Abstract

Strongyloidiasis is widely distributed in tropical and subtropical areas. Disseminated strongyloidiasis may develop in patients with immunodeficiencies. In the absence of early diagnosis and treatment, the prognosis of disseminated strongyloidiasis is extremely poor. We report a case of pulmonary strongyloidiasis that was successfully treated. The patient was an 83-year-old woman who had been receiving long-term oral prednisolone therapy for uveitis. The patient visited our emergency department complaining of breathing difficulties and diarrhea. A chest X-ray revealed a diffuse enhancement of interstitial shadows. A bronchoalveolar lavage (BAL) was performed, and both Gram staining and Grocott’s staining revealed the presence of multiple filariform larvae of Strongyloides stercoralis in the bronchoalveolar lavage fluid (BALF). A stool examination performed at the same time also yielded S. stercoralis. The patient was diagnosed as having pulmonary strongyloidiasis and was treated with thiabendazole and ivermectin, in addition to antimicrobial agents; her respiratory symptoms and diarrhea improved, and S. stercoralis was not detected in subsequent follow-up examinations thereafter. In endemic areas of S. stercoralis, pulmonary strongyloidiasis should be considered as part of a differential diagnosis if chest imaging findings like alveolar and interstitial shadow patterns or lobar pneumonia are seen in patients with immunodeficiencies.

Key words: pulmonary strongyloidiasis, BAL

Introduction

Strongyloidiasis is a parasitic disease that is usually caused by one of two species of Strongyloides, an intestinal nematode. Infection with Strongyloides stercoralis is the most frequent cause of strongyloidiasis in humans, while infection with Strongyloides fuelleborni is rare (1, 2). S. stercoralis is widely distributed in tropical and subtropical areas, such as Africa, Southeast Asia, Southeastern United States and Puerto Rico (2, 3). Okinawa is a subtropical area of Japan and is also regarded as an endemic area. Asato et al in Okinawa, reported that the prevalence rate is 16.0% in males and 7.7% in females (4). Most infected patients are over the age of 40 years. Disseminated strongyloidiasis may develop in patients with immunodeficiencies. As with hyperinfection syndrome, disseminated strongyloidiasis has been reported to occur in 1.5–2.5% of all strongyloidiasis (5). In the absence of early diagnosis and treatment, the prognosis of disseminated strongyloidiasis is extremely poor (6–9). One study reported that the mortality rate for disseminated strongyloidiasis is as high as 77% among compromised hosts (10).

Thus, an early diagnosis of disseminated strongyloidiasis is extremely important. However, disseminated strongyloidiasis often does not result in respiratory symptoms or may cause only mild pharyngeal discomfort. Here, we present a case of pulmonary strongyloidiasis that was successfully treated, thanks to an early diagnosis.

Case Report

The patient was an 83-year-old woman who was receiving long-term systemic prednisolone therapy for the treatment of cryptogenic uveitis as well as medication for type II diabetes mellitus. She was a non-smoker, and her family history was unremarkable.

The patient became ill on November 18, 2002, and came...
to the emergency department of our hospital on the following day, complaining of breathing difficulties, blood in her spu-
tum, and diarrhea. She was immediately admitted for further
examination.

A physical examination performed at the time of admis-
sion revealed respiratory distress. Her blood pressure was
140/60 mmHg, her body temperature was 37.0°C, her pulse
rate was 104 beats per minute, and her respiratory rate was
24 breaths per minute. Examination of her ears, nose, and
throat revealed non-specific findings. No signs of lymph-
adenopathy were detected by palpation of accessible node
sites. Auscultation of her chest revealed late inspiratory fine
crackles. An abdominal examination revealed hypoactive
bowel sounds and slight distention. Leg edema was not seen.

Laboratory findings at the time of admission revealed an
elevated CRP value, but her peripheral blood leukocyte
count was not elevated. The differential-leukocytic count
was characterized by 3% atypical lymphocytes, with a nu-
clear shift to the left.

The patient’s HTLV-1 antibody titer was negative, but her
serum IgE titer was elevated. An arterial blood gas analysis
showed type I respiratory failure with a PaO₂ of 75.3 Torr.

No elevations in Mycoplasma pneumoniae or Chlamydia
pneumoniae antibody titers or ACE were detected (Table 1).

A chest X-ray taken at the time of admission (Fig. 1A)
showed diffuse reticular and granular shadows and partial
ground-glass shadows. A thoracic CT exam (Fig. 1B) also
showed ground-glass shadows and pleural effusion. An ab-
dominal X-ray (Fig. 2) revealed gas in the small intestine.

