

Legionella pneumophila pneumonia with rhabdomyolysis and myocarditis diagnosed by paired bronchoalveolar lavage fluid and blood metagenomic sequencing: a case report

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Case Report

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Abstract

Background

Legionella pneumophila pneumonia may be missed when extrapulmonary manifestations dominate the early clinical picture. Rhabdomyolysis and myocarditis are uncommon but serious complications that may be overlooked. In patients whose early manifestations are dominated by extrapulmonary abnormalities, paired respiratory and blood metagenomic sequencing may help link the pulmonary source with possible systemic involvement.

Case presentation

We report a 57-year-old previously healthy man who presented with high fever, diffuse myalgia, generalized weakness, abdominal distension, headache, mild disorientation, and dark-colored urine, with limited respiratory symptoms. Laboratory tests showed marked systemic inflammation, rhabdomyolysis, hepatic injury, and elevated cardiac biomarkers. Chest computed tomography revealed unilateral pulmonary consolidation. Because of severe pneumonia with multisystem involvement, bronchoalveolar lavage fluid and whole blood were examined simultaneously by metagenomic next-generation sequencing. *Legionella pneumophila* was detected in both specimens, supporting pulmonary infection with probable systemic involvement. Cardiac magnetic resonance imaging later showed subepicardial late gadolinium enhancement consistent with myocarditis. After targeted anti-*Legionella* therapy, fever and systemic symptoms improved rapidly, followed by gradual resolution of inflammatory abnormalities, muscle injury, cardiac biomarker elevation, and pulmonary infiltrates.

Conclusion

This case suggests that *Legionella* pneumonia should remain in the differential diagnosis when severe systemic inflammation is accompanied by rhabdomyolysis or unexplained myocardial injury, even if respiratory symptoms are not prominent. Paired respiratory and blood metagenomic sequencing may provide complementary diagnostic information in selected patients with severe atypical pneumonia when extrapulmonary organ involvement is disproportionate to respiratory symptoms.

Background

Legionella pneumophila is a Gram-negative intracellular pathogen and an important cause of atypical community-acquired pneumonia, particularly in middle-aged and older adults [1]. Severe Legionnaires' disease may progress rapidly and is associated with substantial morbidity and mortality, especially when diagnosis and appropriate antimicrobial treatment are delayed [2]. Although the disease is usually recognized as a pulmonary infection, its early presentation may not always be dominated by respiratory symptoms.

Extrapulmonary manifestations are well described in *Legionella* infection and may include gastrointestinal symptoms, neurologic abnormalities, hepatic injury, acute kidney injury, and

rhabdomyolysis [2–6]. These findings can complicate the initial clinical assessment, particularly when fever, myalgia, altered mental status, or dark-colored urine precede prominent cough or dyspnea. Rhabdomyolysis is an uncommon but clinically important complication and may contribute to renal injury and poor outcomes [3–5]. Cardiac involvement is much less frequently reported. Myocarditis associated with *Legionella pneumophila* remains rare, and may be overlooked when cardiac biomarker elevation is mild or when systemic symptoms dominate the clinical picture [7].

Conventional diagnostic methods for *Legionella* infection, including culture, urinary antigen testing, and serology, have important limitations. Culture is technically demanding and often insensitive, while urinary antigen testing mainly detects *Legionella pneumophila* serogroup 1 and may miss other *Legionella* species or serogroups [1, 8]. Metagenomic next-generation sequencing has increasingly been used for the diagnosis of severe or atypical pneumonia, especially when routine microbiological tests are negative or when unusual pathogens are suspected [5, 8, 9]. In patients with severe pneumonia and multisystem involvement, testing both respiratory and blood specimens may provide useful information not only for pathogen identification, but also for assessing possible systemic involvement.

