

Strongyloides Hyperinfection in a Corticosteroid-Treated Patient – A Case Report and Literature Review

Ko-Hui Hu, Chun-Chi Chang, Ching-Hsiung Lin

Strongyloides stercoralis is a widespread, soil-transmitted, intestinal nematode common in tropical and subtropical countries. The unique ability of this nematode to replicate in the human host permits cycles of autoinfection, leading to chronic disease that can last for several decades without prominent symptoms. However, hyperinfection syndrome caused by *S. stercoralis* in iatrogenically immunocompromised patients may occur. We reviewed the relevant literature and presented a recent case of Strongyloides hyperinfection in a patient treated with corticosteroids for chronic obstructive pulmonary disease (COPD). This patient was a farmer, had initial manifestations of shortness of breath and wheezing breathing sounds that mimicked acute exacerbation of COPD, and chronic gastrointestinal symptoms of anorexia. Subsequent complications of Strongyloides hyperinfection led to ileus, acute respiratory failure, *Trichosporon asahii* fungemia, and aseptic meningitis. Therefore, we should keep the diagnosis in mind when dealing with immunocompromised patients who present with gastrointestinal or pulmonary symptoms or unexplained sepsis caused by enteric pathogens. (*Thorac Med* 2011; 26: 27-32)

Key words: *Strongyloides stercoralis*, hyperinfection, corticosteroids

Introduction

Strongyloidiasis is an infection caused by *S. stercoralis* with manifestations that can range from asymptomatic eosinophilia in the immunocompetent host to disseminated disease with septic shock in the immunocompromised host. *S. stercoralis* is a widespread, soil-transmitted, intestinal nematode common in tropical and subtropical countries, and was first reported in 1876 in the stools of French soldiers on duty in Vietnam who had severe diarrhea, and the

disease the organism produced was known for many years as Cochin-China diarrhea [1].

Strongyloidiasis affects 30 to 100 million people worldwide and is endemic in Southeast Asia, Latin America, sub-Saharan Africa, and parts of the southeastern United States [2]. In contrast to other helminthic parasites, *S. stercoralis* can complete its life cycle entirely within the human host by autoinfection [3]. Most patients have a chronic asymptomatic disease that may last for several decades. However, in patients with impaired cell-mediated immunity,

Division of Chest Medicine, Department of Internal Medicine, Changhua Christian Hospital, Changhua, Taiwan
Address reprint requests to: Dr. Chun-Chi Chang, Division of Chest Medicine, Department of Internal Medicine, Changhua Christian Hospital, 135 Nanxiao St., Changhua County 500, Taiwan

autoinfection may give rise to potentially fatal hyperinfection with disseminated disease [4-5]. Herein, we report a patient with *S. stercoralis* hyperinfection who was previously treated with corticosteroids for chronic obstructive pulmonary disease (COPD).

Case Report

A 73-year-old man, a farmer with a smoking history of about 1/2 pack of cigarettes per day for 40 years, had a history of COPD and type 2 diabetes with poor glycemic control; he presented with productive cough, progressive dyspnea and wheezing breathing sounds in November 2009. Combination therapy with inhaled long-acting β_2 agonist plus inhaled corticosteroid was prescribed at the outpatient services of our chest division. He was admitted because of shortness of breath, fever, and having experienced anorexia for a period of time before admission. He was a well-nourished man with weight of 70 kg and height of 165 cm. Vital signs on admission showed a temperature of 38.3°C, heart rate of 88 beats/min, respiratory rate of 24 breaths/min, and blood pressure of 142/70 mmHg. Chest auscultation revealed diffuse wheezing breathing sounds. The initial laboratory evaluation revealed a white blood cell count of 13,500 cells/mm³ (91.4% neutrophils, 0% eosinophils), hemoglobin of 12.2g/dl and platelet count of 424,000 cells/mm³. Arterial blood gas demonstrated a pH of 7.558, PaCO₂ of 34.9 mmHg, PaO₂ of 123 mmHg, and bicarbonate of 31 mmol/L on nasal cannula at 3 L/min. The chest radiograph at admission showed mild increased axial interstitial infiltrates in the bilateral lung fields, as compared with previous chest films.

