SUBCUTANEOUS IVERMECTIN AS A SAFE SALVAGE THERAPY IN
STRONGYLOIDES STERCORALIS HYPERINFECTION SYNDROME:
A CASE REPORT

JEROME PACANOWSKI, MARIE DOS SANTOS, ANTOINE ROUX, CHRISTINE LE MAIGNAN, JACQUES GUILLOT,
VERONIQUE LAVARDE, AND MURIEL CORNET*

Départements de Microbiologie, Soins Intensifs de Pneumologie, et d'Oncologie Médicale, Hôpital Européen Georges Pompidou,
Assistance Publique des Hôpitaux de Paris, Paris, France; Université Paris V, Paris, France; Département de Parasitologie-Mycologie,
Ecole Nationale Vétérinaire d’Alfort, Maisons-Alfort, France

Abstract. Strongyloides stercoralis hyperinfection syndrome due to the acceleration of the autoinfective cycle of the nematode
is a life-threatening form of the infection occurring in immunocompromised hosts. Intestinal ileus, which is commonly encountered in this form, may reduce the bioavailability and thus the efficacy of oral anthelminthic drugs used
in the treatment of the S. stercoralis hyperinfection syndrome. We report the efficacy and safety of subcutaneous administration of ivermectin in a patient infected with human T cell lymphotropic virus type I with S. stercoralis
hyperinfection syndrome who was unresponsive to an oral combination of ivermectin and albendazole.

INTRODUCTION

Strongyloidiasis is an intestinal parasitic disease caused by the nematode Strongyloides stercoralis1 and is common in
tropical countries. In immunocompetent hosts, the infection commonly leads to minor symptoms such as transient diar-
rhea and abdominal pain, and may be asymptomatic and latent for decades due to the ability of the parasite to sustain
itself by autoinfection. In immunocompromised hosts, the overwhelming accelerated autoinfective cycle can potentially
lead to a life-threatening illness with multi-organ failure due to a massive larval invasion known as hyperinfection syn-
drome.2 The reported mortality of this hyperinfection syndrome is high (up to 87%), highlighting the importance of prophylactic anthelminthic treatment in immunocompromised patients.3 The intestinal ileus associated with the hyperinfection syndrome can reduce the bioavailability and the efficacy of an oral formulation of antiparasitic drugs. We report a case of a S. stercoralis hyperinfection syndrome that was refractory to a combination of two oral drugs and was successfully treated with subcutaneous ivermectin.

CASE REPORT

A 28-year-old African man born in Côte d’Ivoire who lived in France since he was seven years old was diagnosed with a human T cell lymphotropic virus type 1 (HTLV-1)-associated T cell leukemia lymphoma. He was treated with two cycles of doxorubicine, dacarbazine, vinblastine, bleomycine, and methylprednisolone (120 mg on days 1 and 15) alternating with two cycles of vesepide, ifosfamide, cisplatine, and methylprednisolone (120 mg/day on days 1–5). He had diarrhea and a weight loss of 10 kg. He showed complete remission at the end of the induction treatment. However, soon after the fourth cycle, he complained of asthenia, fever, abdominal pain, and incoercible vomiting. A painful tender abdomen and palpable cervical lymphadenopathies were noted. Computed tomography of the abdomen demonstrated distension of the stomach and dilatation of both the duodenum and the proximal jejunum. Diffuse wall edema in the stomach and the small bowel and compressive retroperitoneal lymphadenopathies were observed. A diagnosis of relapse was considered.

Gastro-duodenal aspiration was started and a steroid bolus (methylprednisolone, 120 mg/day) was given for seven days. At day 7, his condition worsened and he was admitted to the Oncology Department of the Hôpital Européen Georges Pompidou. Physical examination showed fever, intestinal ileus, headache, confusion, and dyspnea. The white blood cell count was 11.3 × 10^9/L with 10.5 × 10^9/L neutrophils and 0.5 × 10^9/L eosinophils. The C-reactive protein level was 66
mg/L. Microbiologic findings showed Klebsiella pneumoniae in a peripheral blood culture and Escherichia coli meningitis. He was then treated with intravenous cefotaxime (2 grams every 4 hours for 48 hours, then 2 grams every 6 hours for 8 or more days) ciprofloxacine (200 mg twice a day for 10 days). Demonstration of numerous S. stercoralis rhabditiform and filariform larvae in the gastric fluid confirmed Strongyloides hyperinfection syndrome. Oral ivermectin (12 mg/day) plus oral albendazole (400 mg/day) were given in a nasogastric catheter. Steroids were decreased rapidly during four days and then discontinued. Two days after initiation of the anthelminthic therapy, the patient showed acute respiratory failure due to interstitial pneumonitis. He was referred to the intensive care unit.

