Legionnaires’ Disease Diagnosed by Bronchoalveolar Lavage

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A 51-year-old woman who had been on steroid therapy for systemic lupus erythematosus (SLE) developed a high fever 3 days after visiting a hot spring resort. Chest X-ray films revealed an interstitial, pneumonia-like shadow in the left lung field, which increased rapidly with a worsening of her symptoms. She died of multiple organ failure one week after the onset of the pneumonia. Although the serum antibody titer was negative, Legionella pneumophila was recovered from her bronchoalveolar lavage (BAL) fluid. BAL seems to be a useful method to diagnose Legionnaires’ disease.

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Introduction

Legionnaires’ disease is an acute respiratory infection commonly caused by Legionella pneumophila. This pneumonic illness is characterized by an initial nonspecific prodrome, followed by the development of patchy bronchopneumonia which frequently progresses to multilobular consolidation (1). Most patients infected by Legionella pneumophila develop severe pneumonia (2). In addition to the pneumonia, unusual systemic manifestations such as liver function abnormalities, toxic encephalopathy and renal dysfunction frequently develop (1).

It is difficult to culture Legionella pneumophila, and the demonstration of these organisms in the tissues requires special stains (3). A definitive diagnosis through serologic testing is usually retrospective because of the time-consuming examination (3, 4). Therefore, it can be safely assumed that the diagnosis of Legionnaires’ disease during the acute stage is difficult, and a careful assessment is essential in arriving at a working diagnosis.

We describe here a female patient with severe pneumonia caused by Legionella pneumophila, which was recovered from her bronchoalveolar lavage (BAL) fluid, despite the fact that her serum antibody titer was negative.

Case Report

A 51-year-old woman had been on steroid therapy for her systemic lupus erythematosus (SLE) for 5 years. Prior to admission, she had visited a hot spring resort in Ito, Shizuoka Prefecture, from June 9 to 11, 1996. Three days later, she developed a high grade fever (39°C) and was admitted to our hospital as a returning patient to the Department of Circulating Medicine on June 17, 1996. Chest X-ray films taken on the day of admission showed an interstitial, pneumonia-like shadow in the left lung field (Fig. 1, Left). She was diagnosed with pneumonia and treated with cefotiam dehydrochloride (CTM) 2.0 g per day. However, a rapid spread of diffuse infiltrative shadows in both lung fields was recognized on a chest X-ray film taken on June 19, 1996 in association with a worsening of her symptoms. She was immediately forwarded to the Department of Respiratory Medicine for a closer examination on the same day.

At this time, she had developed acute respiratory distress. Her vitals were as follows: temperature 39.4°C, pulse 140 bpm, and blood pressure 97/45 mmHg. On physical examination, remarkable coarse crackles were noticed in all fields of the lungs. She showed a moon-like face due to the steroid therapy. Her white blood cell (WBC) count was 17,300/μl, and her C-reactive protein (CRP) concentration was 30.6 mg/dl. Arterial blood gas analysis revealed hypoxemia and respiratory alkalosis (partial pressure of oxygen (PaO2) 69.5 torr; partial pressure of carbon dioxide (PaCO2) 20.7 torr; and pH 7.55 under a reservoir mask at 15 l/min). A laboratory examination demonstrated elevated levels of glutamic oxaloacetic transaminase (GOT) (56 IU/l), serum lactate dehydrogenase (LDH) (493 IU/l), blood urea nitrogen (BUN) (25.6 mg/dl) and serum creatinine (1.44 mg/dl). We tentatively diagnosed this patient with...
Figure 1. Left, chest X-ray film taken on the day of admission showing an interstitial, pneumonia-like shadow in the left lung field. Right, chest X-ray film taken on the day of death showing the marked progression of the infiltrates.

Figure 2. Clinical course of the patient with Legionnaires’ disease. CTM: cefotiam dehydrochloride, mPSL pulse: methylprednisolone pulse therapy (arrowheads indicate the days of administration), EM: erythromycin, IMP/CS: imipenem/cilastatin, PI: pentamidine isoniazate, WBC: white blood cell, CRP: C-reactive protein, BP: blood pressure, BAL: bronchoalveolar lavage, iv: intravenous administration, it: intratracheal administration.
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Acute interstitial pneumonia occurring in an immuno-compromised host. Figure 2 shows the clinical course of this patient.

