J Microbiol Immunol Infect 2010;43(3):215–221

Contents lists available at ScienceDirect

Journal of Microbiology, Immunology and Infection

Journal homepage: http://www.e-jmii.com

Original Article

Comparisons of Clinical Characters in Patients with Pneumococcal and *Legionella* Pneumonia

Yuan-Pin Hung[a,e], Chi-Jung Wu[a,c], Chiung-Zuei Chen[b], Hsin-Chun Lee[a,c,d], Chia-Ming Chang[a,c], Nan-Yao Lee[a,c], Chih-Huan Chung[a], Wen-Chien Ko[a,c,d]*

[a]Division of Infectious Diseases, Department of Internal Medicine, National Cheng Kung University Hospital, Tainan, Taiwan.

[b]Division of Pneumology, Department of Internal Medicine, National Cheng Kung University Hospital, Tainan, Taiwan.

[c]Center for Infection Control, National Cheng Kung University Hospital, Tainan, Taiwan.

[d]Department of Medicine, National Cheng Kung University Medical College, Tainan, Taiwan.

[e]Graduate Institute of Clinical Medicine, National Cheng Kung University Medical College, Tainan, Taiwan.

BACKGROUND/PURPOSE: The etiology of pneumonia is usually unknown, but the availability of urinary pneumococcal and *Legionella* antigen tests can improve the diagnostic yield. Our aim was to provide clinical clues to help clinicians perform the appropriate urinary antigen tests.

METHODS: A retrospective study of patients admitted to the National Cheng Kung University Hospital between July 2006 and June 2008 was conducted. Patients aged over 18 years presenting with clinical symptoms and signs, radiological findings compatible with pneumonia, and a positive pneumococcal or *Legionella pneumophila* urinary antigen test, were included. Medical records were reviewed for data collection.

RESULTS: Overall, 55 adults with pneumonia, including 42 with pneumococcal pneumonia (PP) and 13 with *Legionella* pneumonia (LP), were enrolled. On admission, patients with PP tended to be older (73.5 years *vs.* 59.1 years; $p=0.001$), had lower body weights (52.0 kg *vs.* 69.7 kg; $p<0.001$), more frequent respiratory symptoms (59.5% *vs.* 0%; $p<0.001$), and lower systolic (123.0 mmHg *vs.* 141.0 mmHg; $p=0.004$) and diastolic blood pressures (68.3 mmHg *vs.* 81.7 mmHg; $p=0.008$), compared with patients with LP. However, those with LP had higher body temperatures (39.0 °C *vs.* 37.5 °C; $p<0.001$), a higher incidence of relative bradycardia (45.5% *vs.* 0%; $p<0.001$), diarrhea (15.4% *vs.* 0%; $p=0.053$), and lower platelet counts ($178.5\times10^3/mm^3$ *vs.* $233.7\times10^3/mm^3$; $p=0.026$). Radiological findings showed that the major abnormality, lobar consolidation, was indistinguishable between LP and PP. The percentage of patients requiring

*Corresponding author. Department of Internal Medicine, National Cheng Kung University Hospital, 138 Sheng Li Road, Tainan 70403, Taiwan.

E-mail: winston@mail.ncku.edu.tw

Article History:
Received: Dec 31, 2008
Revised: Mar 27, 2009
Accepted: Jul 23, 2009

intensive care (35.7% *vs.* 38.5%) or ventilator support (31% *vs.* 23.1%) and in-hospital crude mortality rates (9.5% *vs.* 7.7%) was similar in both groups.

CONCLUSION: Some clinical and laboratory characteristics may be regarded as important clues indicating the need for an appropriate urinary antigen test in patients with pneumonia.

