

Case Report

COVID-19–Associated Acute Respiratory Distress Syndrome with Legionella Co-Infection: A Case Report and Treatment Insights

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SUMMARY

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has led to numerous complications, including secondary bacterial infections that worsen clinical outcomes. Among these, *Legionella pneumophila*, the causative agent of Legionnaires' disease, poses a significant threat, particularly in critically ill patients. This report presents a case of a 63-year-old male with severe COVID-19 complicated by Legionnaires' disease, resulting in acute respiratory distress syndrome. Despite requiring intensive care and mechanical ventilation, early diagnosis and timely administration of levofloxacin led to a successful recovery. The case highlights the challenges of distinguishing Legionnaires' disease from COVID-19 due to overlapping symptoms and underscores the importance of rapid diagnostic testing. Early identification and targeted antibiotic therapy are crucial in improving patient outcomes. This report also emphasizes the necessity of considering bacterial co-infections in critically ill COVID-19 patients and the need for vigilant monitoring to prevent fatal complications.

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1. Introduction

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was declared a pandemic by the World Health Organization (WHO) in March 2020. The disease ranges from asymptomatic to critical illness, with severe cases often developing pneumonia and acute respiratory distress syndrome (ARDS), both of which have high mortality rates.¹ As of June 6, 2022, WHO has reported over 528 million cases and 6.29 million deaths worldwide. In Taiwan, the number of confirmed cases has exceeded 2.45 million, with 3,090 deaths according to the Central Epidemic Command Center.

Co-infections involving SARS-CoV-2 and bacterial or fungal pathogens have been increasingly reported worldwide, although their prevalence varies across regions and healthcare settings.^{2,3} Studies indicate that secondary bacterial infections contribute to mortality rates ranging from 16% to 100%.² Common bacterial co-infections include *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Staphylococcus* species, and *Candida* species.⁴

Legionella pneumophila, an intracellular, aerobic, gram-negative bacillus, is the causative agent of Legionnaires' disease, an atypical pneumonia primarily acquired from contaminated water sources. Symptoms include fever, non-productive cough, dyspnea, and gastrointestinal manifestations such as nausea, vomiting, and diarrhea. The incubation period ranges from 2 to 14 days.⁵ *L. pneumophila* and SARS-CoV-2 co-infection may be life-threatening if untreated.⁶ Most patients with Legionnaires' disease develop acute respiratory failure

requiring intensive care, with high fatality rates.⁷ However, diagnosing *L. pneumophila* infection in COVID-19 patients is challenging due to overlapping clinical presentations.⁸

Since May 2021, Taiwan has faced multiple COVID-19 outbreaks. More than 200 COVID-19 patients were admitted to MacKay Memorial Hospital in Taipei in 2021, with 29 developing severe pneumonia requiring ICU admission. The standard management was performed according to the consensus guidelines established by the Taiwan Centers for Disease Control (TCDC).⁹ Bacterial co-infections were relatively uncommon during the initial ICU phase. Here, we present a case of *L. pneumophila* co-infection in a critically ill COVID-19 patient, highlighting diagnostic challenges and management strategies.

2. Case presentation

A 63-year-old male, a heavy smoker with poorly controlled type 2 diabetes mellitus and stage 4 chronic kidney disease, presented with fever, dry cough, and sore throat for five days. He developed a high fever (38.8 °C), general malaise, and loss of appetite. Due to a recent COVID-19 outbreak in his community, he sought medical attention, where reverse transcription-polymerase chain reaction (RT-PCR) confirmed SARS-CoV-2 infection. He was subsequently quarantined in an isolation ward.

Within hours of quarantine, he developed worsening dyspnea, requiring oxygen escalating from 2 L/min via nasal cannula to 15 L/min via a non-rebreathing mask within 48 hours to maintain peripheral oxygen saturation (SpO₂) ≥ 94%. Due to respiratory deterioration, he was transferred for intensive care.

Upon arrival at the emergency department, his vital signs were

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as follows: temperature, 37.9 °C; respiratory rate, 28 breaths/min; blood pressure, 155/96 mmHg; pulse rate, 108 beats/min; SpO₂, 95% with a non-rebreathing mask at 15 L/min. Signs of acute respiratory failure, including accessory muscle use and supraclavicular retractions, were noted. Chest radiography revealed bilateral patchy consolidations predominantly in the lower lung zones, consistent with ARDS (Figure 1A).¹⁰ Laboratory tests showed leukopenia with neutrophilia and lymphocytopenia, elevated blood urea nitrogen, creatinine, lactate dehydrogenase, C-reactive protein, and hyponatremia (Table 1). Multiple samples were collected to identify potential pathogens, and urinary antigen testing for *L. pneumophila* was positive. No known exposure history was identified.

