International Journal of Gerontology 5 (2011) 53–55

Contents lists available at ScienceDirect

International Journal of Gerontology

journal homepage: www.ijge-online.com

Case Report

Acute Respiratory Distress Syndrome Complicating *Strongyloides stercoralis* Hyperinfection†

Ming-Ju Tsai [1‡], Tzung-Shiun Wu [1‡], Kun-Bow Tsai [2], Huang-Chi Chen [3*], Jhi-Jhu Hwang [4,5], Ming-Shyan Huang [4,6]

[1] *Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University,* [2] *Department of Pathology, Kaohsiung Municipal Hsiao-Kang Hospital, Kaohsiung Medical University,* [3] *Department of Internal Medicine, Kaohsiung Municipal Hsiao-Kang Hospital, Kaohsiung Medical University,* [4] *Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University,* [5] *Department of Respiratory Therapy, College of Medicine, Kaohsiung Medical University,* [6] *Department of Internal Medicine, School of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan.*

ARTICLE INFO

Article history:
Received 7 February 2010
Accepted 26 April 2010
Available online 5 March 2011

Keywords:
acute respiratory distress syndrome,
bronchoscopy,
pneumonia,
sepsis,
Strongyloides stercoralis

SUMMARY

Strongyloidiasis is endemic in tropic and subtropic areas, but is currently seldom encountered in developed area like Taiwan. We present an elder man with acute respiratory distress syndrome complicating *Strongyloides stercoralis* hyperinfection. There was no significant clue initially for diagnosing this patient as having *S. stercoralis* hyperinfection. Neither peripheral eosinophilia nor significant hemoptysis was noted. Bronchoscopy played a critical role to define the unexpected cause of his progressive pulmonary infiltrates. The correct diagnosis was soon made by recognition of the worm in bronchioloalveolar lavage cytology, and specific treatment was initiated promptly. For a septic patient with progressive pulmonary infiltrates, bronchoscopic studies including cytology may be necessary for defining the cause. Hyperinfection strongyloidiasis should be considered as a cause of acute respiratory distress syndrome in immunocompromised patient, especially with the presence of chronic gastrointestinal symptoms.

1. Introduction

Strongyloidiasis is endemic in tropic and subtropic areas[1,2], but is currently seldom encountered in developed area like Taiwan. We report here a case of acute respiratory distress syndrome complicating *Strongyloides stercoralis* hyperinfection.

2. Case Report

A 72-year-old man with a history of chronic obstructive pulmonary disease, chronic gouty arthritis, and chronic kidney disease had suffered from intermittent chest pain for more than 10 years. The chest pain was dull in character, locating in anterior chest wall, relieved by rest or nitroglycerin, and aggravated by exertion. No radiation was noted, and the duration of each episode was about 15 minutes. He lived at home with poor self-care and hygiene. He did not receive regular medical follow-up, but he took medications from local pharmacy, which included herbs, pain killers, and steroids.

He came to the emergency department of our hospital for general weakness, intermittent chest tightness, and diarrhea for about a week, presenting with normal vital signs and cushingoid appearance. Electrocardiography showed Q wave in inferior wall, but no serial change or elevation in cardiac enzymes was noted. Laboratory examination showed pyuria and impaired liver and renal functions, but no leukocytosis was also noted. He was admitted to our hospital under the impression of urosepsis.

Unfortunately, his consciousness deteriorated on the fifth hospital day, and high C-reactive protein level, thrombocytopenia, and severe metabolic acidosis were noted. He was intubated for his respiratory failure. Because of persisted diarrhea and the abdominal radiograph showed severe ileus, empirical antibiotic treatment with cefpirome and metronidazole was prescribed for suspected intra-abdominal infection. No parasitic ova were isolated from his stool. Because bilateral pulmonary infiltrates developed rapidly with the appearance compatible with the diagnosis of acute respiratory distress syndrome (Fig. 1), antibiotic was adjusted to

* *Correspondence to:* Dr Huang-Chi Chen, Department of Internal Medicine, Kaohsiung Municipal Hsiao-Kang Hospital, Kaohsiung Medical University, 482 Shan-Ming Rd, Hsiao-Kang District, 812, Kaohsiung, Taiwan. Tel.: +886 7 803 6783x3441; fax: +886 7 8063346.
E-mail address: huangchichen@gmail.com (H.-C. Chen).

