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CASE REPORT

Strongyloides stercoralis Hyperinfection and Disseminated Tuberculosis

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Abstract

Asymptomatic infection due to *Strongyloides stercoralis* may result in severe disease after treatment with systemic steroids. A case of *S. stercoralis* hyperinfection in a woman who was treated with systemic steroids for cerebral tuberculosis is reported. A 52-year-old female patient was admitted for a brain space–occupying lesion. A biopsy revealed tuberculoid-like giant cells necrotizing granulomatous reaction. Antituberculous (anti-tb) therapy and corticosteroids were started for suspected cerebral tuberculosis. Ten days after admission, the patient developed respiratory failure. A chest computed tomography showed multiple dense peripheral nodular infiltrates not seen at admission chest x-ray. Taking the patient's epidemiological background into account, ivermectin treatment was initiated, leading to clear improvement in her clinical condition. *S. stercoralis* was isolated from a fecal sample. Ivermectin empirical treatment before initiation of high-dose corticosteroids in patients from endemic areas could be the best strategy for prevention of hyperinfection by this parasite.

Introduction

Strongyloidiasis is a parasitosis widely distributed in tropical and subtropical regions of the world. The infection prevalence is variable in Argentina, with a heterogeneous distribution; the northeast and northwest are the two main endemic areas, with over 30 percent of the population infected.[1, 2]

In immunosuppressed individuals, strongyloidiasis can have potentially fatal complications, such as hyperinfection syndrome and disseminated strongyloidiasis.[3]

This article presents a *S. stercoralis* hyperinfection case to highlight the importance of suspecting and preventing the presence of this infection in patients who are due to receive immunosuppressive drugs, such as corticosteroids.

Case Description

A 52-year-old healthy female from Santiago del Estero was admitted to the hospital with aphasia, disorientation, and fever lasting for one month. She had been previously evaluated in another institution for several brain space–occupying lesions. A biopsy revealed tuberculoid-like giant cells necrotizing granulomatous reaction with multinucleated Langhans-type cells. She was lost to follow-up, resulting in no treatment initiation.

At present admission, the vital signs were temperature 37.8 °C, arterial blood pressure 100/60 mmHg, and heart rate 82 beats/minute. Physical examination revealed disorientation, ataxia, and mutism, but there was no other abnormal finding. Our laboratory results reported no anemia, white blood cell elevation, or platelet count abnormality. A differential with eosinophil count was not performed. No renal or hepatic function abnormalities were found. C-reactive protein (CRP) was 14 (normal range: 0–5 mg/L). A brain computed tomography (CT) showed multiple supra- and infratentorial isodense lesions, with mild perilesional edema and post-surgical changes at the biopsy site. A cerebrospinal fluid exam showed normal glucose and proteins. The acid fast stain was negative. Antituberculous (anti-tb) therapy and systemic corticosteroids were started for suspected cerebral tubercu-

losis.

After ten days of treatment and slow improvement of neurological symptoms, the patient developed diarrhea, persistent fever of 39 °C and hypoxemia. A chest CT showed multiple dense peripheral nodular infiltrates in the upper lobes, middle lobe, and lingula, as well as laminar bilateral pleural effusions. Piperacillin-tazobactam was started for hospital-acquired infection. Furthermore, oral metronidazole and vancomycin for *Clostridium difficile* (toxin A and B positive in stool sample) were started while anti-tb treatment was continued. Given the patient's worsening respiratory status (PaO_2/FiO_2 142) and the persistence of diarrhea, a new chest CT was obtained, which showed progression of lung nodules and involvement of inferior lobes with predominance of apical and posterior segments (**Figure 1**).

Taking the epidemiological background into consideration, as well as the clinical and radiological findings, a *S. stercoralis* hyperinfection was suspected. Empirical treatment with ivermectin was started. Smears of peripheral blood showed 38 percent eosinophils. Immunoglobulin E was 2,348 Ul/ml. The stool specimen parasitological examination revealed the presence of the nematode *S. stercoralis.*After starting treatment with ivermectin, the patient´s clinical condition improved, and the need for oxygen decreased. A bronchoscopy was performed, and the bronchoalveolar lavage culture was positive for *M. tuberculosis*. A new CT showed resolution of the infiltrates (**Figure 2**), and the patient was discharged 30 days after admission with outpatient follow-up recommended.