The patient was admitted to the ICU on the first day. Empirical intravenous ceftriaxone and levofloxacin were initiated for severe community-acquired pneumonia (CAP). On ICU day 2, dexamethasone and tocilizumab were administered due to suspected cytokine release syndrome, per TCDC guidelines.^{9,11} Low-dose enoxaparin (20 mg/day, subcutaneously) was used for thrombosis prevention. Despite treatment, he developed severe hypoxia (SpO₂ 70–80%) but remained asymptomatic. Arterial blood gas analysis confirmed hypoxemia (partial pressure of arterial oxygen (PaO₂): 45 mmHg [normal: 75–100 mmHg]) with oxyhemoglobin saturation of 78%.

Initially, the patient refused intubation and was managed with awake prone positioning for 1.5 hours, which improved SpO₂ to 95%. However, SpO₂ declined to 85% two hours after resuming the supine position. After thorough discussion, he consented to intubation on day 3. Lung-protective ventilation (tidal volume: 6 mL/kg of ideal body weight) was implemented, along with sedation and muscle relaxation. His condition improved, with oxygenation stabilizing by day 5. Follow-up chest radiography on day 7 showed resolution of bilateral lung opacities (Figure 1B). Weaning from ventilation was initiated on day 6, and he was successfully extubated on day 8.

The patient required simple mask support after extubating and was transferred to the general ward on day 10. Serial RT-PCR testing revealed a decreasing viral load: cycle threshold (Ct) values were 28.63 (day 7), 33.02 (day 11), and undetectable (day 18). He completed a 15-day course of levofloxacin and was discharged on day 19 without oxygen dependence or activity limitations (Figure 2).

3. Discussion

Legionnaires' disease is transmitted through contaminated water sources, including hot-water systems and cooling towers. In many countries, its incidence peaks during summer, though in Taiwan, the seasonal variation is less pronounced.¹² Host-related risk factors for Legionnaires' disease and exacerbation of pneumonia include older

age (≥ 50 years), smoking habits, chronic obstructive pulmonary disease, diabetes, compromised immune system, renal impairment, male sex, malignancies, and history of a transplant or chemotherapy.^{5,13} The age distribution of Legionnaires' disease in Taiwan is similar to that in other countries, and its incidence increases with the advancement in age.¹⁴ Over the past decade, the incidence of Legionnaires' disease in Taiwan has gradually increased,¹² likely due to improved laboratory diagnostics and greater awareness of pneumonia pathogens.¹⁵ The incidence rate increased from 1.19 per 100,000 in 2019 to 1.38 per 100,000 in 2020, coinciding with the COVID-19 pandemic.¹² Viral infections may facilitate bacterial superinfection, as observed in influenza and COVID-19.³ Increased awareness of respiratory infections following the pandemic may have contributed to more Legionnaires' disease diagnoses.

Most *L. pneumophila* infections require hospitalization, with a high risk of acute respiratory failure.⁸ Our patient exhibited multiple risk factors, including age, male sex, smoking, and renal impairment, and developed ARDS secondary to *L. pneumophila* and SARS-CoV-2 co-infection. SARS-CoV-2 damages bronchial and alveolar epithelial cells, creating a favorable environment for bacterial adhesion and invasion, leading to severe inflammation.¹⁶ Studies estimate that 14% of ICU COVID-19 patients experience bacterial co-infections, with *Mycoplasma pneumoniae*, *Pseudomonas aeruginosa*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Staphylococcus species*, and *Candida species* being the most common pathogens.^{2,4} An article conducted at a northern Taiwanese medical center between January

Table 1

Laboratory findings of the patient with COVID-19 pneumonia upon initial admission to our hospital.

