Strongyloides Hyperinfection Syndrome:
A Curious Case of Asthma Worsened by Systemic Corticosteroids

Patient: Male, 84-year-old
Final Diagnosis: Strongyloides hyperinfection syndrome
Symptoms: Acute respiratory failure • dyspnea
Medication: —
Clinical Procedure: Bronchoalveolar lavage
Specialty: Pulmonology
Objective: Unusual clinical course

Background: Strongyloidiasis, caused by infection with Strongyloides stercoralis parasitic nematodes, is most prevalent in tropical regions of the world, such as South America, Southeast Asia, and sub-Saharan Africa, but its incidence has increased in nonendemic areas of the United States due to immigration. The majority of patients remain asymptomatic or have only mild gastrointestinal, respiratory, or dermatologic symptoms. Unrecognized strongyloidiasis can progress to Strongyloides hyperinfection syndrome, a highly fatal complication that can occur in response to immunosuppressive therapy. This rare complication is easily misdiagnosed because of its similar presentation to asthma or exacerbation of chronic obstructive pulmonary disease.

Case Report: We report a case of worsening therapeutic response to systemic corticosteroids in an elderly Colombian man who presented with symptoms of acute exacerbation of asthma. His history was positive for residence in a region endemic to S. stercoralis, and he had undergone multiple hospitalizations over the past few years for pulmonary, gastrointestinal, and dermatologic complaints. Laboratory results were significant for increased eosinophilia, and chest radiography showed blunting of the left costophrenic angle. The patient was found to have S. stercoralis hyperinfection after parasitic larvae were detected in a bronchoalveolar lavage sample. Symptoms improved after a course of ivermectin, and the patient was subsequently discharged.

Conclusions: This unusual presentation of Strongyloides hyperinfection syndrome showcases the dangers of corticosteroid therapy in individuals with undiagnosed Strongyloides infection who present with a presumed diagnosis of asthma exacerbation. Clinicians should maintain a high level of suspicion when treating patients from S. stercoralis endemic regions presenting with pulmonary, gastrointestinal, and/or dermatologic symptoms. Ivermectin is the current standard of care for both asymptomatic and complicated strongyloidiasis.

MeSH Keywords: Glucocorticoids • Ivermectin • Nematode Infections • Strongyloides stercoralis • Strongyloidiasis

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Authors' Contribution:
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Data Collection B
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Background

*S. stercoralis* is an intestinal nematode that can establish a chronic parasitic infection in the human host through its potential for autoinfection. The parasite can cause reinfection through its cyclical migratory pathway, which includes the gastrointestinal tract, vasculature, lungs, trachea, and esophagus.

Strongyloidiasis is a common condition primarily found in tropical regions of the world, such as South America, Southeast Asia, and sub-Saharan Africa. The estimated prevalence is reported to be 100 million worldwide [1]. Although strongyloidiasis primarily occurs in underdeveloped countries, its incidence has increased in nonendemic areas of the United States due to immigration [2]. Presentation of *S. stercoralis* infection varies from asymptomatic to symptomatic with multisystem involvement. Most chronically infected patients remain asymptomatic, although a sizable minority can present with persistent abdominal, pulmonary, and dermatologic symptoms [1].

In patients with an underlying immunocompromised status or in patients undergoing immunosuppressive therapy (e.g., systemic glucocorticosteroids), unrecognized strongyloidiasis carries an increased risk for hyperinfection syndrome and disseminated strongyloidiasis. These conditions have a high mortality rate and represent the primary causes of death due to *Strongyloides* infection [1,3].

Patients with hyperinfection syndrome may develop signs of acute dyspnea that mimic an exacerbation of asthma or chronic obstructive pulmonary disease (COPD) [4,5].

We present an unusual case of *S. stercoralis* hyperinfection syndrome mimicking acute asthma exacerbation, with pulmonary symptoms worsening upon glucocorticoid administration. We review the presentation, course, and treatment of this case to highlight the need for screening and preemptive treatment of strongyloidiasis in immigrants or travelers from endemic regions who present with respiratory symptoms.

