



Severe Legionnaire Disease Complicated by Multi-Organ Dysfunction: The Heart is not Spared

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Abstract

Background: *Legionella pneumophila* is a common cause of Community Acquired Pneumonia (CAP) which is often associated with a severe clinical course and a mortality rate of 5% to 25% among immunocompetent patients. Complications of *Legionella* infection include acute renal and respiratory failures, disseminated intravascular coagulation and septic shock which often require intensive level of medical care. Reported cases of myocardial dysfunction and acute systolic heart failure from *legionella* disease are rare. This case describes an atypical presentation of *legionella* pneumonia in a previously healthy patient complicated by multi-organ failure.

Case Presentation: A 63 year old female with medical history of hypertension was admitted to the intensive care unit for acute onset of altered mental status, decreased oral intake, subjective fevers, dizziness and diarrhea. Physical exam was remarkable for temperature of 101.2 F, pulse rate 112 beats/minute, respiratory rate 22 cycles/minute and blood pressure 88/60 mmHg.

Laboratory studies showed leukocytosis, markedly elevated serum Creatinine Kinase (CPK), and creatinine and lactic acid levels. Troponin was elevated; however no evidence of cardiac ischemia on electrocardiogram. Chest X-ray revealed right mid-lung opacities consistent with pneumonia. A Transthoracic Echo (TTE) showed reduced ejection fraction of 35% and urine *legionella* antigen test was positive for *Legionella pneumophila* group 1 antigen. She was admitted to the medical Intensive Care Unit (ICU) and initiated on Intravenous (IV) fluids and empiric antibiotics for CAP (IV Ceftriaxone 2 g daily and Azithromycin 500 mg daily) and by day 5 of hospitalization, her fever had completely resolved and neurological status returned to normal. Her serum CPK and creatinine levels significantly improved and troponin levels normalized. She was discharged home to follow up with infectious disease and cardiology team outpatient. A repeat TTE six weeks later showed normal ejection fraction of 60% to 65% and a normal cardiac stress test.

Conclusion: *Legionella pneumohila* is primarily a respiratory illness, however it has extra-pulmonary manifestations. Cardiac complications of *Legionella* infection are uncommon. Studies have linked atypical organisms that cause CAP with cardiovascular disease through atherogenesis and atherosclerosis. *Legionella* infection should be considered as a possible etiology of systolic heart failure in patients with CAP and sepsis.

Keywords: Infection; Cardiovascular; Critical; Heart failure; *Legionella*

Abbreviations

CAP: Community Acquired Pneumonia; CPK: Creatine Phosphokinase; WBC: White Blood Count; TTE: Transthoracic Echocardiogram; ICU: Intensive Care Unit; IV: Intravenous

Introduction

Legionella pneumophila is a common cause of Community Acquired Pneumonia (CAP) which is often associated with a severe clinical course and a mortality rate of 5% to 25% among immunocompetent patients [1,2]. In adults, about 10% of CAP that requires inpatient care is caused by *Legionella*. The signs and symptoms are usually non-specific, however more than 90% of infected

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individuals present with respiratory illness [3]. *Legionella* infection is largely under diagnosed due to its atypical presentation, low suspicion among clinicians and inadequate testing [4]. The diagnosis is more clinically challenging in the absence of respiratory symptoms.

Legionella pneumonia has reportedly been associated with acute renal and respiratory failures, disseminated intravascular coagulation and septic shock requiring intensive level of medical care [5-7]. However, cases of myocardial dysfunction and acute systolic heart failure are rare. This case describes an atypical presentation of *legionella* pneumonia in a previously healthy patient complicated by multi-organ failure.

Case Presentation

A 63 years old African-American female with a medical history of hypertension was brought into the emergency room with confusion and altered mental status. Collateral history was obtained from the son who stated that patient had experienced decreased oral intake, subjective fevers, dizziness and multiple episodes of diarrhea for five days prior to presentation. She had not been sick before then and no recent inpatient hospitalization. She was a non-smoker and did not have a family history of cardiovascular disease. On physical examination, she was conscious, however delirious and febrile with a temperature of 101.2 F. Her pulse rate was 112 beats/minute, regular with a normal rhythm, respiratory rate was 22 cycles/minute and blood pressure was 88/60 mmHg. The rest of the physical examination was otherwise unremarkable. Though she was lethargic and disoriented, there were no obvious focal neurological deficits.

Laboratory investigation revealed elevated White Blood Count (WBC): 24.4 k/mL, serum Creatine Phosphokinase (CPK): 8,336 u/L, creatinine: 5.4 mg/dl (baseline creatinine: 0.8 mg/dl) with creatinine clearance: 22 mL/min, lactic acid: 4.9 mmol/L and troponin: 0.10 ng/mL. Serum sodium was slightly low; 132 mmol/L while other electrolytes were within normal limits. Her Arterial blood gases were notable for hypoxemia with PaO₂ of 50 mmHg, Electrocardiogram showed sinus tachycardia without evidence of ischemia. Chest X-ray revealed right mid-lung opacities.