KEYWORDS: *Streptococcus pneumoniae, Legionella pneumophila*, urinary antigen tests, differential diagnosis

Introduction

Streptococcus pneumoniae and *Legionella pneumophila* are among the most common pathogens causing pneumonia, whether it is community-acquired pneumonia (CAP) or hospital-acquired pneumonia (HAP). *S. pneumoniae* is regarded as the cause in about one-third of patients with CAP,[1–3] and is an important cause of early-onset HAP with a definitive diagnosis.[4]

L. pneumophila is the leading cause of CAP in some countries,[2] and hospital-acquired *Legionella* pneumonia has a fatality rate of up to 28%.[5] Moreover, *S. pneumoniae* and *Legionella* are two major pathogens causing severe cases of CAP that require admission to intensive care units.[1] Therefore, it is important to distinguish the clinical characteristics and radiographic findings of pneumonia caused by these two pathogens.[6–8]

In order to improve the etiological diagnosis of pneumonia, a non-invasive diagnostic tool, the detection of antigens in urine, had been developed and is widely utilized.[1,9] The use of urinary antigen tests (UAT) to diagnose *S. pneumoniae* or *Legionella* infections has a high sensitivity (94–100%), a high specificity (95–100%), and is time-saving.[9] However, the urinary *Legionella* antigen test can detect only *L. pneumophila* serogroup 1. Using both UAT in patients with pneumonia has increased the diagnostic yield from 36.4% to 41.1% with non-concentrated urine samples, and to 49.5% with concentrated urine samples.[1] In some studies, the UAT was thought to be able to provide rapid detection of *S. pneumoniae* or *L. pneumophila* infections.[1,10,11] Thus in the Infectious Disease Society of America/American Thoracic Society guidelines, patients with severe CAP should have some etiological assays, including blood and sputum cultures, and UAT for *S. pneumoniae* or *L. pneumophila*.[12] However, the routine use of both types of UAT in every patient with pneumonia may be not cost-effective. The present study is intended to provide clinical, laboratory or radiographic characteristics that distinguish pneumococcal pneumonia (PP) from *Legionella* pneumonia (LP), and to help clinicians to choose the appropriate UAT.

Methods

A retrospective study of patients admitted between July 2006 and June 2008 at the National Cheng Kung University Hospital, a medical center in Southern Taiwan, was conducted. Those aged over 18 years, presenting with symptoms and signs of lower respiratory tract infections, new infiltrations consistent with pneumonia on chest films, and positive urinary *S. pneumoniae* or *L. pneumophila* antigen tests (NOW, Binax, Scarborough, Maine, USA) were enrolled. For each patient, UAT for both pathogens were done. However, patients with recent *S. pneumoniae* or *L. pneumophila* infections in the month prior to admission, or hospitalized or followed up at the hospital for less than 2 days, were excluded from the study. Medical records were reviewed for demographic information, underlying diseases, microbiological results, laboratory data, clinical course and outcome.

A patient was regarded as having HAP, if he had been hospitalized within the previous 10 days, or pneumonia developed at least 72 hours after admission.[4] Otherwise, a patient was diagnosed as having CAP. A patient was considered to be a smoker if he smoked every day and had not tried to quit during the past 5 years, and an alcoholic if he consumed more than 80 g of alcohol per day,[13] according to chart records. End stage renal disease (ESRD) was defined as an estimated creatinine clearance rate of < 15 mL/min/1.73 m^2, or receiving hemodialysis or peritoneal dialysis. Chronic obstructive pulmonary disease (COPD) and a

previous history of pulmonary tuberculosis were grouped together as chronic pulmonary disease.

Relative bradycardia was defined as an increase in heart rate of less than 10 beats/min/1°C increase in temperature, with the pulse rate ranging from 38.9°C to 41.1°C.[14] Chest X-ray films were revealed by a pulmonologist who was unaware of the UAT results. The radiological findings were classified as lobar consolidation, interstitial infiltrations (reticular, reticulonodular, or nodular patterns), pleural effusions, pneumothorax, or increased infiltration without any the above described characteristics.

Statistical analysis was performed by using SPSS version 12.0 (SPSS Inc., Chicago, IL, USA). Continuous data were presented as mean ± standard deviations. The χ^2 test or Fisher's exact test were used for comparing categorical variables, and the Student's *t* test for continuous variables. A two-tailed *p* value of less than 0.05 was considered to be statistically significant. The logistic regression model was used to test the variables with $p \leq 0.1$ in the χ^2 test, Fisher's exact test or Student's *t* test.