Case Report

An 84-year-old Colombian man who was a nonsmoker presented to the Emergency Department (ED) reporting a worsening shortness of breath and a productive cough with green-colored sputum. He reported having intermittent shortness of breath for the past 2 months. The patient had a past medical history of coronary artery disease, coronary artery bypass grafting, pacemaker implant, hypertension, dyslipidemia, and adult-onset asthma that was diagnosed several years earlier in his home country. The patient was not immunosuppressed or on any long-term immunosuppressive medications. Due to the worsening shortness of breath and increased sputum production, he decided to visit the ED. The patient arrived in the United States 7 years ago and had a remarkable history of multiple asthma exacerbations and hospitalizations since then. He did not see a respiratory specialist before his ED visit and thus clear information about his diagnosis was not available. The patient’s home medication for asthma consisted of combination therapy with an inhaled long-acting beta-adrenergic agonist, inhaled corticosteroids, and an oral leukotriene inhibitor. The patient’s admission history indicated multiple instances of asthma exacerbations; interestingly, at least one of those exacerbations occurred shortly after treatment with corticosteroids for respiratory distress. In addition, he received treatment 1 month earlier for a pruritic rash and acute pancreatitis of unknown etiology. These symptoms developed shortly after being treated with corticosteroids in the ED for asthma exacerbation. Oral prednisone at 40 mg daily for 5 days was prescribed for acute exacerbation of asthma at our ED about 1 week prior to presentation.

Systemic review was negative for rash, abdominal pain, nausea, vomiting, diarrhea, or constipation. Physical examination on admission revealed a frail-appearing elderly man in moderate respiratory distress. His temperature was 36.9°C, and he had a pulse of 78 beats/min and a respiratory rate of 19 breaths/min. Bilateral expiratory wheezes and diffuse rhonchi were noted on physical examination, and no skin lesions or urticaria was observed.

Based on laboratory testing, the patient’s hematocrit was 29.3%, the white blood cell count was 16.2×10^3/mm³ (59% segs, 14% bands, 10% lymphocytes, 7% monocytes, 7% eosinophils, 3% myelocytes), the platelet count was 381×10^3/mm³, and the absolute eosinophil count was 1100 cells/mm³. The patient experienced respiratory failure and developed significant respiratory distress. Oxygen saturation was measured at 89% on admission and was decreasing. Given the patient’s deteriorating condition, the decision was made to commence bilevel positive airway pressure (BiPAP). The patient was placed on BiPAP with FIO₂ 60%, inspiratory positive airway pressure 10 cm H₂O, and expiratory positive airway pressure 5 cm H₂O. Arterial blood gas analysis revealed a pH of 7.45, PaCO₂ of 39 mmHg, PaO₂ of 212 mmHg, and bicarbonate of 27.1 mmHg. The patient’s condition improved, and he was transitioned to nasal cannula, saturating at 93%. Chest radiography showed blunting of the left costophrenic angle, but it was negative for any focal infiltrates (Figure 1). This result combined with the laboratory finding of 14% bands left us unable to rule out a possible small pleural effusion with underlying pneumonia. The patient was diagnosed with acute asthma exacerbation and acute respiratory failure.

Treatment consisted of intravenous (IV) methylprednisolone (40 mg daily), empiric antibiotic treatment with IV vancomycin...
(1000 mg) and IV piperacillin-tazobactam (3.375 g), combination therapy with nebulized short-acting beta-adrenergic agonist and nebulized corticosteroids, and an anticholinergic agent. Nevertheless, the patient continued to report worsening dyspnea and a productive cough over the next couple days. This unusual course prompted us to employ a more invasive approach.

Bronchoscopy was performed and revealed a normal nasopharynx/oropharynx, larynx, vocal cords, and subglottic space. The trachea was of normal caliber but appeared mildly inflamed. The carina was sharp. The tracheobronchial tree was examined to at least the first subsegmental level. Bronchial mucosa throughout appeared inflamed. Copious amounts of thick, mucoid secretions were found throughout the tracheobronchial tree, particularly on the left side. A mucus plug was obstructing the left lower lobe bronchi and was suctioned. Washings were obtained in the left upper lobe and in the left lower lobe and sent for cell count (differential and bacterial) and acid-fast bacilli (AFB), fungal, and viral analysis. The return was mucoid. Protected brushings were obtained in the lateral and posterior basal segments of the left lower lobe and sent for bacterial, AFB, and fungal analysis. There were no mucus plugs after washing, and no endobronchial lesions were seen in the visualized portion of the airway.

