First Sporadic Cases of Non-pneumonic Legionellosis, Pontiac Fever in Japan

Tetsuo Sakai, Yasutaka Kobayashi, Toshihiro Misawa, Manabu Takabatake, Masanori Shimada*, Yoshitaka Totani**, Takeshi Ishizaki**, Isamu Miyamori** and Atsushi Saito***

Pontiac fever has rarely been found in sporadic cases. Here, we report the first sporadic cases of non-pneumonic legionellosis, Pontiac fever in Japan. Case 1. A 53-year-old man with spinocerebellar degeneration was presented to our hospital. He had an acute onset of high fever and consciousness disturbance. A chest X-ray film on admission was normal, but transient bilateral pleural effusions were revealed on hospital day 14. Case 2. A 77-year-old woman with gastric ulcer was presented to our hospital. She had an acute onset of high fever. A chest X-ray film on admission was normal, but transient bilateral pleural effusions were revealed on hospital day 7. High fever, resistant to β-lactam antibiotics, continued in both cases. Both had serologic confirmation of legionellosis by indirect fluorescent antibody assay for Legionella pneumophila without seroconversion for Mycoplasma pneumoniae, and Chlamydia pneumoniae, and had a good prognosis. Both were thought to be sporadic community-acquired cases rather than epidemics. (Internal Medicine 37: 1068-1071, 1998)

Key words: high fever, Legionella pneumophila

Introduction

Legionella pneumophila (L. pneumophila) is the causal agent of both Legionnaires' disease and Pontiac fever, two different manifestations of legionellosis (1, 2). Legionnaires' disease, a severe pneumonic disease affects not only elderly or immunocompromised individuals but also immunologically normal ones. On the other hand, Pontiac fever which is a self-limited influenza-like state without pneumonia, has been found in many recent epidemics (3–14). It has rarely been found in sporadic cases (1). We reported sporadic cases of Pontiac fever.

Case Report

Case 1

A 53-year-old man with spinocerebellar degeneration was admitted to Fukui General Hospital on December 20, 1995. He had an acute onset of high fever and consciousness disturbance. There was no nausea or abdominal pain. He had smoked one pack of cigarettes per day for 23 years.

His temperature was 40.6°C, his heart rate was 120 beats per minute, and his respiratory rate was 30/min. Inspiratory wheeze was noted in the anterior lung fields. He had a normal chest roentgenogram. Laboratory analysis showed the following values: white blood cells, 14.3×10³/μl, associated with 85.2% neutrophils, 6.5% lymphocytes, 7.7% monocytes, and 0.1% eosinophils; aspartate aminotransferase, 29 IU/ℓ; alanine aminotransferase, 29 IU/ℓ; lactate dehydrogenase (LDH), 647 IU/ℓ; creatine phosphokinase (CPK), 466 IU/ℓ; and sodium, 148 mEq/ℓ. Arterial blood gas values while the patient was breathing oxygen via nasal cannula (5 ℓ/min) were as follows: pH, 7.365; partial pressure of oxygen (PaO₂), 85.1 mmHg; and partial pressure of carbon dioxide (PaCO₂), 49.7 mmHg.

Consciousness disturbance gradually improved after ventilatory support. Lumbar puncture revealed unremarkable findings. Magnetic resonance imaging of brain also revealed unremarkable findings without cerebellar atrophy. Transient bilateral pleural effusions were revealed on hospital day 14, while high fever continued. Thoracocentesis yielded an exudate (protein concentration 3.8 g/dl) with a negative Gram stain and cultures (bacteria, mycobacteria). Then, the patient was treated with oxygen via nasal cannula. High fever, resistant to β-lactam antibiotics, continued in this case. Then, erythromy-
Sporadic Cases of Pontiac Fever

<table>
<thead>
<tr>
<th>Date</th>
<th>Admission</th>
<th>Operation (decubitus)</th>
<th>Discharge</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dec. 1995</td>
<td>PAPM/BP</td>
<td>EM SBT/CPZ, CLDM</td>
<td>FLCZ</td>
</tr>
<tr>
<td>Jan.</td>
<td></td>
<td></td>
<td>Dantrolene sodium</td>
</tr>
<tr>
<td>Feb.</td>
<td></td>
<td></td>
<td>Mechanical Oxygen mask</td>
</tr>
<tr>
<td>Mar.</td>
<td></td>
<td></td>
<td>Ventilation</td>
</tr>
</tbody>
</table>