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Pneumocystis carinii (P. carinii) pneumonia was initially
suspected, based on the diffuse ground-glass appearance of
the shadows. The patient had been receiving long-term sys-
temic prednisolone therapy (10–25 mg/day) for 4 years for
the treatment of uveitis and also had type II diabetes mellitus,
so an immunodeficient state was suspected.

A bronchoalveolar lavage (BAL) was performed on the
second day of hospital admission. The BAL fluid (BALF)
appeared bloody, and the neutrophil fraction was elevated to
39%. When the BALF was examined using Gram stain, mul-
tiple gram-negative rods and S. stercoralis were detected.
Staining with Grocott’s also revealed the presence of
filariform larvae characteristic of strongyloidiasis (Fig. 3),
but P. carinii cysts were not seen.

A stool examination performed on the same day also

<table>
<thead>
<tr>
<th>Table 1. Laboratory Data</th>
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<tbody>
<tr>
<td><strong>Hematology</strong></td>
</tr>
<tr>
<td>WBC 6,700/mm³</td>
</tr>
<tr>
<td>Stab 27.0%</td>
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<tr>
<td>Seg 59.0%</td>
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<tr>
<td>Mono 2.0%</td>
</tr>
<tr>
<td>At-Ly 3.0%</td>
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<tr>
<td>Hb 11.3 g/dl</td>
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<tr>
<td>Ht 38.8%</td>
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<tr>
<td>Plt 26.0x10⁴/mm³</td>
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<tr>
<td><strong>Chemistry</strong></td>
</tr>
<tr>
<td>Na 134 mEq/l</td>
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<tr>
<td>K 3.4 mEq/l</td>
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<tr>
<td>Cl 94 mEq/l</td>
</tr>
<tr>
<td>BUN 181 mg/dl</td>
</tr>
<tr>
<td>Cre 0.5 mg/dl</td>
</tr>
<tr>
<td>Ca 8.51 mg/dl</td>
</tr>
<tr>
<td>T-Bil 0.7 mg/dl</td>
</tr>
<tr>
<td>AST 31 U/l</td>
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<tr>
<td>ALT 47 U/l</td>
</tr>
<tr>
<td>γ-GTP 23 U/l</td>
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<tr>
<td>ALP 253 U/l</td>
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<tr>
<td>LDH 369 U/l</td>
</tr>
<tr>
<td><strong>Serology</strong></td>
</tr>
<tr>
<td>CRP 9.1 mg/dl</td>
</tr>
<tr>
<td>HTLV-1 Ab 16&gt;</td>
</tr>
<tr>
<td>ACEI 6.0 U/l</td>
</tr>
<tr>
<td>IgE 529 IU</td>
</tr>
<tr>
<td>Cold agglutinin titres 4&gt;</td>
</tr>
<tr>
<td>C. pneumoniae IgA 1.63</td>
</tr>
<tr>
<td>C. pneumoniae IgM 8&gt;</td>
</tr>
<tr>
<td>M. pneumoniae Ab( PA) 40&gt;</td>
</tr>
<tr>
<td><strong>Smear test</strong></td>
</tr>
<tr>
<td>Gram’s stain:</td>
</tr>
<tr>
<td>Gram-negative rod (2+)</td>
</tr>
</tbody>
</table>
| Ziehl-Neelsen stain: nega-
| tive                        |
| Grocott’s staining:       |                             |
| Pneumocystis carinii (–), |                             |
| Strongyloides stercoralis (+) |
| **Culture**               |                             |
| Bacterials: E. coli (2+), | K. pneumoniae (2+)          |
| Acid-fast bacteria: nega-
| tive                        |                             |
yielded *S. stercoralis*. *Escherichia coli* and *Klebsiella pneumoniae* were isolated in bacterial cultures of the BALF, but both smears and cultures were negative for acid-fast bacteria. Based on these findings, the patient was diagnosed as having pulmonary strongyloidiasis as a local manifestation of disseminated strongyloidiasis, secondary to a compromised immune system as a result of prednisolone therapy.

The administration of thiabendazole was started after the BAL was performed, and sulfamethoxazole/trimethoprim (SMX, 400 mg; TMP, 80 mg) was used in combination because 1) super-infection with *P. carinii* was a concern until the grocott’s staining later revealed the absence of *P. carinii* cysts, and 2) enterobacterial infection in conjunction with the disseminated strongyloidiasis was a possibility. The patient’s fever promptly resolved after the start of treatment, and her
Respiratory condition and diarrhea also improved. Thiabendazole was later switched to ivermectin (12 mg) because of abdominal distension, which was thought to be an adverse effect of the thiabendazole. Subsequent laboratory data revealed hyponatremia, and the patient developed a fever once again. We suspected that these findings were adverse effects of the SMX/TMP, and this treatment was therefore discontinued on day 5 (Fig. 4). The hyponatremia improved, and the patient’s body temperature returned to normal. During the first week of drug therapy, a CT scan showed only mild ground-glass shadows (Fig. 5A). A chest X-ray performed on the 17th day of hospital admission showed the regression of the reticular and granular shadows (Fig. 5B).