Here, we report a case of severe *Legionella pneumophila* pneumonia in a previously healthy man whose early presentation was dominated by high fever, diffuse myalgia, rhabdomyolysis, neurologic symptoms, and myocardial injury, with limited respiratory symptoms. *Legionella pneumophila* was detected by metagenomic sequencing in both bronchoalveolar lavage fluid and whole blood, and cardiac magnetic resonance imaging supported the diagnosis of myocarditis. This case highlights the need to consider *Legionella* infection in patients with severe systemic inflammation accompanied by muscle or cardiac injury, and suggests that paired respiratory and blood metagenomic sequencing may be useful in selected patients with atypical severe pneumonia. This case is reported in accordance with the CARE guidelines.

Case presentation

A 57-year-old man with no known chronic medical illness was admitted because of intermittent high-grade fever and diffuse myalgia lasting five days. His highest recorded temperature was 40°C. At the early stage of illness, respiratory complaints were not prominent. Instead, he mainly reported chills, generalized weakness, arthralgia, abdominal distension, poor appetite, headache, dark-colored urine, and progressive fatigue. He had received cefixime and traditional herbal medication at a local hospital before admission, without clinical improvement.

On admission, the patient appeared ill, lethargic, and mildly disoriented. His temperature was 40°C, blood pressure was 121/62 mmHg, pulse rate was 78 beats/min, and respiratory rate was 22 breaths/min. Oxygen saturation was 96.2% while receiving oxygen at 5L/min through a nasal cannula. Physical examination did not show obvious focal neurologic deficits. At this point, the main concern was a severe systemic infection with extrapulmonary involvement, rather than an isolated pulmonary process.

Laboratory tests showed marked inflammation and evidence of muscle injury. C-reactive protein was 249.49 mg/L. The white blood cell count was $10.8 \times 10^9/L$, with 92.8% neutrophils and 4.8% lymphocytes. Creatine kinase was 2178 U/L, accompanied by elevated myoglobin at 539.3 ng/mL, lactate dehydrogenase at 372 U/L, and aspartate aminotransferase at 89 U/L. These findings, together with dark-colored urine and diffuse myalgia, were consistent with rhabdomyolysis. Cardiac biomarkers were also abnormal, including high-sensitivity troponin I of 29.2 ng/L and creatine kinase-MB of 8.1 ng/mL. Mild hepatic injury was present, whereas renal function was relatively preserved during hospitalization.

Arterial blood gas analysis showed respiratory alkalosis with metabolic acidosis. Based on his vital signs and mental status at admission, the National Early Warning Score 2 was estimated to be 9[10], suggesting a high risk of clinical deterioration. The Sequential Organ Failure Assessment score was calculated as 3 according to the available admission data[11]. Electrocardiography showed T-wave inversions in the precordial leads. Chest computed tomography revealed consolidation and inflammatory infiltrates predominantly involving the left lung, supporting the diagnosis of severe pneumonia. The clinical course and dynamic changes in laboratory parameters are summarized in Fig. 1.

Because the patient had persistent high fever, severe pneumonia, rhabdomyolysis, abnormal cardiac biomarkers, and neurologic symptoms, bronchoscopy was performed soon after admission to clarify the pathogen. Initial microbiological testing did not identify a causative organism. Blood cultures were negative, and cultures of sputum and bronchoalveolar lavage fluid showed no bacterial growth. Tests for common respiratory viruses, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, influenza virus, and SARS-CoV-2 were also negative. *Legionella* urinary antigen testing was not performed during the initial diagnostic work-up.

Metagenomic next-generation sequencing of bronchoalveolar lavage fluid detected 800 sequence reads of *Legionella pneumophila*. Whole-blood metagenomic sequencing performed at the same time also detected *Legionella pneumophila*, with 14 sequence reads. Sequencing results were interpreted together with clinical findings, imaging features, conventional microbiological results, and the laboratory's background-control criteria. In the setting of severe pneumonia, negative conventional microbiological tests, and multisystem abnormalities, these results supported *Legionella pneumophila* infection, with probable systemic involvement.

The patient initially received intravenous omadacycline at 100 mg once daily, together with antipyretic treatment and hydrocortisone 50 mg every 6 hours for five days. During treatment, he developed visual disturbance described as a "cloud-like" sensation, bilateral hand numbness, and worsening liver enzyme abnormalities. Considering possible drug-related adverse reactions, antimicrobial therapy was changed to intravenous levofloxacin at 500 mg once daily.

