

A Case Report of Severe Legionnaires' Disease in Tehran, Iran

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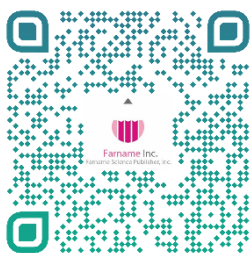
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Introduction

Legionella spp. is considered to play a key role in hospital-acquired (HA) and community-acquired pneumonia (CAP), especially in high-risk patients such as people over 50 years with immune system disorders or chronic lung diseases (1). Among *Legionella* species, *L. pneumophila* accounts for 3-15% of all CAP cases and is considered as the primary leading cause of Legionnaires' disease (LD), which is an acute and atypical type of pneumonia (2). It has been reported that one in ten patients with LD dies due to the disease complications (3). Additionally, the mortality rate of patients developed LD during their stay in medical centers seems to be 25% (4). This discrepancy could be due to the similarity of the signs and symptoms of this disease and other respiratory ones, uncommon testing methods for this pathogen, and empiric antibiotic therapy for *Legionella* infections (2). Moreover, its mortality rate has been reported to be more than 60%

ABSTRACT

Legionella pneumophila is a thin, aerobic, Gram-negative, pathogenic bacillus and the leading cause of Legionnaires' disease (LD) in human, especially those with high risk conditions including immune system disorders or chronic lung diseases. The mortality rate of LD has been reported to be 60% or higher in inappropriately treated cases. Investigating the prevalence of *L. pneumophila* and identifying contaminated sources in hospital settings are essential steps that should be taken to control the disease and evaluate the efficacy of interventional strategies. Currently, the culture method is considered as the "gold standard" for detection of *L. pneumophila* and LD diagnosis. In this case report of severe LD in Iran, we studied a 60-year-old male patient with underlying chronic obstructive pulmonary disease (COPD). We also presented the clinical and pathophysiological features of LD as well as its diagnostic and therapeutic methods. The importance of early diagnosis of *L. pneumophila* infection in patients with COPD is also highlighted.

Keywords: *Legionella pneumophila*, Chronic obstructive pulmonary disease, Legionnaires' disease, Pneumonia, Iran

in inappropriately-treated patients, which could be reduced to 10–20% by proper treatment (5).

Case Report

In December 2017, a 60-year-old male patient with a history of COPD (chronic obstructive pulmonary disease) referred to the emergency section of a 310-bed hospital (Tehran, Iran) complaining about high fever, dyspnea, productive cough and fatigue, which lasted for three days. His vital signs at admission were as follows: body temperature: 38.4 °C, pulse rate: 120 beats/minute, respiration rate: 26 breaths/minute, and blood pressure: 120/73 mmHg. Wheezing and scattered bilateral crackles, especially at the base of the right lung, were identified through physical examination. The pressure of oxygen and carbon

dioxide in his blood was assessed using arterial-blood gas test, the results of which revealed hypoxia and excessive alkalinity of the respiratory system (alkalosis) due to hyperventilation (PO₂: 46 mmHg, PCO₂: 27 mmHg, pH: 7.49, and HCO₃: 21.3 mmol/L). Initial chest radiograph showed an abnormal edematous appearance of his chest, which was compatible with adult respiratory distress syndrome (ARDS) (Figure 1).

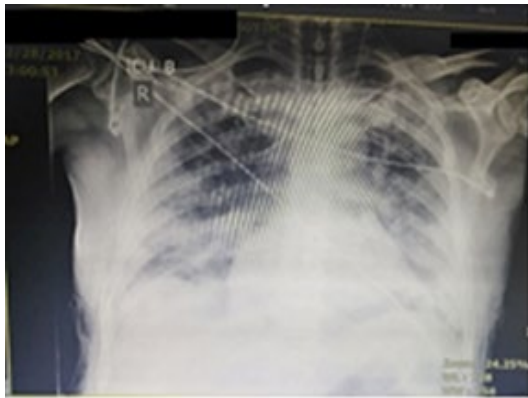


Figure 1. Chest X-ray at admission showing the features of adult respiratory distress syndrome (ARDS).

The patient was transferred to the intensive care unit (ICU) and was provided with primary care to avoid acute respiratory failure by endotracheal intubation. The results of his blood test were as follows: 134 mmol/L for sodium, 4.7 mmol/L for potassium, 106 mmol/L for chloride, 8.1 mmol/L (20 mg/dL) for BUN (blood urea nitrogen), and 118 μmol/L (1.3 mg/dL) for creatinine. The results of laboratory tests were remarkable for white blood cell count (WBC) (12.5/cumm), polymorphonuclear leukocytes (PMN) (73.9%), procalcitonin (PCT) (0.6 μg/L-1, with a normal range of >0.05 μg/L-1), and C-reactive protein (CRP) (118 mg/L-1, with a normal range of >5 mg/L-1). However, Influenza A (H1N1) RT-PCR, bronchoalveolar lavage (BAL) cytology, and Bacille de Koch (BK) smear of respiratory secretions were negative. Respiratory secretions were also tested for presence of *Mycoplasma pneumoniae* by culturing on PPLO (pleuropneumonia-like organism) broth and agar at Pathobiology Department of Tehran University of Medical Sciences and there was no growth of this pathogen. Molecular testing using 16S rRNA and *pl* genes (6) was also negative for *M. pneumoniae*. Patient underwent empiric therapy using intravenous injection of piperacillin/tazobactam, vancomycin, imipenem, metronidazole, and Oseltamivir for five days, significantly deteriorated the clinical symptoms.

