Pneumonia and Osteomyelitis Due to *Legionella longbeachae* in a Woman with Systemic Lupus Erythematosus

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A patient with risk factors of systemic lupus erythematosus, corticosteroid use, and malignancy received a diagnosis of concomitant pneumonia and osteomyelitis caused by *Legionella longbeachae*. In this report, the first description of *Legionella* osteomyelitis, previous cases of extrapulmonary *Legionella* infection are detailed.

A 48-year-old woman with a history of corticosteroid-dependent systemic lupus erythematosus sought care at the emergency department of the Santa Clara Valley Medical Center (San Jose, CA) with a 4-day history of fever and left ankle pain and swelling. She also had a cough with production of clear sputum, as well as dyspnea on exertion, that had worsened over the previous 3 days. Her history was remarkable for chronic corticosteroid use (20 mg daily of prednisone) for >1 year’s duration. She was not receiving trimethoprim-sulfamethoxazole. She did not smoke cigarettes or have preexisting pulmonary disease. She had not traveled recently and did not work outdoors or with potting soil.

At examination, her temperature was 39.8°C, her pulse was 120 beats/min with normal blood pressure, and her respiratory rate was 18 breaths/min. Initial oxygen saturation was 98% while breathing room air. The findings of a physical examination were normal except for an erythematous, tender, and swollen left ankle that was consistent with cellulitis. There was no appreciable joint effusion found during the physical examination. The findings of plain radiographs of the ankle were normal except for soft tissue swelling, and the findings of an ultrasound were negative for deep venous thrombosis. Initial chest radiograph findings were unremarkable. The patient’s WBC count was $8.6 \times 10^3$ cells/L with a differential showing 70% neutrophils and 23% lymphocytes. Her serum electrolyte levels and renal function were normal. She initiated therapy with ticarcillin-clavulanate intravenously. Shortly after admission to the hospital, she developed respiratory distress and rales bilaterally on lung auscultation. The results of an arterial blood gas test were remarkable for a pH of 7.51, a PCO$_2$ of 33 mm Hg, and a PO$_2$ of 42 mm Hg while breathing ambient air, and the findings of a chest radiograph revealed bilateral consolidation. Intravenous levofloxacin therapy was initiated.

Findings of a subsequent CT scan of the thorax revealed mediastinal and axillary lymphadenopathy up to 1.5 cm in diameter; hazy patchy infiltrates in the lingula and right middle lobe; and the development of a small cavity in a right upper lobe area of consolidation. Cultures of blood, sputum, and bronchoalveolar lavage samples showed no growth, including culture of bronchoalveolar lavage samples for acid-fast bacilli, fungi, and culture on buffered charcoal yeast extract (BCYE) agar. There was no *Pneumocystis carinii* seen on special stains of the lavage fluid samples. The results of an antibody test for HIV were negative. However, a sputum culture obtained on the evening of admission (before initiating therapy with levofloxacin) that was incubated on BCYE agar grew *Legionella longbeachae* serogroup 1.

Despite antibiotic therapy, the patient’s ankle became increasingly swollen. MRI findings were highly suggestive of osteomyelitis in the distal tibia with adjacent abscess (figure 1). Aspiration of the fluid revealed frank pus, and the patient was taken to the operating room for emergency surgical debridement. Routine bacterial, fungal, and acid-fast bacilli cultures of tissue and bone were unremarkable, but culture of bone on BCYE agar again grew *L. longbeachae* serogroup 1. Infection was confirmed by direct inspection of bone intraoperatively. Rifampin therapy was added. The patient’s ankle and respiratory function improved considerably during antibiotic therapy. However, she had a persistent pancytopenia, with an absolute neutrophil count nadir of 0.5 × 10^9 neutrophils/L. Bone marrow biopsy and aspiration were performed, and flow cytometry demonstrated the presence of a diffuse large B cell lymphoma. Chemotherapy was deferred, however, until the patient recovered from her acute infections.

After ~3 weeks of inpatient antibiotic treatment, the patient’s condition improved clinically. However, as an outpatient, she...
stopped her antibiotic therapy, and she deteriorated rapidly. The patient was readmitted with respiratory failure, and chest radiograph findings revealed bilateral air space disease. Cultures of bronchoalveolar lavage fluid samples on BCYE agar showed no growth. Open lung biopsy demonstrated diffuse alveolar damage. The patient had a prolonged stay in the intensive care unit and eventually died of multiorgan system failure. A postmortem autopsy was not performed. Of note, the hospital had not reported other cases of *L. longbeachae* infection.

