Concurrent Infection with Legionella pneumophila and Pneumocystis carinii in a Patient with Adult T Cell Leukemia

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A 48-year-old woman was admitted to our hospital with high fever, chills, cough, and exertional dyspnea. On admission, the chest roentgenogram and computed tomography scan showed bilateral alveolar infiltration in the middle and lower lung fields. Microscopic examination of the bronchial lavage fluid showed flower cells typical for adult T-cell leukemia (ATL) and cysts of Pneumocystis carinii, and Legionella pneumophila serogroup 1 grew on buffered charcoal yeast extract (BCYE)-α agar. The patient was successfully treated with antibiotics including trimethoprim/sulfamethoxazole, erythromycin, and sparfloxacin. Remission of ATL was achieved after three courses of antileukemic chemotherapy. Mixed infection of opportunistic pathogens should be considered in patients with ATL.

Key words: severe pneumonia, opportunistic pathogens

Introduction

Adult T-cell leukemia (ATL) is a T-cell malignant condition closely related to infection with human T-cell leukemia virus type 1 (HTLV-1) (1, 2). It is well known that patients with ATL have an immunocompromised state and are prone to develop various types of pulmonary complications, such as opportunistic infections, leukemic cells infiltration, interstitial pneumonia or pulmonary hemorrhage (3). The frequency of these pulmonary complications during the clinical course of ATL is higher than in other hematological malignancies (3). A variety of pathogenic microorganisms may cause pulmonary infection in these patients such as bacteria, fungi, Pneumocystis carinii (P. carinii) and cytomegalovirus. Therefore, a rapid and accurate diagnosis of pulmonary complications is necessary for the successful treatment of patients with ATL.

We report the first case of severe pneumonia caused by P. carinii and Legionella pneumophila (L. pneumophila) serogroup 1, associated with leukemic pulmonary infiltration in a patient with acute ATL.

Case Report

A 48-year-old woman was admitted to our hospital with high fever, chills, cough, exertional dyspnea and yellow jelly-like sputum for five days before admission. The patient had undergone a conization surgery for an early stage of uterine cervical carcinoma one year earlier.

On admission, the patient was alert but slightly excited and talkative. The body temperature was 38.4°C, blood pressure 100/60 mmHg, pulse regular at 88 bpm, and respiratory rate 32 breaths/min. Superficial lymphadenopathy and mild splenomegaly were noted. Heart sounds were clear, mild coarse crackles were noted in both lower lung fields. Chest roentgenogram showed bilateral alveolar infiltration in the middle and lower lung fields (Fig. 1). Chest computed tomography (CT) scan showed right pleural effusion and alveolar infiltrates in both lung fields (Fig. 2). Laboratory tests on admission showed a white blood cell count of 70,200/µl with 25% neutrophils, 43% lymphocytes, 31% abnormal lymphocytes which were typical ATL cells, and 1% monocytes, an erythrocyte sedimentation rate of 36 mm/h and C-reactive protein (CRP) of 22.3 mg/dl, although red blood cell and platelet counts were within the normal range. Biochemical tests showed total serum protein of 6.0 g/dl with 8% α1-globulin, 15.7% α2-globulin, 11.4% β-globulin and 13.9% γ-globulin; total bi-
L. pneumophila and P. carinii Pneumonia in ATL

Figure 1. Posteroanterior chest radiograph on admission showing bilateral alveolar infiltration in the middle and lower lung fields, and a blurred right costophrenic angle.

Figure 2. Chest CT scan showing right pleural effusion and alveolar infiltrates on both lung fields. Note the air-space consolidation on the right lower lung field.

Serum HTLV-1 antibody was positive (1:4,096), the surface phenotype of peripheral blood lymphocytes with CD45 blastgating method showed that CD2, CD3, CD4 and CD5 were positive. In addition, HTLV-1 proviral DNA monoclonal integration in peripheral blood was confirmed by Southern blot analysis. A provisional diagnosis of acute ATL was made based on the criteria described by Shimoyama (4).

Bronchoscopic examination was performed on admission and approximately 6 ml of bronchial lavage fluid at rB9 was obtained. Giemsa staining of the fluid showed 70% abnormal cells with flower cells and toluidine blue O (TBO) stain of the lavage showed cysts of P. carinii (Fig. 3). Based on these results, a diagnosis of P. carinii pneumonia (PCP) and pulmonary infiltration of ATL cells was made at that stage. Gram stain and culture of both sputum and bronchial lavage fluid did not show any bacteria.

The titer of the serum antibody against Mycoplasma pneumoniae and cold agglutination with paired sera did not show significant elevation. Urinalysis showed fungal infection of the urinary tract, examination of the fundus of the eye showed Candida retinitis. The plasma 1,3-β-D-glucan level was increased to 30.1 pg/ml, although the polysaccharide antigen of Cryptococcus neoformans and manno-protein antigen of Candida albicans were negative. It was considered that the elevation of the plasma 1,3-β-D-glucan was caused by the infection with P. carinii (5). Anti-cytomegalovirus immunoglobulin M titer was not elevated. Purified protein derivative of tuberculin test was negative, although the result of an earlier test was unclear. The responses of peripheral blood mononuclear leukocytes to phytohemagglutinin and concanavalin A were attenuated.

