AUCTORES
Globalize your Research

International Journal of Clinical Case Reports and Reviews
Xuecheng Tong *

Open Access

Case Report

Legionella Pneumophila Pneumonia with Rapid Clinical Course in two Patients with Drug-Induced Liver Injury : Case Report

Yali Qiu [1#], Ying Feng [1#], Ruanping Zhou [2#], Qian Liu [1], Qing Sun [1], Xuecheng Tong [2*]

[1]Department of Respiratory and Critical Care Medicine, Changzhou Third People's Hospital, Changzhou Medical Center, Nanjing Medical University.

[2]Department of Infectious Diseases, Changzhou Third People's Hospital, Changzhou Medical Center, Nanjing Medical University.

[3]Department of Osteopathic Medicine, Changzhou Third People's Hospital, Changzhou Medical Center, Nanjing Medical University.

[#]These authors contributed equally to this work and share first authorship.

***Corresponding Author:** Xuecheng Tong, Department of Infectious Diseases, The Third People's Hospital of Changzhou, No.300, the north road of Lan ling, Changzhou, People's republic of China.

Received Date: December 08, 2025 | **Accepted Date:** December 17, 2025 | **Published Date:** December 23, 2025

Citation: Yali Qiu, Ying Feng, Ruanping Zhou, Qian Liu, Qing Sun, et al, (2025), Legionella Pneumophila Pneumonia with Rapid Clinical Course in two Patients with Drug-Induced Liver Injury : Case Report, *International Journal of Clinical Case Reports and Reviews*, 32(1); **DOI:10.31579/2690-4861/953**

Abstract:

Drug-induced liver injury complicated by Legionella pneumophila pneumonia is rare and often associated with poor outcomes, including death. Early diagnosis and prompt treatment are crucial for these patients. Due to its low incidence, complex clinical presentation, atypical lung lesions, and challenges in pathogen culture, Legionella infection is frequently misdiagnosed or overlooked. The inability to identify the pathogen early often leads to inappropriate anti-infective therapy, resulting in a 15 % to 30 % mortality rate, primarily due to respiratory failure, shock, and multiorgan failure. The risk of infection is significantly higher in immunocompromised individuals, such as those with malignancies, chronic obstructive pulmonary disease, diabetes, liver failure, or those on glucocorticoid therapy. While hepatic and renal involvement is uncommon, we present two cases of drug-induced liver injury complicated by Legionella pneumonia.

Key words: legionella pneumophila; liver injury; rapid diagnostics; metagenomic next-generation sequencing; case report

Introduction

Legionella pneumophila (L. pneumophila, Lp), responsible for 1.9 % to 9 % of community-acquired pneumonia, is prone to underdiagnosis due to its low incidence, complex clinical presentation, atypical lung lesions, and difficulty in culturing pathogenic bacteria [1]. The failure to identify the pathogen early results in the administration of ineffective anti-infective treatments, leading to a high mortality rate of 15 % to 30 % due to respiratory failure, shock, and multiorgan failure [2]. Risk factors include male sex, age over 50, diabetes, and smoking [1]. The risk of *L. pneumophila* infection is notably increased in immunocompromised patients, such as those with malignancy, chronic obstructive pulmonary disease (COPD), diabetes mellitus, liver failure, and glucocorticoid use[3]. In this report, we review two cases of drug-induced liver injury complicated by *L. pneumophila* pneumonia, a rare clinical occurrence.

Case Report

Case 1 : A 37-year-old woman was admitted to our hospital after experiencing one week of nausea, anorexia, and fatigue. Ten days before admission, she had self-medicated with compound paracetamol (1 tablet, three times a day), amantadine hydrochloride (100 mg, three times a day), and cefaclor tablets (0.25 g, three times a day) for a respiratory infection. Three days after taking the medications, she developed malaise, nausea, fatigue, loss of appetite, and dark urine. Liver function tests revealed significant abnormalities, prompting her transfer to our hospital for treatment of drug-induced liver injury. Currently, the diagnosis of DILI still follows the strategy of exclusion. The threshold of liver biochemistry should meet any one of the following criteria for acute DILI: (1) ALT ≥ 5 × ULN; (2) ALP ≥ 2 × ULN (particularly accompanied by an increased GGT level with bone disease ruled out); (3) ALT ≥ 3 × ULN and TBil ≥ 2 × ULN[4,5]. We added relevant content in the manuscript. The patient had a history of chronic conditions, including hypertension and type 2 diabetes, for over a year. She had been using irbesartan/hydrochlorothiazide, amlodipine benzenesulfonate, dapagliflozin, and extended-release metformin to manage her conditions. She has no family history of genetic disorders and is mentally healthy.

