Original Article

Mycoplasma pneumoniae infection in hospitalized adult patients with community-acquired pneumonia in China

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Abstract

Introduction: This study aimed to investigate the prevalence, clinical and radiographic features, and antibiotic responses of *Mycoplasma pneumoniae (M. pneumoniae*) infections in hospitalized adults with community-acquired pneumonia (CAP) in China.

Methodology: Serum specimens collected from 189 CAP patients in both acute phase and convalescence were tested for IgG, IgA, and IgM mixed antibodies specific to *M. pneumoniae*. The clinical and radiographic characteristics and efficacy of three antibiotic regimens were compared between patients with *M. pneumoniae* infection and those without.

Results: Among 189 CAP patients, 88 (46.6%) were positive for *M. pneumoniae* infection. Compared to the negative patients, patients with *M. pneumoniae* infection were significantly younger, had higher rates of dry cough, and had white blood cell counts of $<10^{10}$/L, but had less purulent sputum. Radiography further showed more centrilobular nodules, ground-glass opacities, tree-in-bud patterns and thickened bronchovascular bundles, but less pleural effusion and larger tracts of real opacities in patients with *M. pneumoniae* infections. Among the three regimens used, patients with moxifloxacin required significantly shorter fever abatement, treatment, and hospitalization times than those with azithromycin plus ceftriaxone and ceftriaxone only.

Conclusions: *M. pneumoniae* infection was present in almost half of the CAP population in east China, with some distinct clinical and radiographic features. Moxifloxacin was an effective antibiotic for this infection.

Key words: *Mycoplasma pneumoniae*; community-acquired pneumonia; clinical; radiological; treatment.

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Introduction

Mycoplasma pneumoniae (*M. pneumoniae*) is one of the main pathogens causing community-acquired respiratory tract infections, especially in children and young adults, although it also causes about 15% of pneumonias in patients older than 40 years of age [1]. In recent years, community-acquired pneumonia (CAP) has become a common infectious disease, especially among the elderly and those with chronic diseases [2]. Despite substantial progress in therapeutic options, CAP remains a significant cause of morbidity and death worldwide [3], including in China [4], where *M. pneumoniae* infection is associated with about 20% of CAP cases, and is most likely co-infected with other atypical pathogens. In fact, up to 30% of all pneumonia cases are reportedly caused by *M. pneumoniae* in the general population [1]. However, diagnosis of the cause of CAP is difficult due to the co-infections with mixed pathogens. Thus, identification of unique clinical and radiographic features in CAP patients caused by different pathogens is critical to help improve the diagnosis of the pathogenic cause of CAP, and thus guide the treatment of the disease. Whereas clinical and radiographic features of CAP caused by more common pathogens, including *Haemophilus influenzae* (*H. influenzae*) and *Staphylococcus aureus* (*S. aureus*) [5], have been categorized, little is known about the clinical and radiographic features of CAP associated with *M. pneumoniae* infection.

In a community-based population, the most common clinical consequences associated with *M.*

pneumoniae infection are acute bronchitis, pharyngitis, and otitis; a small percentage of patients may develop severe neurologic, hematologic, or dermatologic disease such as erythematous lesions [6]. *M. pneumoniae* infection can result in a wide spectrum of symptoms ranging from a classic presentation with fever, cough, and sputum production to more subtle and nonspecific manifestations such as fatigue, malaise, and myalgia [1]. Thus, generally, clinical manifestations of *M. pneumoniae* infection appear non-specific. However, whether CAP patients with *M. pneumoniae* infection also present with unique symptoms and signs remains unclear. More importantly, radiographic evaluation prior to laboratory investigation, such as sputum smear, culture, PCR, serology, *etc.,* would prove to be a very valuable method in diagnosing *M. pneumoniae* infection in CAP patients if the unique features of *M. pneumoniae*-associated CAP are identified and characterized. Several studies [1,3,7] reported on the radiographic features, including computed tomography (CT); however, there is little information on the clinical and radiographic features in Chinese CAP patients with *M. pneumoniae* infection. Therefore, in the present study, we investigated the prevalence, clinical and radiological features, and antibiotic response of *M. pneumoniae* infection in hospitalized adult patients with community-acquired pneumonia in China.

