CASE REPORT

Secondary *Strongyloides stercoralis* prophylaxis in patients with human T-cell lymphotropic virus type 1 infection: report of two cases

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**Introduction**

Vigilance for *Strongyloides stercoralis* infection is important, even in non-endemic regions. Although endemic to tropical and subtropical regions, this intestinal helminth is increasingly common in other areas, due to the popularity of travel to and immigration from endemic areas. Chronic infection is often asymptomatic or accompanied by vague gastrointestinal symptoms, and may remain undetected for up to six decades.\(^1\) Although chronic strongyloidiasis frequently carries low morbidity, it does have the potential to develop into one of the complicated forms of infection — hyperinfection and disseminated infection — which carry a mortality rate of up to 70%, even with appropriate therapy.\(^2\)\(^–\)\(^4\)

Immunosuppression, most notably human T-cell lymphotropic virus type 1 (HTLV-1) infection and chronic corticosteroids, are the greatest risk factors for complicated strongyloidiasis in the infected individual. Therefore, empiric therapy is recommended prior to at-risk patients undergoing chemotherapy, chronic corticosteroid use, or other severe forms of immunosuppression such as organ transplant.\(^5\)\(^–\)\(^6\) However, treatment failures have been reported, and there are case reports of patients developing complicated strongyloidiasis even after a recommended dose of prophylactic antihelminthics.\(^7\) This is not surprising when considering the autoinfective nature of the parasite. Therefore, it may be more appropriate to view strongyloidiasis as a

**Summary**

Secondary ivermectin prophylaxis for strongyloidiasis in two patients with human T-cell lymphotropic virus type 1 (HTLV-1)-associated malignancies and fully treated complicated strongyloidiasis is described. Treatment was well tolerated and neither patient developed further manifestations of hyperinfection. As treatment failure for complicated strongyloidiasis has been documented in severely immunosuppressed patients, secondary prophylaxis may be indicated.

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chronic infection that can often be suppressed, but not completely eradicated. Continued prophylactic/empiric treatment in immunosuppressed patients with prior strongyloidiasis or at high risk of infection should be considered. The current literature is limited in this area, although some authors state that ongoing prophylactic treatment may be beneficial for patients with a history of previously treated \textit{S. stercoralis} infection and risk factors for hyperinfection/dissemination. There is, however, no literature to date reporting ivermectin use in this way. This paper reviews two cases of patients with HTLV-1-associated malignancies and strongyloides infection who were maintained on long-term intermittent ivermectin following complicated strongyloidiasis.

**Case reports**

In the first case, a 26-year-old female immigrant from Haiti, seropositive for HTLV-1 and undergoing active chemotherapy for T-cell leukemia, presented to The Ottawa Hospital with nausea, vomiting, diarrhea, and syndrome of inappropriate antidiuretic hormone (SIADH). Her course was complicated by Gram-negative bacterial meningitis, polymicrobial gram-negative bacteremia, endocarditis, and a massive upper gastrointestinal bleed. Pathology of gastric and duodenal esophagogastroduodenoscopy (EGD) samples revealed the etiology as \textit{S. stercoralis} infection, 21 days following admission. Thiabendazole was initially administered, but discontinued after seven days due to adverse effects. Clinical remission was achieved with two days of ivermectin therapy (200 \(\mu\)g/kg/day), followed by a third dose taken 10 days later. Remission was confirmed with three repeated negative stool samples, and an EGD biopsy taken 17 days later revealed no living parasites, granulomas from dead parasites, and ulcers in various stages of activity and repair. The patient recovered from her acute illness and was discharged from hospital with the plan of ongoing intermittent ivermectin prophylaxis (200 \(\mu\)g/kg for two days) every four to six weeks. She received two prophylactic doses with no reported adverse effects or relapse of strongyloidiasis. She succumbed to the leukemia a couple of weeks later.

In the second case, a previously healthy 41-year-old male immigrant from Togo presented to The Ottawa Hospital with post-prandial epigastric pain and diarrhea. On work-up, HTLV-1 serology was positive, and EGD biopsy revealed \textit{S. stercoralis} infection, HTLV-1-associated T-cell non-Hodgkin's lymphoma, \textit{Helicobacter pylori}, giardiasis, and Candida esophagitis. Chronic strongyloidiasis was treated with thia bendazole (1.5 g twice a day for two days). Stool samples to determine clearance of infection were sent 10 days post-treatment, and chemotherapy was initiated prior to receiving these results. The post-treatment stool samples were positive for larvae, and one dose of ivermectin at 200 \(\mu\)g/kg was administered. Eight days later, the patient presented with a high fever and pneumonia, clinically suspected to be strongyloides hyperinfection. Symptoms resolved with 12 days of thia bendazole and broad-spectrum antibiotics, and repeated stool samples were negative. Over the next nine months, the patient underwent several more cycles of chemotherapy. Although he had several further admissions for febrile neutropenia, \textit{S. stercoralis} was not identified on repeat stool samples, and no clear source of infection was identified. Each of these episodes resolved with a combination of ivermectin and broad-spectrum antibiotics. Due to risk factors for strongyloides hyperinfection, he was placed on prophylactic ivermectin (200 mg/day) for two days every four to six weeks. Nine months after initial presentation, the patient succumbed to a gram-negative bacteremia (\textit{Escherichia coli}). It is not known if this may have been secondary to refractory strongyloidiasis or his immunocompromised state, as no autopsy was performed. However, since the gastrointestinal lymphoma and chemotherapy predisposed him to gram-negative bacteremia, and there were no other concurrent gram-negative infections, it is presumed the bacteremia was not due to disseminated strongyloidiasis.