Discussion

S. stercoralis can evolve over decades as a chronic parasitization in humans. Its cycle begins when the filariform larvae of the soil penetrate the skin and reach the pulmonary alveoli through the bloodstream; from there, they ascend through the tracheobronchial tree, are swallowed, and reach the duodenum and jejunum, where they mature to adult female worms. These then lay eggs by parthenogenesis and give rise to rhabditiform larvae that are not infectious for humans. Some of these larvae can transform into filariform larvae in the intestine itself and auto-infect the host through the colorectal mucous membrane.[4–5] Hyperinfection by *S. stercoralis* can produce a severe clinical picture with high mortality (30–60%). The manifestations of pulmonary strongyloidiasis occur as a result of two different situations: larval migration and hyperinfection. Larval lung migration is part of the parasite's ordinary cycle and is generally asymptomatic. In a minority of cases, larval migration triggers a marked hypersensitivity reaction that causes cough, dyspnea, chest pain, and fever with pulmonary infiltrates associated with peripheral eosinophilia called Löffler's syndrome. Perforation of the pulmonary alveoli causes small vessel bleeding, exudation, and local inflammation. Many parasites reach the adult state when they stay in the lung for an extended period. Hyperinfection is characterized by excessive worm burden. The massive larval invasion of the lung generates cough and hemoptysis by the migration of the larvae from the capillary bed to the alveoli and can even lead to diffuse alveolar hemorrhage. A patient will present with cough, fever and dyspnea and may be in a potentially catastrophic condition. The absence of eosinophilia may indicate a significant alteration of the immune response and a worse prognosis.[2–6] Chest images may show diffuse interstitial infiltrates, consolidation, or abscesses. When the infection involves other organs besides the intestine and lung, such as the heart, liver, lymph nodes, central nervous system, stomach, or skin, it is considered a disseminated form. There is a known association between *S. stercoralis* hyperinfection and secondary bacterial infections, usually related to Gram-negative rod bacteremia from injured intestinal mucous membranes.[7, 8]

Corticosteroid use and HTLV-1 infection are the factors most associated with hyperinfection syndrome.[9] Other predisposing conditions include neoplastic disease, chronic lung disease, autoimmune diseases, transplantation, malnutrition, and immunosuppressive treatments. Corticosteroid therapy is associated with two to three times the risk of triggering a chronic asymptomatic infection with *S. stercoralis* to a severe form of the disease. In addition, symptoms associated with hyperinfection may relapse because of corticosteroid use (for cerebral tuberculosis in this case) and the delay of effective therapy for strongyloidiasis.[10] One of the explanations for corticosteroids inducing hyperinfection is acute suppression of eosinophilia and activation of lymphocytes. It has also been suggested that corticosteroids could directly affect parasites by accelerating their transformation from filariform to rhabditiform larvae.[8]

In cases of hyperinfection and dissemination, the diagnosis is made by the direct examination of biological samples: fecal matter, sputum, bronchial washing or bronchoalveolar lavage.[6] Ivermectin is the treatment of choice given that compared to albendazole and thiabendazole, ivermectin has a better safety profile.[11–12]

In our case, the infection of brain tuberculosis demanding corticosteroid therapy resulted in *S. stercoralis* hyperinfection. Although some authors argue that the initial T cell response to *M. tuberculosis* infection may play a role in *S. stercoralis* hyperinfection, we believe that in our patient, treatment with steroids was the main cause based on the temporal correlation between its initiation and the manifestations of the disease.

