

## CLINICAL VIGNETTE

# A Classic Case of Legionella Pneumonia

Xiaomeng Deng, MD, Kevin Eng, MD and Jaime Betancourt, MD

### Introduction

*Legionella pneumophila* is a pathogenic gram-negative bacterium typically found in freshwater systems including lakes, rivers, and hot springs. They also may be found in man-made water systems including cooling towers, hot tubs, and plumbing systems. Illness from *Legionella* ranges from “Pontiac Fever,” a self-limited flu-like illness to “Legionnaire’s Disease,” a severe lung infection famously named after an outbreak at an American Legion Convention in 1976. *Legionella* is an important cause of community-acquired pneumonia, accounting for up to 10% of cases depending on the geographic area.<sup>1-5</sup> While some patients present with mild symptoms, studies report up to 30% of patients with Legionnaire’s disease are treated in intensive care units.<sup>6,7</sup> Legionnaire’s disease has reported mortality between 5~10% as patients develop respiratory failure, shock, and multi-organ failure.<sup>6,8,9</sup>

### Case Description

A 72-year-old male presented with one week of subjective fevers, mild dyspnea, dry cough, nausea, and diarrhea. Prior medical history includes hypertension, type 2 diabetes mellitus,

stage 3 chronic kidney disease, coronary artery disease status post multi-vessel coronary artery bypass graft surgery, ischemic cardiomyopathy, and chronic systolic heart failure. Initial evaluation noted fever of 37.5 degrees Celsius, intermittent delirium, mild tachycardia, and relative hypotension. Labs included normal leukocyte count, moderate hyponatremia, mild transaminase elevation and acute kidney injury. The initial anterior-posterior chest radiograph did not demonstrate any acute cardiopulmonary process. Given the lack of clear indicators of sepsis or localizing infection, the patient was admitted for observation and antibiotics were deferred. Due to persistent cough and rales on physical exam, repeat posterior-anterior and lateral chest radiograph on hospital day 3 (Figure 1) demonstrated new opacities in the left upper and left lower lung zones. CT chest on hospital day 4 demonstrated dense left upper and lower lobe consolidation (Figure 2), and Cefepime and Azithromycin were started. On hospital day 5, urine *Legionella* antigen returned positive. Cefepime was discontinued, and the patient was discharged on a 10-day total course of Azithromycin. After hospital discharge, his symptoms had completely resolved. Follow-up CT chest and labs 1 month after hospitalization returned to baseline.

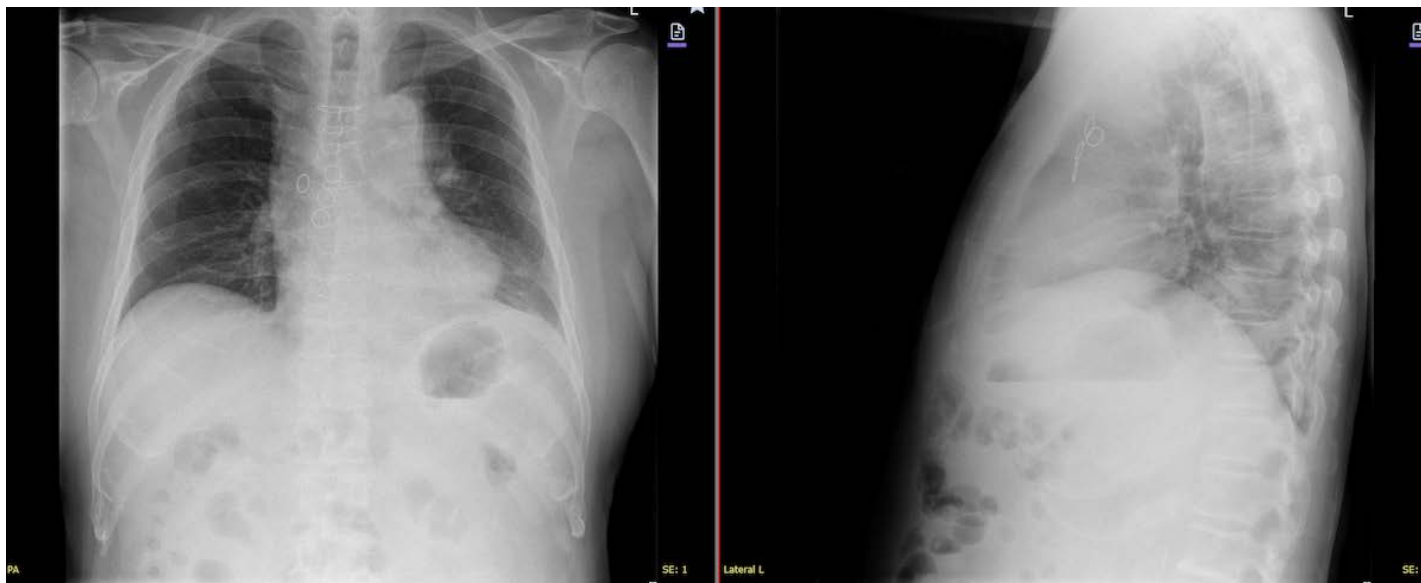


Figure 1.



