need for further studies about IL-17 immunomodulation in *S. stercoralis* and HTLV-1 coinfecting patients.

INTRODUCTION

Strongyloides stercoralis is the main etiological agent of human strongyloidiasis.¹ The host can develop severe forms of strongyloidiasis, as hyperinfection and/or disseminated disease, depending on alterations in the immune status and it is commonly associated with alcoholism, corticosteroid use, and human T cell lymphotropic virus type 1 (HTLV-1) coinfection.²

Human T cell lymphotropic virus type 1 is a retrovirus highly prevalent in some areas of Japan, Papua New Guinea, South America, and West Africa.³ It is transmitted through mother-to-child (mainly through breastfeeding), sexual intercourse, blood transfusions, contaminated blood products, and needle sharing.⁴ Infected individuals are at risk of developing a rapidly progressive malignancy, adult T-cell leukemia, and a debilitating and sometimes fatal neurologic condition, myelopathy/tropical spastic paraparesis (HTLV-I associated myelopathy [HAM]/TSP).⁴ Moreover, HTLV-1 acts to reduce the ability of the infected host to develop an adequate immune response to organisms that require a T-helper 2 (Th2) response.^{5,6} This phenomenon is likely to be associated with an elevation in the inflammatory and regulatory cytokine levels.⁷ As a result, patients infected with HTLV exhibit increased susceptibility to infection with *S. stercoralis* and progression to severe forms of strongyloidiasis. Herein, we describe a case report of an individual coinfecting with *S. stercoralis* and HTLV-1, excreting several parasitic forms in the stool.

CASE REPORT

The patient, a 13-year-old boy, lives with his 16 membered family in a precarious rural settlement, in the Baía de Camamú,

located 300 km off Salvador (Bahia, Brazil). His mother was diagnosed with HAM/TSP in July 2013 and has been treated at a reference center for HTLV. Subsequently, an active search was conducted in the settlement for evaluating the family (May 2015) (Figure 1). The family lived in a precarious condition with an outside adapted kitchen and no bathroom, sewage, or potable water. The peridomicile was used for bodily functions. Blood and feces samples were collected from 14 individuals (except for two children under 2 years old). Thirteen members of the family tested positive to HTLV-1 by enzyme-linked immunosorbent assay and confirmed by Western blotting. All individuals were breast fed when they were children, and nine of them were under 13 years old; the probable route of HTLV-1 transmission was through breastfeeding.

The 13-year-old boy reported alternating diarrhea and intestinal constipation, in addition to abdominal pain and dyspnea. He was in a regular general condition, and his height and weight were compatible with age. The main laboratory findings were as follows: white blood cell count of 6,100/µL (neutrophils: 28.4%, lymphocytes: 50.6%, and eosinophils: 11.6%), hemoglobin of 13.9 g/dL, platelet count of $2.2 \times 10^4/\mu\text{L}$, and total immunoglobulin E (IgE) of 228 UI/mL. The patient tested negative for hepatitis, Chagas' disease, syphilis, and human immunodeficiency virus serologies.

The parasitological examination was performed using Baermann–Morales,⁸ spontaneous sedimentation and agar plate culture methods. It showed a large amount of filariform (about 3,000 larvae/gram of feces) and rhabditiform larvae (about 2,000 larvae/gram of feces). Free-living adult females (about 50 parasites/gram of feces) with 1-mm length and presenting rhabditiform esophagus, uterus filled with eggs and vulva were also found in the direct smear. In addition, *Strongyloides*-like eggs (about 60/gram of feces) (Figure 2), and eggs of *Ascaris lumbricoides* and *Trichuris trichiura* were present. The boy was then diagnosed with *S. stercoralis* hyperinfection as a manifestation of HTLV-1. He was then treated with ivermectin 200 µg/kg (twice, 2 weeks apart) and albendazole 600 mg (single dose).

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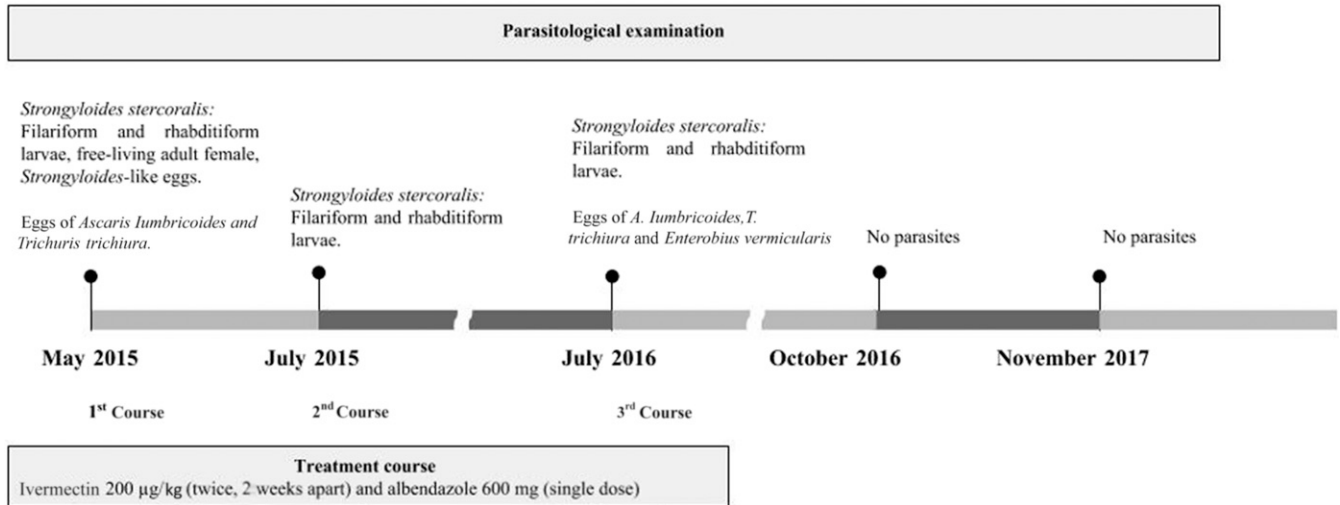