Methodology

Patients

Between January 2009 and December 2010, adult (over 18 years of age) patients who were hospitalized due to the diagnosis of pneumonia according to the international guideline for definition and criteria for enrollment of CAP [8] and the Chinese diagnosis and treatment manual for CAP [9] (based on the presence of selective clinical features and image of chest radiography) at the Third Affiliated Hospital of Wenzhou Medical University were enrolled. Patients who were confirmed with human immunodeficiency virus (HIV) infection, hospital-acquired pneumonia, viral or fungal infection, tuberculosis, lung tumors, chronic obstructive pulmonary disease, who had an organ transplant, serious complications, and/or were treated with immunosuppressive drugs, were excluded.

All eligible patients were invited to participate in the study, and gave written informed consent. This study was approved by the Ethics Committee of the Third Affiliated Hospital to Wenzhou Medical University (No. 2009001).

Specimen collection

Blood samples were collected from the patients on the second day after hospitalization and then at a three- or four-week intervals. Serum samples were separated and kept at -80°C until use. The laboratory tests, including serological diagnosis and physical examinations including radiological diagnosis, were performed and the results were recorded at each time point. Pathogenic tests such as bacterial culture were performed on the sputum and bronchoalveolar lavage fluid of some patients.

Serological diagnosis

The serum specimens in both the acute phase and convalescence were used for detecting *M. pneumoniae* infection using a passive agglutination test (Serodia-Myco II, Fujirebrio Inc., Japan), which measures the mixed antibody titer of *M. pneumoniae* IgG, IgA, and IgM, as described previously [10,11]. *M. pneumoniae* infection was defined as a serum sample that showed a fourfold change of antibody titer during the acute or convalescence period with a mixed antibody titer of ≥ 1:160 [9].

Radiological diagnosis

The CT or chest X-ray images were reviewed and the reports were verified by a radiological expert and a respiratory physician. Patients with the presence of a sheet or patchy shadow of invasion in the lung, or changes of interstitial lung diseases by chest X-ray or CT, were diagnosed with pneumonia.

Treatment of pneumonia with confirmed or suspected M. pneumoniae infection

The treatment of pneumonia is empirical based on the Chinese diagnosis and treatment manual for CAP [9]. Patients with confirmed *M. pneumoniae* infection received one of the following empirical regimens: moxifloxacin (group A), azithromycin plus ceftriaxone (group B), or ceftriaxone (group C) for 48 to 72 hours at the treating physicians' discretion. The treatment was replaced with other antibiotics (piperacillin/tazobactam for group A, or moxifloxacin for groups B and C), if there was no improvement in body temperature and clinical symptoms. Patients who were finally confirmed as having pneumonia with *M. pneumoniae* infection were included in the analysis on the efficacy of treatment regimens.

Statistical analysis

Numerous data were expressed as mean ± standard deviation (SD), where appropriate, and categorical

data were expressed as percentage. Statistical analysis was performed using SPSS 13.0 software (SPSS Inc., Chicago, USA). The incidence of underlying conditions, clinical findings, and radiographic findings were analyzed using the Chi-square test or Fisher's exact test. The mean age of patients and laboratory data were compared using the Student's *t* test. Statistical significance was defined as $p < 0.05$.

Results

Prevalence of M. pneumoniae *infection in patients with CAP*

One hundred and eighty-nine CAP adult patients were hospitalized in the Third Affiliated Hospital of Wenzhou Medical University between January 2009 and December 2010. Patients between 18 and 86 years with a mean age of 40.6 ± 14.1 years were enrolled in the present study. Overall, 88 (46.6%) patients were serologically positive for *M. pneumoniae* infection and were thus diagnosed as having pneumonia with *M. pneumoniae* infection. Of the 101 (53.4%) patients negative for *M. pneumoniae* infection, 15 (7.9%) were found to be infected with *Streptococcus pneumoniae*, 10 (5.3%) with *H. influenzae*, 5 (2.6%) with *Moraxella catarrhalis*, 4 (2.1%) with *Klebsiella pneumoniae*, 3 (1.6%) with *Escherichia coli*, 2 (1.1%) with *S. aureus*, and 1 (0.5%) with *Pseudomonas aeruginosa*. No pathogens were found in the remaining 61 (32.3%) patients.

