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Original Study Role of Atypical Pathogens in Nursing Home—Acquired Pneumonia

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ABSTRACT

Objectives: No international consensus has been reached on the empirical use of antibiotics with atypical coverage in nursing home–acquired pneumonia (NHAP). Aspiration is an important cause of NHAP, but it may not require antimicrobial treatment. This study aimed to investigate the prevalence and clinical characteristics of AP infections and review the need for empirical antibiotics with atypical coverage in NHAP.

Design: A prospective cohort study.

Setting: Four nursing homes with a total number of 772 residents.

Participants: Patients were aged \geq 65 years, hospitalized for NHAP, which was defined as the presence of respiratory symptoms and abnormal chest radiographs, from April 2006 to March 2007.

Measurements: Demographics, clinical parameters, and investigation results were recorded. Microbial investigations comprised sputum routine and mycobacterial cultures, blood and urine cultures, serology, and nasopharyngeal aspirate viral culture and polymerase chain reaction tests. Suspected aspiration pneumonitis was arbitrarily defined as NHAP without pathogens identified.

Results: After excluding lone bacteriuria, 108 episodes of NHAP in 94 patients were included. Twelve APs were detected in 11 patients. There was no clinical feature to distinguish between infections caused by APs and other pathogens. The commonest APs were *Mycoplasma pneumoniae* (6) and *Chlamydophila pneumoniae* (3). No *Legionella pneumophila* was detected by urinary antigen test. None of the patients with AP infection received antibiotics indicated for AP infections. However, AP infections did not result in mortality. No pathogen was isolated in 31.5% of cases. Patients without pathogens isolated were less likely to have purulent sputum and crepitations on chest auscultation, compared with those with pneumonia caused by identified pathogens.

Conclusions: Atypical pathogens (APs) were not associated with mortality even in cases where the prescribed antibiotics did not cover APs. NHAP may not necessarily be treated with empirical antibiotics covering APs.

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Pneumonia is a common cause of death among nursing home residents. *Streptococcus pneumoniae* and *Haemophilus influenzae* are the commonest bacterial pathogens in patients who are able to expectorate.¹ Aspiration is an important contributing factor. Aspiration pneumonitis, which is caused by chemical injury to the lung parenchyma without bacterial infection, does not necessitate antibiotic treatment.² In contrast, aspiration pneumonia is caused by

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bacterial pathogens of oropharynx, including gram-negative bacilli, *Staphylococcus aureus*, and anaerobic bacteria, which are commonly isolated in intubated patients.³ Aspiration pneumonitis is difficult to differentiate from pneumonia clinically.

The empirical use of antibiotic regimens covering atypical pathogens (APs) in the management of community-acquired pneumonia (CAP) in adults is controversial. According to the Cochrane Systematic Review, the empirical use of antibiotics with atypical coverage, compared with those without atypical coverage, did not provide survival benefit or clinical efficacy in patients hospitalized for lowseverity pneumonia.⁴ The British Thoracic Society guidelines, however, recommend the empirical use of combination regimen of penicillin and macrolide antibiotics in patients hospitalized for moderate- to high-severity pneumonia.⁵ The Infectious Diseases Society of America/American Thoracic Society guidelines have no

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recommendation on the empirical use of antibiotics with atypical coverage in nursing home–acquired pneumonia (NHAP).⁶

The importance of APs (*Mycoplasma pneumoniae*, *Chlamydophila* spp., and *Coxiella burnetii*) and *Legionella pneumophila* in older patients with pneumonia is unclear. APs were more likely to infect older people with multiple comorbidities than younger ones,⁷ and were more common in CAP than in NHAP.^{8,9} There is little information regarding the prevalence and mortality of AP infections in NHAP and CAP, which are the major determining factors on the empirical use of antibiotic regimens with atypical coverage. Such information is needed to establish the role of APs and *L pneumophila* in NHAP.¹⁰

We performed a subgroup analysis of NHAP in a study on influenza-like illness (ILI) in old people living in nursing homes. This study aimed to investigate the prevalence and clinical characteristics of AP infections in NHAP and review the need for empirical antibiotic therapy with atypical coverage in NHAP.

Methods

Patient Recruitment

The methodology of this study was described elsewhere.¹¹ Four nursing homes, which were located in the Shatin district of Hong Kong and had a total number of 772 residents, participated in this study from April 2006 to March 2007. Research staff liaised with the nurse or doctor of the Community Geriatric Outreach Team of the Hong Kong Hospital Authority to identify residents with ILI every day. An ILI episode was defined as fever \geq 37.8°C or 100°F (oral temperature) or an acute deterioration in physical or mental condition, plus either new onset of one or more respiratory symptoms or acute worsening of a chronic condition involving respiratory symptoms.

A chest radiograph was taken in those with a chronic cough lasting ≥ 2 weeks or taken when pneumonia was suspected. Respiratory and urinary specimens were collected within the first 2 days of illness and serology 2 weeks later, no matter whether the patients were in the hospital or in the nursing homes.

Patients with ILI were managed by the physician of the Community Geriatric Outreach Team in the nursing homes. Residents were hospitalized if they were in critically ill condition or could no longer be managed in nursing homes. A follow-up visit was arranged by the research nurse after recovery of the illness.

This study was approved by the Research Ethics Committee of the Chinese University of Hong Kong. Appropriate informed written consent was obtained from the patients or their proxy.