† All contributing authors declare no conflict of interest.

‡ M.-J. Tsai and T.-S. Wu contributed equally to this article.

1873-9598/$ – see front matter
doi:10.1016/j.ijge.2011.01.010

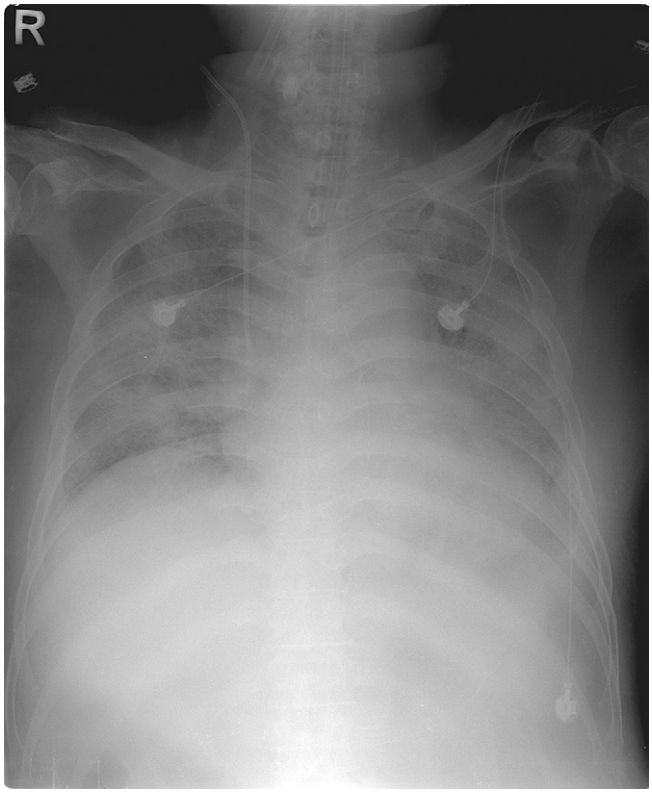

Fig. 1. Chest radiograph showed bilateral pulmonary infiltrates, which was compatible with the diagnosis of acute respiratory distress syndrome.

piperacillin/tazobactam 2 days later to cover *P*seudomonas *aeruginosa* for suspected nosocomial pneumonia. He developed septic shock soon, requiring inotropic support. Abdominal computed tomography was not able to be obtained because of his high-oxygen requirement. Blood culture later yielded *Escherichia coli* and *Klebsiella pneumoniae*, which were both susceptible to piperacillin/tazobactam. Bronchoscopy was done, which revealed coffee ground discharge in posterior segment of left upper bronchi, and bronchioloalveolar lavage (BAL) cytology found filariform larvae of *S. stercoralis* (Fig. 2). Ivermectin was administered for 2 days. Colonofiberoscopy was arranged to survey the cause of his diarrhea, which revealed erosive lesions in right transverse colon, and biopsy showed parasite-like tissue fragments with granulomatous reaction (Fig. 3). He developed oliguric acute kidney injury with hyperkalemia and severe metabolic acidosis. Continuous veno-venous hemofiltration was started soon. However, profound shock developed few hours later, which was not reversed with full-dosed vasopressors and any aggressive treatment. He succumbed to his illness soon.

3. Discussion

S. stercoralis is a soil-living nematode that is considered endemic in tropic and subtropic areas[1,2]. It is able to complete its life cycle within the host through an asexual autoinfective cycle, allowing the infection to persist in the host indefinitely[2,3]. Risk factors of *S. stercoralis* infection include white patients, men, corticosteroid use, hematologic malignancy, prior gastric surgery, and hypochlorhydria or achlorhydria[4,5].

