CASE REPORT

Legionnaires’ Disease Associated with Habitual Drinking of Hot Spring Water

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Abstract

A 57-year-old man presented with pneumonia, respiratory distress, and myelodysplastic syndrome. A diagnosis of Legionnaires’ disease due to Legionella pneumophila (L. pneumophila) was established. The patient had long been drinking tap water via a conduit from a hot spring resource, from which L. pneumophila was also isolated. Both the patient’s strain and the water strain of L. pneumophila were identified as serogroup 1, and the genetic relatedness between the two strains as seen by pulsed-field gel electrophoresis was 87%. The patient was successfully treated with erythromycin, fluoroquinolone, and rifampicin. This case raises an important issue on public health represented by legionellosis in Japan.

Key words: legionellosis, pulsed-field gel electrophoresis, immunocompromised host, public health

Introduction

Since its first description by Fraser and colleagues in 1977 (1), Legionnaires’ disease has become widely recognized as an important cause of either hospital-acquired or community-acquired fatal pneumonia. The leading organism, Legionella pneumophila, serogroup 1 (2), has been consistently isolated from a variety of man-made water reservoirs in many community-acquired legionellosis cases. Here, we describe a case of community-acquired Legionnaires’ disease in an immunocompromised patient who habitually drinks water via a conduit from a hot spring resource. This case raises an important issue of public health represented by Legionnaires’ disease, a community-acquired infectious disease whose etiologic organism frequently resides in hot spring “On-Sen”, where a large population of community people spend their time to bathe or even purchase On-Sen water for domiciliary use.

Case Report

A 59-year-old male office worker was referred to Saga Medical School Hospital on August 10, 1999, complaining of fever, non-productive cough, dyspnea, and myalgia of the trunk and extremities. These symptoms were unresponsive to three days of therapy with oral cefdinir and intravenous ceftriaxone. Upon admission, the patient was in respiratory distress. His body temperature was 38.5°C, heart rate 120/min, respiratory rate 44/min, and blood pressure 108/60 mmHg. Physical examination disclosed diminished breath sounds of the right mid-lower lung field, ipsilateral pleuritic chest pain upon deep breath, and severe myalgia of the trunk induced by light touch. The patient’s chest film (Fig. 1) and computed tomography (CT) scan on admission revealed air-space consolidation in the right lower lobe and pleural effusion. Laboratory analyses were as follows: WBC 400/μl (meta. 2%, neu. 48%, lym. 26%, mono. 14%, eosin. 10%), RBC 323x10^4/μl, platelet count 7.9x10^4/μl, serum C-reactive protein 31.4 mg/dl, creatine phosphokinase (CPK) 266 IU/l, sodium 133 mEq/l, coagulation analyses were: prothrombin time 67%, activated partial thromboplastin time 51.3%, fibrinogen 1,121 mg/dl, fibrinogen degradation products, 207 ng/ml, and antithrombin-III 71.3%. Arterial blood gas analysis while the patient was breathing oxygen via a reservoir mask (15 l/min) were; pH 7.44, PaO2 65.9 mmHg, PaCO2 31 mmHg.

Although the patient recalled no episode of bathing in hot springs prior to the onset of his symptoms, since the patient’s clinical features (i.e., acute respiratory failure, severe myalgia, sepsis, disseminated intravascular coagulation) and accompanying respiratory infection were strongly suggestive of Legionnaires’ disease (3), he was started on therapy with intravenous erythromycin (EM: 1,500 mg/day) and imipenem/cilastatin (IPM/CS: 1 g/day) followed by a combination therapy with oral rifampicin (RFP: 450 mg/day) and levofloxacin (LVFX: 300 mg/day) (Fig. 2). The diagnosis of Legionnaires’ disease...
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was established by 1): isolation from the patient's bronchial lavage fluid (BLF) of colonies on BCYE (buffered charcoal yeast extract)-α agar plate (Oxoid), all of which were identified by DNA-DNA hybridization procedure (4) as *Legionella pneumophilia* (LP), 2): positive antigenuria for LP (Biotest Legionella Urine Antigen EIA), and 3): serum antibody titer against LP serogroup 1 was eventually demonstrated by indirect immunofluorescent antibody method to be increased to 1,024.

It turned out in the second interview with the patient following diagnosis of Legionnaires' disease that the patient had been purchasing tap water for almost one year via a conduit from a hot spring resource in the vicinity. He had been using the hot spring water at home for drinking, but not for brushing his teeth, washing his face, or bathing. He reported that each time upon purchase he connected the tap to his vessel using a long, thin tube, and that water splash was generated each time he poured the water by himself. Therefore, the tap water this patient had utilized as well as the water from the hot tub of probably the same resource were cultured for bacteria, both of which grew *L. pneumophilia*. The quantitative culture for LP in the former yielded >1×10⁴ CFU (colony forming unit)/100 ml tap water, and in the latter 10² CFU/100 ml tub water. All six LP strains from patient’s BLF, five out of six LP strains from tap water, and all three LP strains from tub water were identified as *Legionella pneumophilia* serogroup 1 (Denka Seiken). In an attempt to further clarify the genetic relatedness, three

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**Figure 1.** Chest X-ray film on admission revealed infiltrative shadows in the middle and lower fields of the right lung.