Laboratory tests, including antibodies for hepatitis A, C, and E viruses, as well as hepatitis B serology and autoantibodies, were negative (Table 1). Chest computed tomography (CT) showed no abnormalities.

Following her hospital admission, the patient was treated with magnesium isoglycyrrhizinate, polyene phosphatidylcholine, reduced glutathione, and Kuhuang injection. Over time, her liver function improved. However, after one week of treatment, the patient developed a fever and generalized rash, which was diagnosed as a drug rash. The suspected drug was discontinued, and she was treated with intravenous methylprednisolone. The rash gradually subsided, but the patient continued to experience recurrent high fevers, peaking at 40°C. Additionally, she reported generalized aches, headache, and chest tightness. There were no respiratory symptoms such as cough or sputum production, but she displayed signs of shock, including elevated lactate levels and hypotension. Her laboratory results are shown in **Table 2**. A chest CT scan revealed new consolidation in the dorsal and basal segments of the right lower lobe, raising concern for pneumonia (**Figure 1)**. The patient was diagnosed with hospital-acquired pneumonia (HAP) and started on biapenem. Metagenomic next-generation sequencing (mNGS) identified *L. pneumophila* in her peripheral blood with a sequence number of 207 and a relative abundance of 100 %. Biapenem was discontinued, and she was initiated on anti-infective therapy with azithromycin (400 mg daily) and doxycycline (100 mg every 12 hours). After a period of treatment, the patient's temperature normalized, symptoms improved, and the lung lesions resolved, leading to her discharge.

Case 2: A 66-year-old female patient was admitted with a 1-week history of malaise, dark-colored urine, and pruritus. She had sustained a left scapula fracture from trauma one month prior and had taken an unspecified Chinese herbal medicine (contain Gynura segetum). Following the medication, she developed weakness, loss of appetite, and dark-colored urine. Laboratory tests at another hospital revealed abnormal liver function, prompting her referral for further treatment at our institution, where she was diagnosed with drug-induced liver injury. The patient also had a history of type 2 diabetes, treated with metformin extended-release tablets. She has no family history of genetic disorders and is mentally healthy.

Her laboratory results, shown in **Table 1**, were negative for antibodies to hepatitis A, C, and E, and serologic tests for hepatitis B were also negative. CT of the chest showed no abnormalities. She was diagnosed with drug-induced hepatitis with intrahepatic cholestasis and was treated with ursodeoxycholic acid, compound monoammonium glycyrrhizinate, and polyene phosphatidylcholine to protect the liver. On the 11th day of admission, the patient developed a high fever without significant respiratory symptoms such as cough or sputum. Her laboratory results are shown in **Table 2**. Chest radiograph showed extensive, patchy hyperdense shadows in both lungs, with partial consolidation, especially in the right lung (**Figure 2**). The patient was diagnosed with hospital-acquired pneumonia (HAP) and was treated with biapenem, an anti-infective agent. Despite this, the patient continued to exhibit a high fever, along with cough, sputum production, chest tightness, delirium, and hallucinations. Additionally, the patient developed intractable hyponatremia and hypochloremia. On the 18th day of hospitalization, a follow-up chest CT revealed significant progression of the pulmonary lesions. Concurrently, the patient's oxygen saturation levels dropped, and type I expiratory failure occurred, requiring immediate non-invasive ventilation. A combined IgM antibody test for nine respiratory pathogens yielded a strong positive result for *L. pneumophila* type 1, and urine testing confirmed the presence of the *Legionella* antigen. These findings confirmed the diagnosis of *L. pneumophila* infection. The patient was subsequently treated with moxifloxacin (400 mg once daily) and doxycycline (100 mg every 12 hours) for three weeks. Following this regimen, the patient's fever subsided, symptoms improved, and the lung lesions showed signs of absorption, allowing for discharge.

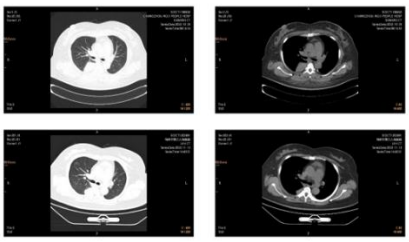

Fig. 1 CT scan of the lungs at the peak of the patient's illness: multiple nodular, mass-like lesions in the right lung.