S. stercoralis may cause hyperinfection in immunocompromised hosts with high-mortality rate (up to 90%)[3,6–8]. Glucocorticoid treatment and human T-lymphotropic virus type 1 infection are the two conditions most specifically associated with hyperinfection,

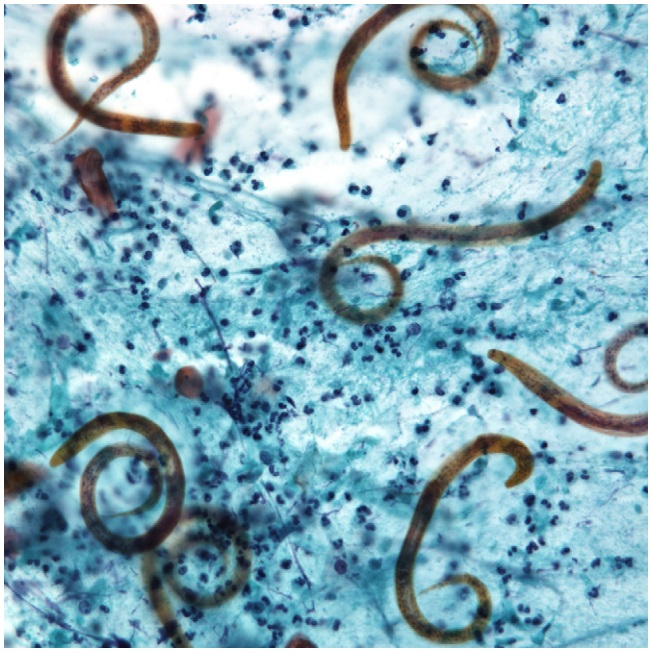

Fig. 2. Bronchioloalveolar lavage cytology showed numerous aggregated neutrophils and eosinophils, suggesting respiratory tract infection. Filariform larvae of *Strongyloides stercoralis* were identified by their worm-like appearance with characteristic notch at the tail end. (Papanicolaou stain; original magnification, ×40).

whereas cases have been reported in association with hematologic malignancy, malnutrition, hypogammaglobulinemia, acquired immunodeficiency syndrome, transplant recipients, and patients receiving chemotherapy[1–3,6,9–11].

Strongyloidiasis may present with a variety of clinical manifestations, including constitutional, cutaneous, gastrointestinal, and pulmonary symptoms. This includes weight loss, skin rash,

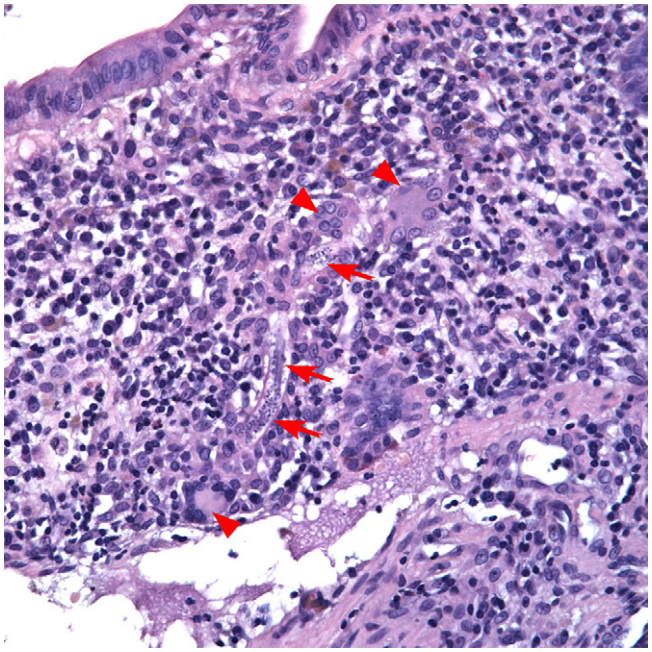

Fig. 3. The specimens from colonofiberoscopic biopsy showed inflammatory lamina propria mainly infiltrated by lymphocytes and plasma cells. There was a parasite-like tissue fragment (arrows) with granulomatous reaction. Several multinucleated foreign body giant cells (arrow heads) were also seen. (Hematoxylin and eosin stain; original magnification, ×40).

indigestion, nausea, vomiting, gastrointestinal bleeding, small bowel obstruction, cramping, abdominal pain, watery diarrhea, constipation, asthma-like symptoms such as cough and wheezing, symptoms mimicking acute exacerbation of chronic obstructive pulmonary disease, pulmonary hemorrhage, and pleural effusion[1,2,12,13].

