

## CLINICAL CASE OF THE MONTH

# A 64 Year-Old Woman Presenting With Fever, Confusion, Ophthalmoplegia and Pneumonia

Daniel H. Johnson, MD; Michael Modica, MD; Rachel Coleman, MD; Charles V. Sanders, MD; Fred A. Lopez, MD

### INTRODUCTION

*Legionella pneumophila* is a major cause of atypical community-acquired pneumonia, which is commonly severe enough to require hospitalization.<sup>1,2</sup> Though primarily a respiratory infection, Legionellosis involves the central nervous system (CNS) in up to 50% of patients, and diagnosis can be obscured by the absence of obvious respiratory symptomatology.<sup>3</sup> A reversible diffuse encephalopathy is the most common neurologic complication, but focal CNS involvement can sometimes be the initial presentation.<sup>4,5,6</sup> We report a case of a woman infected with *Legionella pneumophila* presenting with vague symptomatology and focal neurologic findings. This report highlights the challenges of early recognition of *Legionella* infection when neurologic symptoms predominate.

### CASE REPORT

We describe the case of a 64-year-old woman with a past medical history of chronic hepatitis C infection and hypertension presenting to the emergency department with several days of generalized weakness, lethargy, subjective fevers, chills, and poor oral intake. The patient's family mentioned that she was also confused during this period. On initial presentation, the physical exam was significant for a left lateral gaze palsy, slowed mentation, and crackles on auscultation of the base of the left lung. Laboratory values were significant for a serum sodium of 128 mmol/L (normal 135-145 mmol/L) and a platelet count of 89,000/ $\mu$ L (normal 130,000-400,000/ $\mu$ L). There was also a mild elevation in creatinine to 1.12 mg/dL. Chest radiograph was significant for an infiltrate in the area of the left lower lobe, consistent with pneumonia (Figure 1).

The patient was initially admitted to the medical intensive-care unit for close monitoring of her focal neurologic findings. The patient was empirically started on ceftriaxone, ampicillin, acyclovir, and vancomycin to treat a potential central nervous system (CNS) infection. A lumbar puncture was attempted at the bedside, but was unsuccessful. The patient later refused a lumbar puncture attempt with interventional radiology. Due to the pneumonia, she was also started on ciprofloxacin and oseltamivir. Blood cultures, sputum culture, and legionella urine antigen were collected prior to administration of antibiotics. Overnight the ophthalmoplegia resolved spontaneously, and on day two of admission, the patient was transferred to the medicine ward. Antibiotics were de-escalated to ceftriaxone and levofloxacin, and the patient's mental status was noted

to have improved. Her hyponatremia and elevated creatinine normalized by the third day of hospitalization. By day four of her hospital stay, the patient's presenting symptoms had completely resolved, and she was discharged to complete a fourteen-day course of levofloxacin. One week after admission, her urine legionella antigen resulted as positive and the diagnosis of Legionellosis was confirmed.

### DISCUSSION

#### Epidemiology

*Legionella pneumophila* was first recognized as a causative pathogen of severe pneumonia in 1976 after an outbreak among American Legion conventioners at Philadelphia's Bellevue Stratford Hotel.<sup>7</sup> *Legionella* species are aerobic Gram-negative bacteria found naturally in fresh water environments, and Legionnaires' disease outbreaks are usually associated with manmade fresh-water reservoirs, such as building-associated water systems.<sup>8</sup> There has been a recent increase in reported cases of Legionellosis since the turn of the century, but it is still unclear whether this represents a true increase in incidence or changes in testing and reporting practices.<sup>8</sup> The most common presenting symptoms are cough, dyspnea, and high fevers, but extrapulmonary manifestations such as diarrhea and neurologic deficits can also be seen.<sup>9</sup>