A bedside Transthoracic Echocardiogram (TTE) showed low ejection fraction of 35% to 40% without valve abnormalities or vegetation. She had a retroperitoneal ultrasound which demonstrated normal kidneys. Urine analysis was notable for 3+ hemoglobin with scanty red blood cells. She was diagnosed with sepsis presumably from pneumonia, complicated by multi-organ dysfunction. She was admitted to the medical Intensive Care Unit (ICU) and initiated On Intravenous (IV) fluids and empiric antibiotics for CAP (IV Ceftriaxone 2 g daily and Azithromycin 500 mg daily). On the third day of ICU care, her urine resulted positive for *Legionella pneumophila* Group 1 antigen. Blood and stool microbiological studies were however normal. By hospital day 5, her fever had completely resolved and neurological status returned to normal. Also, serum CPK and creatinine levels had improved from 8,336 u/L to 1,882 u/L and 5.4 mg/dl to 2.1 mg/dL (creatinine clearance: 39 mL/min) respectively.

Her troponin level gradually trended down to normal levels with clinical improvement. She was discharged on oral Azithromycin to complete 10 days course treatment (In-hospital IV therapy inclusive). At post discharge follow up four weeks later, she was doing well clinically and she had a repeat TTE which showed normalized ejection fraction of 60% to 65% without evidence of diastolic dysfunction. She also had a cardiac stress test which did not reveal an area of ischemia.

Table 1: Frequency of symptoms commonly seen in Legionella infection.

Symptoms	Frequency (%)
Cough	41%-92%
Fever >102 F	88%-90%
Chills	42%-77%
Dyspnea	20%-62%
Headache	40%-48%
Myalgia/Arthralgia	20%-40%
Diarrhea	21%-50%
Nausea/Vomiting	8%-49%
Neurologic abnormalities	4%-53%
Chest pain	13%-35%

Discussion

Legionnaires' disease is a respiratory infection caused by *Legionella* bacteria and a common cause of atypical pneumonia [1,4]. It is transmitted to humans primarily through inhalation of colonized aerosols or droplets [1]. Risk factors for legionnaire's disease include advanced age, immunosuppression, and chronic lung disease [8]. It predominantly presents with respiratory symptoms, however as seen in this case and few others in the literature it can present with extra-pulmonary symptoms and manifestations [3,9,10] (Table 1).

Notable, in this case, is the finding of systolic heart failure diagnosed with TTE. Our patient does not have a documented personal or family history of coronary artery disease or heart failure. She had not experienced angina or heart failure symptoms prior to her hospital admission. Though she is hypertensive, it was well controlled with blood pressure medications and her systolic heart failure resolved with the resolution of *Legionella* infection which suggests a causal-effect relationship.

Cases of myocarditis have been described as a rare complication of severe *Legionella* infection from infiltration of inflammatory cells [11-14]. Though our patient did not have an endomyocardial biopsy done, there was no myocardial wall thickening or wall motion abnormalities on TTE which made myocarditis unlikely. Similar to this case, Suzuki et al. [14] also reported a case of transient left ventricular failure in a patient with *legionella* infection and negative biopsy. The association between CAP and myocardial dysfunction has been studied extensively; however, the precise etiology remains unclear. It has been postulated that respiratory infections lead to the production of cytokines, endothelin-1, prostanoids, and nitric oxide which increase myocardial oxygen demand, reduce myocardial oxygen delivery and ultimately depress myocardial contractility [12-14].

Another possible etiology of myocardial dysfunction is the atherogenesis, atherosclerosis and consequent cardiac vasoconstriction from *Legionella* infection through inflammatory and immunological mechanisms [15,16]. Respiratory infections like influenza virus, *Chlamydia pneumoniae*, and *Mycoplasma pneumoniae* have been directly associated with cerebrovascular disease and the presence of *Chlamydia pneumoniae* has also been demonstrated in atherosclerotic plaques [17,18]. *Legionella pneumophila* is a gram-negative, intracellular bacterium like *Chlamydia pneumoniae* with similar microbiological, clinical and neurological features that may also exert a chronic immunological response. More research should

be done to study the possible direct damage to coronary vessels by *Legionella* pathogen. Additionally, studies have demonstrated that cytokine synergy significantly contributes to myocardial dysfunction in sepsis [19,20]. Thus, it is quite possible that extensive cytokine production with *Legionella* infection is partly responsible for the systolic heart failure in this case [21].

We attribute our patient's elevated troponin to myocyte necrosis from reduced myocardial oxygen supply, hypotension and exertional demand on the heart from CAP sepsis and not necessarily Acute Coronary Syndrome (ACS) due to the absence of chest pain. Furthermore, the troponin levels trended down with improvement in the patient's clinical condition. Nevertheless, the absence of chest pain does not preclude AMI and sometimes, it could be difficult to differentiate acute coronary syndrome from infection as a cause of myocardial dysfunction.

Conclusion

Cardiac complications of *Legionella* infection are uncommon. *Legionella pneumophila* should be considered as a possible etiology of systolic heart failure in patients with CAP and sepsis.

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