Bronchoalveolar lavage fluid, gastric fluid, and stool specimens showed persistent numerous S. stercoralis rhabditiform and filariform larvae. The eosinophil count increased to 1.79 × 10^9/L. Due to the persistence of the intestinal ileus, the absorption and efficacy of the oral treatment were uncertain. As a life-saving therapy, after informed consent of the patient’s family and agreement of the French drug administration (Agence Française de Sécurité Sanitaires des Produits de Santé) were obtained, a veterinary formulation of parenteral ivermectin (Ivomec®; Merial, Lyon, France) was given (6 mg twice a day) by subcutaneous injections in the thighs or abdominal wall. Treatment with oral albendazole was continued. The patient’s condition improved rapidly and the amount of living larva in the stools decreased dramatically 48 hours after the initiation of parenteral ivermectin. Four days later, no larva could be demonstrated in the stool, gastric fluid, or sputum. Parenteral ivermectin was administered for six days (6 mg twice a day) and was then replaced by the oral route (12
mg/day) for six additional days. The tolerance of the injec-

* Address correspondence to Muriel Cornet, Laboratoire de Microbiologie, Hôtel-Dieu, 1, Place du Parvis Notre-Dame, 75181, Paris Cedex 04, France. E-mail: mucornet@aol.com
tions was good, except for transient pain at the injection site in the abdomen. The eosinophil count remained high (1.0 × 10^9/L) for two weeks after the beginning of oral treatment and then decreased to a stable count of 0.2 × 10^9/L. The patient did not have any relapse of the S. stercoralis infection after discontinuation of treatment, but he died five weeks later of progressive lymphoma, despite a new regimen of interferon-α and zidovudine.

**DISCUSSION**

*Strongyloides stercoralis* hyperinfection syndrome has been described in immunocompromised patients. The most common predisposing factors are the use of steroids and HTLV-I infection. Other underlying diseases leading to immunodeficiency such as lymphomas, leukemias, or infection with human immunodeficiency virus have been reported to facilitate *Strongyloides* hyperinfection. As in our patient, initial features of *S. stercoralis* hyperinfection may be bacteremias, pneumonias, or meningitis due to enteric bacteria that can be carried by the larvae. Patients with such bacterial infections without an obvious cause should be investigated for the carriage of *S. stercoralis*. Bacterial infections associated with strongyloidiasis are very severe and mortality may be as high as 87%. The use of an early effective anthelmintic treatment in association with appropriate antibacterial therapy is crucial for improving the prognosis.

Currently available regimens for treatment of strongyloidiasis in humans include only oral agents. Ivermectin is now recognized as the drug of choice because it showed comparable and better rates of larval clearance than thiabendazole and albendazole, respectively, and fewer and comparable side effects than thiabendazole and albendazole, respectively. Albendazole has been used successfully in treating *S. hyperinfection syndrome.* However, since the clinical features of *S. stercoralis* hyperinfection include intestinal ileus, oral absorption of the drugs may be impaired. Only a few reports of non-oral therapy for hyperinfection syndrome have been published. One patient with bowel obstruction was successfully treated by rectal administration of thiabendazole. Tarr and others reported the use of rectal ivermectin enemas concurrently to oral albendazole and ivermectin in a patient with ileus but without diarrhea. Only two previous reports described the successful subcutaneous administration of ivermectin to human patients with *S. stercoralis* hyperinfection syndrome (Turner SA and others, unpublished data). In two of the three patients, as in our patient, the hyperinfection syndrome was associated with an HTLV-I infection. Since these studies reported a daily dose of 200 μg/kg/day, up to 14 consecutive days in the patient described by Turner and others (unpublished data), we chose the same daily regimen. No significant accumulation of ivermectin was seen in the patient described by Turner and others (unpublished data). In our patient, the subcutaneous treatment was replaced by the oral route after six days because no larva could be detected in the specimen collected and the condition of the patient improved.

Several veterinary avermectins (including ivermectin) are now available. These drugs are frequently used for the treatment and prophylaxis of gastrointestinal strongyloidiasis in cattle at a dosage of 200 μg/kg. However, the approval process for drugs for veterinary use is different from those for human use. Many parenteral formulations are licensed for use in cattle because these formulations are much more convenient to use than oral formulations and the dosage is not variable. The present case confirms the efficacy and safety for the salvage therapy of humans of a parenteral administration of veterinary ivermectin that is not currently licensed for human use. However, oral albendazole was concurrently given to our patient and could have provided a partial and late positive effect.

An association between HTLV-I infection and *S. stercoralis* increased prevalence, treatment failure, recurrent strongyloidiasis, and hyperinfection syndrome has been reported. However, this association remains controversial. Conversely, it has been suggested that *S. stercoralis* might be a cofactor in the pathogenesis of HTLV-I-induced T cell lymphomas. As observed in our patient before treatment, the lack of eosinophilia is typical in patients infected with HTLV-I infection; this retrovirus enhances the production of interferon-γ, and decreases the production of interleukin-5 and the IgE response. In our patient, corticosteroid therapy could have contributed to the lack of eosinophilia.

This report confirms that the subcutaneous use of a veterinary ivermectin preparation is a safe salvage therapy in patients with *S. stercoralis* hyperinfection syndrome unresponsive to oral therapy. Further studies assessing on a larger scale the pharmacokinetics parameters and tolerance of parenteral ivermectin are urgently needed.

Received September 28, 2004. Accepted for publication January 19, 2005.


**REFERENCES**


