

# Failed Outpatient Therapy in Community Acquired Pneumonia

## A Case Report and Clinical Pearls

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### Abstract

We present the case of a patient with community-acquired pneumonia unresponsive to empiric azithromycin, and discuss the diagnostic and therapeutic considerations of this clinical scenario.

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### Clinical Case:

A 64 year-old Caucasian male smoker with a history of chronic lymphocytic leukemia (CLL) initially presented to his primary care physician with several days of a mild productive cough, dyspnea on exertion, and subjective fever. A chest radiograph obtained in the office demonstrated right upper lobe consolidation (Figure 1).



Fig. 1: Chest radiograph at outpatient presentation.

He was prescribed a course of azithromycin 500 mg daily for five days for presumed community acquired pneumonia (CAP). Over the next three days, the patient became increasingly dyspneic and lethargic despite taking the prescribed antibiotic. He subsequently presented to the emergency department notably confused. He was febrile to 101.8° F, his blood pressure was 85/50 mmHg, and heart rate was 88. His respiratory rate was 36, and oxygen saturation was 75% on room air. Repeat chest X-ray showed near complete consolidation of the right hemithorax (Figure 2).



**Fig. 2: Chest radiograph at hospital presentation, 3 days later.**

The patient was intubated for hypoxemic respiratory failure and started on broad spectrum antibiotics with vancomycin and piperacillin-tazobactam. He was transferred to the medical intensive care unit with the following laboratory data:

Table 1. Laboratory Values at Hospital Admission.

Test	Value	Reference Range
White blood cell count	13,500/mm <sup>3</sup>	3,000 – 10,000/mm <sup>3</sup>
Sodium	132 mmol/L	134 – 142 mmol/L
BUN	41 mg/dL	7 – 20 mg/dL
Creatinine	1.5 mg/dL	0.7 – 1.3 mg/dL
Blood culture	No data	N/A
Mini-bronchoalveolar lavage	No data	N/A
Streptococcus urinary antigen	Negative	Negative
Legionella urinary antigen	Negative	Negative

### Quiz: How do you interpret these findings, in this clinical context?

- A. The patient likely has a resistant pathogen causing a severe pneumonia. Vancomycin and piperacillin-tazobactam provide adequate broad-spectrum antimicrobial coverage. No changes in antibiotics are needed.
- B.) The Legionella urinary antigen could represent a false negative. An IV macrolide or fluoroquinolone should be added.
- C.) The patient likely has an aspiration pneumonia. IV clindamycin would provide better anaerobic coverage and should be added.
- D.) The patient likely developed a post-obstructive pneumonia. Bronchoscopy with airway inspection and bronchoalveolar lavage (BAL) should be performed.

### Discussion

*Legionella* is relatively common among hospitalized patients with pneumonia. In a recent U.S. population-based study, it estimated that 8,000-18,000 persons are hospitalized each year with *Legionella* pneumonia, and it remains in the top four microbial causes of hospitalization due to community acquired pneumonia (CAP).<sup>1</sup> Worldwide incidence varies based on geography, but overall *Legionella* is estimated to represent approximately 2-15% of community acquired pneumonia that requires hospitalization.<sup>2</sup> Further, the CDC has reported that the incidence of pneumonia due to *Legionella* has been increasing since its first recognition in the 1970's. From 2000 to 2009 the age-adjusted incidence in the United States has increased 170%, from 0.40 to 1.08 cases per 100,000 persons.<sup>3</sup> Currently there are 48 known species that comprise 70 distinct serogroups in the genus *Legionella*. Specifically, *Legionella pneumophila* is the major cause of *Legionella* pneumonia (91.5%), and serogroup 1 is the predominant serotype representing approximately 84% of cases.<sup>4,5</sup>