The patients were treated with a course of anti-neoplastic agents consisting of vincristine, cyclophosphamide, Adriamycin, ranimustine, vindesine, etoposide, carboplatine and prednisolone for ATL. This therapy was based on a multicenter phase II study of Lymphoma Study Group 15 (ATL 93). First, 1 mg/m² vincristine, 350 mg/m² cyclophosphamide and 40 mg/m² Adriamycin were administered intravenously (i.v.) on day 1. Additionally, 30 mg/m² Adriamycin and 60 mg/m² ranimustine were administered i.v. on day 8, 2.4 mg/m² vindesine, 100 mg/m² etoposide, 250 mg/m² carboplatine were administered i.v.
on day 15, 100 mg/m² etoposide was administered days 15–17. And 80 mg/m² prednisolone was administered i.v. days 1, 8, 15–17, rhG-CSF was given subcutaneously at doses of 2.5 μg/kg on day 3–6, 9–13 and 18–27. She was treated simultaneously with trimethoprim/sulfamethoxazole for PCP, together with broad spectrum antibiotics which included meropenem, clindamycin and clarithromycin for bacterial infection. However, her condition continued to deteriorate, including a progressive worsening of respiratory failure, inspite of this treatment.

On the 7th day of admission, clarithromycin was replaced with 2 g of erythromycin (i.v.) and 300 mg of sparfloxacin per day due to the isolation of *L. pneumophila* serogroup 1 from the bronchial lavage fluid on admission. This was followed by a marked fall in CRP and improvement in arterial blood gases, 14 days after admission. In addition, most alveolar infiltrates also disappeared on a chest roentgenogram taken 24 days after admission (Fig. 4). With continued improvement in her condition, the patient was discharged from our hospital on July 22, 1997.

Remission of ATL was achieved by three courses of antileukemic chemotherapy. After the chemotherapy, the abnormal lymphocyte level has persisted within 1,000–4,000/μl. No relapse of ATL nor pulmonary complications has occurred during the last 9 months after discharge.

### Discussion

ATL is endemic in southwest Japan, the West Indies and southeast of the United States (1–3). It is well known that ATL patients are in a state of immunodeficiency which often leads to various types of infectious diseases. Shimoyama (4) examined 818 cases with ATL and reported that the infection rate in these patients at the time of diagnosis was 26% (acute type; 27%, chronic type and smoldering type; 36%, lymphoma type; 10%) (6). Consequent to the dysfunction of T-cells, the rates of fungal (8%), parasitic (5%), and viral (2%) infections are higher than bacterial infections (12%) (6). On the other hand, Yoshioka et al (3) compared ATL with other hematological malignancies and showed a high frequency of respiratory complications in ATL patients (93.1%), consisting of infiltration of tumor cells and/or infection (3).

In the present case, we first made a provisional diagnosis of acute ATL associated with infiltration of abnormal lymphoid cells and PCP for pulmonary complications, *Candida* retinitis, and fungal infection of the urinary tract. Accordingly, the patient was treated with anti-neoplastic agents, sulfamethoxazole-trimethoprim, anti-fungal agents, and broad spectrum antibiotics including carbapenem and an oral form of macrolide were also administered empirically. In spite of such therapy, respiratory function continued to progressively deteriorate. Isolation of *L. pneumophila* from bronchial lavage fluid collected on admission confirmed the diagnosis of *Legionella* pneumonia on day 7.

Figure 3. Top: Flower cell in the bronchial lavage obtained from rB9. (Giemsa stain, original magnification ×1,000). Bottom: Cysts of *Pneumocystis carinii* in the lavage (TBO stain, magnification ×1,000).

Figure 4. Chest roentgenogram showing disappearance of alveolar infiltrates on February 24, 1997.
Although *Legionella* species is an important cause of severe pneumonia, establishment of an early diagnosis is often difficult. The frequency of community acquired pneumonia caused by *Legionella* species is 2–6% or more and these organisms were reported to cause from 0 to 47% of community acquired pneumonias requiring hospitalization (7, 8). The diagnostic accuracy of tests for *L. pneumophila* varies with the laboratory and test method (7, 8). Although failure to diagnose Legionnaires’ disease in the early stages is likely to lead to increased morbidity and mortality, a prompt and definite diagnosis is still difficult.

Taguchi et al reported that the chest roentgenogram of *Legionella* pneumonia included bilateral shadow findings, pleural effusion and rapid progression of shadow were characteristic and were clinically useful for diagnosis (9). The patient’s chest roentgenogram was characteristic for *Legionella* pneumonia, although we thought the abnormal shadow on the chest roentgenogram mainly consisted of infiltration of leukemic cells. The findings of the gram stain of the sputum and bronchial lavage, the chest roentgenogram and the progressive pneumonia with poor response to prior antibiotics was triggered by suspecting *Legionella* pneumonia. Fortunately, in spite of the delay in intravenous administration of erythromycin, the patient recovered from severe pneumonia. Examination of paired serum samples from the patient showed a four-fold rise in the titer of IFA (titers increased from 1:128 to 1:512). We also evaluated urinary antigen test for *L. pneumophila* serogroup 1 retrospectively, the urine samples continued to be positive for the antigen for three months after admission. Furthermore, we performed IFA studies of the family as well as close friends and contacts, but the titer was not high in any of these individuals. In addition, cooling water tower samples from the office and shower water from the home of the patients were examined also.

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In the present case, the patient was diagnosed with severe pneumonia caused by *L. pneumophila* and *P. carinii*, and the patient was a known pathogen in immunocompromised patients, being a well known pathogen in immunocompromised patients. The detection of human T-cell leukemia virus proviral DNA and its application for classification and diagnosis of T-cell malignancy. Blood **63**: 1235–1240, 1984.

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**References**