**Discussion.** The patient described herein had classic signs and symptoms of *Legionella* pneumonia, including dyspnea, hypoxemia, scant sputum production, fever, and radiographic infiltrates, as well as microscopic hematuria. This case represents an unusual confluence of factors; namely, osteomyelitis caused by an unusual species of *Legionella*. However, there is a fairly high degree of certainty regarding the diagnosis in this patient. For one, the isolation of the same species of *Legionella* from a respiratory specimen and from an intraoperative bone specimen is noteworthy. Second, several studies have indicated that, for osteomyelitis, MRI is an excellent diagnostic tool, having a sensitivity of 92%–100% and a specificity of 89%–100% [1, 2]. Third, a latency period of 4 days between the onset of pneumonia and hematogenous seeding is within the realm of plausibility. Finally, the patient’s multiple levels of immunosuppression—corticosteroid use, systemic lupus erythematosus, and hematologic malignancy—rendered her susceptible to opportunistic infections.

This case represents what, to our knowledge, the first description of osteomyelitis due to a *Legionella* species. Bone involvement would not be expected a priori, given the relatively weak vascular supply of the bone cortex. However, hematogenous dissemination of *Legionella* species from the lungs to various other sites has been reported in the literature. Previously described sites of infection include spleen [3–5], liver [6], kidney [5, 7, 8], CNS [8], lymph nodes [6, 7], skeletal muscles [7], myocardium [8, 9], pericardium [10–12], heart valves [13], skin and soft tissue [14], and others [6, 15]. There are reports of cutaneous [16] and perirectal [17] *Legionella* abscesses after episodes of pneumonia. The most common species in such reports is *L. pneumophila*, probably because of its predominance among *Legionella* species as a cause of pneumonia. One report describes a 58-year-old man with involvement of 10 organs.
Table 1. Patients with pertinent cases of soft tissue infection due to *Legionella* species.

<table>
<thead>
<tr>
<th>Patient age</th>
<th>Sex</th>
<th>Site of infection</th>
<th>Concurrent pneumonia?</th>
<th>Species</th>
<th>Confirmatory test</th>
<th>Immunocompromising condition(s)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>48 years</td>
<td>F</td>
<td>Osteomyelitis</td>
<td>Yes</td>
<td><em>Legionella longbeachae</em></td>
<td>Culture</td>
<td>SLE, lymphoma, corticosteroid therapy</td>
<td>Present case</td>
</tr>
<tr>
<td>65 years</td>
<td>F</td>
<td>Myositis</td>
<td>Yes</td>
<td><em>Legionella pneumophila</em></td>
<td>DFA</td>
<td>None identified</td>
<td>[7]</td>
</tr>
<tr>
<td>66 years</td>
<td>M</td>
<td>Cellulitis</td>
<td>Yes</td>
<td><em>L. pneumophila</em>, serogroup 1</td>
<td>Urine antigen, DFA, culture</td>
<td>Lymphoma</td>
<td>[14]</td>
</tr>
<tr>
<td>62 years</td>
<td>F</td>
<td>Cutaneous abscess</td>
<td>Yes</td>
<td><em>Legionella micdadei</em></td>
<td>DFA, culture</td>
<td>Rapidly progressive glomerulonephritis, corticosteroid use, cyclophosphamide use</td>
<td>[16]</td>
</tr>
<tr>
<td>46 years</td>
<td>F</td>
<td>Perirectal abscess</td>
<td>Yes</td>
<td><em>L. pneumophila</em>, serogroup 1</td>
<td>Culture</td>
<td>Idiopathic diffuse proliferative glomerulonephritis, corticosteroid use</td>
<td>[17]</td>
</tr>
<tr>
<td>85 years</td>
<td>F</td>
<td>Sternal wound</td>
<td>No</td>
<td><em>Legionella dumoffii</em></td>
<td>Culture</td>
<td>None identified</td>
<td>[22]</td>
</tr>
<tr>
<td>3 weeks</td>
<td>F</td>
<td>Sternal wound</td>
<td>No</td>
<td><em>L. pneumophila</em></td>
<td>Culture</td>
<td>None identified</td>
<td>[22]</td>
</tr>
<tr>
<td>27 years</td>
<td>M</td>
<td>Sternal wound</td>
<td>No</td>
<td><em>L. dumoffii</em>, <em>L. pneumophila</em></td>
<td>Culture</td>
<td>None identified</td>
<td>[22]</td>
</tr>
<tr>
<td>71 years</td>
<td>M</td>
<td>Postoperative hip wound</td>
<td>No</td>
<td><em>L. pneumophila</em>, serogroup 4</td>
<td>DFA, culture</td>
<td>None identified</td>
<td>[23]</td>
</tr>
<tr>
<td>39 years</td>
<td>F</td>
<td>Necrotizing cellulitis</td>
<td>No</td>
<td><em>L. micdadei</em></td>
<td>DFA, culture</td>
<td>Receipt of renal transplant</td>
<td>[25]</td>
</tr>
<tr>
<td>73 years</td>
<td>F</td>
<td>Soft tissue abscesses on the jaw, wrist, and arm</td>
<td>No</td>
<td><em>Legionella cincinnatiensis</em></td>
<td>PCR, culture</td>
<td>IgA gammopathy</td>
<td>[26]</td>
</tr>
</tbody>
</table>