	Study case	Normal references
White blood cell count × 10 ⁹ /L	3.9	4.0–10.0
Neutrophil count × 10 ⁹ /L	3.1	2.2–7.5
Lymphocyte count × 10 ⁹ /L	0.4	0.8–4.0
Hemoglobin, g/dL	13.1	13–18
Platelet × 10 ⁹ /L	261	140–450
Lactate, mmol/L	1.64	0.50–2.20
Sodium, mmol/L	133	136–144
Aspartate aminotransferase, mmol/L	42	15–41
Blood urea nitrogen, mmol/L	18.9	2.9–7.1
Creatinine, μmol/L	291.7	35.4–106.1
C-reactive protein, mg/dL	8.0	0–0.79
LDH, U/L	379	98–192
Procalcitonin, ng/mL	0.16	< 0.09
ESR, mm/h	59	0–20
D-dimer, μg/L	1188	< 500
HbA1c, %	12.0	4.0–6.0

ESR, erythrocyte sedimentation rate; HbA1c, glycated hemoglobin; LDH, lactate dehydrogenase.

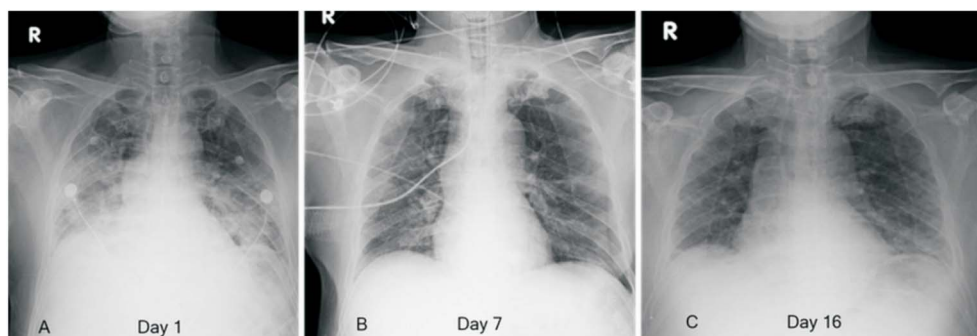


Figure 1. (A) Chest radiography performed on day 2 showing prominent bilateral infiltrations and ill-defined patchy opacities in the right and left lungs, suggestive of acute respiratory distress syndrome. (B) Chest radiography performed on day 7 showing obvious resolution of the bilateral opacities. (C) Chest radiography performed on day 16 shows marked improvement.

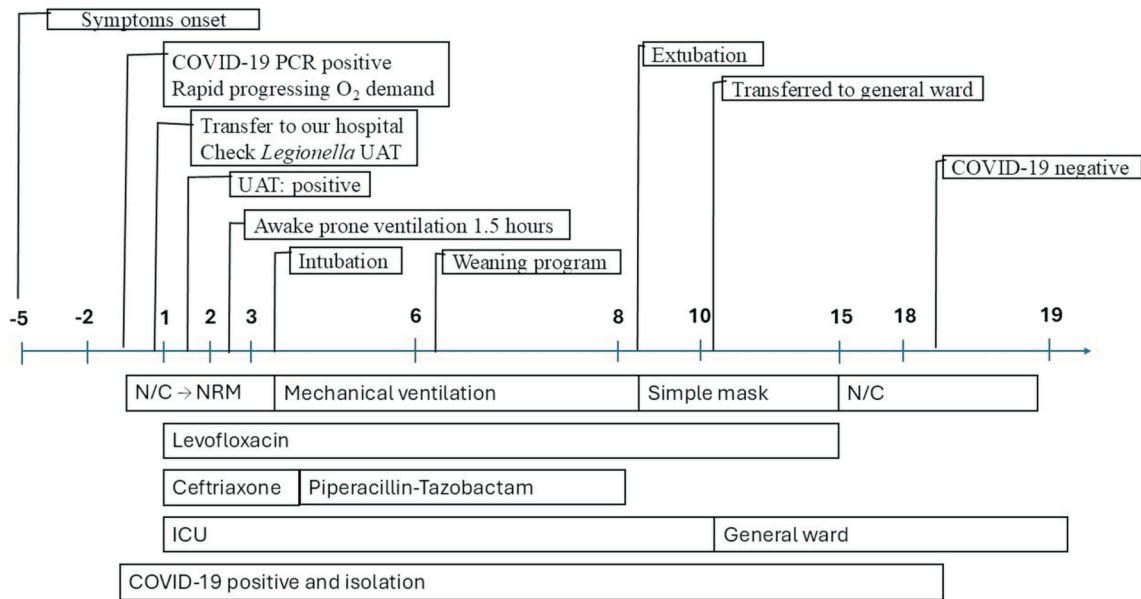


Figure 2. Patient Hospital Course Timeline. Abbreviations: COVID-19: coronavirus disease 2019; ICU: intensive care unit; N/C: nasal cannula; NRM: non-rebreathing mask; PCR: polymerase chain reaction; UAT: urine antigen test.