Clinical characteristics of patients with M. pneumoniae infection

The detailed comparison of patients with without *M. pneumoniae* infection are listed in Table 1. Patients

Table 1. Comparison of demographic, clinical, and laboratory characteristics of patients with and without *M. pneumoniae* infections

Characteristics	With *M. pneumoniae* (n = 88)	Without *M. pneumoniae* (n = 101)	÷²	*P*
Male (%)	34 (38.6)	50 (49.5)	2.25	0.134
Age (mean ± SD [range]), years	34.6 ± 10.1 (18–81)	45.8 ± 15.7 (18–86)	*t* = 5.90	<0.001
Symptoms & signs (%)				
Fever	81 (92.0)	91 (90.1)	0.22	0.640
Fever ≥ 39°C	41 (46.6)	42 (41.6)	0.48	0.490
Cough	86 (97.7)	97 (96.0)	0.44	0.509
Dry cough	48 (54.5)	19 (18.8)	26.24	<0.001
Purulent sputum	23 (26.1)	41 (40.6)	4.39	0.036
Dyspnea	9 (10.2)	14 (13.9)	0.58	0.450
Chest pain	5 (5.7)	12 (11.9)	2.201	0.137
Hemoptysis	2 (2.3)	6 (5.9)	1.25	0.264
Physical and laboratory examinations (%)				
Normal	66 (75.0)	64 (63.4)	2.96	0.085
Dry rales	1 (1.1)	4 (4.0)	1.46	0.228
Moist rales	21 (23.9)	33 (32.7)	0.85	0.355
WBC<10^{10}/L	83 (94.3)	80 (79.2)	9.05	0.003
CRP >8 mg/L	41/60 (68.3)	48/62 (77.4)	1.28	0.260

WBC: white blood cell count; CRP: C-reaction protein

Table 2. Comparison of radiological characteristics of patients with and without *M. pneumonia* infection.

Characteristics	With *M. pneumoniae* (n = 88)	Without *M. pneumoniae* (n = 101)	χ^2	*P*
Lesions (%)				
Single unilateral lesions	52 (59.1%)	72 (71.3%)	3.100	0.078
Unilateral multifocal leaves	14 (15.9%)	14 (13.9%)	0.156	0.693
Bilateral multiple leaves	22 (25.0%)	15 (14.9%)	3.076	0.079
Large opacities	19 (21.6%)	38 (37.6%)	5.739	0.017
Patchy opacities	52 (59.1%)	74 (73.2%)	2.726	0.099
Centrilobular nodules	63 (71.6%)	27 (26.7%)	37.94	<0.001
Ground-glass opacities	45 (51.1%)	20 (19.8%)	20.463	<0.001
Tree-in-bud pattern	51 (58.0%)	6 (5.9%)	60.403	<0.001
Thickened bronchovascular bundles	41 (46.6%)	3 (12.9%)	50.099	<0.001
Pleural effusion	8 (9.1%)	26 (25.7%)	8.838	0.003
Mediastinal and hilar lymph nodes	9 (10.2%)	13 (12.9%)	0.320	0.570

with *M. pneumoniae* infection were significantly younger than those without *M. pneumoniae* infection (34.6 ± 10.1 *vs.* 45.8 ± 15.7 years, $t = 5.90$, $p < 0.001$); more patients with *M. pneumoniae* infection were younger than 50 years of age, compared with those without *M. pneumoniae* infection (88.6% [78/88] *vs.* 58.4% [59/101], $\chi^2 = 21.54$, $p < 0.001$). Dry cough was more common (54.5% *vs*. 18.8%, $\chi^2 = 26.24$, $p < 0.001$), while purulent sputum was less common (26.1% *vs*. 40.6%, $\chi^2 = 4.39$, $p = 0.036$) in patients with than in patients without *M. pneumoniae* infection. Moreover, normal white blood cell (WBC) counts ($<10^{10}$/L) were observed in 94.3% of patients with *M. pneumoniae* infection and in 79.2% of those without *M. pneumoniae* infection ($\chi^2 = 9.05$, $p = 0.003$).