**NOTE.** DFA, direct fluorescent antibody; SLE, systemic lupus erythematosus.
systems, including lung, liver, kidney, brain, thyroid, pancreas, muscle, testes, prostate, and heart [6]. There is a report of an infected hemodialysis fistula, demonstrating that the organism can infect prosthetic material [18]. It has been found in bone marrow, as well [7, 19]. Legionella has also been cultured directly from blood, serving as mechanistic evidence of hematogenous spread [20, 21]. Taken together, these reports suggest that the organism, albeit fastidious in culture in vitro, may be more durable and robust in vivo.

Extrapulmonary Legionella infections have also been described as primary infections in the absence of pneumonia. The mode of spread in such cases is probably direct inoculation of susceptible tissues and wounds. One case series by Lowry et al. [22] describes a cluster of L. dumoffii sternal wound infections after cardiac surgery due to periwound site cleaning with contaminated hospital tap water. Another report describes the case of a patient who developed Legionella infection in a postoperative hip wound from a water bath used for rehabilitation after hip surgery [23]. Other sites of de novo infection include sinusitis in a patient with HIV infection [24], necrotizing cellulitis [25], soft tissue abscess [26], and endocarditis [13].

In cases of extrapulmonary legionellosis, there appears to be a preponderance of immunocompromised hosts. This is especially true of soft tissue infections, in which 6 of 11 reported cases, including the present case, were in patients who were immunocompromised (table 1). Other factors, such as a positive result on a direct fluorescent antibody test, the presence of specific Legionella species, and the route of infection, do not appear to predict which patients will develop extrapulmonary soft tissue infections.

Environmental sources of Legionella species have been well established. The most common species, L. pneumophila, which accounts for 70%–90% of diagnosed cases in the United States [27, 28], usually enters the respiratory tract via aerosolized droplets. Demonstrated sources of large-scale outbreaks of this organism have included water supplies capable of aerosolizing organisms or spreading them via direct contact, such as large decorative water fountains [29], whirlpool spas [30], and hospital water distribution systems [22]. Traditional environmental sources for L. longbeachae include potting soil, as demonstrated by studies conducted in the United States [31], Japan [32], and Australia [33]. Recently, however, epidemiological studies have identified multiple species of Legionella, including L. longbeachae, in drinking water in residential distribution systems [34]. Our case patient had no obvious exposure to potting soil, raising the question of whether this organism is indeed more ubiquitous than was previously believed. As compared with the more prevalent L. pneumophila, L. longbeachae is probably less virulent [35], possibly explaining why it is less often a pathogen but may be more common in immunocompromised hosts. Also, because the urine antigen test (which is sensitive only for L. pneumophila serogroup 1) is so widely used now for diag-

Figure 2. Reported sites of extrapulmonary infection due to Legionella species. *Site at which infection without concurrent pneumonia has been described.
nosis, it may be that many infections caused by non-
*pneumophila* species remain undiagnosed.

In summary, this culture-proven case of *L. longbeachae* osteomyelitis demonstrates that *Legionella* species are capable of hematogenous dissemination to bone. Because of the difficulty of diagnosing *Legionella* infections, both of pulmonary and nonpulmonary origin, it is probably underreported as an etiology. A high index of suspicion must be maintained for *Legionella* infections and other atypical infections, especially in immunocompromised hosts, who are particularly susceptible.

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**References**