CASE REPORT

Can we truly rely on the urinary antigen test for the diagnosis? Legionella case report

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Abstract
It is critical to diagnose and treat Legionella pneumonia (LP) immediately after infection because of the associated high mortality. The urine antigen test (UAT) is often used for the diagnosis of LP; however, it cannot detect the serogroups of all Legionella species. A detailed medical history and several clinical findings such as liver enzyme elevation and hyponatremia are useful in diagnosis. Some specific types of Legionella are found in compost. Herein, we report a case of LP in which the patient’s medical history and several clinical findings were useful for diagnosis.

KEYWORDS
compost, gardening, Legionella longbeachae, Legionella pneumonia, loop-mediated isothermal amplification, urine antigen test

1 | INTRODUCTION

The urine antigen test (UAT) is often used in the primary care setting for the diagnosis of Legionella pneumonia (LP); however, the test is not adequately sensitive and the results are frequently uncertain. For the present case, the patient’s medical history and several clinical findings proved essential for LP diagnosis. The UAT results could not aid the diagnosis owing to its limited sensitivity.

2 | CASE PRESENTATION

A 69-year-old Japanese man presented to the emergency department for a 3 day history of a fever and chills. He did not have a cough, rhinorrhea, pharyngalgia, dyspnea, nausea, diarrhea, or loss of appetite. He had diabetes mellitus (HbA1c 7.0% 11 days before admission) and atrial fibrillation, and he was receiving glimepiride, sitagliptin, and warfarin medication. In terms of risk factors for LP, he was an ex-smoker and a gardener, but had not traveled abroad or taken a public bath.

On physical examination, his body temperature was 36.3°C, his heart rate was 91 beats per minute, his blood pressure was 99/68 mm Hg, his respiratory rate was 16 breaths per minute. and his SpO2 was 98% in room air. Coarse crackles were heard in his right lower lung field. The rest of the physical examination was normal.

His laboratory test results are shown in Table 1. The blood test showed anemia, thrombocytopenia, liver enzyme elevation, hyponatremia, and elevated creatinine phosphokinase. Proteinuria and microhematuria were revealed via urine analysis. The result of a Legionella UAT was negative. We assessed his sputum Gram stain and classified it as Geckler group 6; no bacteria were detected in the smear. The sputum culture test showed the presence of only alpha-hemolytic Streptococcus and Candida. It was negative for Legionella though we did not use the buffered charcoal yeast extract agar base to detect Legionella species. A chest radiograph and a computerized axial tomography scan showed consolidation in the right lower lobe (Figures 1 and 2).

Despite the negative UAT result, we initiated ceftriaxone, azithromycin, and minocycline treatment for LP because of a high clinical suspicion based on the clinical history and physical and laboratory findings. We confirmed the diagnosis using a sputum loop-mediated isothermal amplification (LAMP) test (Eiken Chemical Co. Ltd, Japan). We administered levofloxacin because his body temperature was elevated (without relative bradycardia) and his bloody sputum persisted.
Following treatment, he recovered and he was discharged on day 12 (Figure 3).

3 | DISCUSSION

LP comprises 2% to 9% cases of community-acquired pneumonia.\(^1\)\(^-\)\(^5\)  

Generally, legionellosis is caused by infections acquired from a water reservoir or hot spring contamination. The common risk factors of LP are cigarette smoking, chronic lung disease, increasing age, and immunosuppression. This patient had history of smoking and diabetes mellitus, which we considered risk factors of LP.

Generally, in cases of LP, respiratory symptoms such as cough and sputum are not prominent at first. Hyponatremia occurs frequently in legionellosis.\(^6\)\(^-\)\(^10\) Renal and hepatic dysfunction, elevated creatinine phosphokinase, thrombocytopenia, and leukocytosis are considered the common laboratory abnormalities. Hematuria and proteinuria are also common abnormalities. In this case, the patient only complained of a fever and chills, and he did not have a cough or sputum. However, he eventually presented all the aforementioned laboratory features. A Gram stain of his sputum resulted in its classification as Geckler group 6, which did not aid the diagnosis.