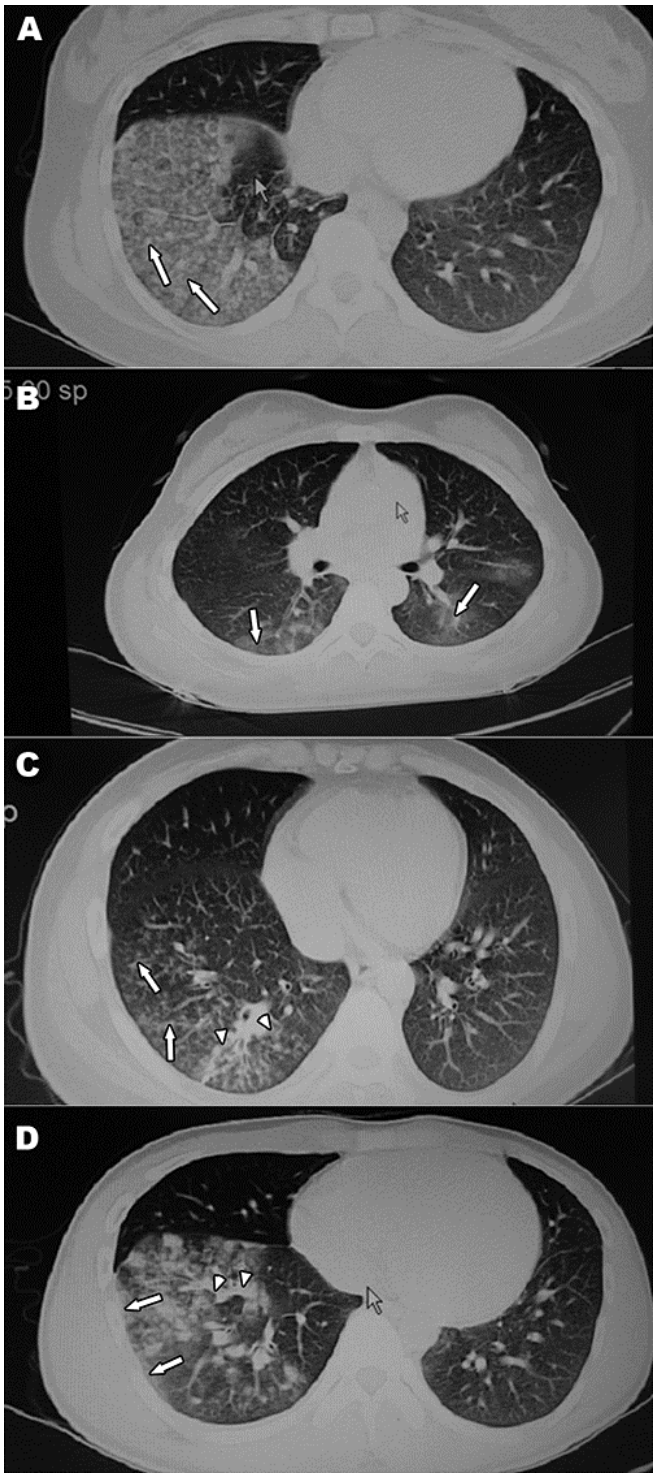
Radiographic characteristics of patients with M. pneumoniae *infection*

The radiographic characteristics of the two groups are shown in Table 2. Centrilobular nodules (Figure 1A), ground-glass opacities (Figure 1B), tree-in-bud patterns (Figure 1C), and thickened bronchovascular bundles (Figure 1D) were more commonly presented in patients with *M. pneumoniae* infection than in those without *M. pneumoniae* infection (all $p < 0.001$). However, pleural effusion and large opacity were significantly less in patients with *M. pneumoniae* infection than in those without *M. pneumoniae* infection ($\chi^2 = 8.84$, $p = 0.003$; and $\chi^2 = 5.74$, $p = 0.017$, respectively).

Treatment of patients with M. pneumoniae *infection*

Initially, of the 189 patients, 66, 62 and 61 patients were assigned into groups A, B and C, respectively, based on the differences in clinical treatment. Among the 88 patients with confirmed *M. pneumoniae* infection, 32 patients received moxifloxacin (group A), 30 received azithromycin plus ceftriaxone (group B), and 26 received ceftriaxone only (group C) (Table 3). There was no difference among the three groups in age, sex, and major clinical and laboratory parameters. When compared with groups B and C, group A had a significantly different fever abatement time, treatment progress, number of cases with antibiotic drugs switching, and average hospitalization time (all $p < 0.001$). Moreover, the proportion of cases with an antibiotic drug switch was significantly lower and the average hospitalization duration was significantly shorter in group B than in group C (both $p < 0.001$).

Figure 1. Representatives of major radiological characteristics of pneumonia with *M. pneumoniae* as shown in computed tomography. **A:** Centrilobular nodules (arrows) in a 29-year-old woman with *M. pneumoniae* pneumonia; **B:** Ground-glass opacities (arrows) in a 35-year-old woman with *M. pneumonia*e pneumonia; **C:** Tree-in-bud pattern (arrows) and bronchial wall thickening (arrowheads) in a 25-year-old man with *M. pneumonia*e pneumonia; and **D:** Wall thickening (arrowheads) and ground-glass attenuation (arrows) and in a 42-year-old man with *M. pneumonia*e pneumonia.