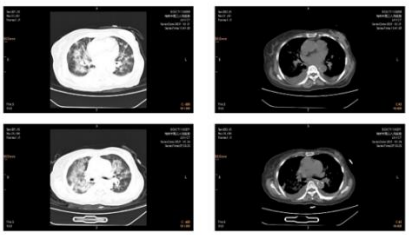

Fig. 2 CT scan of the lungs at the peak of the patient's illness: multiple patchy hyperdense shadows in both lungs, partly solid

Laboratory test	Result (normal range), case 1	Result (normal range), case 2
White blood cell	82,800/μL(35,000-95,000/μL)	138,500 (35,000-95,000/μL)
neutrophil percentage	84.70% (40-75%)	96.30 (40-75%)
glycosylated haemoglobin	7.4 (4-6.5)	/
Prothrombin time	16.10 s (11-15 s)	12.00 s (11-15 s)
prothrombin activity	61.72% (75-160%)	121.13% (75-160%)

Activated partial thromboplastin time	40.50 s (24-40 s)	31.60 s (24-40 s)
Alaninetransaminase	1081.3 U/L (7-40 U/L)	29.3 U/L (7-40 U/L)
aspartate aminotransferase	863 U/L (13-35 U/L)	14 U/L (13-35 U/L)
alkaline phosphatase	133 U/L (35-100 U/L)	518 U/L (35-100 U/L)
gamma-glutamyltransferase	628.4 U/L (7-45 U/L)	630.7 U/L (7-45 U/L)
lactate dehydrogenase	386 U/L (109-245 U/L)	309 U/L (80-285 U/L)
total bilirubin	164.6 µmol/L (3.4-22 µmol/L)	66.9 umol/L (3.4-22 µmol/L)
direct bilirubin	125.2µmol/L(1.7-10.3umol/L)	61.3µmol/L (1.7-10.3 umol/L)
albumin	33.8 g/L (40-55 g/L)	26.2 g/ L (40-55 g/L)

Table 1: Initial relevant Laboratory Values on Presentation

Laboratory test	Result (normal range), case 1	Result (normal range), case 2
White blood cell	138,700/µL (35,000-95,000/µL)	148,100 (3,5000-9,5000/µL)
neutrophil count	93,000 (18,000-63,000µL)	108,000 (18,000-63,000µL)
C-reactive protein	24.43 mg/L (0-5 mg/L)	85 mg/L (0-5 mg/L)
calcitonin	0.278 ng/L (0-0.05 ng/L)	0.845 ng/L (0-0.05 ng/L)
potassium	3.56 mmol/L (3.5-5.3 mmol/L)	3.73 mmol/L (3.5-5.3 mmol/L)
sodium	117.3 mmol/L (137-147 mmol/L)	118.1 mmol/L (137-147 mmol/L)
chlorine	87.0 mmol/L (99-110 mmol/L)	86.0 mmol/L (99-110 mmol/L)

Table 2: Relevant Laboratory Values during the course of the disease

Discussion

L. pneumophila is genetically diverse, comprising 32 species and 51 serogroups[6], with *Legionella* pneumophila serogroup 1 (Lp1) being the most frequently implicated in global outbreaks [7]. Upon inhalation, the pathogen infects alveolar macrophages and replicates within them. The body's Toll-like receptors on cell surfaces recognize *L. pneumophila* markers, triggering the activation of transcription and nuclear factors[8]. This leads to the production of inflammatory cytokines, macrophage activation, and dendritic cell maturation, which initiates a robust immune response. Consequently, individuals with weakened immune systems, including those with advanced age, smoking history, diabetes, or those receiving glucocorticoids or immunosuppressants, are particularly vulnerable[9]. In our study, both patients had diabetes mellitus and drug-induced liver injury, which compromised their immune systems and heightened their susceptibility to infection due to extensive hepatocellular necrosis, severe dysfunction of the intrahepatic monocyte-macrophage system, impaired leukocyte adhesion, and serum complement deficiencies.

L. pneumophila is a bacterium associated with human infections, causing various clinical manifestations, including the pneumonic form (Legionnaires' disease) and the non-pneumonic form (Pontiac fever) [10]. Pontiac fever is typically a mild, self-limiting illness resembling influenza, with rapid onset. In contrast, Legionnaires' disease is a severe pneumonia that can result in permanent lung damage or death. Its incubation period ranges from 2 to 14 days. The disease often begins subtly, with respiratory symptoms initially absent or mild. Instead, the onset of toxaemia-characterized by high fever and muscle aches-is more prominent [11], and these symptoms can easily be mistaken for viral infections or sepsis. Pulmonary infections are twice as likely in patients with diabetes compared to the healthy population due to a certain degree of immunosuppression and metabolic disorder[12]. Legionnaires' disease has been shown to result in hepatic dysfunction at higher rates compared to other causes of pneumonia. However, it is necessary to further explore the pathological mechanism of how diabetes and drug-induced liver injury synergistically led to immune deficiency and Legionella pneumonia combined with liver injury.