Medications on admission included intra-

venous steroids with methylprednisolone 40 mg every 12 hours, nebulized bronchodilator of ipratropium 0.5 mg/salbutamol 2.5 mg every 8 hours, and empiric intravenous antibiotic with ampicillin/sulbactam 1500 mg every 6 hours. Initially, the patient felt abdominal distension, and the abdominal plain film showed paralytic ileus. Besides, multiple ulcerative lesions in the colon, duodenal bulb and second portion of the duodenum had been found by colonoscopy and panendoscopy. Biopsy of the colonic ulcerative lesions revealed non-specific chronic inflammation with leukocytic infiltrates. Several days later, septic shock with acute respiratory failure occurred. The follow-up chest radiograph showed exacerbated bilateral axial interstitial pulmonary infiltrates (Figure 1) and *Trichos-*



Fig. 1. Chest radiograph shows axial interstitial infiltrates of bilateral lung fields, which were suggestive of atypical pneumonia related to *Strongyloides* hyperinfection with pulmonary involvement.

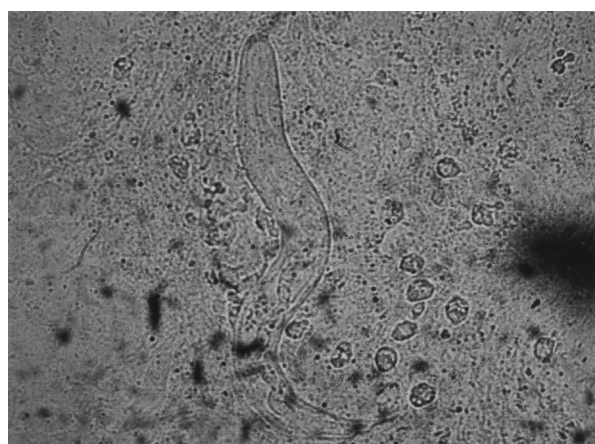
poron asahii was isolated from blood culture.

Thereafter, the diagnosis of *Strongyloides* hyperinfection was made by detection of *Strongyloides* larvae in the stool and sputum smear (Figure 2). Because of the patient's drowsy consciousness with positive meningeal signs, brain MRI was arranged, but revealed no specific abnormalities except senile brain parenchyma atrophic change. Lumbar puncture was performed and examination showed clear colorless cerebrospinal fluid (CSF) with a pH of 8.0, white blood cell count of 20 cell/mm³ (0%

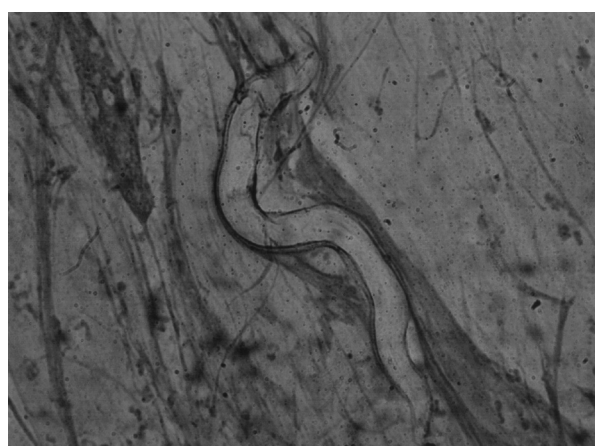
neutrophil, 98% lymphocyte), protein at 26.96 mg/dL, and glucose at 139.40 mg/dL. India ink stain of the CSF for cryptococcus, a direct smear for fungus (KOH preparation), and serum cryptococcal Ag all yielded negative findings. We prescribed a prolonged 9-day treatment course of ivermectin (200 µg/kg daily) for *Strongyloides* hyperinfection due to the persistent drowsy consciousness. The patient had a good response to the course of antihelminthic therapy and his consciousness became clear thereafter. Follow-up chest radiography revealed ongoing resolution of the pulmonary interstitial infiltrates. He received regular follow-up at our outpatient services for several months without sequelae of the pulmonary symptoms or neurologic complications.

Discussion

Strongyloides stercoralis is an intestinal nematode endemic to tropical and subtropical areas of the world. Infection of *S. stercoralis* begins when human skin contacts infective filariform larvae of *S. stercoralis*, which are found in soil or other materials contaminated with human feces. Immunocompetent hosts infected by the parasite can be asymptomatic for several decades. Most clinical manifestations of localized strongyloides infection include gastrointestinal symptoms of anorexia, abdominal pain, nausea, vomiting and diarrhea; and pulmonary symptoms of cough, dyspnea and wheezing breathing sounds [2, 6-7]. However, overwhelming hyperinfection can occur in carriers who become immunocompromised, leading to sepsis, respiratory failure, hemoptysis, paralytic ileus, gastrointestinal bleeding, cutaneous lesions, and meningitis [2, 8]. The likelihood of developing the hyperinfection



(A)



(B)

Fig. 2. Microscopic examination of sputum smears demonstrates the *Strongyloides stercoralis* larvae (A: wet mount, B: Gram stain; original magnification 400×)

syndrome is increased if cell-mediated immunity is impaired by congenital immunodeficiency, underlying malignancy, malnutrition, hypogammaglobulinemia, alcoholism, hematopoietic stem cell transplantation, human T-lymphotropic virus type 1 infection or the administration of corticosteroids or cytotoxic drugs [4, 9-11].