FIGURE 1. A timeline of parasitological examination and treatment course of a 13-year-old boy with *Strongyloides stercoralis* hyperinfection as a manifestation of human T cell lymphotropic virus type 1.

After 2 months of treatment (July 2015), he no longer complained of dyspnea. However, the parasitological examination of feces revealed a large amount of *S. stercoralis* rhabditiform and filariform larvae (more than 1,000 larvae/gram of feces). The patient was then treated with a new course of ivermectin and Albendazol at the same therapeutic regimen.

One year later (July 2016), a new parasitological examination was performed and a large amount of *S. stercoralis* larvae, *A. lumbricoides*, *T. trichiura*, hookworm, and *Enterobius vermicularis* eggs, as well as *Endolimax nana* cysts were present in feces. A new course of ivermectin and albendazole was given, at the same regimen. Parasitological examinations of

feces performed in October 2016 and November 2017 showed no parasites, indicating parasitological cure (Figure 1).

The levels of cytokines in sera were measured by cytometric bead array during *S. stercoralis* infection (mean of the three points before cure), and following the parasitological cure in October 2016. T-helper 1 (IL-2, IL-6, and interferon [INF]-γ), Th-2 (IL-4), and Treg (IL-10 and tumor necrosis factor [TNF]-α) cytokine levels were similar before and after parasitological cure. IL-17 level presented a 19-fold elevation following parasitological cure (Table 1). In addition, a decrease in the white blood cell and eosinophil counts, total IgE and specific IgE and immunoglobulin G1 (IgG1) levels were observed after parasitological cure (Table 1).

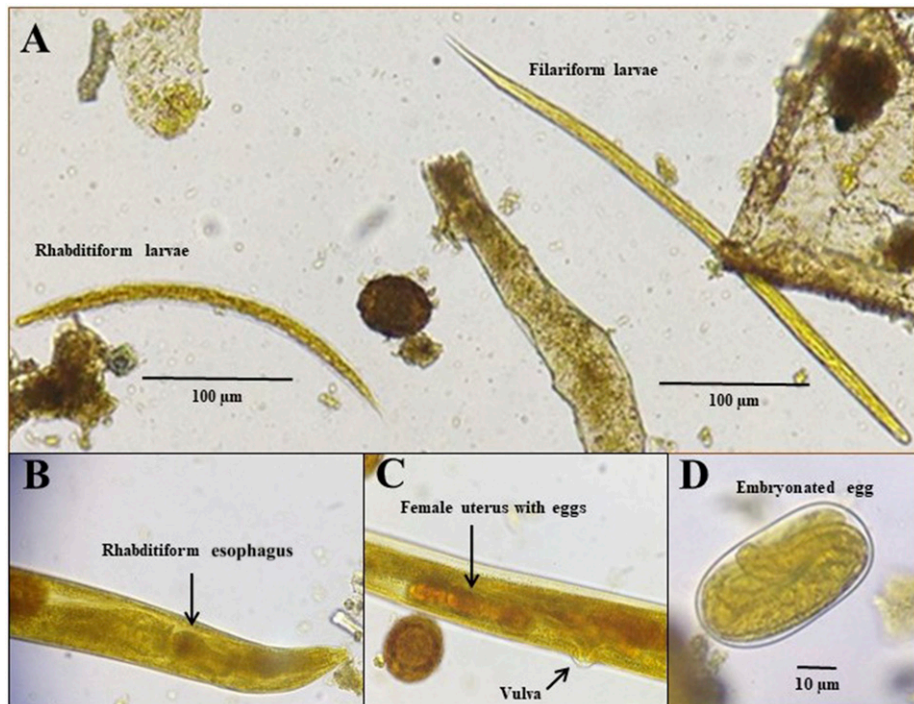


FIGURE 2. Photomicrographies of *Strongyloides stercoralis* stages in fecal smear stained with iodine showing rhabditiform and filariform larva (A), free-living female rhabditiform esophagus (B) and uterus (C), and an embryonated egg (D). This figure appears in color at www.ajtmh.org.