Current diagnostic methods for *L. pneumophila* include urine antigen detection, nucleic acid amplification tests (NAAT), high-throughput gene sequencing, antibody detection, and bacterial culture. Among these, culture remains the gold standard for diagnosis [10]. Urinary antigen detection has a sensitivity of 74 % and a specificity of 99.1 %, providing results within 2 to 3 days. However, caveats to sole dependence on urinary antigen testing are due to its specificity to L pneumophila subtype 1, with Legionellosis caused by other subtypes and species being potentially missed[13]. The rapid development of metagenomic next-generation sequencing (mNGS) has significantly improved diagnostic accuracy, allowing earlier detection and intervention for infected patients [14]. This technique sequences all nucleic acids in a sample, and has extensive coverage, as it is capable of detecting over 10,000 pathogens. mNGS testing can be completed within 24-36 h, but mNGS costs almost ten times more than conventional microbiological testing. In our cases, mNGS detected *Legionella* in peripheral blood, suggesting partial release of bacterial fragments into the bloodstream. While bacterial culture remains the diagnostic gold standard, it is not routinely used as a first-line test due to the absence of clear respiratory symptoms in the early stages of infection and the demanding culture conditions. *Legionella* requires a specialized medium and up to 15 days for proper growth. Changes in double serum Legionella-specific antibody titers, increasing fourfold or more between the acute and recovery phases, can also aid in diagnosis, but this method is limited to serotype 1 and is not useful for early detection, as most patients do not produce antibodies until approximately three weeks into the infection. Furthermore, the test requires an interval of 3 to 10 weeks, limiting its utility in acute cases.

Delayed treatment of *L.* pneumophila infections with appropriate antibiotics increases mortality. The choice of antibiotic depends on its activity and its ability to reach high intracellular concentrations in macrophages. The most effective antibiotics against *Legionella* include quinolones, macrolides, tetracyclines, rifampicin, and telithromycin, with quinolones and telithromycin showing particularly high efficacy [15]. For patients with underlying conditions or those whose symptoms do not improve with initial therapy, combination therapy is recommended. In the cases of the two patients in our study, both had a history of chronic diseases and presented with poor general conditions. Given the rapid progression of the disease and the unknown pathogen, we initially administered biapenem, which is effective against pneumococcus, Enterobacteriaceae, and anaerobes. After identification of *L. pneumophila* via peripheral blood mNGS, we switched to a combination of moxifloxacin and doxycycline. These antibiotics are the first-line treatment for Legionnaires' disease due to their bactericidal action, high intracellular concentrations, and ability to penetrate lung tissue, making them particularly effective against *Legionella*.

L. pneumophila pneumonia is known to be the most common cause of elevated serum hepatic transaminases and has been historically considered a clinical marker distinguishing it from other types of pneumonia [16]. Both patients in our study had diabetes mellitus and drug-induced liver injury, which compromised their immune systems and increased their susceptibility to *Legionella* infection. This was exacerbated by severe hepatocellular necrosis, dysfunction of the intrahepatic monocyte-macrophage system, impaired leukocyte adhesion, and serum complement defects. This case report's strength is highlighting the rare co - occurrence of drug - induced liver injury and *Legionella* pneumophila pneumonia, with advanced diagnosis like mNGS. However, it has limitations. The sample size of two cases restricts generalizability, and the retrospective nature may bring biases. Despite this, it offers valuable insights, and further large - scale, prospective studies are needed.

In conclusion, for immunocompromised patients with significant risk factors for *L. pneumophila* infection, clinical suspicion should be heightened if symptoms of infectious toxicity or multisystem involvement are present. Given the complexity of lung imaging and its lack of specificity, respiratory specimens should be prioritized for mNGS as a rapid diagnostic tool in patients at high risk for *Legionella* infection. Antibiotic selection should be tailored based on the patient's condition and the identified pathogen.

Acknowledgements: The authors would like to thank all the persons who participated in the research.

Disclosure: The authors declare that they have no competing interests.

Grants: This work was supported by grant from: Yali, Qiu, Department of Respiratory and Critical Care Medicine, Changzhou Medical Center project of Nanjing Medical University (Grant No. CMCB202323).

Availability of data and materials: Please contact the corresponding author for data on reasonable request.

Ethics approval and consent to participate: The studies involving human participants were reviewed and approved by the Institutional Review Board at Changzhou Third People's Hospital (No. 02A-A2024004).

Authors' contributions: YQ, YF and RZ designed the experiments and wrote the manuscript. QS performed the experiments. XT, as a corresponding author, designed the experiments and funded. All authors read and approved the final manuscript.