Discussion

Despite rapid economic development during the last decade in China, *M. pneumoniae* infection remains a great public health problem in the country. In the present study, the infection rate of *M. pneumoniae* detected by serology was 46.6% among hospitalized CAP patients. This rate was significantly higher than those (6.8%–29.6%) previously detected by various methods in most studies [12-16]. However, this rate is consistent with the one recently reported by Tao *et al.* in Chinese patients with CAP, in whom *M. pneumoniae* infection was the most frequently identified pathogen, detected by serological tests in 38.9% of CAP patients and in 45.7% and 24.4% of young (< 65 years of age) and old patients, respectively [10]. The high detection rates of *M. pneumoniae* infection in the present study and the study by Tao *et al.* might be caused by regional sporadic infection, because the incidence of *M. pneumoniae* infection has occurred approximately every three to five years, mostly during summer, autumn, and winter [17,18]. The unrecognized community outbreak of *M. pneumoniae* infection is consistent with the observation in Rhode Island, USA [6].

Because serological diagnosis of *M. pneumoniae* infection requires specimens collected in both acute phase and convalescence, the diagnosis based on clinical symptoms and chest CT were more sensitive and specific than rapid serologic detection of IgM antibody of *M. pneumoniae* at the initial stage of CAP [19]. In this study, patients with *M. pneumoniae* infection were younger than those without *M. pneumoniae* infection, and most of them (88.6%) were younger than 50 years of age (Table 1), suggesting that CAP patients < 50 years are most frequently associated with *M. pneumoniae* infection, which is in agreement with the findings of a previous study [17]. Dry cough occurred more frequently, while purulent sputum occurred less frequently in patients with *M. pneumoniae* infection, compared with those without *M. pneumoniae* infection, suggesting that *M. pneumoniae* infection can cause dry cough with little phlegm. Baseline laboratory examinations showed that most of the patients (94.3%) with *M. pneumoniae* infection had normal WBC counts, while only 20.8% of patients without *M. pneumoniae* infection had normal WBC counts. Because there was no significant difference in increased levels of C-reactive protein (CRP) ($p = 0.260$) between the two groups (68.3% and 77.4%, respectively), this data indicated the effect of *M. pneumoniae* infection on CRP; it does, however, require further investigation.

In order to understand the radiological characteristics and improve the diagnosis of *M. pneumoniae* infection in patients with pneumonia, we

Table 3. Efficacy of three antibiotic regimens in patients with *M. pneumoniae* pneumonia

	Group A (n = 32)	Group B (n = 30)	Group C (n = 26)	$\div^2$	P
Age (years)	33.8 ± 11.4	37.4 ± 11.6	32.2 ± 7.5	$F = 1.117$	0.332
Male	11 (34.4%)	14 (46.7%)	9 (34.6%)	$\div^2 = 1.24$	0.54
Major symptoms and laboratory parameters at baseline (%)					
Fever	29 (90.6%)	27 (90.0%)	25 (96.2%)	0.86	0.65
Fever ≥ 39°C	16 (50.0%)	13 (43.3%)	12 (46.2%)	0.28	0.87
Cough	31 (96.9%)	30 (100%)	25 (96.2%)	1.09	0.58
Dry cough	18 (56.3%)	15 (50.0%)	15 (57.7%)	0.39	0.82
Purulent sputum	8 (25.0%)	8 (26.7%)	7 (26.9%)	0.03	0.98
Dyspnea	3 (9.4%)	3 (10.0%)	3 (11.5%)	0.08	0.96
White blood cells < 10^{10}/L	30 (93.8%)	29 (96.7%)	24 (92.3%)	0.52	0.77
Antibiotic therapy					
Fever abatement (days)	2.3 ± 1.2*	4.1 ± 1.5	5.0 ± 1.6	$F = 26.31$	<0.001
Treatment duration (days)	5.5 ± 0.8*	8.2 ± 1.1	8.6 ± 1.2	$F = 54.47$	<0.001
Changed program (%)	0*	11 (36.7%)**	19 (73.1%)	$\div^2 = 34.23$	<0.001
Moxifloxacin	0	11	14		
Macrolide	0	0	1		
Macrolide (azithromycin) plus ceftriaxone	0	0	4		
Hospitalization duration (mean ± SD, days)	4.9 ± 0.7	6.5 ± 1.2**	8.6 ± 1.5	$F = 73.43$	<0.001