Given the elevated cardiac biomarkers and electrocardiographic abnormalities, cardiac magnetic resonance imaging was performed to further evaluate myocardial involvement. It showed subepicardial late gadolinium enhancement in the inferolateral wall of the left ventricle, a pattern compatible with

myocarditis (Fig. 2). The patient did not report chest pain, and cardiac evaluation did not show reduced left ventricular ejection fraction or regional wall motion abnormalities. There was no clinical evidence of an acute coronary event. The patient had no previous cardiovascular disease, and no prior electrocardiographic abnormalities had been documented. In the context of severe *Legionella* infection, the myocardial findings were considered most consistent with infection-associated myocarditis.

After adjustment of antimicrobial therapy, the patient became afebrile within two days, and his myalgia, weakness, mental status, and systemic symptoms gradually improved. Serial laboratory testing showed parallel decreases in inflammatory markers, creatine kinase, myoglobin, and cardiac biomarkers. He completed eight days of intravenous levofloxacin and was discharged with an additional 14-day oral course. At one-month follow-up, chest computed tomography showed marked absorption of the pulmonary infiltrates compared with the initial images, as shown in Fig. 3A(b), 3B(b), and 3C(b).

Discussion and Conclusions

In this patient, *Legionella pneumophila* infection first appeared as a systemic febrile illness, rather than as a straightforward pneumonia. Fever, diffuse myalgia, dark-colored urine, mild disorientation, rhabdomyolysis, and myocardial injury were more striking than respiratory symptoms at the time of admission. Such a presentation may delay recognition of Legionnaires' disease, especially when cough, sputum production, or dyspnea is absent or mild at presentation.

Rhabdomyolysis was one of the earliest clues in this case. The patient had diffuse muscle pain, dark-colored urine, and marked elevations of creatine kinase and myoglobin. Rhabdomyolysis has been reported in *Legionella* infection and may be complicated by acute kidney injury or severe systemic deterioration [3, 4, 12–15]. Its pathogenesis remains uncertain, but direct bacterial injury, toxin-mediated muscle damage, systemic inflammation, electrolyte disturbances, and tissue hypoxia during severe infection have all been proposed as possible mechanisms [12, 15]. In the present case, renal function was relatively preserved despite definite muscle injury. Early recognition, supportive care, and timely anti-*Legionella* treatment may have contributed to this outcome. The subsequent decline in creatine kinase and myoglobin also supported infection-associated rhabdomyolysis rather than a primary neuromuscular disease.

Myocardial involvement was another important finding. Cardiac complications in Legionnaires' disease are uncommon, and myocarditis is rarely described. In severe infection, a mild or moderate increase in cardiac biomarkers may be attributed to sepsis-related myocardial injury, demand ischemia, or nonspecific critical illness. In this patient, however, the elevated high-sensitivity troponin I, precordial T-wave inversions, absence of previous cardiovascular disease, and cardiac magnetic resonance findings together supported myocarditis. The subepicardial late gadolinium enhancement in the inferolateral wall showed a non-ischemic inflammatory pattern. Cardiac magnetic resonance imaging is a useful noninvasive tool for evaluating suspected myocarditis, especially when endomyocardial biopsy is not

performed [16]. This case suggests that cardiac evaluation should be considered when *Legionella* infection is accompanied by unexplained biomarker elevation or electrocardiographic abnormalities.

The simultaneous detection of *Legionella pneumophila* in bronchoalveolar lavage fluid and whole blood by metagenomic next-generation sequencing was clinically informative. BALF mNGS identified the pulmonary pathogen, whereas whole-blood mNGS provided additional evidence suggesting possible systemic involvement. *Legionella* bloodstream infection is difficult to confirm by conventional methods, and the detection of *Legionella* DNA in blood should be interpreted cautiously [17]. In this patient, the blood mNGS result was considered meaningful because it was concordant with the BALF result and matched the broader clinical picture, including severe pneumonia, neurologic symptoms, rhabdomyolysis, myocardial injury, and clinical response to targeted therapy. However, because the number of reads in blood was low, we regarded this finding as evidence of probable systemic involvement rather than definitive bacteremia.

