

Case report

Recurrent *Strongyloides stercoralis* infection in an HIV+ patientKelli Bagwell^{a,*}, Jaya Vasudevan^a, Kristin Mondy^b^a University of Texas at Austin Dell Medical School, Department of Internal Medicine, 1500 Red River St, Austin, TX 78701, USA^b University of Texas at Austin Dell Medical School, Department of Infectious Diseases, 1500 Red River St, Austin, TX 78701, USA

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ABSTRACT

Although infection with *Strongyloides stercoralis* is often subclinical, some infections persist for decades due to the parasite's autoinfective lifecycle. Hyperinfection syndrome, however, characterized by a massive increase in parasite burden as a result of host immunosuppression causes a myriad of clinical symptoms and is associated with high mortality. Use of corticosteroids and infection with HTLV-1 virus are the biggest traditional risk factors for hyperinfection syndrome, though its development can occur with virtually any degree of immunosuppression. Recurrent hyperinfection syndrome, though rare, has also been demonstrated in persons with ongoing immunosuppression, prompting many experts to recommend continued prophylactic treatment in at risk populations. We present the case of a recurrent *S. stercoralis* hyperinfection occurring four years after previous treatment with anti-helminthic therapy in a patient with AIDS with intermittent adherence to antiretroviral therapy (ART), highlighting diagnostic and treatment issues in the management of recurrent *S. stercoralis* infection.

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Introduction

Although endemic in the tropics and subtropics, infection with the intestinal nematode *S. stercoralis* is becoming increasingly common in non-endemic regions due to increased travel and immigration. In immunocompetent hosts, infection is typically indolent and asymptomatic, persisting for years due to the parasite's unique lifecycle that allows for perpetual host autoinfection [1]. With any insult to the immune system, however, a massive increase in parasitic burden ensues, resulting in a clinical syndrome known as hyperinfection, with symptoms resulting from increased parasitic dissemination throughout the body. Rapidly fatal if unrecognized, hyperinfection can result in gastrointestinal bleeding, respiratory distress and frequent development of polymicrobial bacteremia and sepsis, as enteric organisms translocate through the gut wall during parasitic invasion [2,3].

Case presentation

A 44-year-old African woman with a history of advanced HIV complicated by intermittent adherence to ART presented to the hospital with progressive, severe abdominal pain as well as fever,

anorexia and diarrhea for over one week. Shortly after her immigration to the United States from Southern Africa four years prior, she had required hospitalization for treatment of *S. stercoralis* hyperinfection, diagnosed via positive stool studies, with resolution of infection after two weeks of anti-helminthic therapy and initiation of ART. At the time of this initial infection, a serum *S. stercoralis* antibody was negative, though a CD4 count was only 36 cells/ μ L. After completion of two weeks of combination therapy with albendazole and ivermectin, a subsequent stool study was negative and no further anti-helminthic therapy was given. The patient unfortunately had frequent lapses in her HIV care and had poor medication adherence. Upon readmission four years later, the patient was febrile to 39.1C, but had otherwise stable vital signs. She denied recent travel outside of the United States. Physical exam revealed cachexia and a distended, diffusely tender abdomen, though without peritoneal signs. Complete blood count revealed no leukocytosis or eosinophilia. A complete metabolic panel showed a sodium level of 121 mm/dL and albumin of 2.6 g/dL. Serum and urine studies were consistent with the syndrome of inappropriate antidiuretic hormone (SIADH). Other metabolic parameters were within normal limits. CD4 count was 72 cells/ μ L. A serum *S. stercoralis* antibody level was not checked due to the patient's prior negativity with active infection and persistently low CD4 count. Interestingly, an initial stool study for ova and parasites was only notable for *Blastocystis hominis* with no evidence of *S. stercoralis* larvae, though only one stool sample was sent for evaluation. CT scan of the abdomen and pelvis