Data are expressed as mean ± standard deviation or number (%), where appropriate.
Group A, treatment with moxifloxacin; group B, treatment with azithromycin plus ceftriaxone; group C, treatment with ceftriaxone only.
* $P < 0.001$, when compared with Groups B and C;
** $P < 0.01$, when compared with Group C.

compared the CT results of CAP patients with and without *M. pneumoniae* infection. We found that centrilobular nodules, ground-glass opacities, tree-in-bud patterns, and thickened bronchovascular bundles were more common in patients with *M. pneumoniae* infection than in those without *M. pneumoniae* infection (Table 2), which likely resulted from *M. pneumoniae*-induced bronchiolitis [20]. High rates (88%–93%) of centrilobular nodules, ground-glass opacities, and thickened bronchovascular bundles in patients with *Chlamydia pneumoniae* (*C. pneumoniae*) pneumonia were also previously reported [21]. In addition, we found that pleural effusion was less common in patients with *M. pneumoniae* infection than in those without *M. pneumoniae* infection. In the present study, there was no specific difference in radiographic findings between *M. pneumoniae* and other atypical pneumonia; however, chest CT data are helpful for rapid diagnosis of *M. pneumoniae* infection because of the reported sensitivity of 73% and specificity of 85% for the diagnosis of *M. pneumoniae* infection based on the CT characteristics of chest high-resolution computed tomography [19].

We also compared the prognosis of different treatment of *M. pneumoniae* infection. Table 3 shows that patients treated with moxifloxacin had significantly shorter fever abatement time, treatment progression, and hospitalization duration than did those treated with azithromycin plus ceftriaxone or ceftriaxone only. In addition, patients treated with azithromycin plus ceftriaxone showed a shorter fever abatement time and better treatment progress than those treated with ceftriaxone only (Table 3). Interestingly, no patients treated with moxifloxacin needed to switch to another antibiotic program due to any clinic symptoms, while 73.1% of patients treated with ceftriaxone needed to switch to another antibiotic regimen, which may be due to the fact that *M. pneumoniae* has no cell wall and is resistant to drugs such as beta-lactams, including ceftriaxone, that target the cell wall [22]. Generally, *M. pneumoniae* is susceptible to macrolides and related antibiotics, tetracyclines, and fluoroquinolones [19]. However, high resistant rates to macrolides including azithromycin (69%–92%) in *M. pneumoniae* isolates have been observed in pediatric and adult patients with respiratory tract infections in China [23-25], which may further explain our clinical findings, though susceptibility testing was not performed in the present study. No CAP patients with *M. pneumoniae* infection died in the present study, which supports the observation of a previous study in China that infection with *M. pneumoniae* as well as *C. pneumoniae* was associated with a low pneumonia severity index, indicating low CAP severity and low risk for death [26].

There are some limitations in the present study. First, we used a passive agglutination test measuring the mixed antibody titer of *M. pneumoniae* IgG, IgA and IgM. Ideally, serology, culture and fluorescence quantitative polymerase chain reaction (FQ-PCR) should be incorporated in the establishment of *M. pneumonia* infection in clinical practice [27]. However, culture is slow and FQ-PCR is expensive, and both have low sensitivity [27]. Therefore, we applied the serological method, which is rapid and practical, with considerable sensitivity, specificity and accuracy, and has thus been used in many previous studies [10,27,28]. Second, although we further examined bacterial pathogens in samples of 101 patients without *M. pneumonia* infection, most of them (60.4%, 61/101) remained unclear. Thus, there may be heterogeneity in the group without *M. pneumonia* infection. However, the main focus of the present study was to determine the prevalence, clinical and radiographic features, and antibiotic response of *M. pneumonia* infection in hospitalized adults with CAP, and current analysis already produced some significant results; however, further sub-analysis may not be more meaningful, considering the relatively small sample size. Finally, we did not carry out susceptibility testing *in vitro*, due to technical issues, and thus it is unknown whether the responses to the antibiotic treatment were associated with the antibiotic susceptibility in the bacteria.

Conclusions

In conclusion, *M. pneumoniae* infection is present in almost half of the CAP population and has distinct clinical and radiographic features, which indicates that it is possible to screen *M. pneumoniae* infection in CAP patients for early effective antibiotic intervention. Moxifloxacin is an effective antibiotic in the treatment of *M. pneumoniae* infection.