The paired use of respiratory and blood mNGS was helpful in this case because the extrapulmonary findings were disproportionate to the initial respiratory symptoms. A respiratory specimen is usually more useful for identifying the pulmonary source, while blood testing may help assess whether there is possible systemic spread or circulating microbial DNA. For patients whose early manifestations are dominated by extrapulmonary abnormalities, this dual-site approach may help link the lung lesion with systemic findings. In the present case, paired mNGS helped establish a coherent diagnosis of severe *Legionella* infection complicated by rhabdomyolysis and myocarditis. Even so, mNGS should not be interpreted alone. The clinical value of the result depends on the specimen type, read number, background contamination risk, imaging findings, conventional microbiology, and treatment response [5, 17]. Therefore, paired mNGS should be viewed as a complementary diagnostic tool rather than a replacement for culture, urinary antigen testing, serology, or conventional clinical assessment.

The treatment course should be interpreted with caution. Fluoroquinolones and macrolides remain standard options for *Legionella* pneumonia. Omadacycline was used initially in this patient, but was later replaced by levofloxacin because of suspected adverse reactions, including visual disturbance, bilateral hand numbness, and worsening liver enzyme abnormalities. Fever resolved within two days after the treatment adjustment, followed by gradual improvement in inflammatory markers, muscle enzymes, cardiac biomarkers, and pulmonary infiltrates. However, this single case cannot determine the independent effect of omadacycline, levofloxacin, or corticosteroids. The more important therapeutic message is that early pathogen recognition and timely use of active anti-*Legionella* therapy are essential when severe pneumonia is accompanied by extrapulmonary organ involvement [1, 2, 18].

Several limitations should be acknowledged. First, *Legionella pneumophila* was identified by mNGS, but *Legionella* urinary antigen testing was not performed, and culture confirmation with antimicrobial susceptibility testing was not available. Second, whole-blood mNGS supported possible systemic involvement, but the low read number cannot prove bloodstream infection. Third, myocarditis was diagnosed on the basis of cardiac biomarkers, electrocardiographic abnormalities, and cardiac magnetic

resonance imaging; endomyocardial biopsy was not performed. Finally, this is a single case, and the diagnostic value of paired BALF and blood mNGS in similar patients needs further clinical observation.

In conclusion, *Legionella pneumophila* pneumonia may present as a severe multisystem disease in which extrapulmonary manifestations dominate the early course. Rhabdomyolysis and unexplained myocardial injury should prompt consideration of *Legionella* infection, even when respiratory symptoms are limited. Paired metagenomic sequencing of bronchoalveolar lavage fluid and whole blood may be useful in selected patients with severe atypical pneumonia, particularly when pulmonary infection and possible systemic involvement need to be assessed together.

Abbreviations

BALF Bronchoalveolar lavage fluid

CT Computed tomography

mNGS Metagenomic next-generation sequencing

NEWS2 National Early Warning Score 2

SOFA Sequential Organ Failure Assessment

Declarations

Ethical approval and consent to participate

This case report was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Beijing Anzhen Hospital, Capital Medical University (approval No.2026167X).

Clinical trial number

Not applicable.

Consent for publication

Written informed consent for publication of the clinical details and any accompanying images was obtained from the patient.

Availability of data and materials

De-identified patient data underlying this study are available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Author contributions

All authors contributed to the study conception and design. Yu Gu and Peixi Zhou contributed equally to this work, drafted the manuscript and performed literature review. Jinghan Lei and Shunyao Cui collected and analyzed clinical data. Yuanxing Wu, as the corresponding author, conceived and designed the study, revised the manuscript, and supervised the research. All authors read and approved the final manuscript.