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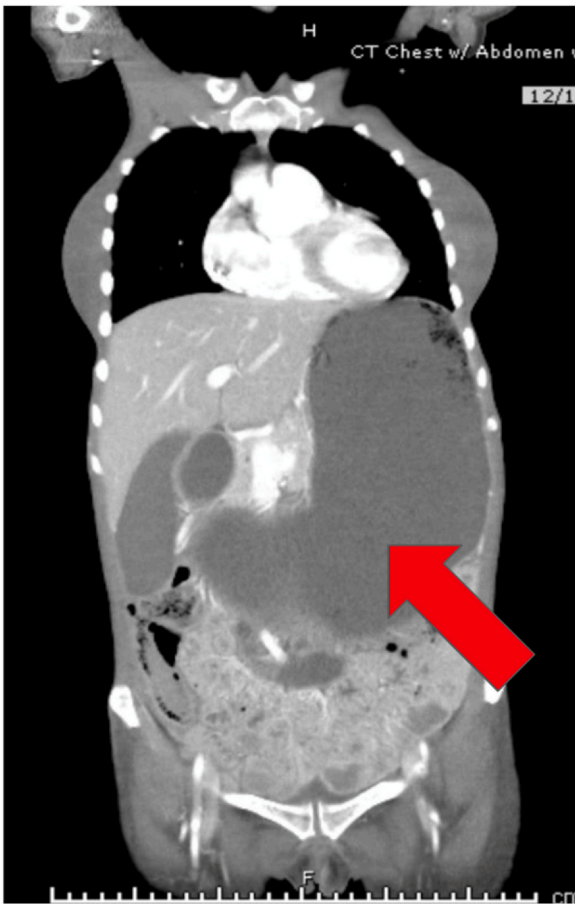


Fig. 1. CT Chest/Abdomen/Pelvis revealing distended stomach (red arrow) and proximal duodenum, consistent with SMA syndrome. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

revealed cardiomegaly, enterocolitis and a distended stomach and proximal duodenum (Fig. 1).

Broad spectrum antibacterials were initiated. *Escherichia coli* and *Citrobacter* sp. promptly grew in the aerobic bottles of two sets of blood cultures drawn at admission. Esophagogastroduodenoscopy (EGD) revealed a distended stomach with multiple nodular duodenal erosions from which biopsies were taken. Despite antibacterials and subsequent clearance of her blood cultures, the patient's abdominal pain continued to worsen, as did her abdominal distension and anorexia. In addition, new systolic cardiac murmurs were detected in multiple valvular regions. Finally, pathology from endoscopic biopsies returned, revealing *S. stercoralis* in the stomach and duodenum (Fig. 2). Transthoracic echocardiogram demonstrated vegetations up to 1.3 cm in size involving the tricuspid, aortic and mitral valves, suspicious for Loeffler's endocarditis given her biopsy results and negative repeat blood cultures (Fig. 3). These findings, indicative of parasitic involvement in both the gastrointestinal tract and cardiac system, suggested the diagnosis of *S. stercoralis* hyperinfection. Two weeks after antimicrobial and anti-helminthic therapies were initiated, her symptoms had resolved and repeat duodenal biopsies were negative for *S. stercoralis*. The patient was discharged on ART with bictegravir-emtricitabine-tenofovir alafenamide, trimethoprim-sulfamethoxazole for *Pneumocystis jirovecii* prophylaxis and monthly ivermectin for secondary *S. stercoralis* prophylaxis. After hospitalization, the patient was followed by the local community HIV clinic for further care. Repeat endoscopic biopsies two months after hospital discharge revealed no evidence of persistent infection,

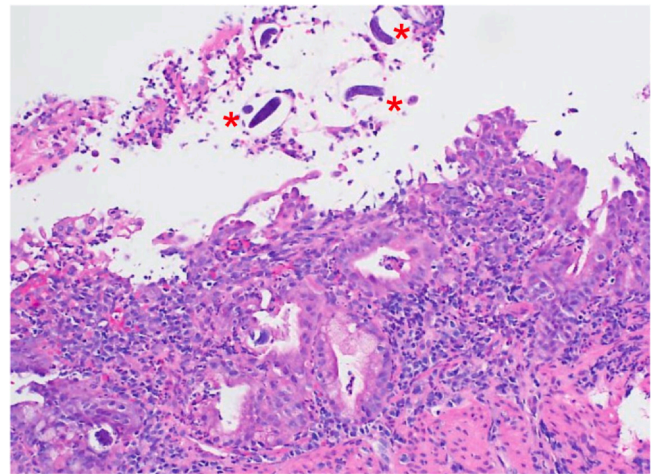


Fig. 2. Gastric biopsy pathology slide revealing *Strongyloides stercoralis* larvae (see red asterisks). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

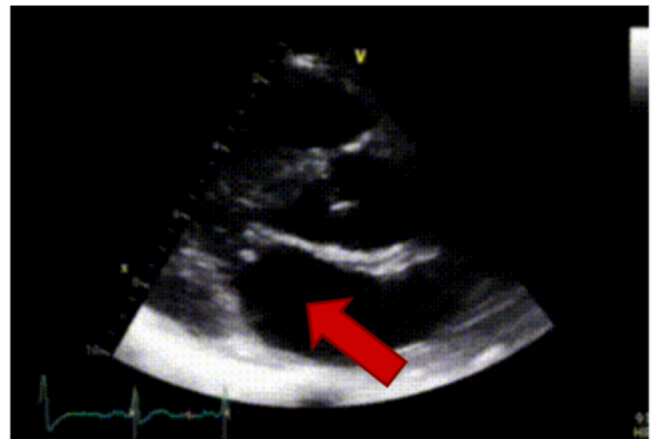


Fig. 3. Transthoracic echocardiogram parasternal long axis view with sterile mitral valve vegetations (red arrow) suggestive of Loeffler's endocarditis. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

however, she remains on continued monthly antiparasitic therapy as her CD4 count has not been reliably above 200 cells/ μ L.