Bronchial washings exhibited *S. stercoralis* larvae under microscopy (Figure 2), which suggested *Strongyloides* infection. The patient was consequently prescribed oral ivermectin 9 mg (200 μg/kg) daily for 2 weeks by the infectious disease team and weaned off systemic corticosteroids. The patient reported feeling better in the following days with improvement of his cough as well as decreased sputum production. He was discharged with instructions to complete the oral ivermectin course.

**Discussion**

Strongyloidiasis is a parasitic infection caused by the multicellular helminth *S. stercoralis* of the phylum Nematoda. There are over 50 species of *Strongyloides*, but the most common species in human infections is *S. stercoralis*. This species has a worldwide distribution and is found mostly in rural regions of tropical and subtropical countries. In the United States, some southeastern states are endemic areas; however, sporadic cases are reported throughout the United States, with patients mostly being immigrants, travelers, and military personnel with a travel history to endemic regions of the world [2,6,7].

Chronic strongyloidiasis is characterized by the parasite’s ability to autoinfect the human host and remain undetected for decades [5]. Figure 3 shows the parasitic cycle of the *S. stercoralis* nematode [8]. *Strongyloides* infection is established initially through direct skin penetration by the infective filariform larvae present in contaminated soil [1]. After entering the skin, the larvae travel via the bloodstream to the alveoli in the lungs. The migratory larvae in the lungs cause the pulmonary symptoms, which are often misdiagnosed as new-onset asthma or an exacerbation of asthma or COPD [5,6,9,10]. From the lungs, the larvae ascend the trachea and are eventually swallowed and descend down the esophagus into the gastrointestinal tract. Molting of the infective filariform larvae into the adult parthenogenetic female form allows them to produce eggs that are either excreted or remain in the gastrointestinal tract. The eggs then hatch into the noninvasive and noninfectious rhabditiform larvae [5]. These rhabditiform larvae can transform into filariform larvae, which have the ability to penetrate the intestinal mucosa and restart the parasitic cycle [6]. Our patient was from Colombia, a country where *S. stercoralis* is endemic. Thus, it is likely that he was infected before arrival to the United States.
Chronic infection by *S. stercoralis* can be asymptomatic or present with cutaneous, pulmonary, or gastrointestinal symptoms [1,6]. Gastrointestinal symptoms include diarrhea, abdominal discomfort, nausea, and anorexia [1,5,6]. Dermatologic manifestations of strongyloidiasis include pruritus or a pathognomonic rash called larva currens, which is an urticarial wheal with a tortuous track created by migrating larvae [6,10]. Pulmonary symptoms include cough, shortness of breath, wheezing, and hemoptysis [1,4,6]. These symptoms can mimic acute exacerbation of COPD or asthma [9]. Some of these symptoms were apparent in our patient's history of dyspnea, cough, dermal pruritus, and acute pancreatitis. The patient's history of asthma might actually have been an overlooked indicator of strongyloidiasis, which was erroneously attributed to adult-onset asthma.

Acute pancreatitis is a rare complication of *Strongyloides* hyperinfection syndrome, with only 5 prior cases being reported in the literature [11]. The exact mechanism has not been established, but it has been theorized that inflammation of the duodenal ampulla and pancreatic duct plays a role in its pathogenesis [11]. As stated above, our patient had an episode of acute pancreatitis that developed shortly after treatment of respiratory distress with corticosteroids. A possible explanation is that the glucocorticoids caused immunosuppression, which then incited hyperinfection leading to acute pancreatitis. However, this possibility cannot be proved without serology or stool samples taken at the time.

Because the symptoms of strongyloidiasis are nonspecific and the disease has a low incidence in the United States, the diagnosis can be challenging. This circumstance explains why there is a delay in the diagnosis of chronic strongyloidiasis of about 5 years in the United States [5].

The worsening of pulmonary symptoms in our patient could be explained by hyperinfection brought on by the systemic glucocorticoids he had been prescribed a week prior. Hyperinfection syndrome involves the phenomena of accelerated autoinfec- tion and increased parasite load [1,4,10]. Autoinfection and hyperinfection are distinguished by the development or exacerbation of gastrointestinal and pulmonary symptoms and an increase in the number of larvae found in sputum or stool samples [10]. These phenomena differ from disseminated infection, which occurs when larvae migrate away from the organs normally involved in the autoinfection cycle to infect additional organ systems such as the brain and skin [1,4,10].