TABLE 1

Biological markers in an individual coinfecting with *Strongyloides stercoralis* and human T cell lymphotropic virus type 1 before and after parasitological cure

Description	Before parasitological cure*	After parasitological cure
IL-2 (pg/mL)	1.782	1.870
IL-6 (pg/mL)	2.172	2.263
INF- γ (pg/mL)	19.640	19.830
IL-4 (pg/mL)	1.866	1.618
IL-10 (pg/mL)	2.130	2.111
TNF- α (pg/mL)	1.869	1.648
IL-17 (pg/mL)	0.973	19.031
IgG1 anti- <i>S. stercoralis</i>	0.260	0.178
IgE anti- <i>S. stercoralis</i>	0.140	0.106
White blood cell count (/ μ L)	6.100	5.500
Eosinophils (%)	11.6	5.0
Total IgE (UI/mL)	228	141.4

* Mean of three measurements before the parasitological test became negative.

The Committee of Ethics in Research of the Nursing School, Federal University of Bahia, Brazil, approved the study and a written informed consent for this case report publication was assigned by the child legal guardian.

DISCUSSION

The case reported herein presents a typical *S. stercoralis* hyperinfection syndrome, with a high parasite load, and gastrointestinal and pulmonary symptoms, in a HTLV-1 coinfecting individual. However, a very unusual presentation appeared when filariform larvae, eggs, and free-living adult female were found in feces. Indeed, this is the first case report, to our knowledge, presenting *S. stercoralis* free-living adult females in human stool. The *S. stercoralis* free-living and parthenogenetic females differ morphologically. The two main differences are the size and the esophageal morphology. The parasitic forms measure around 2.5 mm in length and have filariform esophagus that occupies about a third of their body size, whereas the free-living females are smaller, measuring up to 1 mm in length and with a rhabditiform esophagus occupying only 10% of the body of the parasite.⁹ Besides, parasitic female worms live in the small intestinal mucosa, forming tunnels in the epithelium at the bases of villi in the small intestines, being rarely found in feces. The presence of a free-living form in the individual feces is probably due to the intestinal constipation, and could indicate that both parthenogenetic and sexual reproduction may be occurring in the host, which could enhance the parasite load, as was observed in the infected individual before the treatment.

Human T cell lymphotropic virus type 1 induces a spontaneous cell proliferation, generating an exacerbated Th1 response, with high levels of INF- γ , TNF- β , and IL-2, along with a decline in IL-4, IL-5, and IL-10 production, which could leave the coinfecting host more susceptible to severe strongyloidiasis.^{10,11} Although, increased IgE levels and a high eosinophil count have been associated with the host immune response against *S. stercoralis*, they are usually decreased in coinfecting *S. stercoralis* and HTLV-1 individuals.^{6,10,12–14} However, in this case report, the levels of Th1, Th2, and Treg cytokines were similar before and after the parasitological cure. Along with the elevated IgE levels and eosinophils count before the treatment, it may indicate a T-cell balance and preserved immune response, which could prevent *Strongyloides* dissemination to other organs and a fatal outcome.

IL-17 is a pro-inflammatory cytokine associated with the induction and maintenance of inflammation, resulting in the recruitment of neutrophils to the tissue.¹⁵ Human T cell lymphotropic virus type 1 tax protein induces IL-17 gene expression in HTLV-1 infected T-cell lines, which could contribute to the pathogenesis of neurological disease related to HTLV-1 infection.^{16–18} On the other hand, in *S. stercoralis* infection, cluster of differentiation 4⁺ Th17 cell frequency are decreased in an Ag-specific manner.¹⁹ In this case report, an increase in IL-17 level following strongyloidiasis treatment in a HTLV-1 coinfecting individual was observed for the first time, to our knowledge, which could reflect an inhibition of HTLV-1 inflammation response by *Strongyloides*. This could indicate a protection against inflammatory complications caused by HTLV-1, such as HAM/TSP. This finding raises the need for further studies.

The recommended treatment for *Strongyloides* hyperinfection syndrome is ivermectin 200 μ g/kg in two doses, 2 weeks apart.^{19–23} However, studies reported successive failure in the treatment of patients coinfecting with HTLV-1.²⁴ In the current case, the patient was treated three times with ivermectin before achieving a parasitological cure. Because the patient lived in a high-risk condition—without basic sanitation and with the habit of walking barefoot—it is difficult to establish whether there was a treatment failure or a reinfection. In addition to the absence of larvae in the feces, after the last treatment, a decrease in specific IgG1 and IgE levels was observed, which could indicate a reduction and/or elimination of the parasite. In summary, this is the first case report, to our knowledge, where it was possible to observe an adult free-living female elimination in human feces and where an increase in IL-17 levels following *Strongyloides* treatment was observed in a HTLV-1 coinfecting patient.

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