**Table 1. Serologic Analysis of Two Cases with Legionellosis (Indirect Fluorescent Antibody Titer)**

<table>
<thead>
<tr>
<th>Antigens</th>
<th>Case 1 Convalescent</th>
<th>Case 1 Discharge</th>
<th>Case 2 Admission</th>
<th>Case 2 Convalescent</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>L. pneumophila</em> serogroup 1</td>
<td>×128</td>
<td>&lt;×32</td>
<td>×128</td>
<td>×256</td>
</tr>
<tr>
<td><em>L. pneumophila</em> serogroup 1-3 (poly)</td>
<td>×128</td>
<td>&lt;×32</td>
<td>×64</td>
<td>×128</td>
</tr>
<tr>
<td><em>L. pneumophila</em> serogroup 4-6 (poly)</td>
<td>×128</td>
<td>&lt;×32</td>
<td>×64</td>
<td>×128</td>
</tr>
<tr>
<td><em>L. micdadei</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>L. bozemanii</em> (poly)</td>
<td>×32</td>
<td>&lt;×32</td>
<td>×64</td>
<td>×64</td>
</tr>
<tr>
<td><em>L. dumoffii</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Case 1**
A 77-year-old woman with gastric ulcer was presented to Fukui General Hospital on June 3, 1996. She had an acute onset of high fever. There was no cough or nausea. Her temperature was 38.5°C, her heart rate was 66 beats per minute, and her respiratory rate was 20/min. No rales were audible on lung fields. She had a normal chest roentgenogram. Laboratory analysis showed the following values: white blood cells, 5.7×10⁹/μl, associated with 76% neutrophils, and 9% lymphocytes, 15% monocytes; aspartate aminotransferase, 31 IU/μl; alanine aminotransferase, 21 IU/μl; LDH, 487 IU/μl; CPK, 206 IU/μl; and sodium, 135 mEq/l. Transient bilateral pleural effusions were noticed on hospital courses.

*Pneumocystis carinii* (1,000 mg/day) was given intravenously. Cultures of blood, sputum, urine were all negative for bacteria and mycobacteria. Assays of paired serum samples (drawn on admission and one month later) were negative for antibodies to *Mycoplasma pneumoniae* and *Chlamydia pneumoniae*. Though decubitus infection superimposed afterwards, he had a good prognosis (Fig. 1).

Convalescent serum samples (drawn one month later and on discharge) were obtained from the patient. *Legionella* serologic testing was performed with the use of several serogroup antigens by indirect fluorescent antibody assay, as previously described (13, 14). It demonstrated serologic evidence of infection with *L. pneumophila* by indirect fluorescent antibody assay. Seroconversion was defined as a four-fold or greater rise [or fall (7)] in titer, which was observed in this case in which paired serum samples were available (Table 1).

**Case 2**
A 77-year-old woman with gastric ulcer was presented to Fukui General Hospital on June 3, 1996. She had an acute onset of high fever. There was no cough or nausea. Her temperature was 38.5°C, her heart rate was 66 beats per minute, and her respiratory rate was 20/min. No rales were audible on lung fields. She had a normal chest roentgenogram. Laboratory analysis showed the following values: white blood cells, 5.7×10⁹/μl, associated with 76% neutrophils, and 9% lymphocytes, 15% monocytes; aspartate aminotransferase, 31 IU/μl; alanine aminotransferase, 21 IU/μl; LDH, 487 IU/μl; CPK, 206 IU/μl; and sodium, 135 mEq/l. Transient bilateral pleural effusions were noticed on hospital courses.

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day 7. Thoracocentesis yielded a transudate (protein concentration 2.3 g/dl) with a negative Gram stain and cultures (bacteria, mycobacteria). Culture on buffered charcoal yeast extract agar (BCYE) was also negative. High fever, resistant to β-lactam antibiotics, continued in this case. Then, erythromycin (1,000 mg/day) was given intravenously, in addition to antituberculous drugs. Cultures of blood, sputum, urine were all negative for bacteria and mycobacteria. Assays of paired serum samples (drawn on admission and one month later) were negative for antibodies to Mycoplasma pneumoniae and Chlamydia pneumoniae. She had a good prognosis (Fig. 2).