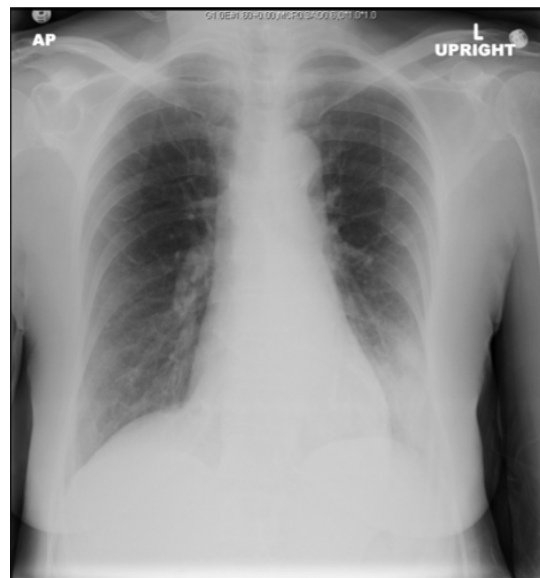


FIGURE 1. An AP chest radiograph reveals a left lower lobe consolidation

## Clinical Presentation

Here we describe a patient presenting with lethargy, confusion, and an ophthalmoplegia, who was subsequently diagnosed with a *Legionella* infection. Legionellosis involves the CNS in up to 50% of patients, commonly presenting with headache, somnolence, and varying degrees of encephalopathy.<sup>3</sup> Focal neurologic findings are uncommon, but cerebellar dysfunction, pyramidal dysfunction, and psychiatric symptoms have been reported.<sup>6,10-15</sup> Legionellosis presenting with an ophthalmoplegia or cranial nerve palsy as in our patient is even less frequent.<sup>14,16-18</sup> Proposed theories for the pathogenesis of *Legionella*-associated neurologic dysfunction include direct invasion of brain parenchyma,<sup>14,16</sup> neurotoxin production, and autoimmune mechanisms.<sup>4,14,16</sup> The prognosis of neurologic deficits associated with *Legionella* infection is not well studied, but there are numerous case reports and case series of persistent neurologic symptoms.<sup>4,6,14</sup> Our patient's neurologic symptoms resolved with antibiotics, an outcome that has also been reported in other cases in the literature.<sup>3,5,11,14,16</sup>

## Diagnosis

Timely diagnosis of *Legionella* infection can be challenging when there is a lack of sputum production, only mild respiratory symptoms, or a predominance of extrapulmonary manifestations.<sup>9</sup> Early recognition of the disease is important, as delay in appropriate therapy has been associated with increased mortality.<sup>19</sup> Diagnosis of serotype 1 *Legionella* infection can be confirmed by urinary antigen tests, which have a specificity of 99% but a lower sensitivity of 74%.<sup>20</sup> Due to poor sensitivity, limited detection of non-serotype 1 *Legionella*, and the inability in certain settings to obtain these results rapidly, empiric antibiotic coverage is often needed before a diagnosis can be confirmed.

Though the heterogeneity of clinical presentation can make recognition of *Legionella* infection challenging, there are some unique clinical predictors which can help assess the likelihood of *Legionella* pneumonia. Higher fevers (sometimes with a relative bradycardia), absence of sputum production, hyponatremia, elevated LDH, and low platelets have been shown to be independent predictors of *Legionella*-associated community-acquired pneumonia (CAP).<sup>9</sup> In addition, highly elevated serum ferritin levels (mean level at initial presentation 1698 ng/mL) have been associated with *Legionella* CAP while matched patients with non-*Legionella* CAP had levels less than twice the normal value.<sup>21</sup>

## Treatment & Prognosis

Macrolides and fluoroquinolones are the IDSA-recommended first-line treatment for *Legionella* pneumonia.<sup>22</sup> Although studies showed superiority of respiratory fluoroquinolones to the older macrolides,<sup>23,24</sup> more recent trials comparing azithromycin and levofloxacin have shown no difference in mortality or length of hospital stay.<sup>25,26</sup> Also shorter antibiotic courses (7-14 days) have been found to have the same cure rates as the previously recommended duration of 21 days.<sup>27,28</sup> A large-scale study from

the CDC showed a decrease in the case-fatality rate for *Legionella* CAP from 26%-10% for the period 1980-1998.<sup>29</sup> Implementation of community-acquired pneumonia (CAP) guidelines, which recommend empiric use of either azithromycin or a respiratory fluoroquinolone, could be a reason for the dramatic mortality reduction seen in community-acquired *Legionella* pneumonia.<sup>30</sup> With recent data showing 90-day mortality non-inferiority of beta lactam monotherapy compared to beta-lactam-macrolide combination or fluoroquinolone monotherapy for community-acquired pneumonia,<sup>31</sup> empiric use of therapy effective against *Legionella* may decline. This would make clinical recognition of *Legionella* infection even more important.

## CONCLUSION

*Legionella* is an atypical pneumonia pathogen that can present with extrapulmonary symptoms including neurologic deficits. Early recognition and initiation of appropriate therapy against *Legionella* species improves mortality. Awareness of the unique clinical presentations of *Legionella*-associated infections is essential for the appropriate antimicrobial management of patients with community-acquired pneumonia.

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**Dr. Johnson** is a chief resident in the Department of Internal Medicine at Louisiana State University Health Sciences Center in New Orleans; **Dr. Modica** is a second-year resident in the Department of Internal Medicine at LSUHSC-New Orleans; **Dr. Coleman** is a chief resident in the Department of Internal Medicine at LSUHSC-New Orleans; **Dr. Sanders** is the Chairman of the Department of Medicine, the Edgar Hull Professor of Medicine, and a Professor of Microbiology, Immunology, and Parasitology at the LSUHSC-New Orleans; **Dr. Lopez** is the Richard Vial Professor and Vice Chair of Education in the Department of Internal Medicine at LSUHSC-New Orleans.