Recurrence of *Strongyloides stercoralis* infection in a patient with Hansen’s disease: A case report

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**Summary** In patients with immunosuppressive disorders, *S. stercoralis* infection may develop into a hyperinfection syndrome which, on rare occasions, may be a life-threatening condition. Therapy of *S. stercoralis* infection with thiabendazole has been limited, due to its numerous side effects, and has been replaced by albendazole and ivermectin. The present case report describes a case of *Strongyloides* Hyperinfection Syndrome (SHS) in a patient with Hansen’s disease and lack of response to first-line anthelmintic treatment. A 38 year-old man was diagnosed as having borderline lepromatous leprosy. He developed Erythema Nodosum Leprosum and was treated with thalidomide and prednisone. In May 2010 he was diagnosed with *S. stercoralis* infection and was treated with albendazole. One year later, the stool examination showed continued presence of *S. stercoralis* larvae. He was treated with ivermectin (6 mg) in a double dose (given 1 month apart) which resulted in larvae excretion clearance. The absence of infection was confirmed three times during a 1 year follow-up period by stool examination and non-detection of anti-*S. stercoralis* IgG levels.

**Introduction**

The *S. stercoralis* infection affects 30 to 100 million people throughout the world, mainly in tropical and sub-tropical areas. 1 In immunocompetent patients, *S. stercoralis* infection
usually results in a chronic intestinal infection, which can remain undetected for decades.\textsuperscript{2,3} However, \textit{S. stercoralis} may cause hyperinfection syndrome (SHS) in immunocompromised patients. SHS is not precisely defined, but an increase in the number of larvae in the stool along with manifestations confined to the gastrointestinal and respiratory systems are suggestive of hyperinfection syndrome.\textsuperscript{2}

A definitive diagnosis of strongyloidiasis is usually made by the detection of larvae in stools.\textsuperscript{4} However, \textit{S. stercoralis} is one of the most difficult intestinal parasites to diagnosis because of the low parasite load and the irregular larval output.\textsuperscript{5} The detection of circulating antibodies by ELISA has high sensitivity and it is used as a tool to support the diagnosis of strongyloidiasis.\textsuperscript{6} Options for therapy for strongyloidiasis include albendazole, thiabendazole and ivermectin.\textsuperscript{7}

This case report describes a case of \textit{Strongyloides stercoralis} hyperinfection in a patient with Hansen’s disease under long-term steroid therapy and discusses the importance of a very careful follow-up of patients with \textit{S. stercoralis} infection, since the treatment may not promptly eliminate the parasite.

\textbf{Case report}

In August 2003 a 38 year-old male patient, resident in an urban area of Salvador, Bahia, Brazil, was hospitalised with high fever (40\textdegree C), night sweats, pain in the lower and upper limbs, and difficulty in walking. The patient also complained of pain in the left hand (mainly in the fourth and fifth metatarsal), reduction in muscle strength, numbness in the left arm, and edema in the ankle. The patient was diagnosed as having borderline lepromatous leprosy according to the clinical presentation, skin smear and histopathology results; he was then started on multibacillary multi-drug therapy (MDT). Subsequently, he developed a Type 2 reaction (Erythema Nodosum Leprosum, ENL), associated with neuritis and, since then, he has been treated with thalidomide and prednisone. The prednisone was slowly tapered from 60 mg/day to a maintenance dose of 5 mg/day, with interruption of treatment during remission of the signs and symptoms of ENL. Before starting corticosteroid therapy, albendazole (400 mg in a single dose) was used as precautionary treatment for helminthic diseases that may be present.

Elevated eosinophilia was observed 5 years after the diagnosis of Hansen’s disease and mebendazole (200 mg for 3 days) was prescribed. In May 2010 the patient was diagnosed with \textit{S. stercoralis} infection for the first time, by the presence of \textit{S. stercoralis} larvae in stool by Baermann-Moraes and Agar Plate Culture (APC) methods. Treatment with albendazole (400 mg/day) was administered for 3 days and a parasitological cure was observed by the absence of \textit{S. stercoralis} larvae in stool by Baermann-Moraes and APC methods. At this time, he was under corticosteroid therapy (prednisone 5 mg/day) and his eosinophil count was 2,016/mm\textsuperscript{3} (14\%). Ten months after the albendazole treatment (March 2011), the patient complained of abdominal pain, nausea, shortness of breath and coughing. Stool examination, by Baermann-Moraes method, revealed numerous larvae of \textit{Strongyloides stercoralis} (4,000 larvae/gram of feces) and IgG anti-\textit{S. stercoralis} antibodies were positive on serological examination. Laboratory investigations revealed a pronounced eosinophilia (32\%). The patient was treated with a single oral dose of ivermectin (6 mg) and, after one month, no parasitological cure was observed; however, there was a significant reduction in larval output (96.3\% - 150 larvae/g of feces). In addition, normal liver and kidney function was observed.
The levels of total serum immunoglobulins A (345 mg/dl) and G (1,800 mg/dl) were slightly elevated and total serum IgE level was markedly elevated, above 700 IU/ml (normal level < 150 IU/ml). The level of immunoglobulin M was normal (62.9 mg/dl), as were complement proteins C3 (107 mg/dl) and C4 (17.6 mg/dl). The evaluation of the cellular response through the measurement of the number of CD4 (1,382 cell/µl) and CD8 cells (1,430 cell/µl) was normal. In addition, the patient tested negative for HIV, hepatitis A, B and C, by ELISA commercial kits.