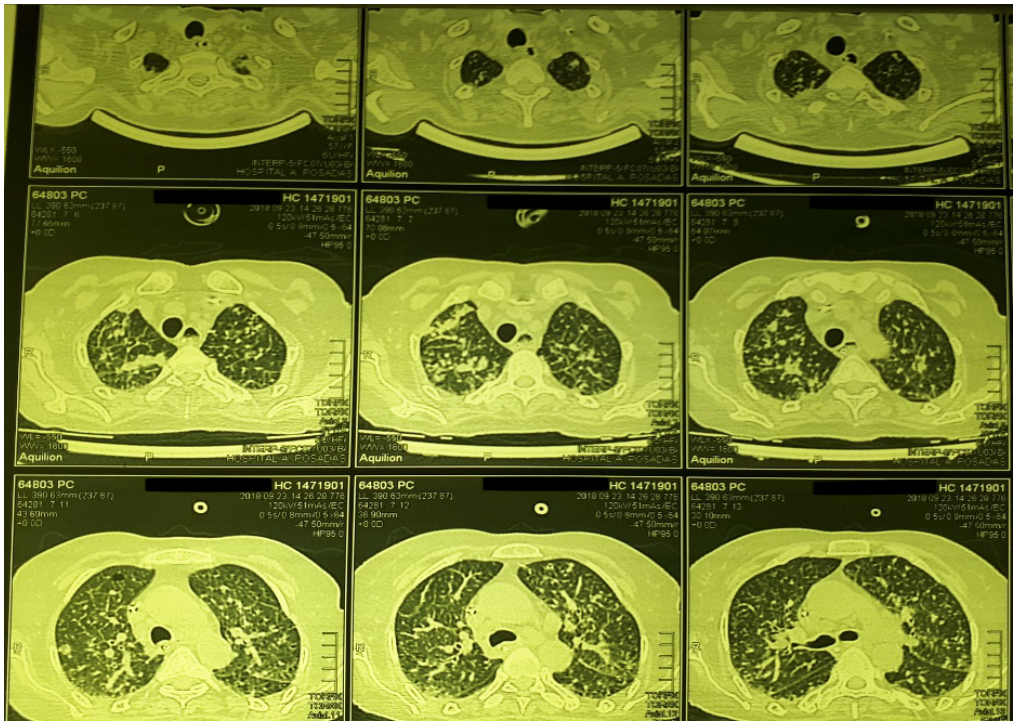

Figure 1. A chest computed tomography (CT), showing multiple dense peripheral nodular infiltrates in the upper andm iddle lobes and the lingula ten days after admission.

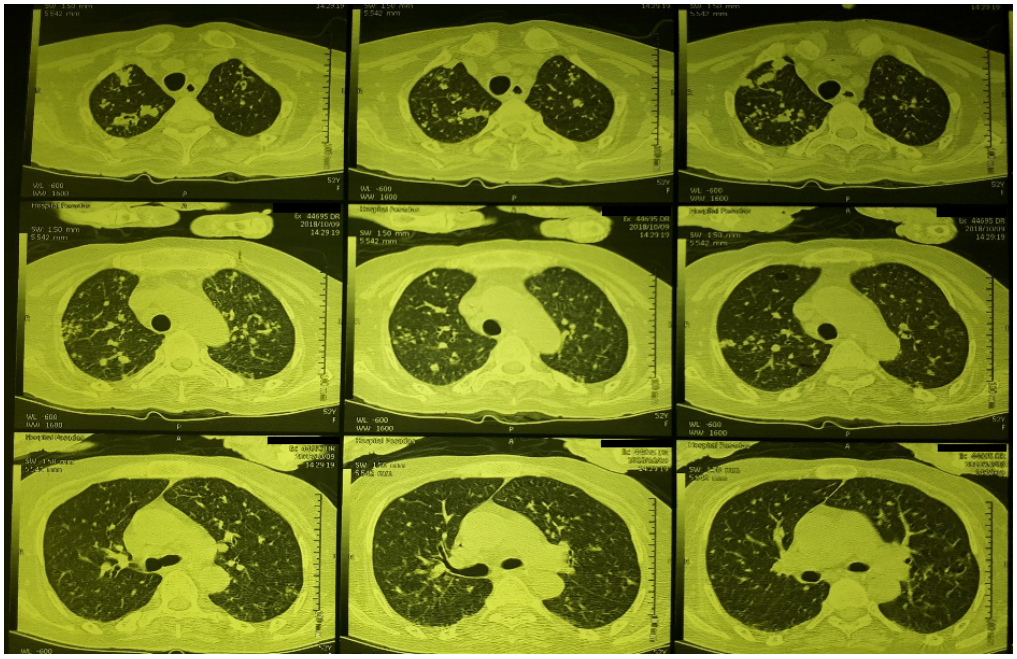

Figure 2. A chest computed tomography (CT) showing resolution of peripheral nodular infiltrates 26 days after admission.

Conclusion

S. stercoralis hyperinfection should be suspected in patients with acute pulmonary symptoms who receive immunosuppressive treatment and/or suffer from an immunodeficiency illness in an endemic area of this parasite.

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