Convalescent serum samples (drawn two months later) were obtained from the patient. Legionella serologic testing was performed with the use of several serogroup antigens by indirect fluorescent antibody assay, as previously described. It demonstrated serologic evidence of infection with L. pneumophila by indirect fluorescent antibody assay. Seroconversion in this case was defined as an unpaired convalescent titer of 256 or more detected by indirect fluorescent antibody assay (Table 1).

**Discussion**

*L. pneumophila*, a Gram-negative bacillus, is the causal agent of both Pontiac fever and Legionnaires’ disease (1, 2). Pontiac fever is a self-limited influenza-like condition without pneumonia. Pontiac fever, non-pneumonic legionellosis has been found in many recent epidemics (3–14). Girod et al discussed that not only epidemics but also sporadic cases of nonpneumonic illness may represent a bridge between subclinical illness and pneumonia. Moreover, they reported that sporadic case was indistinguishable clinically from epidemics, suggesting that Pontiac fever is not always restricted to an epidemic disease.

Clinical symptoms of Pontiac fever reported previously were non specific and influenza-like condition such as fever, headache, myalgias, and cough. Our first case (Case 1) seemed to be atypical because he had a severe clinical condition and a prolonged clinical course. Prior underlying illness (spinocerebellar degeneration) could modify such a condition. However, consciousness disturbance from confusion to coma was sometimes one of the clinical manifestations in Legionnaires’ disease (15), suggesting that there could be neurologic manifestations also in Pontiac fever. Moreover, confusion was one of the neurologic findings in the first report (3).

High fever, resistant to β-lactam antibiotics, continued in these cases, suggesting that Mycoplasma, Chlamydia or Legionella infections were occurring. Legionella infection was the most likely as both cases had nonpneumonic form. Then, they were treated with erythromycin.

Pontiac fever has been associated with six species of Legionella, which are pneumophila serogroup 1 (1, 4–6, 16), 6 (7, 9) and 7 (14), L. anisa (12), L. feeleii (8), and L. micdadei (10, 11). Our serological findings suggested that seroconversions to L. pneumophila were detected in both cases with cross-reactions (17) among L. serogroups but not L. species.

It was unclear whether or not pleural effusion was experienced frequently by the patients. One patient had a pleural friction rub two weeks after the acute illness in the first outbreak (3). Repeat examinations of chest X-rays after onset should be performed on such patients, as pleural effusions were recognized one week or two weeks later in our cases. Pleural effusion...
in case 2 showed a transudate, but she had not had any specific diseases, such as congestive heart failure, liver cirrhosis or nephrotic syndrome, suggesting that pleural effusion may be a nonspecific phenomenon in Pontiac fever.

It is difficult to diagnose Pontiac fever based only on the clinical symptoms. The epidemiological aspect is a more important key for the diagnosis of Pontiac fever. The first epidemic of Pontiac fever reported in Japan occurred in a training center building of a company in Shibuya-ku, Tokyo in August 1994 (13, 14). Forty-five people fell ill with Pontiac fever caused by L. pneumophila serogroup 7. It was speculated that a cooling tower of a cylindrical open style which was located at the top of the center, sent the mist containing L. pneumophila which flowed in through the open windows of the training rooms.

Regarding the exposure to L. pneumophila of the present cases, twelve hours after arrival to a leisure hotel, the first case (Case 1) became ill. The source of L. pneumophila in this case was the heated pool where he regularly went for rehabilitation (two or three times monthly) for the underlying disease, but further investigation was not done. However, after detailed questioning, no other possible exposure to L. pneumophila in this case was identified. Moreover, no other family members became ill. Thus, we could not identify the source of L. pneumophila in case 1. The second case (Case 2) also had no exposure previously associated with L. pneumophila and no other family members became ill. These findings indicated that both were sporadic community-acquired cases but not epidemics. Here, we reported the first sporadic cases of Pontiac fever in Japan, although Pontiac fever has been found in many epidemics (3–14). It is important to recognize such cases associated with acute onset of high fever, and the late development of bilateral pleural effusion, which in the present cases, was not responsive to the typical antibiotic therapy.

References