Treatment with ivermectin was repeated, resulting in larvae excretion clearance, confirmed by three stool-sample examinations by modified Baermann-Moraes and agar plate culture methods. There were follow-up visits for one year to confirm the absence of the *S. stercoralis* infection. During this period, at each visit (1, 4 and 12 months) the parasitological cure was confirmed. In the final visit (1 year after the treatment with ivermectin), ELISA to detect circulating IgG anti-*S. stercoralis* was negative, IgE levels were normal and eosinophilia was absent. At this point, the patient was not under corticosteroid therapy and was free of leprosy reaction.

The patient had a low exposure to exogenous risk factors for *Strongyloides stercoralis* infection, and parasitological examinations of all members of his family were negative, suggesting that he was resistant to anthelmintic therapies. After the last strongyloidiasis treatment and at the end of 1 year follow-up period the patient did not complain of any strongyloidiasis symptoms.

**Discussion**

In patients under corticosteroid therapy, the immune response is altered. Moreover, corticosteroids increase levels of ecdysoyroid-like substances, which stimulate the transformation of rhabditiform larvae into the infective filarioid form, favoring hyperinfection and the dissemination of *S. stercoralis* infection.

Worldwide, two million people are estimated to be disabled by leprosy. Indian leprosy manuals mention *S. stercoralis* infection as a contraindication for steroid therapy in patients with Hansen’s disease. In Cambodia, the National Leprosy Programme included albendazole therapy before the use of corticosteroids. In Brazil, there is no agreement on how to proceed with leprosy patients who have *S. stercoralis* infection, but in some cases, before the start of immunosuppressive therapy, treatment with anthelmintics is recommended to avoid *S. stercoralis* hyperinfection. We describe the fifth case, to our knowledge, of *S. stercoralis* hyperinfection in a patient with Hansen’s disease.

In general, the Th2 immune response is dominant in patients with helminthic infections and the eosinophils play a major role in host defence. In this case report, despite corticosteroid therapy, the patient presented eosinophilia and high levels of IgE, which can be responsible for protecting the individual against the dissemination of infection. Moreover, elevated levels of IgG and IgA, and normal levels of IgM were found. Previous studies have shown that both IgM and IgG antibodies can be associated with protection against *S. stercoralis* infection.

There is no single ideal screening or diagnostic test for detecting *S. stercoralis* infection. Therefore, an approach that combines the most sensitive parasitological method (agar plate culture), immunological methods, such as ELISA and laboratory findings (eosinophilia and total serum IgE levels) is the best way to diagnose a *Strongyloides* infection. In this case
report, a robust protocol for the diagnosis of \textit{S. stercoralis} infection was not used, which may have contributed to the long-term duration of the infection. Early diagnosis and the correct treatment are the best options to prevent hyperinfection.

Some studies have demonstrated that ivermectin in a single-dose is efficacious compared with multiple-doses of thiabendazole and is better tolerated.\textsuperscript{22} However, in a study performed by Zaha \textit{et al.},\textsuperscript{23} a regimen of two single doses of 200 \textmu g/kg ivermectin, given 2 weeks apart, is more clinically suitable for the treatment of chronic strongyloidiasis. In our case, the single dose could be the reason for the apparent resistance or non-responsiveness to the first treatment with ivermectin. Failure of therapy for chronic strongyloidiasis may result in the persistence of the infection, with potential risk of disseminated disease.\textsuperscript{24} This can occur due to the low sensitivity of the methods applied to assess the efficacy of treatment, the time spent between treatment and follow-up examinations, and re-infection from the environment. Therefore, highly sensitive diagnostic methods are necessary for the follow-up examinations. Studies have reported marked declines in the \textit{S. stercoralis}-specific IgG antibodies levels for a majority of subjects, 6 months after treatment.\textsuperscript{24} Thus, the follow-up should be performed for at least 1 year after treatment. Along with the parasitological results, total serum antibodies and eosinophil count, tests which are usually available in clinical laboratories, should also be examined. Because of the higher costs to produce \textit{S. stercoralis} antigens, the determination of specific antibodies to the parasite may be implemented in reference laboratories for groups at high risk of SHS or dissemination of \textit{Strongyloides} infection, such as Hansen’s patients on corticosteroids.

In summary, clinicians must be aware of the need to follow the efficacy of anthelmintic treatment for \textit{S. stercoralis} infection in leprosy patients. Patients with Hansen’s disease should be carefully screened by searching for larvae in stool samples or by detecting specific serum antibodies, before and during corticosteroid therapy, to prevent the severe forms of \textit{S. stercoralis} infection.

References