Reference

1. Du R., Feng Y., Wang Y., Huang J., Tao Y., Mao H. (2023). Metagenomic next-generation sequencing confirms the diagnosis of Legionella pneumonia with rhabdomyolysis and acute kidney injury in a limited resource area: a case report and review. Front Public Health, 11:1145733.
2. Orsini J, Frawley BJ, Gawlak H, Gooch R, Escovar J (2020). Severe Sepsis with Septic Shock as a Consequence of a Severe Community-Acquired Pneumonia Resulting from a Combined Legionella pneumophila and Streptococcus pneumoniae Infection. Cureus, 12(10): e10966.
3. Eidy H., Senger B., Steele J., Kathawa J. (2024). An Atypical Presentation of Legionnaires' Disease. Cureus, 16(5): e60856.
4. Huo B., Lin L., Zhao L., Yu R., Yang J. (2023). First reported case of ANCA-associated vasculitis induced by oxaliplatin, capecitabine, and trastuzumab. Ren Fail, 45(2):2282710.
5. Mao Y, Ma S, Liu C, Liu X, Su M, et al., (2024). Technology Committee on Dili Prevention MCMBA, Study Group on Drug-Induced Liver Disease CSoHCMA: Chinese guideline for the diagnosis and treatment of drug-induced liver injury: an update. *Hepatol Int*, 18(2): 384-419.
6. Zhao X, Wang Y, Lai R, Wang X, Yu Y, et al., (2024). Validation of the revised electronic version of RUCAM for diagnosis of DILI in Chinese patients. Hepatol Commun, 8(4).
7. Kozak-Muiznieks N. A., Morrison S. S., Mercante J. W., Ishaq M. K., Johnson T., et al., (2018)., Comparative genome analysis reveals a complex population structure of Legionella pneumophila subspecies. Infect Genet Evol, 59:172-185.
8. Ricci M. L., Fillo S., Ciammaruconi A., Lista F., Ginevra C., et al., (2022)., Genome analysis of Legionella pneumophila ST23 from various countries reveals highly similar strains. Life Sci Alliance, 5(6).
9. Rogers J., Hakki A., Perkins I., Newton C., Widen R., Burdash N., Klein T., Friedman H. (2007). Legionella pneumophila infection up-regulates dendritic cell Toll-like receptor 2 (TLR2)/TLR4 expression and key maturation markers. Infect Immun, 75(6):3205-3208.
10. Kikuchi T., Kobayashi T., Gomi K., Suzuki T., Tokue Y., et al., (2004). Dendritic cells pulsed with live and dead Legionella pneumophila elicit distinct immune responses. *J Immunol*, 172(3):1727-1734.
11. Hamilton KA, Prussin AJ, 2nd, Ahmed W, Haas CN (2018). Outbreaks of Legionnaires' Disease and Pontiac Fever 2006-2017. Curr Environ Health Rep, 5(2): 263-271.
12. Mondino S., Schmidt S., Rolando M., Escoll P., Gomez-Valero L., Buchrieser C. (2020). Legionnaires' Disease: State of the Art Knowledge of Pathogenesis Mechanisms of Legionella. Annu Rev Pathol, 15:439-466.
13. Gattuso G., Rizzo R., Lavoro A., Spoto V., Porciello G., et al., (2022). Overview of the Clinical and Molecular Features of Legionella Pneumophila: Focus on Novel Surveillance and Diagnostic Strategies. Antibiotics (Basel), 11(3).
14. Fiocca Vernengo F, Rowekamp I, Boillot L, Caesar S, Dorner PJ, et al., (2024). Diabetes impairs IFN gamma-dependent antibacterial defense in the lungs. Mucosal Immunol.
15. Eidy H, Senger B, Steele J, Kathawa J (2024). An Atypical Presentation of Legionnaires' Disease. Cureus, 16(5): e60856.
16. Bellew S., Grijalva C. G., Williams D. J., Anderson E. J., Wunderink R. G., ET AL., (2019). Pneumococcal and Legionella Urinary Antigen Tests in Community-acquired Pneumonia: Prospective Evaluation of Indications for Testing. Clin Infect Dis, 68(12):2026-2033.
17. Cunha BA (2006). The atypical pneumonias: clinical diagnosis and importance. Clin Microbiol Infect, 12 Suppl 3: 12-24.
18. Hunter JM, Chan J, Reid AL, Tan C (2013). Acute Legionella pneumophila infection masquerading as acute alcoholic hepatitis. BMJ Case Rep, 2013.

DOI:10.31579/2690-4861/953