Our patient was a farmer, which increased the risk of contact with soil contaminated by human feces. He also had gastrointestinal (anorexia) and pulmonary (shortness of breath) symptoms before admission. We supposed that he may have been previously infected with *S. stercoralis*. Corticosteroid therapy for COPD can play an important role in the transformation of chronic infection to hyperinfection. Moreover, augmentation of intravenous methylprednisolone on admission for acute exacerbation of COPD may have worsened our patient's hyperinfection syndrome, resulting in septic shock with acute respiratory failure several days after admission. Although peripheral blood eosinophilia, a well-known clue of parasitic infection, is a common finding in chronic *Strongyloides* infection [2], our patient did not show eosinophilia on admission. This tells us that the absence of eosinophilia in patients cannot completely exclude the diagnosis. Furthermore, eosinophil levels of less than 400 cells per microliter are generally considered poor prognostic indicators for patients with severe strongyloidiasis infection [7].

The definitive diagnosis of strongyloidiasis is usually made on the basis of detection of larvae in the stool. However, the standard stool examination is insensitive (<50% sensitivity) [12], especially for uncomplicated cases of strongyloidiasis, since the intestinal worm load is usually low and the output of larvae is minimal [13]. Repeated examination of stool specimens can

increase diagnostic sensitivity. In some studies, diagnostic sensitivity increased to 50% with 3 stool examinations, and can approach 100% if 7 serial stool samples are examined [14-15]. In disseminated strongyloidiasis, filariform larvae can be found in stool, sputum, bronchoalveolar lavage fluid, and ascites [16-18]. Currently, the most reliable diagnostic test available to clinicians is a *S. stercoralis* ELISA developed by the Centers for Disease Control and Prevention for detecting serum IgG antibodies to *S. stercoralis*. In 1 study, 2 commercially available ELISAs (IVD-ELISA and Bordier-ELISA) were found to have sensitivity of 89% and 83%, respectively, and specificity of 97.2% for both in the diagnosis of strongyloidiasis [19]. However, ELISA results can be falsely negative in immunocompromised hosts and false positive results may occur in the presence of other helminth infections due to cross-reactivity with hookworms, filariae, and schistosomes [2].

Even in the asymptomatic state, strongyloidiasis must be treated due to the ability of the parasite to replicate in the hosts and its potential for a subsequent fatal hyperinfection. In the past, thiabendazole was the drug of choice for the treatment of strongyloidiasis. Recently, ivermectin (200 µg/kg daily for 2 days) has been found to be the most effective drug in the treatment of disseminated strongyloidiasis and is registered as the drug of choice in the World Health Organization's list of essential drugs for the treatment of strongyloidiasis [20]. For hyperinfection syndrome and disseminated strongyloidiasis, treatment with ivermectin should be extended for at least 5 to 7 days or until the clinical syndrome has resolved and the larvae have not been identified for at least 2 weeks. Follow-up examinations for larvae in stool or sputum are necessary, with repeat dos-

ing if the infection persists [21].

In conclusion, *Strongyloides* hyperinfection syndrome mostly occurs in immunocompromised hosts who are receiving corticosteroid therapy for underlying disease. It is often associated with sepsis from enteric pathogens and can lead to high mortality rates. Therefore, patients at risk for acquiring *S. stercoralis* infection should always be screened, identified, and treated, especially before administration of corticosteroid therapy.