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Figures

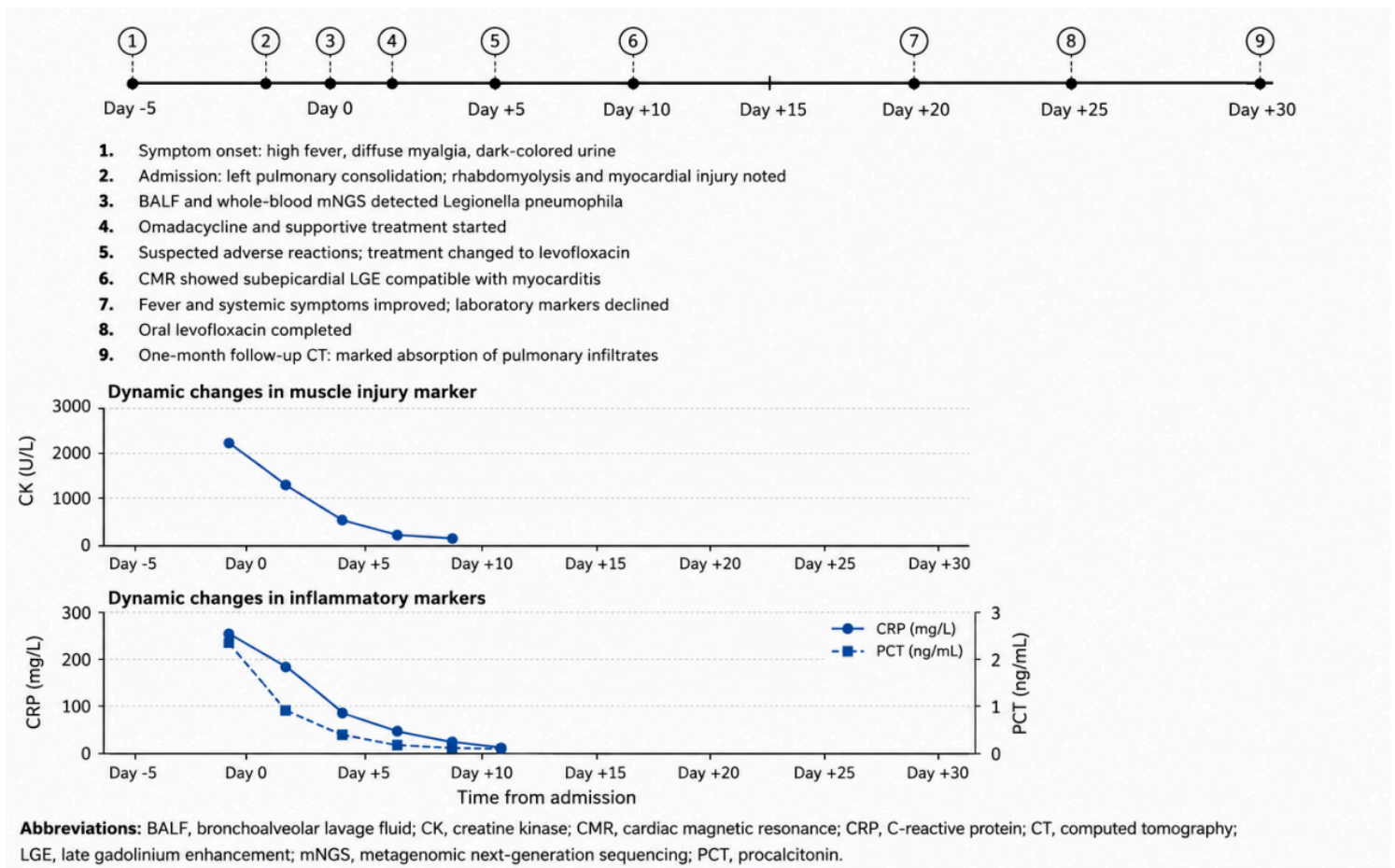


Figure 1

Clinical timeline of *Legionella pneumophila* pneumonia complicated by rhabdomyolysis and myocarditis.