Results

During the study period, 787 urinary samples underwent the *Legionella* antigen test and 429 the pneumococcal antigen test. Thirteen (1.65%) of the urinary *Legionella* antigen tests and 122 (28.44%) of the pneumococcal antigen tests were positive. The 122 urine samples containing pneumococcal antigens were obtained from 120 patients, 78 (65.0%) of whom were children. Therefore, 55 adults with pneumonia, including 42 adults with urinary pneumococcal antigen and pneumonia diagnosed as PP, and 13 with urinary *L. pneumophila* serotype 1 antigen and pneumonia (LP), were included. Their demographic characteristics and underlying illnesses are shown in Table 1. Patients with PP were older (73.5 years *vs.* 59.1 years, $p=0.001$) and had lower body weights (52.0 kg *vs.* 69.7 kg, $p<0.001$) than patients with LP. No difference was noted in terms of gender or underlying conditions. PP was more often community-acquired than LP (95.2% *vs.* 76.9%, $p=0.080$), though this was not statically significant. LP tended to prevail in patients with alcoholism (15.4% *vs.* 4.8%, $p=0.234$) and ESRD

Table 1. Demographic characteristics and underlying illness of patients with pneumococcal and *Legionella* pneumonia[a]

	Pneumococcal pneumonia ($n=42$)	*Legionella* pneumonia ($n=13$)	*p*
Mean age (yr)	73.5 ± 14.1	59.1 ± 11.5	0.001
Body weight (kg)	52.0 ± 11.4	69.7 ± 15.7	< 0.001
Sex, male	30 (71.4)	10 (76.9)	1.000
Community-acquired pneumonia	40 (95.2)	10 (76.9)	0.080
Underlying illness	31 (73.8)	8 (61.5)	0.489
Hypertension	16 (38.1)	5 (38.5)	1.000
Diabetes mellitus	12 (28.6)	4 (30.8)	1.000
Chronic pulmonary disease	10 (23.8)	1 (7.7)	0.266
Chronic obstructive pulmonary disease	6 (14.3)	1 (7.7)	1.000
Previous pulmonary tuberculosis	6 (14.3)	0 (0)	0.317
Malignancy	8 (19.0)	2 (15.4)	1.000
Smoking	6 (14.3)	2 (15.4)	1.000
Stroke	6 (14.3)	1 (7.7)	1.000
Bed-ridden status	6 (14.3)	0 (0)	0.317
Congestive heart failure	3 (7.1)	0 (0)	1.000
Alcoholism	2 (4.8)	2 (15.4)	0.234
End-stage renal disease	2 (4.8)	3 (23.1)	0.080
Coronary artery disease	1 (2.4)	1 (7.7)	0.420

[a]Data presented as mean ± standard deviations or *n* (%).

Table 2. Clinical presentations of patients with pneumococcal and *Legionella* pneumonia

Characteristics	Pneumococcal pneumonia ($n=42$)	*Legionella* pneumonia ($n=13$)	p
Symptoms			
Fever	35 (83.3)	13 (100)	0.179
Cough	30 (71.4)	7 (53.8)	0.314
Sputum production	25 (59.5)	0 (0)	<0.001
Dyspnea	25 (59.5)	6 (46.2)	0.525
Pleuritic chest pain	5 (11.9)	0 (0)	0.324
GI discomfort[b]	5 (11.9)	3 (23.1)	0.376
Chills	4 (9.5)	1 (7.7)	1.000
Confusion	4 (9.5)	0 (0)	0.562
Sore throat	2 (4.8)	1 (7.7)	0.562
Headache	1 (2.4)	0 (0)	1.000
Rhinorrhea	1 (2.3)	0 (0)	1.000
Signs			
Body temperature (°C)	37.5±0.9	39.0±0.7	<0.001
Pulse rate (/min)	102.9±17.0	110.5±13.9	0.183
Relative bradycardia	0 (0)	5 (45.5)	<0.001
Respiratory rate (/min)	23.1±6.3	21.4±2.2	0.156
Systolic BP (mmHg)	123.0±17.2	141.0±18.1	0.004
Diastolic BP (mmHg)	68.3±14.5	81.7±13.8	0.008
Abnormal breathing sounds	37 (88.1)	9 (69.2)	0.192
Crackles	32 (76.2)	7 (53.8)	0.165
Decreased breathing sounds	6 (14.3)	0 (0)	0.317
Wheezing	4 (9.5)	3 (23.1)	0.337
Clinical outcome			
Hospitalization (d)	12.2±6.8	23.9±21.0	0.071
Fever (d)	3.4±3.4	3.6±2.1	0.224
ICU stay	15 (35.7)	5 (38.5)	0.553
Ventilator support	13 (31.0)	3 (23.1)	0.734
Crude mortality rate	4 (9.5)	1 (7.7)	1.000