Hyperinfection or disseminated strongyloidiasis can occur in individuals who are immunocompromised or those undergoing immunosuppressive therapy. Such situations include steroid therapy, chemotherapy, HIV or HTLV-1 infection, organ transplants, or hematologic malignancy [9,10]. Disseminated strongyloidiasis has a high mortality rate (up to 87%) and is commonly the cause of death in chronic *Strongyloides* infection [1,3]. The complications of dissemination and hyperinfection...
Eosinophilia is a common presentation in people with chronic strongyloidiasis; for example, our patient showed an increase in eosinophil count, with an absolute count of 1100 cells/mm$^3$ [4]. Interestingly, an absence of eosinophilia is associated with a worse prognosis in strongyloidiasis [14]. Other studies have reported a similar absence of eosinophilia, possibly due to suppression of eosinophils caused by administration of systemic corticosteroids [6]. In a systematic review of case reports of 244 cases of hyperinfection syndrome and dissemination, only 22.4% of patients had eosinophilia [4]. Eosinophilia is a common presentation in people with chronic strongyloidiasis; for example, our patient showed an increase in eosinophil count, with an absolute count of 1100 cells/mm$^3$ [4]. Interestingly, an absence of eosinophilia is associated with a worse prognosis in strongyloidiasis [14]. Other studies have reported a similar absence of eosinophilia, possibly due to suppression of eosinophils caused by administration of systemic corticosteroids [6]. In a systematic review of case reports of 244 cases of hyperinfection syndrome and dissemination, only 22.4% of patients had eosinophilia [4].

Strongyloides has been well documented and is accompanied by a high mortality rate if left untreated [1,4,6,9,10]. Complications include disseminated bacterial and fungal infections, septicemia, pneumonia, meningitis, paralytic ileus, and mucosal ulceration [1,9]. Chronic strongyloidiasis has also been associated with reactive arthritis, nephrotic syndrome, chronic malabsorption duodenal obstruction, and hepatic lesions [10]. Penetration of the mucosal wall by a large number of infective filariform larvae introduces gut bacteria to the bloodstream. The larvae are also able to carry bacteria that are linked to infection, and numerous infections can present as focal or bilateral pulmonary infiltrates, lung consolidation, lung cavitation, acute respiratory distress syndrome, mediastinal lymphadenopathy, or pleural effusion [1,15].

Elaboration of the Infectious Form of the Larvae. Ivermectin is widely accepted to be the current criterion standard due to its superior efficacy and tolerability [1,10,12]. Consequently, the World Health Organization has officially designated ivermectin as one of the essential drugs for the treatment of strongyloidiasis [1]. However, there is currently no consensus on the treatment duration or dose of ivermectin [12]. Some studies have reported 200 μg/kg/day to be an effective ivermectin dosage [9,16]. Hyperinfection syndrome is considered a medical emergency, and medication should be started immediately if clinical evidence suggests the diagnosis. Although there is no established treatment regimen for hyperinfection syndrome, ivermectin for a minimum of 2 weeks is considered the de facto treatment [9].

Our patient received oral ivermectin at 200 μg/kg/day for 2 weeks as recommended by the infectious disease team, and he was weaned off systemic glucocorticosteroids. This drug regimen was intended to ensure that all remaining infectious larvae were eliminated and to prevent the cycle of endogenous reinfection. Although stool ova and parasite testing would have been useful to strengthen the diagnosis and confirm clearance of infection, it was not performed after diagnosis in this case.

Thiabendazole and albendazole are alternatives that can be used if ivermectin is not available. Thiabendazole efficacy is limited by a high relapse rate and an unfavorable adverse-effect profile including gastrointestinal symptoms, pruritus, headache, dizziness, visual disturbances, and neuropsychiatric symptoms [1,6,16]. Albendazole is an acceptable alternative in patients who have accompanying high levels of Loa loa microfilariaemia because of the risk of encephalopathy when treated with ivermectin [10].
Conclusions

Clinicians should employ a high level of caution when administering glucocorticoids for symptoms of an asthma exacerbation in patients with a history of travel or prior residence in an area endemic for *S. stercoralis*. Possible complications include *Strongyloides* hyperinfection syndrome and dissemination, both of which can be fatal. Screening efforts should be encouraged in those at risk before commencing immunosuppressive treatment. Ivermectin is the current standard of care for both asymptomatic and complicated strongyloidiasis.

References:


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