<table>
<thead>
<tr>
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<tr>
<td>Admission</td>
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<tr>
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<td>↓ ↓</td>
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<tr>
<td>EM</td>
<td>LVFX</td>
</tr>
<tr>
<td>IPM/CS</td>
<td>RFP</td>
</tr>
<tr>
<td>CZOP</td>
<td>CAM</td>
</tr>
<tr>
<td>Tom</td>
<td>EM</td>
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**Fever**

**Myalgia**

**Headache**

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<tr>
<th>WBC</th>
<th>PLT (×10⁴)</th>
<th>CRP</th>
<th>GOT/GPT</th>
<th>PaO₂/FiO₂</th>
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<tr>
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<td>7.9</td>
<td>31.4</td>
<td>26/23</td>
<td>125</td>
</tr>
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<td>2,200</td>
<td>13</td>
<td>14.6</td>
<td>120/184</td>
<td>156</td>
</tr>
<tr>
<td>3,400</td>
<td>14.5</td>
<td>10.2</td>
<td>35/119</td>
<td>202</td>
</tr>
<tr>
<td>3,000</td>
<td>25.3</td>
<td>10</td>
<td>42/77</td>
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</tr>
<tr>
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<td>0.2</td>
<td>16/13</td>
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**Biotest**

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<th>negative</th>
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<th>negative</th>
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<tr>
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<td>×32</td>
<td>×512</td>
<td>×1,024</td>
</tr>
</tbody>
</table>

**Chest X-p**

G-CSF: granulocyte colony stimulating factor, CZOP: cefozopran, CAM: clarithromycin. Other abbreviations; see text.

**Figure 2.** Clinical course of the patient.
Figure 3. Analysis of Sfi-I-digested genomic DNA of Legionella pneumophila strains by pulsed-field gel electrophoresis (PFGE). Extraction of chromosomal DNA from all the strains and endonuclease digestion were performed as recommended by manufacturer (Gene Path: Group 5, BIO-RAD). PFGE was run in 1% agarose gel for 19 H using Gene Path Strain Typing System (BIO-RAD), then visualized by ethidium bromide staining. Three strains each from three different samples were analyzed. Lane 1-3: BLF (bronchoalveolar lavage) isolates from the patient, lanes 4-6: tap water isolates, lanes 7-9: tub water isolates. Bacteriophage lambda ladders (M) were used as molecular size standards (48.5 kb).

The patient’s clinical course showed a good response to antimicrobial chemotherapy for Legionnaires’ disease. The marked leukocytopenia upon admission initially considered to reflect systemic severe infection was restored at the highest level, and was eventually diagnosed by bone marrow tap as myelodysplastic syndrome. Three weeks following the discharge from the hospital, the follow-up bone marrow tap showed that the patient developed acute myelogenous leukemia presenting 76% myeloblast, and the patient is now treated with anti-leukemic chemotherapy.

Discussion

The clinical features seen in the present case (i.e., male gender, 5th decade in age, complicating hematologic malignancy) have been considered risk factors for Legionnaires’ disease (2, 6, 7). Similar cases of Legionnaires’ disease accompanying myelodysplastic syndrome or disseminated intravascular coagulation have also been reported (8, 9).

Many of the reported cases of legionellosis have been attributed either to inhalation or aspiration of legionellae into the respiratory tract (7, 10–15). The tap water this patient had long used was found to be heavily contaminated with L. pneumophila of $>10^4$ CFU/100 ml, in contrast to the previous reports in which the quantitative culture of L. pneumophila was reportedly $10^3$ CFU/100 ml or less (14, 16). In addition to these findings, the fact that the hot spring bath tub water surveyed was contaminated with less L. pneumophila (10^3 CFU/100 ml) may together suggest that the tap water might have possibly been pooled in a reservoir system in which L. pneumonia proliferates exponentially before reaching the tap outlet. Given that even a negligible amount of L. pneumophila of as low as 3 CFU/100 ml has resulted in Legionnaires’ pneumonia (14), it is very likely that the habitual drinking of heavily LP-contaminated water had resulted in legionellosis in the present patient.

As has previously been documented in a patient (5), colonization of the oropharyngeal mucosa by Legionella pneumophila and subsequent aspiration into the lungs could be an attractive hypothesis in our patient. However, since the antibody titer against L. pneumophila in our patient was not elevated upon admission, chronic colonization (or infection) by L. pneumophila may not be as likely as in the previous case. In view of the report by Bridge and Edelstein that Legionella pneumophila rarely colonizes the oropharyngeal portion (17), another hypothesis is that water splash containing L. pneumophila might have been aspirated into the patient’s airway at the time of purchasing, which ultimately caused Legionnaires’ disease. Alternatively, this patient might have aspirated a small amount of the hot spring water upon drinking, even though he did not recall an overt aspiration event.

Generally, two bacterial strains are considered genetically identical when numerical analysis of genetic relatedness demonstrates a percentage similarity of >95% (18). Therefore, the LP strains from the tap water sampled for investigation may not be considered clonally identical to the strains from the patient’s sputum. However, since the LP strains from the patient and hot tub were genetically identical, a clonal link of L. pneumophila serogroup 1 between the patient and tap water is likely present.

Given that almost half of the hot springs surveyed nationwide up to 1994 were reportedly contaminated by Legionella species (19), implementation of effective measures for inhibiting the growth of Legionellae species would have a strong impact on public health issues surrounding this community-ac-
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quired infection. Maintaining the temperature of the resource water at least above 55°C is considered an effective countermeasure to prevent survival of *Legionella* species (20), or chloramination of the water system may be a cost-effective method for control of Legionnaires’ disease (21). Most importantly, it must be carefully monitored to ensure that the community people are informed that the hot spring water is possibly contaminated by pathogenic *Legionella* species, and drinking and other domiciliary use should be avoided.

References