[a]Data presented as mean±standard deviations or *n* (%); [b]GI discomfort includes nausea, vomiting, diarrhea, and abdominal pain. GI=Gastrointestinal; BP=blood pressure; ICU=intensive care unit.

(23.1% *vs.* 4.8%, $p=0.080$), and PP in those with chronic pulmonary diseases (28.6% *vs.* 7.7%, $p=0.266$).

The clinical symptoms and signs in patients with pneumonia are shown in Table 2. Patients with PP often had increased sputum production (59.5% *vs.* 0%, $p<0.001$), and those with LP were more likely to have diarrhea (15.4% *vs.* 0%, $p=0.053$). As far as clinical signs were concerned, patients with LP had higher body temperatures (39.0°C *vs.* 37.5°C, $p<0.001$), and were more likely to have relative bradycardia (45.5% *vs.* 0%, $p<0.001$). In contrast, patients with PP had lower systolic (123.0 mmHg *vs.* 141.0 mmHg, $p=0.004$) and diastolic (68.3 mmHg *vs.* 81.7 mmHg, $p=0.008$) blood pressures. Therefore, our logistic regression model included age, body weight and underlying diseases. Only lower body weight was independently associated with PP (adjusted odds ratio=1.12; 95% confidence interval=1.01–1.23; $p=0.024$).

The laboratory and radiographic findings of the two groups are presented in Table 3. There was no significant difference between patients with LP and PP in terms of leukocyte counts, hemoglobin, serum aminotransferases, sodium, and creatinine levels. However, patients with LP had lower platelet counts (178.5×10^9/L *vs.* 233.7×10^9/L,

Table 3. Laboratory and radiographic findings of patients with pneumococcal and *Legionella* pneumonia[a]

Characteristics	Pneumococcal pneumonia ($n=42$)	*Legionella* pneumonia ($n=13$)	p
Laboratory findings			
White blood count ($\times 10^9$/L)	14.0±7.8	11.6±2.9	0.108
Neutrophils (%)	80.6±16.3	83.8±15.3	0.532
Hemoglobin (g/dL)	13.8±14.9	11.9±2.4	0.644
Platelet ($\times 10^9$/L)	233.7±111.9	178.5±58.9	0.026
C-reactive protein (mg/L) ($n=54$)	182.9±104.6	238.6±174.5	0.311
Creatine phosphokinase (U/L) ($n=19$)	108.4±108.3	301.7±338.5	0.274
Aspartate aminotransferase (U/L)	75.7±101.7	67.2±53.9	0.775
Alanine aminotransferase (U/L)	48.7±98.4	69.3±77.2	0.492
Serum sodium (mmol/L)	134.1±9.2	136.1±3.7	0.270
Serum potassium (mmol/L)	3.9±0.9	3.8±0.7	0.584
Creatinine (mg/dL)	1.5±1.0	2.6±2.8	0.214
Radiographic findings[b]			
Lobar consolidation	31 (73.8)	11 (91.7)	0.420
Interstitial infiltrations	14 (35.0)	1 (8.3)	0.143
Reticulonodular pattern	10 (25.0)	1 (8.3)	0.421
Reticular pattern	2 (5.0)	0 (0)	1.000
Nodular pattern	2 (5.0)	0 (0)	1.000
Pleural effusion	6 (15.0)	0 (0)	0.316
Increased infiltration	2 (4.8)	1 (7.7)	0.562
Pneumothorax	1 (2.5)	0 (0)	1.000

[a]Data presented as mean±standard deviation or *n* (%); [b]A patient may have more than one radiological finding on the chest film.