Because of its nonspecific clinical features and potentially fatal outcome, a high index of suspicion is needed for early diagnosis of hyperinfection strongyloidiasis. Patients, especially immunocompromised individuals from endemic area, should be evaluated aggressively, particularly when presenting with asthma-like symptoms, acute respiratory distress, gastrointestinal symptoms, eosinophilia, or gram-negative bacteremia[12,13].

Strongyloidiasis is difficult to diagnose because of low-parasite load and the irregular larval output[13]. A specific and sensitive diagnostic test is lacking, and a definite diagnosis of strongyloidiasis usually relies on the detection of larvae in stool or sputum. However, it is inadequate to rely on these studies alone for screening. Conventional examination of a single stool specimen usually fails to detect larvae in up to 70% of cases, whereas examination of several stool specimens on consecutive days may increase the diagnostic yield[2,12,13]. Several techniques discerning larvae in stool samples, including Baermann concentration method, Harada-Mori filter paper culture, formalin-ethyl acetate concentration, direct smear of feces in saline—Lugol iodine stain, and nutrient agar plate cultures, are much more sensitive than single stool smear, but they are rarely standard procedures in clinical parasitology laboratories[13]. Several immunodiagnostic assays, such as skin testing with larval extracts, indirect immunofluorescence analysis of fixed larvae, radioallergosorbent testing for specific IgE, enzyme-linked immunosorbent assay IgG antibody tests, and gelatin particle agglutination, are available, but extensive cross-reactivity with hookworms, filariae, and schistosomes is of concern[2,7,13]. Although examination of duodenal aspirate and histological examination of duodenal or jejunal biopsy specimens may be more sensitive, these invasive methods are usually reserved for immunocompromised children necessitating rapid detection or transplant recipients with suspicious hyperinfection strongyloidiasis[2,13]. A real-time polymerase chain reaction method targeting the small subunit of the rRNA gene has been developed recently for the detection of *S stercoralis* DNA in fecal samples, and this may further increase the detection rate[2,14]. In disseminated disease, larvae and adult parasites can also be seen in urine, sputum, BAL fluid, pleural effusion, and other body fluid[6].

Unexplained eosinophilia is often related to parasitic infection. In hyperinfection strongyloidiasis, however, eosinophilia is not quite common. In a case series about seven patients of hyperinfection strongyloidiasis, all of the three fatal cases had eosinophil count less than 400/μL[15]. In our case, the eosinophil count was only 20/μL. Therefore, the absence of eosinophilia does not exclude the diagnosis of strongyloidiasis or other parasitic infection.

There was no significant clue initially for diagnosing this patient as having *S. stercoralis* hyperinfection. Neither peripheral eosinophilia nor significant hemoptysis was noted. Bronchoscopy played a critical role to define the unexpected cause of his progressive pulmonary infiltrates. The coffee ground discharge in the airway, which was attributed to damaged pulmonary vasculature by larvae, may provide a clue for diagnosis, while considering about the history of chronic diarrhea. The correct diagnosis was soon made by recognition of the worm in BAL cytology, and specific treatment was initiated promptly. For a septic patient with progressive pulmonary infiltrates, bronchoscopic studies including cytology may be necessary for defining the cause.

As in our case, patients with hyperinfection strongyloidiasis often develop acute respiratory distress syndrome and gram-negative septicemia[1,2,6–8,16,17]. These were attributed to the ulcerative bowel mucosa and to the migration of larvae from the gastrointestinal tract to the pulmonary system, carrying enteric bacteria (particularly gram-negative bacilli) on the surface of the migrating worms[6,7,17]. Blood cultures commonly grow *E. coli, K. pneumoniae*, *Proteus mirabilis*, *Pseudomonas*, and *Enterococcus faecalis*[6]. Therefore, broad-spectrum antibiotic treatment in addition to antiparasitic therapy should be initiated as soon as hyperinfection strongyloidiasis is diagnosed[17]. The mechanism of developing acute respiratory distress syndrome is still not well understood. Lung injury caused by direct damage by parasites or endotoxin-mediated injury from associated bacterial sepsis may play a role[16]. Besides, intrapulmonary destruction of larvae after administration of antiparasitic agents can also trigger intense inflammatory reaction, leading to acute respiratory distress syndrome[16,17].