Discussion

Although previously considered an AIDS-defining illness, *S. stercoralis* hyperinfection syndrome in persons with AIDS is fairly uncommon, and is more typically seen in persons with either HTLV-1 infection or chronic steroid use [1,2,4]. Though *S. stercoralis* hyperinfection itself is not infrequent, recurrent hyperinfection is rare. A few cases of recurrent *S. stercoralis* hyperinfection in other immunocompromising conditions have been previously described in persons with HTLV-1 infections and malignancy, but review of those reports demonstrated recurrence within weeks to months of original treatment, suggesting more of a primary treatment failure [5,6].

Our case demonstrates a recurrence of *S. stercoralis* hyperinfection several years after completion of a previous course of appropriate anti-helminthic therapy. We postulate this was due to a lack of regular adherence to ART and failure to maintain immune reconstitution, as the patient had no risk factors to suggest new infection, such as travel to region in which *S. stercoralis* is endemic. To our knowledge, such a relapse years after initial infection has not been previously reported.

This case highlights the complexity of *S. stercoralis* infection in immunocompromised persons, especially those who may have variable immune reconstitution as seen with HIV/AIDS. As prompt diagnosis and initiation of early therapy can greatly improve disease outcomes, this case demonstrates the need to consider recurrent hyperinfection in the differential diagnosis of those patients with AIDS presenting with typical clinical features and to obtain swift diagnosis, which is notoriously difficult. An initial stool examination in this patient was negative, which is not uncommon given the irregular shedding of larvae, even in hyperinfection, with most studies suggesting that at least four successive stool studies are required to effectively rule out infection [2,7]. This case also highlights the importance of documenting clearance of parasites after appropriate treatment through endoscopic biopsy, multiple stool examinations, or serology trends, if previously positive, and to consider secondary prophylaxis in persons with ongoing or relapsed immunocompromise. Due to the low sensitivity of stool examinations and invasiveness of endoscopic procedures, the use of monitoring sequential serum *S. stercoralis* antibody titers has been suggested as a means of evaluating efficacy of treatment in those at high risk for treatment failure [8]. Though adequate research is still lacking regarding the true sensitivity of serum antibody assays, most studies report a sensitivity of 70–100% in those currently available [7,9]. Interestingly, during our patient's initial hospitalization for *S. stercoralis* hyperinfection, her *S. stercoralis* serum IgG levels were negative, which we attribute to her low absolute CD4 count of 36 cells/ μ L at admission causing an inability to mount an antibody response. This false negativity has also been reported in other studies evaluating serologic methods of *S. stercoralis* detection, again attributable to overall reduced antibody production in those with HIV or other immunocompromising conditions [7–9]. Still, for patients with a demonstrable antibody titer, there is some evidence to suggest the use of monitoring patients serially at least 1–2 years post treatment to ensure sustained serologic trend of cure [8].

Review of current literature also supports the use of ongoing suppressive anti-parasitic therapy after initial treatment for hyperinfection in those patients with continued immunosuppression, in part due to the difficulty in assuring complete eradication of infection in this population. Most of this literature, however, is focused on a patient population either with malignancy and need for continued chemotherapy or those patients requiring ongoing treatment with corticosteroids [1,5,10]. We chose to extrapolate this recommendation to our patient with recurrent hyperinfection due to AIDS as she was at high risk of reinfection due to her history of adherence issues with taking ART. Based on this case, we would recommend that patients diagnosed with *S. stercoralis* hyperinfection be closely monitored (potentially over years) for signs or symptoms of

recurrent infection, and that those who have persistent or recurrent immunosuppression be considered as candidates for secondary prophylaxis.

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Consent

No written informed consent was obtained for this case report as it does not contain any patient identifiers in order to protect patient anonymity.

CRedit authorship contribution statement

KB: Data collection, Writing, Editing. **JV:** Writing, Editing. **KM:** General conceptualization, Editing.

Conflicts of interest

No author has any conflicts of interest to declare.

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