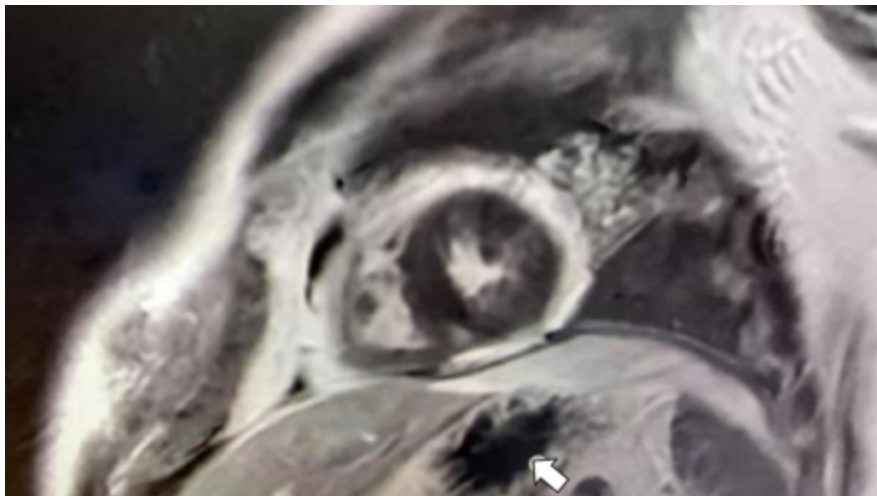


Figure 2

Cardiac magnetic resonance imaging findings compatible with myocarditis. Subepicardial late gadolinium enhancement is seen in the inferolateral wall of the left ventricle.

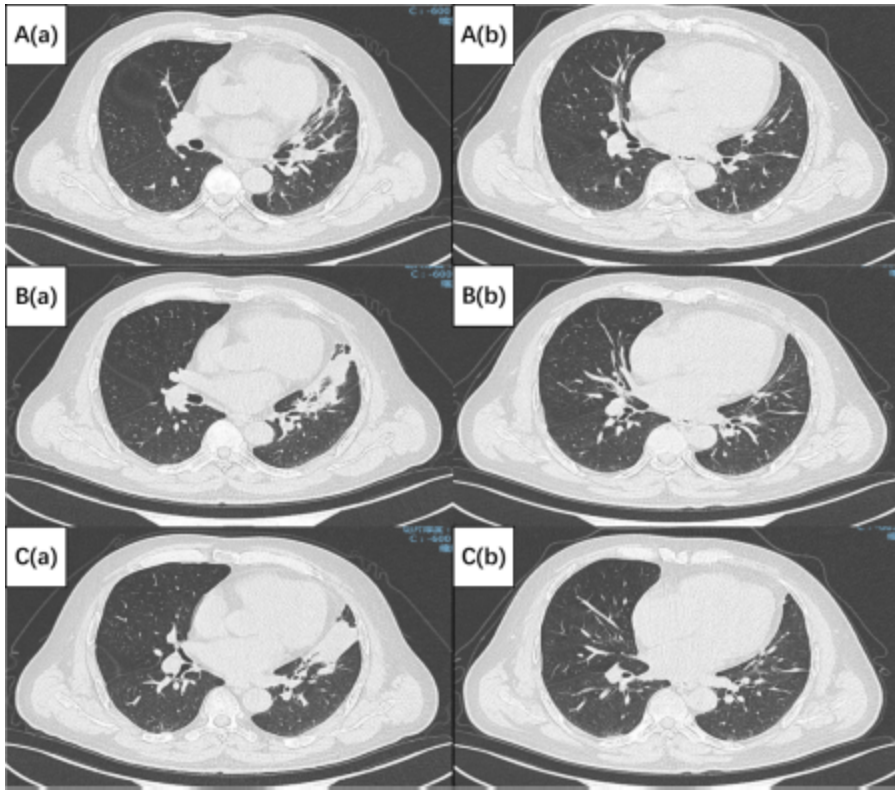


Figure 3

Chest computed tomography findings before and after treatment. Panels A(a), B(a), and C(a) show left-sided pulmonary consolidation and inflammatory infiltrates at presentation. Panels A(b), B(b), and C(b) show marked absorption of the lesions at one-month follow-up.