Clinical Characteristics of 8 Sporadic Cases of Community-Acquired *Legionella* Pneumonia in Advanced Age

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Abstract

Legionella spp are well recognized as one of the etiologic factor in pneumonia, but it is difficult to distinguish the clinical features of *Legionella* infection from pneumonia due to other causes. The objective of the present study was to examine the clinical characteristics of community-acquired *Legionella* pneumonia in elderly patients. We reviewed the clinical, laboratory and radiographic findings in 8 patients diagnosed as having pneumonia caused by *Legionella*. The diagnosis was confirmed by the presence of urinary antigen, bacterial culture, polymerase chain reaction (PCR) and serum antibody. There were 6 men and 2 women, whose ages ranged from 76 to 85 years. All patients had fever and hypoxia, four patients had respiratory symptoms. The initial chest X-ray findings were varied-consolidation, ground glass opacity, pleural effusion and linear shadow. Urinary antigen was positive in 4 patients, bacterial culture in 2, PCR on the sputum in 3 and serum antibody in 2 patients. As pneumonia caused by *Legionella* often becomes life-threatening, especially in elderly people, it is imperative to diagnose it at the initial stage. In this study, urinary antigen proved to be the most useful diagnostic means. However, it is important to confirm the diagnosis through plural examinations.

Key words: *Legionella* pneumonia, community-acquired pneumonia, sporadic cases, elderly person

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Introduction

The potential importance of *Legionella* species as the etiology of community-acquired pneumonia has been reported in the West (1, 2). Ishida et al (3) reported that in Japan, *Legionella* species was the causative pathogen in only about 0.6% of the cases of community-acquired pneumonia unlike the higher frequency reported in the West.

Whether it is possible to identify pneumonia caused by *Legionella* from the clinical features remains a matter of debate. Although there is no single clinical manifestation that distinguishes from other types of community-acquired pneumonia, it has been suggested that if there is a characteristic clinical profile, the likelihood of the diagnosis would increase (4-6). Thus, an accurate presumptive clinical diagnosis could be made on the basis of the proper association of

key signs and symptoms. It is difficult to distinguish the clinical features of *Legionella* infection from other types of pneumonia, especially in sporadic cases. As the clinical condition of patient with *L. pneumonia* rapidly worsens, it is imperative to diagnose it at the initial stage and to control the infection with appropriate antibiotics.

We report the characteristics of 8 patients of advanced age with *L. pneumonia*. The purpose of this study was to contribute to a better understanding of *L. pneumophila* pneumonia by examining the clinical features of thoracic infections caused by these pathogens in the elderly.

Patients and Methods

We retrospectively studied the clinical records of 8 patients of advanced age who were diagnosed with *L. pneumonia*. The diagnosis was based on the criteria proposed by

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Table 1. Profile of the Patients with *Legionella* pneumonia

Case	Age	Sex	Underlying disease	Symptoms	Surmised source of infection
1	84	M	(-)	fever	unknown
2	81	M	old tbc	fever, fatigue	unknown
3	79	F	HT	fever, dyspnea	unknown
4	86	F	HT	fever	unknown
5	81	M	Depression	fever, dyspnea, sore throat	unknown
6	85	M	HT, Renal failure	fever, cough, sputum, dyspnea	unknown
7	81	M	Emphysema	fever, cough, sputum, dyspnea	unknown
8	76	M	HT, DM	fever, consciousness loss	hot spring

Yamaguchi et al (7) in Japan. That is, 1) isolation of *L.* species from sputum or lung tissue, 2) positive urinary antigen, 3) high titer of serum antibody, 4) positive results of PCR. One positive finding among these four criteria, is sufficient to establish the diagnosis of *L. pneumonia*.

At the initial visit and after a complete clinical history taking, the patients were subjected to physical examination and biochemistry and hematologic tests. We also carried out bacteriological, urinary antigen, serological investigations and PCR on the sputum, for each patient.

Bacteriological investigations

Respiratory specimens containing mucus were liquefied with semi-alkaline protease, incubated at 37°C for 10 minutes and then centrifuged. Each specimen was incubated in BCYE α and WYO α . The plates were incubated and were examined for 3 to 10 days. Visible colonies subcultured on BCYE α agar plates and WYO α agar plates were considered as possible *Legionella* species and were tested by direct fluorescence-antibody assay (DFA) for *L. pneumophila* serogroups 1 to 6.

Polymerase chain reaction (PCR)

PCR was performed with primers previously determined to amplify a 386-bp product within the 16S rRNA gene of *L. pneumophila* in respiratory samples (8). It was reported that the sensitivity and specificity of respiratory section were 83~100% and 90~100%, respectively.