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Authors' contributions

Zong-Xiao Shangguan participated in the design and literature search of this study, chest CT reading, patient

treatment, and manuscript preparation. Qing Feng Sun initiated the study design, participated in literature search, performed the statistical analysis and revised and finalized the manuscript. Ming Hua Zhang participated in the study design and patient treatment. Ji Guang Ding participated in the study design and patient treatment. Lin Gao Yi participated in the study design and management of anti-bacterial drugs. Yuan Tong Gao participated in chest CT readings and analyzed the imaging diagnosis. Ai Xia Zhan participated in antibody detection of *M. pneumoniae* and analyzed results of immunological diagnosis. Ren Guo Zhao participated in the study design and patient treatment. Xiao Ci participated in the study design and patient treatment. All authors read and approved the final manuscript.

References

1. Morozumi M, Takahashi T, Ubukata K (2010) Macrolide-resistant Mycoplasma pneumoniae: characteristics of isolates and clinical aspects of community-acquired pneumonia. J Infect Chemother 16: 78-86.
2. Donalisio MR, Arca CH, Madureira PR (2011) Clinical, epidemiological, and etiological profile of inpatients with community-acquired pneumonia at a general hospital in the Sumare microregion of Brazil. J Bras Pneumol 37: 200-208.
3. Miyashita N, Sugiu T, Kawai Y, Oda K, Yamaguchi T, Ouchi K, Kobashi Y, Oka M (2009) Radiographic features of Mycoplasma pneumoniae pneumonia: differential diagnosis and performance timing. BMC Med Imaging 9:7.
4. Liu YN, Chen MJ, Zhao TM, Wang H, Wang R, Liu QF, Cai BQ, Cao B, Sun TY, Hu YJ, Xiu QY, Zhou X, Ding X, Yang L, Zhuo JS, Tang YC, Zhang KX, Liang DR, Lu XJ, Li SQ, Liu Y, Yu YS, Wei ZQ, Ying KJ, Zhao F, Chen P, Hou XN (2006) A multicentre study on the pathogenic agents in 665 adult patients with community-acquired pneumonia in cities of China. Zhonghua Jie He He Hu Xi Za Zhi 29: 3-8.
5. Park DR, Sherbin VL, Goodman MS, Pacifico AD, Rubenfeld GD, Polissar NL, Root RK (2001) The etiology of community-acquired pneumonia at an urban public hospital: influence of human immunodeficiency virus infection and initial severity of illness. J Infect Dis 184: 268-277.
6. Walter ND, Grant GB, Bandy U, Alexander NE, Winchell JM, Jordan HT, Sejvar JJ, Hicks LA, Gifford DR, Alexander NT, Thurman KA, Schwartz SB, Dennehy PH, Khetsuriani N, Fields BS, Dillon MT, Erdman DD, Whitney CG, Moore MR (2008) Community outbreak of Mycoplasma pneumoniae infection: school-based cluster of neurologic disease associated with household transmission of respiratory illness. J Infect Dis 198: 1365-1374.
7. Lee I, Kim TS, Yoon HK (2006) Mycoplasma pneumoniae pneumonia: CT features in 16 patients. Eur Radiol 16: 719-725.
8. Mandell LA, Wunderink RG, Anzueto A, Bartlett JG, Campbell GD, Dean NC, Dowell SF, File TM, Jr., Musher DM, Niederman MS, Torres A, Whitney CG, Infectious Diseases Society of America, American Thoracic Society (2007) Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. Clin Infect Dis 44 Suppl 2: S27-S72.
9. Diagnosis and treament manual for community-acquired pneumonia (CAP) (2006). Chin J Tuberc Respir Dis 29: 651-655.
10. Tao LL, Hu BJ, He LX, Wei L, Xie HM, Wang BQ, Li HY, Chen XH, Zhou CM, Deng WW (2012) Etiology and antimicrobial resistance of community-acquired pneumonia in adult patients in China. Chin Med J 125: 2967-2972.
11. Sohn JW, Park SC, Choi YH, Woo HJ, Cho YK, Lee JS, Sim HS, Kim MJ (2006) Atypical pathogens as etiologic agents in hospitalized patients with community-acquired pneumonia in Korea: a prospective multi-center study. J Korean Med Sci 21: 602-607.
12. Wattanathum A, Chaoprasong C, Nunthapisud P, Chantaratchada S, Limpairojn N, Jatakanon A, Chanthadisai N (2003) Community-acquired pneumonia in southeast Asia: the microbial differences between ambulatory and hospitalized patients. Chest 123: 1512-1519.
13. von Baum H, Welte T, Marre R, Suttorp N, Luck C, Ewig S (2009) Mycoplasma pneumoniae pneumonia revisited within the German Competence Network for Community-acquired pneumonia (CAPNETZ). BMC Infect Dis 9: 62.
14. Song JH, Oh WS, Kang CI, Chung DR, Peck KR, Ko KS, Yeom JS, Kim CK, Kim SW, Chang HH, Kim YS, Jung SI, Tong Z, Wang Q, Huang SG, Liu JW, Lalitha MK, Tan BH, Van PH, Carlos CC, So T (2008) 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 3: 107-114.
15. Martinez MA, Ruiz M, Zunino E, Luchsinger V, Avendano LF (2008) Detection of Mycoplasma pneumoniae in adult community-acquired pneumonia by PCR and serology. J Med Microbiol 57: 1491-1495.
16. Liu Y, Chen M, Zhao T, Wang H, Wang R, Cai B, Cao B, Sun T, Hu Y, Xiu Q, Zhou X, Ding X, Yang L, Zhuo J, Tang Y, Zhang K, Liang D, Lv X, Li S, Yu Y, Wei Z, Ying K, Zhao F, Chen P, Hou X (2009) Causative agent distribution and antibiotic therapy assessment among adult patients with community acquired pneumonia in Chinese urban population. BMC Infect Dis 9: 31.
17. Hauksdottir GS, Jonsson T, Sigurdardottir V, Love A (1998) Seroepidemiology of Mycoplasma pneumoniae infections in Iceland 1987-96. Scand J Infect Dis 30: 177-180.
18. Eun BW, Kim NH, Choi EH, Lee HJ (2008) Mycoplasma pneumoniae in Korean children: the epidemiology of pneumonia over an 18-year period. J Infect 56: 326-331.
19. Miyashita N, Kawai Y, Yamaguchi T, Ouchi K, Oka M (2011) Clinical potential of diagnostic methods for the rapid diagnosis of Mycoplasma pneumoniae pneumonia in adults. Eur J Clin Microbiol Infect Dis 30 : 439-446.
20. Cha SI, Shin KM, Kim M, Yoon WK, Lee SY, Kim CH, Park JY, Jung TH (2009) Mycoplasma pneumoniae bronchiolitis in adults: clinicoradiologic features and clinical course. Scand J Infect Dis 41: 515-519.
21. Okada F, Ando Y, Wakisaka M, Matsumoto S, Mori H (2005) Chlamydia pneumoniae pneumonia and Mycoplasma pneumoniae pneumonia: comparison of clinical findings and CT findings. J Comput Assist Tomogr 29: 626-632.
22. Bebear C, Pereyre S, Peuchant O (2011) Mycoplasma pneumoniae: susceptibility and resistance to antibiotics. Future Microbiol 6: 423-431.
23. Cao B, Zhao CJ, Yin YD, Zhao F, Song SF, Bai L, Zhang JZ, Liu YM, Zhang YY, Wang H, Wang C (2010) High