The initial chemotherapy with CTM was not successful, and interstitial infiltrates developed rapidly. Therefore, the patient was switched to daily intravenous injections of 1.5 g of erythromycin (EM), 1.0 g of imipenem/cilastatin (IPM/CS), 0.5 g of gancyclovir and an intratracheal administration of 300 mg of pentamidine isoniazate beginning on June 19. Mechanical ventilatory assistance was also started (F\textsubscript{O\textsubscript{2}} 1.0; PEEP 10 cmH\textsubscript{2}O) because of acute respiratory failure. Furthermore, she was treated with steroid pulse therapy consisting of a daily administration of 1.0 g of methylprednisolone sodium succinate for 3 days. Unfortunately, the findings from the laboratory examinations indicated multiple organ failure (MOF), including renal, hepatic and cardiac failure. The patient died one week after the onset of the pneumonia. A chest X-ray film taken on the day of her death showed a marked progression of the infiltrates (Fig. 1, Right).

No causative bacteria for the pneumonia were isolated from a culture of her sputum or blood. The serum antibody titer against Legionella pneumophila serogroup 1 was examined by the indirect fluorescent antibody (IFA) method on serum samples obtained from the patient one day before her death. However, the serum antibody titer did not show a positive reaction at 64-fold dilution. The BAL fluid taken from the left upper lobe (taken during bronchoscopy on June 19) was then cultured on a specific WYO culture medium at 35°C under aerobic conditions for 6 days. Light gray colonies were found growing on the dark culture medium (Fig. 3). The organism isolated was identified as Legionella pneumophila serogroup 1 using the anti-sera from Legionella pneumophila serogroups 1–6. Therefore, we finally diagnosed this case as Legionnaires’ disease. An examination of the hot spring water was not performed in the present case, and an autopsy was not permitted.

**Discussion**

It has been reported that Legionnaires’ disease is most likely to develop in immunocompromised hosts (5, 6), and that it is closely related to the travel experience of the patient before the onset of the disease (7). It is known that a high fever is almost always present, and diarrhea and disturbances in consciousness are also typical of Legionnaires’ disease (2, 5, 8). In the present case, the patient showed several symptoms that supported a possible infection with Legionnaires’ disease. It has been reported that small, unilobar infiltrates rapidly progress to consolidation in the area of the initial infiltration, and/or spread to involve other areas within 3 or 4 days (2, 3). This pattern of progression was also seen in the present patient on her chest X-ray films.

To our knowledge, there have been about 96 reported cases of Legionnaires’ disease in Japan. It has been reported that in about 40 out of these 96 cases, Legionella pneumophila was identified from a culture examination (9). The diagnosis of Legionnaires’ disease seems to be difficult because: a) the bacteria do not grow on ordinary culture medium, but grow only on specific media such as B-CYE and WYO (2, 5, 10); b) sputum samples are known to show only a few positive results (10, 11); and c) it takes at least two weeks to show marked increases in the serum levels of the antibody (3).

Since an early diagnosis of Legionnaires’ disease is difficult, the mortality rate is relatively high in Japan. Previous reports have shown that 45 patients died out of 85 patients traced (53%), and that only 6 patients survived out of 19 patients who had required mechanical ventilatory assistance (9). In those patients who did not survive, EM had generally been prescribed for the treatment in most cases under the suspicion of Legionnaires’ disease. In the United States, it has been reported that when EM therapy is administered, the fatality rate is closer to 5 percent (2). The fatality rate is much higher in Japan than in the United States, and it is assumed that these patients did not survive because the drug administration was started too late. In the present case, the appropriate treatment was also delayed. The patient was treated with EM, but not with rifampicin (RFP), which is known to be more effective against Legionella pneumophila when used in combination with EM (5, 9). We had suspected the possibility of other infections such as cytomegalovirus, Pneumocystis carinii or other fungal infections. It is assumed that the patient did not survive for these reasons.

In order to increase the rate of early detection of Legionnaires’ disease, it is important to be able to generate a high index of suspicion for this infection based on the general history and symptoms of the patient. It is then necessary to obtain specimens such as the BAL fluid, and to culture these specimens with the specific culture media. To our knowledge, there have been only 2 reported cases of Legionnaires’ disease diagnosed by the culture of BAL fluid in our country (9, 12). However, it should be noted that at least 2 to 5 days are necessary to identify the bacterial colonies on the culture medium (5, 10). Recently, the usefulness of urinary antigen detection and polymerase chain reaction (PCR) methods have been reported for the early diagnosis of Legionnaires’ disease (13–17), although we did not use these methods in the present case. The BAL fluid can...
also be used to detect *Legionella pneumophila* in the PCR assay (16, 17), and therefore seems to be a useful specimen material in diagnosing Legionnaires’ disease. It is expected that the early diagnosis of this disease could be made more effectively by a combination of these methods in the future.

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**References**