Urinary antigen and serological investigations

Legionella antigens in urine samples were examined by immunochromatographic assay (Binax, Portland, OR, USA) and urinary antigen enzyme immunoassay (Binax). The serum antibody titer was determined by the microplate agglutination test (Denka Seiken, Tokyo, Japan).

Results

Table 1 shows the profile of the present 8 patients. *L. pneumophila* pneumonia infection was identified in 6 men and 2 women, whose ages ranged from 76 to 85 years. Seven patients had an underlying disease. All patients had fever, however, 4 patients had no respiratory symptoms such

as cough, sputum or dyspnea. In one patient, we could surmise the source of infection (hot spring).

Table 2 shows the laboratory data on admission. All patients had hypoxia and a high CRP value. Six patients had a high WBC count. Three patients had a high CPK score, but no complicating rhabdomyolysis or acute renal failure. There were no patients with hyponatremia.

Treatment and outcome are shown in Table 3. Seven patients had been under treatment with antibiotics such as imipenem/cilastatin (IPM/CS), meropenem (MEPM), ceftazidime (CAZ), clindamycin (CLDM), cefazopran (CZOP), sulfamycin tosylate (SBTPC). As for the therapy for *L. pneumophila* pneumonia, all patients were treated with two or more antibiotics, mainly ciprofloxacin (CPFX), erythromycin (EM) and rifampicin (RFP). A corticosteroid was used in 4 patients. With regard to their outcome, 6 patients were cured and two patients died.

Chest radiographic findings are shown in Table 4. Consolidation, which tended to be seen in peripheral lung, was present in 7 patients. Ground glass opacity was seen in 5 (in four it was located around the consolidation, and in one it was solitary). An interstitial shadow was seen in one patient. Pleural effusion was identified in 2 patients. No cavity or nodular infiltration was detected. Most patients showed a lobar pneumonia pattern. There were four patients who presented bilateral infiltrates and the radiographic shadow occupied more than one-third of the lung field.

The results of tests indicating a definite diagnosis are shown in Table 5. Gimenez staining was positive in 2 of 8 cases, sputum culture in 2 (*L. pneumophila*, serogroup 1) cases, urinary antigen in 4 cases, PCR on the sputum in 3, and serum antibody in 2 of 8 cases (*L. pneumophila*, serogroup 1, 256 titer).

Discussion

L. pneumophila pneumonia was first reported in Japan in 1981 by Saito et al. (9) Since then, several types of *L. pneumophila* pneumonia have been reported in Japan. Lieberman et al, (1) reported that *L.* species were the causative patho-

Table 2. Laboratory Data on Admission

Case	WBC/mm ³	CRP mg/dl	ESR mm/hr	PaO ₂ torr	PaCO ₂ torr	GOT IU/l	GPT IU/l	LDH IU/l	CPK IU/l	Na mEq/l
1	12000	21	12	58.5	31	146	89	737	356	141
2	5200	16.3	62	49.7	36.3	77	45	435	110	143
3	16600	23.8	147	58.3	32.5	36	17	485	135	134
4	12500	20.7		52.5	35.7	54	44	316	248	140
5	12700	7.9		62.8	33	26	14	245	39	155
6	9700	18.8		60.8	31	40	19	237		
7	11400	14.5		48.6	30.3	322	186	838	671	155
8	7000	30	117	58.1	30.3	23	27	255	83	137

Table 3. Treatment and Outcome

Case	Pretreatment	Treatment	Supportive therapy	Outcome
1	MEPM	CPFX+EM	Mechanical Ventilation, methylpredonisolone	Cure
2	IPM/CS	CPFX+CAM	(-)	Cure
3	CAZ+CLDM	CPFX+EM	methylpredonisolone	Died
4	(-)	EM+RFP	(-)	Cure
5	IPM/CS+CLDM	EM+RFP+MINO	methylpredonisolone	Cure
6	CZOP	CPFX+CAM+RFP	(-)	Cure
7	SBTPC+CLDM	CPFX+EM	methylpredonisolone	Died
8	MEPM	EM+RFP	(-)	Cure

CPFX : ciprofloxacin, EM : erythromycin, CAM : clarithromycin, MINO : minomycin, RFP : refampicin, MEPM : meropenem, IPM/CS : imipenem/cilastatin, CAZ : ceftazidime, CZOP : cefozopran, SBTPC : sultamicillin tosilate, CLDM : clindamycin.

gens in 16.2% of the cases of community-acquired pneumonia in the West. However, the percentage in *Legionella* species causative of community-acquired pneumonia is very low in Japan. It might be suggested that sporadic cases of *L. pneumophila* pneumonia must be overlooked without a definite diagnosis.