By cultivation of the specimens on BCYE agar (buffered charcoal yeast extract), *L. pneumophila* colonies appeared after four days of incubation (Fig. 2) and were confirmed by carbol-fuchsin Gram-staining (Fig. 3).



Figure 2. *L. pneumophila* colonies on BCYE agar.

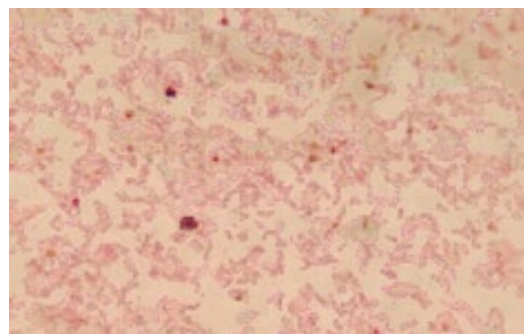


Figure 3. Gram-negative *L. pneumophila* bacilli

Rapid detection of *L. pneumophila* was performed via polymerase chain reaction (PCR) through partial sequencing of the *mip* gene (7). Identification of *L. pneumophila* in respiratory secretions caused antibiotic therapy to be changed and continued with levofloxacin. The patient was extubated four days after the start of intravenous injection of levofloxacin. After 30 days of intensive care, the follow-up appointment was satisfactory according to another chest radiograph, and he was discharged from the hospital with a prescription of oral clarithromycin for 10 days and other supplementary medications.

Discussion

Legionnaires' disease is a severe form of pneumonia. Several LD outbreaks have been reported so far. The first global outbreak of HAP due to LD was reported in Philadelphia in 1976. Relatively late detection of CA diseases seems to lead to delays in therapeutic interventions and proper antibiotic treatment. Improper antibiotic therapy could cause complications and increase mortality rate (as high as 80%) in patients with legionellosis, especially in immunocompromised ones (8). Currently, the culture method is considered as the "gold standard" for detecting Legionella and diagnosing Legionnaires' disease. Suitable and acceptable samples for culture are those collected from the lower airways, including sputum, bronchoalveolar lavage (BAL) fluid, pleural fluid, and bronchial aspirates (Fig. 2). Pulmonary tissue specimens and biopsy samples are also suitable for culturing. Samples

less commonly used for culture are those collected from outside the lungs, such as blood, joint fluids, and soft tissues (9) since Legionella infection is rarely reported in these areas. These areas should be evaluated by culture method only when other etiologies are rejected. Generally, of all the potentially suitable specimens, the most frequently used samples for culture are those collected from sputum; however, most LD patients produce no or little sputum that is not sufficient for culture analysis.

The sensitivity of culture method for detection of Legionella strains in clinical samples varies from <10% to 80%, and isolates recovery depends on several factors, including the type of specimen and the specialized skills and experience of lab staff (10).

Studies have shown that in Iran, *L. pneumophila* was more prevalent during 2009–2016 (9.2%) compared to 2000–2008 (0.7%) (8).

This study was conducted on a case of atypical pneumonia. Recent studies have predicted that COPD would be the seventh most prevalent disease as well as the fourth most common cause of death in humans by 2030 (11). A previous study showed that in most patients with *L. pneumophila* CAP, chest radiographies (X-rays) were abnormal (12). However, distinct radiographic patterns, especially with patchy, pneumonic, infiltrate, or lobar consolidation and cavitation, could not confirm or reject LD in patients (13). Conversely, there is evidence showing that Legionella infections further exacerbate and worsen the disease in COPD patients compared to other respiratory pathogens (14). This could make it difficult for physicians to identify the infectious agent and provide appropriate treatment. Considering the fact that inappropriate treatment of LD could lead to 60–70% mortality (5), prompt diagnosis of LD as well as the initiation of effective therapy could reduce patient mortality. Information about LD in Iran is insufficient.

This study identified and reported a severe case of LD in a COPD patient in Iran and described its successful treatment with antibiotic therapy. The findings of this study suggest that physicians should pay more attention to atypical pathogens, such as *Legionella spp.*, in patients with COPD, presenting an unusual form of pneumonia.

Conclusion

None.

Acknowledgments

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Conflict of Interest

The authors have no conflict of interest to disclose.

Ethics approval and consent to participate

This study was reviewed and approved by Tehran University of Medical Sciences ethics committee (Grant no.: 34054).

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