While the mortality rate among patients with community-acquired legionellosis ranges from 16% to 30%, with or without treatment using

### TABLE 1  Laboratory data on admission

| Complete blood count | Blood Chemistry Serology | Arterial blood gas (Room air) |
|----------------------|--------------------------|-------------------------------|
| White blood cell     | 7700/μL                  | T-protein 6.3 g/dL\(^a\)       | pH 7.433 mm Hg |
| Red blood cell       | 356×10⁴/μL\(^a\)         | T-bil 0.7 mg/dL               | PaCO₂ 36.0 mm Hg |
| Hemoglobin           | 11.2 g/dL\(^a\)          | AST 265 U/L\(^a\)             | PaO₂ 72.5 mm Hg\(^a\) |
| Hematocrit           | 31.5%\(^a\)              | ALT 61 U/L\(^a\)              | HCO₃ 23.7 mmol/L |
| Platelet count       | 11.9×10⁴/μL\(^a\)        | LDH 572 U/L\(^a\)             | BE 0.2 mmol/L  |
|                      |                          | ALP 196 U/L                   | O₂Sat 97.3% |
|                      |                          | CPK 15510 U/L\(^a\)          | AG 12.6 mmol/L |
|                      |                          | Amy 47 U/L                    | Lac 9 mg/dL  |

| Blood coagulation system | | | |
|--------------------------|---|---|---|
| PT                       | 17.7 s\(^a\) | %PT 42.0%\(^a\) | PT-INR 1.54\(^a\) |
| APTT                     | 53.9 s\(^a\) | BUN 28 mg/dL\(^a\) | Cr 1.65 mg/dL\(^a\) |
| Blood sugar              | 382 mg/dL\(^a\) | Na 126 mEq/L\(^a\) | K 3.5 mEq/L\(^a\) |
| CRP                      | 19.79 mg/dL\(^a\) | Cl 92 mEq/L\(^a\) | Blood sugar 382 mg/dL\(^a\) |

**Urinalysis**

| Specific gravity | 1.020 | Ketone body | - | Pneumococcus | - |
| pH               | 6.0   | Blood      | 3+\(^a\) | Legionella | - |
| Protein          | 2+\(^a\) | Leukocyte | - |
| Glucose          | 24+\(^a\) |

\(^a\)Results out of the reference range.

**FIGURE 1** Chest radiography findings. The radiograph shows consolidation in the right lower lobe, which gradually disappeared after day 2.
inactive antibiotics such as beta-lactam agents, it reduces to less than 10% in patients with community-acquired LP treated with potent therapies.\textsuperscript{11–15} In many countries, such as Japan, USA, and UK, cases of legionellosis should be reported immediately to the public health department. This is because earlier detection and appropriate diagnosis and treatment are very important for reducing the associated high mortality risks.

The commercial UAT (Alere BinaxNOW\textsuperscript{®} Legionella Urinary Antigen Card) is an immunochromatographic membrane assay that is used to detect the \textit{Legionella pneumophila} serogroup 1 soluble antigen.
TABLE 2  Correlation between UAT, LAMP, and culture tests

|                | UAT     | LAMP     |
|----------------|---------|----------|
|                | +       | -        | Total   | +       | -        | Total   |
| Culture        | 13      | 9        | 22      | 21      | 1        | 22      |
| -              | 0       | 113      | 113     | 0       | 113      | 113     |
|                | 13      | 122      | 135     | 21      | 114      | 135     |

in human urine.16 A vast majority of community-acquired LP cases are caused by this species and serogroup.4,17,18 Although it is very useful to define a diagnosis of LP, it is of limited use to detect non-serogroup 1 L. pneumophila and other species. The sensitivity and specificity of UAT for detecting other serogroups and species are currently unknown.