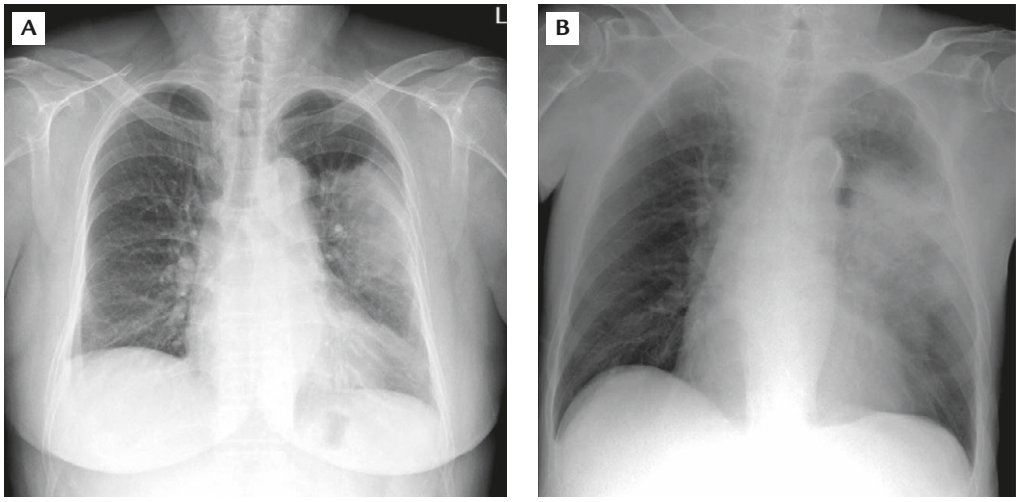

Figure. Typical lobar consolidation in chest X-rays. (A) A 62-year-old female with diabetes mellitus and urinary pneumococcal antigen. (B) A 70-year-old male with chronic obstructive pulmonary disease and urinary *Legionella* antigen.

$p=0.026$). The major radiographic finding on chest films in patients with either PP or LP was lobar consolidation; found in 77.5% of patients with PP and 91.7% with LP. Chest films showing a typical lobar consolidation pattern are shown in the Figure. However, the degree of lobar consolidation was indistinguishable between PP and LP.

When a clinical diagnosis of PP was established, 22 (52.4%) patients were treated with β-lactam agents (mainly

amoxicillin/clavulanate or ampicillin/sulbactam), 18 (42.6%) with penicillin plus fluoroquinolone (moxifloxacin or levofloxacin), and two (4.8%) with fluoroquinolone. In contrast, antimicrobial therapy for LP was fluoroquinolone (moxifloxacin or levofloxacin) in nine patients (69.2%), a macrolide (azithromycin or roxithromycin) in one patient (7.7%), and sequential therapy in one patient (7.7%). Concerning the clinical outcomes of the two groups, there was no difference in fever duration, or in the need for intensive care unit care or ventilator support. Likewise, the crude mortality rate for patients with PP and LP were similar (9.5% and 7.7%, respectively). However, patients with LP tended to have a longer period of hospitalization compared with PP patients (23.9 days *vs.* 12.2 days, $p=0.071$).

Discussion

Though 1.65% of *Legionella* UAT and 28.76% pneumococcal UAT were positive, we did not perform UAT in every patient with pneumonia. These data should not be interpreted as representing the "incidence" of pneumonia. The present study shows that there are characteristic clinical and laboratory findings in patients with PP and LP, which may be helpful in distinguishing one form of the disease from the other. Patients with PP were often older and had a lower body weight. As for underlying diseases, LP tended to prevail in patients with alcoholism and ESRD, and PP in those with chronic pulmonary disease. It has been shown that CAP caused by *S. pneumoniae* is more often associated with patients that have underlying diseases, especially COPD and neoplasms, while CAP caused by *L. pneumophila* is more frequently seen in individuals with alcoholism.[15] However, another study concluded that CAP caused by *L. pneumophila* was often seen in male smokers with alcoholism, but fewer underlying diseases.[16] In some studies, *L. pneumophila* was more prevalent in older males with underlying disease.[17,18] In a German study, most hospitalized patients with LP were older men with underlying diseases, but outpatients were younger, had less co-morbidity, and no gender predominance[19] Therefore, these clinical experiences indicate that the diversity of host factors seen in patients with LP may be related to variable environmental exposure, or to variable degrees of susceptibility in different populations. Using a logistic regression model, we noted that patients with PP had a lower body weight. Though the cause of this finding is not evident, it is likely that those with PP were older and had certain underlying diseases.

