Severe Legionnaires’ disease with false negative urine antigen test complicated by myocarditis and cardiac arrest

Hind El Soufi, Yahya El Soufi, Andrew Mekaiel, Mohammad Aneeb, Farshad Bagheri

ABSTRACT

Introduction: Legionnaires’ disease is defined as severe pneumonia with multi-organ failure caused by Legionella species. Urine antigen test is the most common method used for its diagnosis with a sensitivity reaching 80%. False negative test can be suspected when urine samples used are diluted, when they are obtained later than seven days after the onset of pneumonia, when infection is caused by Legionella non-serogroup 1, and when samples contain excessive antigens relative to antibodies, which prevents antibody-to-antigen crosslinking, phenomenon known as post-zone effect. We report a case of pneumonia with multi-organ damage caused by Legionella pneumophila with initial false negative urine antigen test complicated by myocarditis, cardiomyopathy, and cardiac arrest.

Case Report: A 34-year-old healthy male with recent visit to the Caribbean islands presented with fever, cough, and alteration of mental status. Chest X ray showed consolidation in his right upper lung lobe. Legionella urine antigen test was initially negative. High suspicion for Legionnaire’s disease required repeating the test which subsequently came back positive.

Conclusion: High suspicion for the infection prompts repeating or even using a combination of tests to increase sensitivity and to detect all possible species causing the infection.

Keywords: Legionnaires’ disease, Myocarditis, Urine antigen

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INTRODUCTION

Severe pneumonia with multi-organ failure caused by Legionella pneumophila, an aerobic, gram-negative bacillus, is usually known as Legionnaires’ disease (LD) [1]. In the United States, it accounts for 1.4 to 1.8 cases per 100,000 persons [2]. Legionella infection should be considered in any patient presenting with community acquired or nosocomial pneumonia. The early recognition and treatment are crucial to improve outcome and decrease mortality [3]. Many testing methods are available for detection of Legionella including the common urine antigen test; however, its sensitivity ranges from 70% to 80% when infection is caused by Legionella serotype 1 [4]. We report a rare case of severe Legionella pneumonia infection complicated by multi-organ damage and subsequent cardiac arrest in a young healthy man with initial false negative urine antigen test.

CASE REPORT

A 34-year-old man was brought to the emergency department by his family with complaints of fever, chills, diarrhea, nonproductive cough, and progressive
confusion that started 10 days after his arrival from Saint Lucia, one of the Caribbean’s islands. During his stay, the patient used many hot tubs and swam in public pools. The patient was a non-smoker, had no previous medical or surgical history.

Upon presentation, his blood pressure was 145/69 mmHg, heart rate was 118/min, respiratory rate was 24/min with an oxygen saturation of 95% on room air, and a temperature of 105 F. On physical examination, the patient was oriented only to self. Crackles were heard on auscultation to the right upper lung field with dullness on percussion. Laboratory testing showed mild leukocytosis (WBC 11.7 k/uL), thrombocytopenia (platelets 101 k/uL), hyponatremia (Na 126 mEq/L), rhabdomyolysis [creatinine phosphokinase (CPK) 96,000 U/L], coagulopathy [international normalized ratio (INR) 1.7], transaminitis [alanine aminotransferase (ALT) 168 U/L, aspartate aminotransferase (AST) 715 U/L] with a procalcitonin level of 4.06 ng/mL and creatinine of 1.2 mg/dL. Computed tomography (CT) head was negative for any abnormalities. Chest radiograph and confirmatory CT chest showed consolidation in the right upper lobe. Blood, urine and sputum cultures were sent. Given his hemodynamic instability requiring vasopressors and critical condition requiring Intensive Care Unit admission, the patient was started on broad spectrum antibiotics including Vancomycin, Meropenem, and Levofloxacin along with aggressive intravenous (IV) hydration. Quantiferon-TB Gold Plus test was negative and initial immunochromatographic assay for *Legionella* antigen in urine was negative as well.

Due to high suspicion for *Legionella* infection given the typical clinical presentation, imaging findings and the history of recent use of pools and hot tubs, urine antigen test was re-sent the next day which eventually came back positive confirming *Legionella* infection. Antibiotics were then de-escalated to Levofloxacin. However, due to severe sepsis and continuously worsening respiratory status, Rifampicin was added to his antibiotic regimen. Follow-up lab tests showed preserved kidney function, positive troponin level of 0.123 ng/mL, and worsening CPK of 130,000 U/L. Maintenance fluids were increased and a repeat chest radiograph showed new bilateral pulmonary congestion. Echocardiogram was then done and showed unexplained severely reduced left ventricular function with an estimated ejection fraction of 20% and diffuse wall hypokinesia. Decision was made to continue hydration at a very low rate, start the patient on furosemide and spironolactone, and low dose lisinopril to continue hydration. QuantiFERON-TB Gold Plus test was negative and initial immunochromatographic assay for *Legionella* antigen in urine was negative as well.

DISCUSSION

*Legionella pneumophila* can spread in small droplets from contaminated water systems that people can breathe in [5]. Legionellosis can manifest as mild flu-like syndrome usually known as Pontiac fever or as severe pneumonia with multi-organ failure known as Legionnaires’ disease [6]. In the United States, hospitalization due to *Legionella* infection is estimated to be 8,000 to 18,000 per year with a mortality rate reaching 30% [2, 7]. Clinical manifestations are usually similar to pneumonia caused by other organisms. However, associated gastrointestinal and neurological symptoms, elevated liver enzymes and hyponatremia, can increase the suspicion index for Legionellosis [8]. Diagnosis methods include urine *Legionella* antigen testing, polymerase chain reaction (PCR), or culture of specimens and direct fluorescent antibody test [9]. The urine antigen test is usually the preferred initial diagnostic tool for Legionnaires disease. It is rapid, relatively inexpensive and practical since urine sample is usually easy to get [10]. However, this test can only detect *Legionella pneumophila* serogroup 1 which by itself accounts for more than 80% of Legionnaires’ disease worldwide [9]. False negative urine antigen test for *Legionella* should therefore be suspected in case of infection by *Legionella pneumophila* non-serogroup 1, in case when the sample is not concentrated by ultrafiltration, or when testing is later than seven days post-infection [9]. False negative urine test can also be caused by excessive antigens in samples, preventing antibody-to-antigen crosslinking which is necessary for immunochromatographic detection. This effect is usually referred to as the post-zone phenomenon [11]. When such phenomenon is suspected, serial sample dilutions must be performed in order to improve test sensitivity [11]. Severe infection can lead to end organ failure including rhabdomyolysis, kidney failure, hepatitis, and even myocarditis which can lead to heart failure and arrhythmias and subsequently cardiac arrest as occurred with our patient [12]. The diagnosis of myocarditis was made based on the 2013 European Society of Cardiology position statement criteria for “clinically suspected myocarditis” requiring one clinical presentations of myocarditis including: acute chest pain, new onset dyspnea, unexplained arrhythmia, unexplained cardiogenic shock; and one diagnostic criterion including electrocardiogram (ECG) changes, elevated cardiac enzymes, functional and structural abnormalities on cardiac imaging, tissue characterization by cardiac magnetic resonance imaging [13].

CONCLUSION

It is always important to have a high index of suspicion for *Legionella pneumonia* when the clinical tableau is in favor, even if the initial urine antigen is falsely negative.
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REFERENCES


Author Contributions

Hind El Soufi – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Yahya El Soufi – Conception of the work, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Andrew Mekaiel – Conception of the work, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Mohammad Aneeb – Conception of the work, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Farshad Bagheri – Conception of the work, Drafting the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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Conflict of Interest

Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.

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