2020 and September 2021 reported 178 hospitalized patients with confirmed COVID-19,¹⁷ and bacteria constituted 22% of the respiratory pathogens during early co-infection (length of stay < 7 days) in the rapid progression to death group but no *L. pneumophila* infection was found in that study. One recent meta-analysis includes a total of 10,936 hospitalized patients tested positive for SARS-CoV-2, and the pooled prevalence for *L. pneumophila* was estimated to be at 0.288%, while the pooled estimated case fatality ratio among patients with co-infection of SARS-CoV-2 and *L. pneumophila* was 26.3%.⁷

Bacterial co-infections in COVID-19 patients are associated with increased mortality, particularly among the elderly.⁴ The Legionella score has been proposed for differentiating Legionnaires’ disease from other CAP causes,¹⁸ but it is not reliable for severe pneumonia cases. Early diagnosis is critical to ensure prompt treatment. The American Thoracic Society and Infectious Diseases Society of America recommend urinary antigen testing (UAT) for Legionella in severe CAP cases.¹⁹ Although the culture of lower respiratory tract specimens remains the gold standard in diagnosing Legionnaires’ disease, UAT is widely used due to its rapid turnaround time and cost-effectiveness compared to culture methods.¹⁹ According to current Sanford antibiotic guideline,²⁰ the antibiotic choice included fluoroquinolones, macrolides, and doxycycline. In patients with severe CAP, routine UAT is necessary and should always consider giving empiric antibiotic covering *Legionella*.

Although no environmental source was identified in this case, hospital-acquired Legionnaires’ disease remains a serious concern, especially in ICUs. Public health guidance for community congregate settings, such as long-term care facilities, emphasizes routine flushing of water fixtures, monitoring of water temperature and chlorine residuals, and the development of site-specific water management plans to prevent Legionella growth. Weekly flushing of seldom-used outlets until maximum hot water temperature is reached, maintaining chlorine levels throughout plumbing systems, and pre-planning corrective actions are central components of prevention strategies.²¹

These principles are equally relevant in hospital settings, particularly in intensive care units where older and immunocompromised patients are at high risk. Hospital-acquired Legionella infections can result from exposure to contaminated water systems, and

their mortality can exceed that of community-acquired cases. In addition to prompt clinical recognition and diagnostic testing, health-care facilities should implement multidisciplinary water management programs that include engineering controls, routine water quality surveillance, and outbreak response protocols. Such measures are vital in preventing nosocomial Legionella infections in vulnerable populations.²²

The present case is unique for several reasons. First, the patient lived in his own home and had no known exposure or cluster history related to *L. pneumophila*. The only possible source was the previous hospital; however, he stayed there for only 48 hours, and no other cases of *L. pneumophila* infection were reported from that facility. Second, the patient received levofloxacin as part of combination therapy for severe CAP, and the Legionella urinary antigen test (UAT) returned positive one day after starting antibiotics. We attribute the patient’s excellent outcome to the early administration of appropriate antibiotics. Third, no evidence of other bacterial co-infections was found during admission, including negative blood and sputum cultures, as well as negative tests for *Mycoplasma pneumoniae* and *Streptococcus pneumoniae* antigens. Therefore, *L. pneumophila* was considered the co-infection pathogen in this case.

4. Conclusion

This study presents a case of a COVID-19 patient diagnosed with Legionella pneumophila co-infection on the first day of admission. Empirical treatment with levofloxacin was initiated immediately. Despite developing ARDS, the patient responded well to treatment, was successfully extubated, and fully recovered without oxygen dependence. The favorable outcome highlights the importance of early diagnosis, timely antibiotic therapy, and proper management of COVID-19-related ARDS. This case underscores the need to consider *L. pneumophila* co-infection in severe COVID-19 cases and the critical role of prompt intervention in improving prognosis.

Data availability statement

The original contributions presented in the study are available upon reasonable request to the corresponding author.

Ethics statement

The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of Mackay Memorial Hospital in Taipei, Taiwan (protocol code: 21MMHI369e; date of approval: December 4, 2021), which waived the need for written informed consent.

Author contributions

Conceptualization, TYH; data analysis and interpretation, WLC and WHL; writing, original draft preparation, WLC; writing, review and editing, TYH; supervision, TYH and KHC; project administration, TYH. All authors have read and agreed to the published version of the manuscript.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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