A second administration of ivermectin was performed on hospital day 22. *S. stercoralis* was not detected in subsequent follow-up examinations. The patient’s clinical course was good, and her diabetes mellitus was also well controlled. The patient was able to walk at the time of her discharge from the hospital.
Discussion

Strongyloidiasis is widely distributed in tropical and sub-tropical areas (1, 11). Disseminated strongyloidiasis frequently develops in patients with immunodeficiencies caused by poor nutrition, drug therapy (including steroid therapy) for autoimmune diseases, chronic alcoholism, advanced age, diabetes mellitus, collagen disease, a post-surgery status, or a high titer of HTLV-1 (11, 12).

In the present case, P. carinii pneumonia was first suspected based on the diffuse ground-glass appearance of the shadows. Since the patient had been receiving long-term systemic prednisolone therapy (10–25 mg/day for about 4 years) for the treatment of uveitis and also had type II diabetes mellitus, an immunodeficient state was suspected.

Since P. carinii pneumonia or some other form of pneumonitis, was suspected, additional examinations were performed. The presence of S. stercoralis larvae in the BALF sample enabled us to make properly diagnosis the patient as having pulmonary strongyloidiasis.

The patient’s general condition and pulmonary disease improved after treatment for strongyloidiasis and possibly complicating bacterial infections.

Pulmonary strongyloidiasis is one of the most important signs of disseminated strongyloidiasis. The present patient was elderly, had diabetes mellitus, and had been receiving long-term systemic steroid therapy for the treatment of cryptogenic uveitis. These factors may have allowed the development of disseminated strongyloidiasis, leading to pneumonia and pulmonary hemorrhage. However disseminated strongyloidiasis often does not result in respiratory symptoms or may cause only mild pharyngeal discomfort. Some studies have reported a low body temperature, coughing, laryngismus paralytics, and blood-stained sputum as possible symptoms (7, 8). In the absence of early diagnosis and treatment, the prognosis of disseminated strongyloidiasis is extremely poor (6, 9, 11, 13). Some studies have reported that a patient’s prognosis is related to the severity of their underlying condition (9).

However, the diagnosis of pulmonary strongyloidiasis is difficult and often delayed (14, 15), since the symptoms and laboratory findings are nonspecific. Chest imaging in patients with pulmonary strongyloidiasis reveals non-segmental patchy areas of consolidation, diffuse reticulonodular patterns and diffuse pulmonary opacities (16). Sometimes lung abscess is also seen (9, 12). These chest imaging findings and many of the respiratory symptoms in patients with disseminated strongyloidiasis are thought to be caused by one of the following three mechanisms (11, 14, 17). First, filariform larvae multiply through the augmentation of autoinfection and infiltrate the intestinal mucosa. From there, the larvae reach the pulmonary vascular beds through the circulation system; the filariform larvae then invade the alveoli and evoke responses that are manifested by inflammation, coughing, and bronchial spasms. Pulmonary hemorrhage occurs as a result of the mechanical destruction (6) caused by the above conditions. A second possibility is that bronchitis and mucus plugs are induced as an exacerbation of an underlying lung disease. These underlying conditions may cause respiratory failure, at which time the filariform larvae may also be recognized in the individual’s sputum. At this stage, chest X-rays may reveal various patterns, such as alveolar and interstitial shadow patterns, lobar pneumonia, etc (8, 9, 17). Finally, bacterial pneumonia, a complication of pulmonary strongyloidiasis, might be caused by the “piggyback” transport of bacteria from the intestines (11).

In the present case, E. coli and K. pneumoniae were isolated in bacterial cultures of BALF and sputum samples. Thus, the condition appears to have been caused by enterobacterial infection, resulting from the piggyback transport of bacteria from the intestines. Consequently, the chest X-ray findings in this case are thought to represent pulmonary hemorrhage, pulmonary edema and bacterial pneumonia.

The clinical course of the present case is typical for strongyloidiasis. Initially, however, we did not know that the patient had S. stercoralis, and pulmonary strongyloidiasis was not included in the differential diagnosis performed at the time of admission.

Although S. stercoralis can cause a severe pathologic state, the initial symptoms are very mild and nonspecific (9). In endemic areas of S. stercoralis, strongyloidiasis should be included as a possible cause of pulmonary disease in differential diagnoses, especially in patients with immunodeficiencies and abnormal chest imaging findings, like alveolar and interstitial shadow patterns or lobar pneumonia.

References