Case Report

Acute Respiratory Distress Syndrome Complicating *Strongyloides stercoralis* Hyperinfection

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**S U M M A R Y**

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 bronchialalveolar 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.

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1. Introduction

Strongyloidiasis is endemic in tropic and subtropic areas, 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

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piperacillin/tazobactam 2 days later to cover *Pseudomonas 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 *Strongyloides 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 venovenous 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. 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. Risk factors of *S. stercoralis* infection include white patients, men, corticosteroid use, hematologic malignancy, prior gastric surgery, and hypochlorhydria or achlorhydria.

*S. stercoralis* may cause hyperinfection in immunocompromised hosts with high-mortality rate (up to 90%). Glucocorticoid treatment and human T-lymphotropic virus type 1 infection are the two conditions most specifically associated with hyperinfection, whereas cases have been reported in association with hematologic malignancy, malnutrition, hypogammaglobulinemia, acquired immunodeficiency syndrome, transplant recipients, and patients receiving chemotherapy.

Strongyloidiasis may present with a variety of clinical manifestations, including constitutional, cutaneous, gastrointestinal, and pulmonary symptoms. This includes weight loss, skin rash,
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\textsuperscript{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\textsuperscript{12,13}.

Strongyloidiasis is difficult to diagnose because of low-parasite load and the irregular larval output\textsuperscript{1}. 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\textsuperscript{1,2,13}. Several techniques discerning larvae in stool samples, including Baermann concentration, BA 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\textsuperscript{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\textsuperscript{5,7,13}. Although examination of duodenal aspirate and histological examination of duodenal or jejunal biopsy samples may be more sensitive, these invasive methods are usually reserved for immunocompromised children necessitating rapid detection or transplant recipients with suspicious hyperinfection strongyloidiasis\textsuperscript{14}. A real-time polymerase chain reaction method targeting the small subunit of the RNA gene has been developed recently for the detection of \textit{S. stercoralis} DNA in fecal samples, and this may further increase the detection rate\textsuperscript{2,4}. In disseminated disease, larvae and adult parasites can also be seen in urine, sputum, BAL fluid, pleural effusion, and other body fluid\textsuperscript{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 \text{µl}\textsuperscript{15}. In our case, the eosinophil count was only 20 \text{µl}\textsuperscript{5}. 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 \textit{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\textsuperscript{1,2,6–16,17}. 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\textsuperscript{6,7,17}. Blood cultures commonly grow \textit{E. coli}, \textit{K. pneumonieae}, \textit{Proteus mirabilis}, \textit{Pseudomonas}, and \textit{Enterococcus faecalis}\textsuperscript{6}. Therefore, broad-spectrum antibiotic treatment in addition to antiparasitic therapy should be initiated as soon as hyperinfection strongyloidiasis is diagnosed\textsuperscript{18}. 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\textsuperscript{18}. Besides, intrapulmonary destruction of larvae after administration of antiparasitic agents can also trigger intense inflammatory reaction, leading to acute respiratory distress syndrome\textsuperscript{6,17}.

Treatment options include ivermectin, albendazole, and thiabendazole\textsuperscript{16,20,21}. Ivermectin is generally considered the treatment of choice because of higher clearance rate and a favorable side-effect profile\textsuperscript{16,20}. Oral, rectal, and subcutaneous formulations of ivermectin were available\textsuperscript{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.

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