PP seen in the patients in this study was associated with typical airway symptoms such as dyspnea, pleuritic chest pain, cough, excess sputum, and typical physical findings such as crackles or decreased breath sounds. In contrast, LP was often associated with high fever and less sputum production. Similar results have been observed in other studies.[15,16] Relative bradycardia is claimed to be an important characteristic of *Legionella* infection,[14,20] and was present in 46% of our 13 patients. The incidence of neurological symptoms, such as headache and confusion, were more often found in CAP cases caused by *L. pneumophila*,[15,16] but altered consciousness was not noted in our LP patients. This may be related to the younger age, fewer underlying diseases, and fewer hemodynamic changes in the LP patients.

Patients with pneumonia caused by *L. pneumophila* had more frequent thrombocytopenia, severe hyponatremia (serum sodium < 130 mmol/L), altered liver function and creatine phosphokinase elevation.[15,16,21,22] The patients with positive *L. pneumophila* UATs in our study had lower platelet counts, higher serum alanine aminotransferase, C-reactive protein, and creatine phosphokinase, but these were not significant. Hyponatremia was not noted in the patients with a positive *L. pneumophila* UAT, but this may be due to the relatively small number of patients studied. The culture-positive rate was 14.3% in patients with a positive *S. pneumoniae* UAT. This implies that using culture method for the diagnosis of *S. pneumoniae* or *L. pneumophila* infections is not reliable. Although the patients with a positive *S. pneumoniae* UAT seemed to present more frequently with interstitial patterns and pleural effusion on chest X-ray, there was no significant difference between the two groups. This result is compatible with previous studies.[6,7] Patients with LP generally had longer hospital stays. This may be attributed to the higher percentage of HAP in the LP group, which prolongs hospitalization.

There are several limitations to our study. The first is the relatively small number of patients. Some trends were noted in our study, but they were not statistically significant. Second, we did not include patients with *S. pneumoniae* or *L. pneumophila* grown from originally sterile sites, or those with a negative or no UAT. Only one patient with

pneumococcal antigen in the urine had concurrent pneumococcal bacteremia. According to a previous study conducted in Northern Taiwan, *Legionella* urinary antigens were present in 10 of 317 (3.15%) patients with CAP requiring hospitalization.[23] Since not all patients with pneumonia are tested using either of the UATs, our study did not aim to report the prevalence of PP or LP in our hospitalized patients. However, to our knowledge, there is no other study that directly compares pneumonia patients with positive *S. pneumoniae* or *L. pneumophila* UATs. The results of our study may provide valuable clues for determining whether to perform a UAT.

In conclusion, there are some distinctive clinical and laboratory characteristics in patients with pneumococcal pneumonia and *Legionella* pneumonia. These findings provide significant hints for clinicians in choosing the appropriate UAT.