prevalence of macrolide resistance in Mycoplasma pneumoniae isolates from adult and adolescent patients with respiratory tract infection in China. Clin Infect Dis 51: 189-194.
24. Xin D, Mi Z, Han X, Qin L, Li J, Wei T, Chen X, Ma S, Hou A, Li G, Shi D (2009) Molecular mechanisms of macrolide resistance in clinical isolates of Mycoplasma pneumoniae from China. Antimicrob Agents Chemother 53: 2158-2159.
25. Liu Y, Ye X, Zhang H, Xu X, Li W, Zhu D, Wang M (2009) Antimicrobial susceptibility of Mycoplasma pneumoniae isolates and molecular analysis of macrolide-resistant strains from Shanghai, China. Antimicrob Agents Chemother 53: 2160-2162.
26. Lee YT, Chen SC, Chan KC, Wu TC, Tsao SM, Chan CH (2013) Impact of infectious etiology on the outcome of Taiwanese patients hospitalized with community acquired pneumonia. J Infect Dev Ctries 7: 116-124. doi:10.3855/jidc.2834.
27. Qu J, Gu L, Wu J, Dong J, Pu Z, Gao Y, Hu M, Zhang Y, Gao F, Cao B, Wang C (2013) Accuracy of IgM antibody testing, FQ-PCR and culture in laboratory diagnosis of acute infection by Mycoplasma pneumoniae in adults and adolescents with community-acquired pneumonia. BMC Infect Dis 13: 172.
28. El Sayed Zaki M, Goda T (2009) Clinico-pathological study of atypical pathogens in community-acquired pneumonia: a prospective study. J Infect Dev Ctries 3: 199-205. doi:10.3855/jidc.36.

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