*Legionella* often presents as a very severe and potentially life threatening disease. The WHO estimates a mortality rate of 5-20% worldwide.<sup>6</sup> Treatment usually requires IV antimicrobial therapy and hospital admission. Certain populations such as cigarette smokers, the elderly, patients with chronic lung diseases, immunosuppressed, and solid organ transplant recipients are at the highest risk for developing the disease.<sup>7</sup> Transmission of the bacteria is through contaminated aerosols. Potable water supplies such as cooling towers, respiratory-therapy equipment, and whirlpool bathes have all been implicated in disease transmission. The clinical manifestations typically start with non-specific symptoms including fevers, malaise, and mildly productive cough. Gastrointestinal symptoms, especially diarrhea, are associated with *Legionella* and can be present in 20-40% of cases. Relative bradycardia (pulse-temperature dissociation) and hyponatremia (sodium <130) are also more common but cannot reliably distinguish *Legionella* from other pneumonias. There are no characteristic radiographic findings, but a pleural effusion can be seen in up to one third of patients. As the disease course progresses, patients can develop severe respiratory failure requiring mechanical ventilation. For these patients, progression of infiltrates on chest X-ray despite appropriate antimicrobial therapy is common.

Diagnosis can be made through several different modalities. Sputum culture remains the reference standard; however it can be

very difficult to grow, takes several days to process, and can be affected by antibiotic exposure. For these reasons, the urine antigen test has become a much more common diagnostic tool. The test can be performed quickly, accurately, and is fairly inexpensive with the most recent Medicare midpoint reimbursement cost being \$22. The urine antigen test specifically isolates *Legionella pneumophila* serotype 1 which represents approximately 80% of cases.<sup>5</sup> In a systematic review and meta-analysis published in 2009, the urinary antigen test was shown to have a specificity of 99% and sensitivity of 74% in detecting Legionella pneumonia.<sup>8</sup> The test will remain positive for weeks to months even after antibiotic therapy, making a history of recent pneumonia potentially the only reason for a false positive result. A negative result, on the other hand, should be regarded with caution. The different Legionella serotypes that are not tested in the urine lower the sensitivity and give the test its 26% false negative rate. For this reason, sputum culture should be sent on every patient where the diagnosis of *Legionella* is highly suspected, and empiric antibiotic coverage should be continued at least until sputum culture has been confirmed or another pathogen is implicated. When pairing the sputum with the urinary antigen, the sensitivity increases to almost 90%.<sup>9</sup>

Since its development in the late 1970's, the urine antigen test has become readily available in many hospitals throughout the United States. Because of this, many clinicians are frequently checking for *Legionella* pneumonia on every presentation of community acquired pneumonia. This at least partly explains the dramatic increase in disease incidence reported to the CDC from 2000-2009. However, *Legionella* urine antigen testing should not be routinely ordered on every patient with community acquired pneumonia. The IDSA/ATS guidelines suggest *Legionella* urine antigen testing for only those patients admitted to the intensive care unit, those who have failed outpatient therapy, those who have traveled in the past two weeks, and those with a pleural effusion on chest radiography.<sup>10</sup> While there are always exceptions to guidelines, keeping these in mind prior to ordering the urine antigen test can help reduce cost and excessive testing.

Treatment for pneumonia due to *Legionella* primarily consists of either a respiratory fluoroquinolone or macrolide antibiotic. **Therefore, the quiz answer is B.** Occasionally, patients do not respond to oral therapy alone so parenteral therapy should be initiated on presentation and continued until objective clinical response. In severe cases, limited data suggests improved outcomes with combination therapy. This can be with both a macrolide and a fluoroquinolone or either of these paired with rifampin.<sup>11,12</sup> Total duration of therapy should be 10 to 14 days and can be completed with oral antibiotics once clinically stable. A 21-day course is recommended for the immunosuppressed or patients with extensive disease on chest imaging.

The patient described in this case was admitted to the ICU and IV azithromycin was added for empiric coverage of *Legionella*. A non-bronchoscopic bronchoalveolar lavage (mini-BAL) grew *Legionella* serotype 6 three days into admission. Due to the severity of his illness, combination therapy was added with azithromycin and levofloxacin. By the sixth day of hospitalization, the patient's clinical course had improved enough to be removed from mechanical ventilation. Antibiotics were narrowed to azithromycin monotherapy for a total of 21 days. He was transitioned to an acute rehabilitation hospital where he was eventually able to completely wean off supplemental oxygen.