Figure 2.

### Discussion

Diagnosing *Legionella* pneumonia can be challenging. Although outbreaks are often associated with large, complex water systems such as hotels, hospitals, and cruise ships, studies have shown a steady rise in the incidence of community-acquired *Legionella* pneumonia in the last two decades, with close to two-thirds of reports having no known potential exposure or identifiable source.<sup>10</sup> While the predominant symptoms cannot distinguish *Legionella* from other causes of community-acquired pneumonia (CAP), several other clinical features have been found to occur more often with Legionnaires' disease than other CAPs including gastrointestinal symptoms, high fever, relative bradycardia, hyponatremia, elevated C-reactive protein, and elevated hepatic transaminases.<sup>8,11–13</sup>

Identification of *Legionella* has public health implications and early diagnosis and treatment with effective antibiotic therapy is key to mortality reduction. Both the Infectious Diseases Society of America (IDSA) and the American Thoracic Society (ATS) recommend testing for *Legionella* in adult patients with severe CAP with urine *Legionella* antigen test and collection of lower respiratory tract secretions for *Legionella* culture or nucleic acid amplification testing.<sup>13</sup>

Choosing an effective antimicrobial agent is also crucial in reducing pneumonia morbidity and mortality, including Legionnaires' disease.<sup>14</sup> Before the 1990s, cephalosporins were the empiric antibiotic monotherapy of choice but they are presently ineffective against *Legionella*. More recent ATS/IDSA guidelines published in 2007 and 2019 recommend the addition of a macrolide or a fluoroquinolone to a beta-lactam as empiric therapy for severe CAP.<sup>11,13</sup> While an earlier meta-analysis from 2014 reported findings favoring fluoroquinolones to macrolides,<sup>15</sup> a more recent meta-analysis incorporating more studies and a larger collective sample size concluded that these two classes of antibiotics had similar effectiveness in reducing mortality in *Legionella* pneumonia.<sup>16</sup> This patient was successfully treated with azithromycin.

### REFERENCES

1. **Marchello C, Dale AP, Thai TN, Han DS, Ebell MH.** Prevalence of Atypical Pathogens in Patients With Cough and Community-Acquired Pneumonia: A Meta-Analysis. *Ann Fam Med.* 2016 Nov;14(6):552-566. doi: 10.1370/afm.1993. PMID: 28376442; PMCID: PMC5389400.
2. **Phin N, Parry-Ford F, Harrison T, Stagg HR, Zhang N, Kumar K, Lortholary O, Zumla A, Abubakar I.** Epidemiology and clinical management of Legionnaires'