References

- Grove DI. Human strongyloidiasis. *Adv Parasitol* 1996; 38: 251-309.
- Siddiqui AA, Berk SL. Diagnosis of *Strongyloides stercoralis* infection. *Clin Infect Dis* 2001; 33: 1040-7.
- Siddiqui AA, Genta RM, Berk SL, Strongyloidiasis. Guerrant RL, Walker DH, Weller PF, *Tropical Infectious Diseases - Principles, Pathogens & Practice*, Second edition, Philadelphia, Elsevier, 2006: 1274.
- Keiser PB, Nutman TB. *Strongyloides stercoralis* in the immunocompromised population. *Clin Microbiol Rev* 2004; 17: 208-14.
- Haque AK, Schnadig V, Rubin SA, *et al.* Pathogenesis of human strongyloidiasis: autopsy and quantitative parasitological analysis. *Mod Pathol* 1994; 7: 276-88.
- Fardet L, Genereau T, Poirot J, *et al.* Severe strongyloidiasis in corticosteroid-treated patients: Case series and literature review. *J Infect* 2007; 54: 18-27.
- Newberry AM, Williams DN, Stauffer WM, *et al.* Strongyloides hyperinfection presenting as acute respiratory failure and Gram-negative sepsis. *Chest* 2005; 128: 3681.
- Morrell MR, Dallas J, Kollef MH. A 50-year-old woman with abdominal pain and respiratory failure 3 months after kidney transplantation. *Chest* 2008; 134: 442-6.
- Safdar A, Malathum K, Rodriguez SJ, *et al.* Strongyloidiasis in patients at a comprehensive cancer center in the United States. *Cancer* 2004; 100: 1531-6.
- Orient H, Crawley C, Cwynarski K, *et al.* Strongyloidiasis pre- and post-autologous peripheral blood stem cell transplantation. *Bone Marrow Transplant* 2003; 32: 115-7.
- Concha R, Harrington W Jr, Rogers AI. Intestinal strongyloidiasis: recognition, management, and determinants of outcome. *J Clin Gastroenterol* 2005; 39: 203-11.
- Boulware DR, Stauffer WM III, Walker PF. Hypereosinophilic syndrome and mepolizumab. *N Engl J Med* 2008; 358: 2838-9.
- Liu LX, Weller PF. Strongyloidiasis and other intestinal nematode infections. *Infect Dis Clin North Am* 1993; 7: 655-82.
- Nielsen PB, Mojon M. Improved diagnosis of *Strongyloides stercoralis* by seven consecutive stool specimens. *Zentralbl Bakteriol Mikrobiol Hyg A* 1987; 263: 616-8.
- Pelletier LL. Chronic strongyloidiasis in World War II Far East ex-prisoners of war. *Am J Trop Med Hyg* 1984; 33: 55-61.
- Smith SB, Schwartzman M, Mencia LF, *et al.* Fatal disseminated strongyloidiasis presenting as acute abdominal distress in an urban child. *J Pediatr* 1977; 91: 607-9.
- Williams J, Nunley D, Dralle W, *et al.* Diagnosis of pulmonary strongyloidiasis by bronchoalveolar lavage. *Chest* 1988; 94: 643-4.
- Harris RA Jr, Musher DM, Fainstein V, *et al.* Disseminated strongyloidiasis: Diagnosis by sputum examination. *JAMA* 1980; 244: 65-6.
- van Doorn HR, Koelewijn R, Hofwegen H, *et al.* Use of enzyme-linked immunosorbent assay and dipstick assay for detection of *Strongyloides stercoralis* infection in humans. *J Clin Microbiol* 2007; 45: 438-42.
- Albonico M, Crompton DW, Savioli L. Control strategies for human intestinal nematode infections. *Adv Parasitol* 1999; 42: 277-341.
- Rosenthal PJ. Protozoal and helminthic infections. In: McPhee SJ, Papadakis MA, Tierney LM Jr. *Current Medical Diagnosis & Treatment* 2010, 49th edition, The McGraw-Hill Companies, 2010 online.

接受類固醇治療的病患引發糞小桿線蟲高度感染之 病例報告及文獻回顧

胡克輝 張竣期 林慶雄

糞小桿線蟲是一種經由土壤傳播感染且流行於熱帶及亞熱帶許多國家的腸道寄生蟲。這種線蟲擁有獨特的能力可以在人類宿主體內複製而引發自體感染，並可導致持續數十年無明顯症狀的慢性疾病。然而，高度感染症候群可以發生在因接受免疫抑制治療而導致免疫力低下的病人。在此，我們回顧了相關文獻及提出新近因慢性阻塞性肺疾而接受類固醇治療的病患引發糞小桿線蟲高度感染的病例。此病患是一位農夫，他剛開始的表現是類似慢性阻塞性肺疾急性發作的呼吸急促及喘鳴聲，和食欲不振的腸胃道症狀。接下來因糞小桿線蟲高度感染的併發症導致腸阻塞、急性呼吸衰竭、*Trichosporon asahii*敗血症和無菌性腦膜炎。因此，對於免疫功能低下的病患，如果呈現腸胃道、呼吸道症狀或難以解釋的腸胃道病原菌所引起的敗血症時，吾人應對這個診斷抱持高度警覺。(胸腔醫學 2011; 26: 27-32)

關鍵詞：糞小桿線蟲，高度感染，類固醇