## Legionella Pneumonia: Clinical Pearls

- Legionella can cause an especially severe pneumonia. It often requires admission into the hospital and IV antimicrobial therapy.
- Urine antigen testing is a relatively inexpensive test and, when positive, should prompt immediate therapy. A negative test result should not necessarily change management until further data is obtained.
- Urine antigen testing need not be routinely used on every patient with community acquired pneumonia. Certain clinical situations such as ICU admission, failure of outpatient therapy, or recent travel should prompt testing.
- Respiratory fluoroquinolones and macrolides provide the best coverage for Legionella. In severe cases, combination with both a macrolide and fluoroquinolone or either paired with rifampin can be used.

## References

1. Marston BJ, Plouffe JF, File TM Jr, Hackman BA, Salstrom SJ, Lipman HB, Kolczak MS, Breiman RF. Incidence of community-acquired pneumonia requiring hospitalization. Results of a population-based active surveillance Study in Ohio. The Community-Based Pneumonia Incidence Study Group. Arch Intern Med. 1997 Aug 11-25;157(15):1709-18. PubMed PMID:9250232. [REFERENCE LINK](#)
2. Stout JE, Yu VL. Legionellosis. N Engl J Med. 1997 Sep 4;337(10):682-7. PubMed PMID:9278466. [REFERENCE LINK](#)
3. Legionellosis --- United States, 2000-2009. MMWR Morb Mortal Wkly Rep. 2011 Aug 19;60(32):1083-6. PubMed PMID:21849965. [REFERENCE LINK](#)

4. Fields BS, Benson RF, Besser RE. Legionella and Legionnaires' disease: 25 years of investigation. Clin Microbiol Rev. 2002 Jul;15(3):506-26. PubMed PMID:12097254.  
REFERENCE LINK
5. Yu VL, Plouffe JF, Pastoris MC, Stout JE, Schousboe M, Widmer A, Summersgill J, File T, Heath CM, Paterson DL, Cheresky A. Distribution of Legionella species and serogroups isolated by culture in patients with sporadic community-acquired legionellosis: an international collaborative survey. J Infect Dis. 2002 Jul 1;186(1):127-8. PubMed PMID:12089674.  
REFERENCE LINK
6. Legionella and the prevention of legionellosis. 2007, Geneva: World Health Organization. 1 vol. (pp. XXIV-252).  
REFERENCE LINK
7. Vergis EN, Akbas E, Yu VL. Legionella as a cause of severe pneumonia. Semin Respir Crit Care Med. 2000;21(4):295-304. PubMed PMID:16088740.  
REFERENCE LINK
8. Shimada T, Noguchi Y, Jackson JL, Miyashita J, Hayashino Y, Kamiya T, Yamazaki S, Matsumura T, Fukuhara S. Systematic review and metaanalysis: urinary antigen tests for Legionellosis. Chest. 2009 Dec;136(6):1576-85. PubMed PMID:19318671.  
REFERENCE LINK
9. Centers for Disease Control and Prevention website. Legionella (Legionnaires Disease and Pontiac Fever). 2013.  
REFERENCE LINK
10. 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 consensus guidelines on the management of community-acquired pneumonia in adults. Clin Infect Dis. 2007 Mar 1;44 Suppl 2:S27-72. PubMed PMID:17278083.  
REFERENCE LINK
11. Pedro-Botet ML, Yu VL. Treatment strategies for Legionella infection. Expert Opin Pharmacother. 2009 May;10(7):1109-21. PubMed PMID:19405787.  
REFERENCE LINK
12. Yu VL, Greenberg RN, Zadeikis N, Stout JE, Khashab MM, Olson WH, Tennenberg AM. Levofloxacin efficacy in the treatment of community-acquired legionellosis. Chest. 2004 Jun;125(6):2135-9. PubMed PMID:15189933.  
REFERENCE LINK