- disease. *Lancet Infect Dis*. 2014 Oct;14(10):1011-21. doi: 10.1016/S1473-3099(14)70713-3. Epub 2014 Jun 23. PMID: 24970283.
3. **Jain S, Self WH, Wunderink RG, Fakhran S, Balk R, Bramley AM, Reed C, Grijalva CG, Anderson EJ, Courtney DM, Chappell JD, Qi C, Hart EM, Carroll F, Trabue C, Donnelly HK, Williams DJ, Zhu Y, Arnold SR, Ampofo K, Waterer GW, Levine M, Lindstrom S, Winchell JM, Katz JM, Erdman D, Schneider E, Hicks LA, McCullers JA, Pavia AT, Edwards KM, Finelli L; CDC EPIC Study Team.** Community-Acquired Pneumonia Requiring Hospitalization among U.S. Adults. *N Engl J Med*. 2015 Jul 30;373(5):415-27. doi: 10.1056/NEJMoa1500245. Epub 2015 Jul 14. PMID: 26172429; PMCID: PMC4728150.
  4. **Musher DM, Abers MS, Bartlett JG.** Evolving Understanding of the Causes of Pneumonia in Adults, With Special Attention to the Role of Pneumococcus. *Clin Infect Dis*. 2017 Oct 30;65(10):1736-1744. doi: 10.1093/cid/cix549. PMID: 29028977; PMCID: PMC7108120.
  5. **Barskey AE, Derado G, Edens C.** Rising Incidence of Legionnaires' Disease and Associated Epidemiologic Patterns, United States, 1992-2018. *Emerg Infect Dis*. 2022 Mar;28(3):527-538. doi: 10.3201/eid2803.211435. PMID: 35195513; PMCID: PMC8888234.
  6. **Collier SA, Deng L, Adam EA, Benedict KM, Beshears EM, Blackstock AJ, Bruce BB, Derado G, Edens C, Fullerton KE, Gargano JW, Geissler AL, Hall AJ, Havelaar AH, Hill VR, Hoekstra RM, Reddy SC, Scallan E, Stokes EK, Yoder JS, Beach MJ.** Estimate of Burden and Direct Healthcare Cost of Infectious Waterborne Disease in the United States. *Emerg Infect Dis*. 2021 Jan;27(1):140-149. doi: 10.3201/eid2701.190676. PMID: 33350905; PMCID: PMC7774540.
  7. **Falcone M, Russo A, Tiseo G, Cesaretti M, Guarracino F, Menichetti F.** Predictors of intensive care unit admission in patients with Legionella pneumonia: role of the time to appropriate antibiotic therapy. *Infection*. 2021 Apr;49(2):321-325. doi: 10.1007/s15010-020-01565-7. Epub 2020 Dec 14. PMID: 33315182; PMCID: PMC7734452.
  8. **Allgaier J, Lagu T, Haessler S, Imrey PB, Deshpande A, Guo N, Rothberg MB.** Risk Factors, Management, and Outcomes of Legionella Pneumonia in a Large, Nationally Representative Sample. *Chest*. 2021 May;159(5):1782-1792. doi: 10.1016/j.chest.2020.12.013. Epub 2020 Dec 19. PMID: 33352192.
  9. **Dooling KL, Toews KA, Hicks LA, Garrison LE, Bachaus B, Zansky S, Carpenter LR, Schaffner B, Parker E, Petit S, Thomas A, Thomas S, Mansmann R, Morin C, White B, Langley GE.** Active Bacterial Core Surveillance for Legionellosis - United States, 2011-2013. *MMWR Morb Mortal Wkly Rep*. 2015 Oct 30;64(42):1190-3. doi: 10.15585/mmwr.mm6442a2. PMID: 26513329.
  10. **Baral SD, Grosso A, Holland C, Papworth E.** The epidemiology of HIV among men who have sex with men in countries with generalized HIV epidemics. *Curr Opin HIV AIDS*. 2014 Mar;9(2):156-67. doi: 10.1097/COH.000000000000037. PMID: 24445371.
  11. **Mandell LA, Wunderink RG, Anzueto A, Bartlett JG, Campbell GD, Dean NC, Dowell SF, File TM Jr, Musher DM, Niederman MS, Torres A, Whitney CG; Infectious Diseases Society of America; American Thoracic Society.** Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. *Clin Infect Dis*. 2007 Mar 1;44 Suppl 2(Suppl 2):S27-72. doi: 10.1086/511159. PMID: 17278083; PMCID: PMC7107997.
  12. **Bellew S, Grijalva CG, Williams DJ, Anderson EJ, Wunderink RG, Zhu Y, Waterer GW, Bramley AM, Jain S, Edwards KM, Self WH.** Pneumococcal and Legionella Urinary Antigen Tests in Community-acquired Pneumonia: Prospective Evaluation of Indications for Testing. *Clin Infect Dis*. 2019 May 30;68(12):2026-2033. doi: 10.1093/cid/ciy826. PMID: 30265290; PMCID: PMC7182343.
  13. **Metlay JP, Waterer GW, Long AC, Anzueto A, Brozek J, Crothers K, Cooley LA, Dean NC, Fine MJ, Flanders SA, Griffin MR, Metersky ML, Musher DM, Restrepo MI, Whitney CG.** Diagnosis and Treatment of Adults with Community-acquired Pneumonia. An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America. *Am J Respir Crit Care Med*. 2019 Oct 1;200(7):e45-e67. doi: 10.1164/rccm.201908-1581ST. PMID: 31573350; PMCID: PMC6812437.
  14. **Heath CH, Grove DI, Looke DF.** Delay in appropriate therapy of Legionella pneumonia associated with increased mortality. *Eur J Clin Microbiol Infect Dis*. 1996 Apr;15(4):286-90. doi: 10.1007/BF01695659. PMID: 8781878.
  15. **Burdet C, Lepeule R, Duval X, Caseris M, Rioux C, Lucet JC, Yazdanpanah Y.** Quinolones versus macrolides in the treatment of legionellosis: a systematic review and meta-analysis. *J Antimicrob Chemother*. 2014 Sep;69(9):2354-60. doi: 10.1093/jac/dku159. Epub 2014 May 14. PMID: 24827889.
  16. **Jasper AS, Musuza JS, Tischendorf JS, Stevens VW, Gamage SD, Osman F, Safdar N.** Are Fluoroquinolones or Macrolides Better for Treating Legionella Pneumonia? A Systematic Review and Meta-analysis. *Clin Infect Dis*. 2021 Jun 1;72(11):1979-1989. doi: 10.1093/cid/ciaa441. PMID: 32296816; PMCID: PMC8315122.