**Discussion**

These two cases describe patients with HTLV-1 related hematologic malignancies, who had endemic risk factors for strongyloidiasis and developed the complicated form of the infection. This is compatible with the medical literature, which documents not only an increased prevalence of strongyloidiasis in HTLV-1-positive patients, but also an increased incidence of complicated strongyloidiasis. In one Peruvian study comparing disease patterns of strongyloidiasis, HTLV-1 was identified in 85.7% of patients with hyperinfection, compared to 10% of patients with intestinal strongyloidiasis and 4.7% of patients with negative stool samples for strongyloides. Additionally, strongyloides is more refractory to therapy in HTLV-1-positive patients. In a study by Satoh et al., remission was achieved in only 40.6% of HTLV-1-positive patients receiving albendazole, compared to 66.0% in HTLV-1-negative patients. Data on successful remission with ivermectin in HTLV-1-positive patients is limited to case reports. Both patients described here had endemic risk factors for strongyloidiasis. The patient in case 1 did not receive screening or prophylactic treatment prior to the initiation of chemotherapy. The patient in case 2, who was diagnosed with HTLV-1 and intestinal strongyloidiasis concurrently, did receive appropriate treatment for infection immediately, prior to initiation of chemotherapy. Unfortunately, lymphoma chemotherapy was initiated prior to documented clearance of infection, as the strongyloidiasis was refractory to the initial course of thia bendazole. He subsequently received one dose of ivermectin. Although he was thought to have cleared the infection, symptoms likely due to hyperinfection occurred eight days later. Of note, thia bendazole, which was the first-line therapy at the time of his presentation, is currently not recommended due to problems with supply and due to the availability of ivermectin, which has a better efficacy and lower adverse effect profile.

Screening for strongyloidiasis is recommended in HTLV-1-positive patients, due to its increased prevalence and risk of the complicated form of infection. Patients with epidemiologic risk factors for strongyloidiasis should also be given a preemptive/prophylactic anthelmintic to treat a possible occult infection. However, such treatment is not always successful. The refractoriness to treatment of \textit{S. stercoralis} can be explained by its autoinfective nature. As a single rhabditiform larva can replicate, every parasite must be eradicated to prevent ongoing replication. To make matters worse, complete eradication is impossible to determine. Stool examination, considered the gold standard for diagnosis, is specific, but
lacks sensitivity, as larvae are shed intermittently. Additionally, it is operator-dependent, and has a sensitivity of only 15–60% for the most commonly used methods\textsuperscript{13} (variation dependent on number of samples and method of preparation used).

A potentially promising method for determining response to treatment is following sequential serology, most commonly the ELISA. Antibody titers decrease after therapy, and the ratio of pre- and post-treatment antibody levels, using a cut-off of <0.6, can be used to document response.\textsuperscript{14} Although this method has been useful to determine response to therapy in some studies,\textsuperscript{15,16} it is unclear if serology can determine complete eradication of strongyloides. For this reason and due to the potentially devastating consequences of complicated infection, it may be appropriate to stray from the traditional view that strongyloidiasis can be eradicated, and instead consider it a chronic infection that can be suppressed, but not completely eradicated.

As a result, it may be appropriate to give intermittent prophylactic therapy to patients with HTLV-1 infection, particularly those with a history of complicated strongyloidiasis. Even stronger consideration must be given to those undergoing chemotherapy. The current drug of choice for therapy is ivermectin, with albendazole as the alternative, since ivermectin has few adverse effects and a better success rate than albendazole in treating strongyloides.\textsuperscript{15–18} Ivermectin, at a dose of 200 µg/kg for one to two days every four to six weeks was the anthelmintic used in our cases, and was tolerated well. Neither patient developed further manifestations of complicated strongyloidiasis. 

In conclusion, complicated strongyloidiasis is a serious and frequently fatal infection. Both HTLV-1 infection and chemotherapy predispose previously infected patients to hyperinfection or disseminated strongyloidiasis. Initial screening and prophylactic treatment is necessary in patients with epidemiologic risks for strongyloidiasis. However, complete eradication is impossible to determine by current methods. Therefore it may be appropriate to treat these patients, especially those with associated malignancies or undergoing chemotherapy, with ongoing intermittent ivermectin therapy. Further study in this area will be needed to determine that this is advantageous.

Ethics approval: This work received approval from the Ottawa Hospital Research Ethics Board prior to the initiation of the study and complied with all stipulations.

Conflict of interest: No conflict of interest to declare.

References