In general, *L. pneumophila* pneumonia presents with various symptoms: hyponatremia, impaired level of consciousness, cough, sputum, fever, diarrhea, or a combination of these symptoms (10). In the early phase of *L. pneumophila* pneumonia, 10% of the chest X-rays taken are almost normal (11). According to Heath et al (12), eight of their 39 patients did not have severe pneumonia. Although *L. pneumophila* pneumonia tends to cause severe pneumonia, some patients improve if given appropriate therapy at an early stage. Thus, an early diagnosis is of great importance, we

have described the characteristics of 8 elderly patients with *L. pneumophila* pneumonia.

In this study, all patients had hypoxia and fever. However, there were no specific laboratory data or clinical features in the initial stage. It was our impression that hypoxia was severe, given their shadow on chest X-ray and CT findings. From the viewpoint of differential diagnosis, bacterial pneumonia caused by *Streptococcus pneumoniae* or other bacterial infection might be more important than atypical pneumonia. In four patients, although they had severe pneumonia and hypoxia, no respiratory symptoms such as, cough, sputum, dyspnea, etc., were observed. Thus, when there are no respiratory symptoms other than fever, chest X-ray might not be taken.

It was reported that the delay in appropriate therapy, an underlying disease (cancer, diabetes, renal disease, etc.) and

Table 4. Chest Radiographic Findings

	No. of patients
Location	
bilateral infiltrate	4
right lung infiltrate	3
left lung infiltrate	1
Extent of radiographic shadow expressed as percent of one lung field	
<1/3	2
1/3~2/3	2
2/3<	4
Cavity	0
Pleural effusion	2
Lobar pneumonia	6
Interstitial pneumonia	1
Characteristics of opacity	
Air-space consolidation	2
Mixed air space consolidation and ground glass opacity	4
Ground glass opacity	1

Table 5. The Methods for Definite Diagnosis

Case	Gimenez stain	Sputum culture	PCR on sputum	Urinary antigen	Serum antibody
1	(+)	(+)	(-)	(-)	(-)
		<i>L. pneumophila</i> (serogroup 1)			
2	(-)	(-)	(+)	(-)	(+) 256
3	(-)	(-)	(-)	(-)	(+) 256
4	(-)	(-)	(+)	(-)	(-)
5	(-)	(-)	(-)	(+)	(-)
6	(+)	(+)	(+)	(+)	(-)
		<i>L.pneumophila</i> (serogroup 1)			
7	(-)	(-)	(-)	(+)	(-)
8	(-)	(-)	(-)	(+)	(-)

age were important risk factor for *L. pneumophila* pneumonia (10, 12, 13). In this study, the average number of days from onset to appropriate therapy was 5.0. Six of these 8 patients were cured regardless of their advanced age and existing underlying disease. The number of days to appropriate therapy of 2 patients who died cases (cases 3 and 7) was 8, which was a delayed timing compared to other cases. We found the prognosis was associated with the delay in appropriate therapy. There was not obvious relationship between the use of methylprednisolone and outcome.

There have been numerous reports with regard to the imaging findings of *L. pneumophila* pneumonia. The pulmonary infiltrates seen in *L. pneumophila* pneumonia are predominantly seen in the lower lobe, sometimes bilaterally, and there is rapid progression and pleural effusion (11, 14, 15). In the present study, we found a similar distribution of pulmonary infiltrates and frequency of pleural effusion com-

pared to previous reports. Yagyu et al (10) reported the following imaging findings of *L. pneumophila* pneumonia: multiple segments were affected and peripheral lung consolidation with ground glass opacity was present. Ground glass opacity was mainly located around the consolidation. In our study, there were four patients who had a similar pattern.

In establishing the definite diagnosis of *L. pneumophila* pneumonia, either a bacteriological test, serological examination, urinary antigen or PCR for *Legionella* is needed. There have been reports describing the usefulness of urinary antigen for the diagnosis of Legionnaire's disease (16-18). Urinary antigen was positive in 4 of 8 cases (positive rate 50%) in the present study. Urinary antigen might be the most useful for the initial diagnosis of *L. pneumophila* pneumonia. Although the positive rate of urinary antigen was higher compared with other examinations, there were patients who tested positive only for other examinations. We

consider that each examination was valuable and that they should be carried out when encountering patients with severe pneumonia.

In elderly patients with *L. pneumophila* pneumonia may present as fever without respiratory symptoms. The chest X-ray findings might show a bilateral distribution, multiple segments might be affected, and peripheral consolidation with ground glass opacity is observed. As *L. pneumophila* pneumonia often becomes a life-threatening condition, it is

critical to diagnose it in its initial stage. The key principles of management of *L. pneumophila* pneumonia are early diagnosis and control of the infection with appropriate antibiotics. It is important to be aware of the fact that elderly patients with *L. pneumophila* pneumonia might not present respiratory symptoms and that for an early diagnosis plural examinations will be needed. A detailed analysis of the clinical features might contribute to the diagnosis of *L. pneumophila* pneumonia.

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