LAMP (Loopamp Legionella Detection Kit E) is a nucleic acid amplification method19 to specifically amplify the target gene using four primers specific to six distinct regions. The whole amplification reaction continuously takes place under isothermal conditions. We used this method to support our legionellosis diagnosis. The sensitivity and specificity of this method are 91.3% (21/23) and 100% (112/112), respectively.20 The correlation between UAT, LAMP, and culture tests is shown in Table 2; almost all patients (21/22) with positive cultures tested positive for LP via LAMP, while only 59.1% of patients (13/22) with positive cultures tested positive for LP via a UAT.19 We hypothesized that the cause of this case of LP was non-serogroup 1 L. pneumophila infection or an infection from another species, because the positive results were obtained using the LAMP method, and negative results were observed using the UAT.

Inhalation or ingestion of potting soil is associated with LP. We identified several cases of legionellosis with causes related to gardening (see Table 3). While a few patients were infected by L. pneumophila, most patients were infected by L. longbeachae. This species was first isolated in 1980 from a patient with pneumonia in Long Beach, California.21 Interestingly, the UAT was negative for all patients infected with L. Longbeachae. We also assembled data regarding the distribution of Legionella species in Japanese potting soils (see Table 4). Similar reports have been published for distribution in other areas such as America, Australia, and Europe.22,23 These reports consistently indicate that L. pneumophila is not commonly found in the soil. Therefore, we should consider other Legionella species as the causal agent particularly when the soil is the possible pathway of infection, as in this case. Although we were not able to identify which Legionella species was the pathogen in this case, we speculated it was L. longbeachae or other related species and not L. pneumophila, because this patient was a gardener. This speculation explains both the negative result with the UAT and the positive result of the LAMP test.

In conclusion, the medical history and clinical findings are key to diagnosing LP, because the UAT is not always helpful owing to its limited sensitivity. In particular, when gardening is the route of infection, because the occurrence of L. pneumophila in the soil is rare, other species such as L. longbeachae should be considered as the potential causal pathogen for LP. In addition, in such cases, the clinicians should

TABLE 3  Legionella cases caused by gardening

| Time  | Nation   | Character | Outcome | UAT | Species          | References |
|-------|----------|-----------|---------|-----|------------------|------------|
| 1996/7 | Japan    | 52, m     | Death   | -   | L. longbeachae   | 24         |
| 1999/7 | Japan    | 83, m     | Survive | -   | L. longbeachae   | 25         |
| 2000/5 | USA      | 77, f     | Survive | -   | L. longbeachae   | 22         |
| 2000/5 | USA      | 45, m     | Death   | -   | L. longbeachae   |            |
| 2000/6 | USA      | 46, f     | Death   | -   | L. longbeachae   |            |
| 2000/8 | Netherlands | 81, m   | Death   | -   | L. longbeachae   | 26         |
| 2000/8 | Netherlands | 69, m   | Death   | -   | L. longbeachae   |            |
| 2004/12 | Netherlands | 67, m   | Death   | -   | L. longbeachae   |            |
| 2001/5 | Australia | 40s, m    | Survive | +   | L. pneumophila   | 27         |
| 2004/8 | Japan    | 72, m     | Survive | -   | L. longbeachae   | 28         |
| 2009/10 | Japan    | 74, m     | Survive | -   | L. longbeachae   | 29         |
| Not noted | New Zealand | 79, f   | Death   | -   | L. longbeachae   | 30         |
| Not noted | Switzerland | 60, m   | +       |     | L. pneumophila   | 31         |
be careful in interpreting the result of the UAT, because the results can be negative even when these species are present. The LAMP test is useful with higher sensitivity and specificity than UAT when the clinical suspicion of legionellosis is high although UAT is negative.

CONFLICT OF INTEREST
The authors have stated explicitly that there are no conflicts of interest in connection with this article.

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