References

1. Andreo F, Dominguez J, Ruiz J, Blanco S, Arellano E, Prat C, et al. Impact of rapid urine antigen tests to determine the etiology of community-acquired pneumonia in adults. *Respir Med* 2006;100:884–91.
2. Song JH, Oh WS, Kang CI, Chung DR, Peck KR, Ko KS, et al. Epidemiology and clinical outcomes of community-acquired pneumonia in adult patients in Asian countries: a prospective study by the Asian network for surveillance of resistant pathogens. *Int J Antimicrob Agents* 2008;31:107–14.
3. Jover F, Cuadrado JM, Andreu L, Martinez S, Canizares R, de la Tabla VO, et al. A comparative study of bacteremic and non-bacteremic pneumococcal pneumonia. *Eur J Intern Med* 2008;19:15–21.
4. Sopena N, Sabria M. Multicenter study of hospital-acquired pneumonia in non-ICU patients. *Chest* 2005;127:213–9.
5. Stout JE, Muder RR, Mietzner S, Wagener MM, Perri MB, DeRoos K, et al. Role of environmental surveillance in determining the risk of hospital-acquired legionellosis: a national surveillance study with clinical correlations. *Infect Control Hosp Epidemiol* 2007;28:818–24.
6. Diederen BM. *Legionella* spp. and Legionnaires' disease. *J Infect* 2008;56:1–12.
7. Fields BS, Benson RF, Besser RE. *Legionella* and Legionnaires' disease: 25 years of investigation. *Clin Microbiol Rev* 2002;15:506–26.
8. Edelstein PH. Legionnaires' disease. *Clin Infect Dis* 1993;16:741–7.
9. Charles PG. Early diagnosis of lower respiratory tract infections (point-of-care tests). *Curr Opin Pulm Med* 2008;14:176–82.
10. Dominguez JA, Manterola JM, Blavia R, Sopena N, Belda FJ, Padilla E, et al. Detection of *Legionella pneumophila* serogroup 1 antigen in nonconcentrated urine and urine concentrated by selective ultrafiltration. *J Clin Microbiol* 1996;34:2334–6.
11. Dominguez J, Gali N, Blanco S, Pedroso P, Prat C, Matas L, Ausina V. Detection of *Streptococcus pneumoniae* antigen by a rapid immunochromatographic assay in urine samples. *Chest* 2001;119:243–9.
12. Mandell LA, Wunderink RG, Anzueto A, Bartlett JG, Campbell GD, Dean NC, et al. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. *Clin Infect Dis* 2007;44(Suppl 2):S27–72.
13. Pedro-Botet ML, Sopena N, Garcia-Cruz A, Mateu L, Garcia-Nunez M, Rey-Joly C, et al. *Streptococcus pneumoniae* and *Legionella pneumophila* pneumonia in HIV-infected patients. *Scand J Infect Dis* 2007;39:122–8.
14. Cunha BA. Clinical features of legionnaires' disease. *Semin Respir Infect* 1998;13:116–27.
15. Sopena N, Pedro-Botet ML, Sabria M, Garcia-Pares D, Reynaga E, Garcia-Nunez M. Comparative study of community-acquired pneumonia caused by *Streptococcus pneumoniae*, *Legionella pneumophila* or *Chlamydia pneumoniae*. *Scand J Infect Dis* 2004;36:330–4.
16. Sopena N, Sabria-Leal M, Pedro-Botet ML, Padilla E, Dominguez J, Morera J, et al. Comparative study of the clinical presentation of *Legionella* pneumonia and other community-acquired pneumonias. *Chest* 1998;113:1195–200.
17. Ruiz M, Ewig S, Marcos MA, Martinez JA, Arancibia F, Mensa J, et al. Etiology of community-acquired pneumonia: impact of age, comorbidity, and severity. *Am J Respir Crit Care Med* 1999;160:397–405.
18. Straus WL, Plouffe JF, File TM Jr, Lipman HB, Hackman BH, Salstrom SJ, et al. Risk factors for domestic acquisition of legionnaires disease. *Arch Intern Med* 1996;156:1685–92.
19. von Baum H, Ewig S, Marre R, Suttorp N, Gonschior S, Welte T, et al. Community-acquired *Legionella* pneumonia: new insights from the German competence network for community acquired pneumonia. *Clin Infect Dis* 2008;46:1356–64.
20. Cunha BA, Pherez FM, Nouri Y. Legionella community-acquired pneumonia (CAP) presenting with spontaneous bilateral pneumothoraces. *Heart Lung* 2008;37:238–41.
21. Larsson A, Nilsson B, Eriksson M. Thrombocytopenia and platelet microvesicle formation caused by *Legionella pneumophila* infection. *Thromb Res* 1999;96:391–7.
22. Pedro-Botet ML, Sabria M. Legionellosis. *Semin Respir Crit Care Med* 2005;26:625–34.
23. Yeh KM, Lin JC, Wang NC, Chang FY. Legionnaires' disease in community-acquired pneumonia requiring hospitalization in Taiwan. *J Med Sci* 2007;27:63–6.