Treatment options include ivermectin, albendazole, and thiabendazole[2,7,18]. Ivermectin is generally considered the treatment of choice because of higher clearance rate and a favorable side-effect profile[7,10]. Oral, rectal, and subcutaneous formulations of ivermectin were available[18].

In conclusion, hyperinfection strongyloidiasis should be considered as a cause of acute respiratory distress syndrome in immunocompromised patient, especially with the presence of chronic gastrointestinal symptoms.

References

1. Khasawneh F, Sreedhar R, Chundi V. Strongyloides hyperinfection: an unusual cause of respiratory failure. *Ann Intern Med* 2009 Apr 21;150(8):570–571.
2. Roxby AC, Gottlieb GS, Limaye AP. Strongyloidiasis in transplant patients. *Clin Infect Dis* 2009 Nov 1;49(9):1411–1423.
3. Keiser PB, Nutman TB. Strongyloides stercoralis in the immunocompromised population. *Clin Microbiol Rev* 2004 Jan;17(1):208–217.
4. Davidson RA, Fletcher RH, Chapman LE. Risk factors for strongyloidiasis. A case-control study. *Arch Intern Med* 1984 Feb;144(2):321–324.
5. Cook GC. Infective gastroenteritis and its relationship to reduced gastric acidity. *Scand J Gastroenterol Suppl* 1985;111:17–23.
6. Liu HC, Hsu JY, Chang KM. Strongyloides stercoralis hyperinfection presenting with symptoms mimicking acute exacerbation of chronic obstructive pulmonary disease. *J Chin Med Assoc* 2009 Aug;72(8):442–445.
7. Huston JM, Eachempati SR, Rodney JR, et al. Treatment of Strongyloides stercoralis hyperinfection-associated septic shock and acute respiratory distress syndrome with drotrecogin alfa (activated) in a renal transplant recipient. *Transpl Infect Dis* 2009 Jun;11(3):277–280.
8. Huang MS, Hwang KP, Chiang PC, Hwang JJ. Pulmonary hyperinfection with Strongyloides stercoralis. *J Formos Med Assoc* 1996 Jul;95(7):551–554.
9. Vilela EG, Clemente WT, Mira RR, et al. Strongyloides stercoralis hyperinfection syndrome after liver transplantation: case report and literature review. *Transpl Infect Dis* 2009 Apr;11(2):132–136.
10. Wirk B, Wingard JR. Strongyloides stercoralis hyperinfection in hematopoietic stem cell transplantation. *Transpl Infect Dis* 2009 Apr;11(2):143–148.
11. Seas C, Legua P. A 56-year-old woman with rash, paralytic ileus, and massive gastrointestinal bleeding. *Clin Infect Dis* 2009 Oct 1;49(7):1094–1095, 132–3.
12. Vijayan VK. How to diagnose and manage common parasitic pneumonias. *Curr Opin Pulm Med* 2007 May;13(3):218–224.
13. Siddiqui AA, Berk SL. Diagnosis of Strongyloides stercoralis infection. *Clin Infect Dis* 2001 Oct 1;33(7):1040–1047.
14. Verweij JJ, Canales M, Polman K, et al. Molecular diagnosis of Strongyloides stercoralis in faecal samples using real-time PCR. *Trans R Soc Trop Med Hyg* 2009 Apr;103(4):342–346.
15. Newberry AM, Williams DN, Stauffer WM, et al. Strongyloides hyperinfection presenting as acute respiratory failure and gram-negative sepsis. *Chest* 2005 Nov;128(5):3681–3684.
16. Vigg A, Mantri S, Reddy VA, Biyani V. Acute respiratory distress syndrome due to Strongyloides stercoralis in non-Hodgkin's lymphoma. *Indian J Chest Dis Allied Sci* 2006 Jan–Mar;48(1):67–69.
17. Hauber HP, Galle J, Chiodini PL, et al. Fatal outcome of a hyperinfection syndrome despite successful eradication of Strongyloides with subcutaneous ivermectin. *Infection* 2005 Oct;33(5–6):383–386.
18. Pacanowski J, Santos MD, Roux A, et al. Subcutaneous ivermectin as a safe salvage therapy in Strongyloides stercoralis hyperinfection syndrome: a case report. *Am J Trop Med Hyg* 2005 Jul;73(1):122–124.