Microbial Investigations

All patients with ILI symptoms had the following specimens collected for microbial investigations: sputum, blood and urine samples, nasopharyngeal aspirate (NPA), and serology.

Sputum samples were used for routine bacterial culture that covered *S. pneumoniae*, *H. influenzae*, *Moraxella catarrhalis*, *Pseudo-monas* spp., and other pathogens. Sputum mycobacterial culture for tuberculosis was limited to those with prolonged respiratory symptoms, weight loss, or hospital admission.

NPA samples were sent for routine viral culture, including influenza A and B, parainfluenza virus types 1, 2, and 3, respiratory syncytial virus, and adenovirus. A rapid multiplex nested polymerase chain reaction (PCR) was undertaken to detect atypical organisms (*M. pneumoniae, C. pneumoniae,* and *L. pneumophila*) and viruses (influenza A and B, parainfluenza virus types 1, 2, 3, and 4, respiratory syncytial virus, rhinovirus, adenovirus, enterovirus, coronavirus, and metapneumovirus).¹²

Paired serum samples were taken to identify APs (*M. pneumoniae*, *Chlamydophila* spp., and *C. burnetii*), *L. pneumophila*, and respiratory viruses (influenza A and B, parainfluenza 1, 2, 3, and 4, and adenovirus) by complement fixation tests. Blood and urine samples were collected for routine culture. Urinary antigen tests for *L. pneumophila* serogroup 1 and *S. pneumoniae* were performed in hospitalized patients.

NHAP

NHAP was defined as the presence of respiratory symptoms supported by abnormal findings on chest radiographs, that is, illdefined shadow, consolidation, or pleural effusion. Our study recruited residents hospitalized for NHAP.

Diagnostic Criteria

The cause of NHAP was definitive if one of the following criteria was met: (1) positive blood culture; (2) positive sputum culture for *S. pneumoniae, H. influenzae*, and *M. catarrhalis*; (3) positive NPA viral culture or PCR identification; (4) a seroconversion or 4-fold increase in antibody titer; (5) IgM positive; or (6) positive urinary antigen test for *L. pneumophila*. The cause was probable if one of the following criteria was met: (1) positive sputum culture for other bacteria; (2) a single titer \geq 80 when paired serum samples were not available; or (3) positive urinary antigen test for *S. pneumoniae*.

Documentation of Clinical Course

The following characteristics of the study patients were recorded: demographic characteristics, comorbidities, vaccination status, prior hospitalization, premorbid functional status, Mini-Mental State Examination, body mass index, symptoms and signs of the illness, investigation results, antibiotics, hospitalization, length of stay, and mortality.

Premorbid functional status was assessed by the Barthel index. This score covers a wide range of activities of daily living with a total score of 20. A score of 20 indicates independence, 15–19 indicates mild to moderate functional limitation, and \leq 14 indicates severe limitation.

The burden of medical illnesses was represented by the Charlson comorbidity index and the severity of pneumonia measured by the CURB score (confusion, blood urea level, respiratory rate, and low blood pressure).

Statistical Analysis

Categorical variables were expressed as counts (percentages) and continuous variables as mean (\pm SD) or median (interquartile range). Two groups were compared by χ^2 (or Fisher exact) test for categorical variables and by *t* test (or Mann–Whitney *U* test) for continuous variables. Two-tailed tests with a significance level of 5% ($\alpha = 0.05$) were used for all analyses. The Statistical Package for Social Sciences 13.0 (SPSS Inc, Chicago, Illinois) was used for statistical analyses.

Results

A total of 259 episodes of ILI occurred in 194 patients. Abnormal chest radiographs were present in 128 episodes. All except one required hospitalization. Two episodes were excluded because of missing data. Of the remaining 125 episodes, bacteria were isolated only in the urine samples of 17 episodes, which were further excluded. Finally, 108 episodes of NHAP in 90 patients were included

Table 1

Clinical Characteristics and Investigation Results of the Study Population (N = 108)

Variables	Values (Normal Range)
Demographics	
Age, y, mean $(\pm SD)$	85.6 (±9.2)
Male sex, n (%)	50 (46.3)
Mini-Mental State Examination score, mean $(\pm SD)$	15.8 (±6.2)
Barthel index, median (IQR)	4 (2-10)
Body mass index, kg/m ² , median (IQR)	20.8 (18.1-24.6)
Nasogastric tube feeding, n (%)	20 (18.5)
Charlson comorbidity index, median (IQR)	3 (1-4)
Hospitalization within past 4 weeks, n (%)	29 (26.9)
Flu vaccination within past 6 months, n (%)	57 (52.8)
Flu vaccination within past 6–12 months, n (%)	41 (38.0)
Comorbidities, n (%)	
Cerebrovascular accident	52 (48.1)
Dementia	59 (54.6)
Diabetes	26 (24.1)
Ischemic heart disease	17 (15.7)
Congestive heart failure	18 (16.7)
Chronic obstructive pulmonary diseases	21 (19.4)
Chronic kidney diseases	18 (16.7)
Chronic liver diseases	3 (2.8)
Active malignancy	6 (5.6)
Respiratory symptom, n (%)	
Fever	98 (90.7)
Shortness of breath	81 (75.0)
Cough*	99 (91.7)
Mucoid sputum	45 (41.7)
Purulent sputum	47 (43.5)
Hemoptysis	3 (2.8)
Respiratory signs, n (%)	
Rhonchi	21 (19.4)
Bronchial breath sounds	8 (7.4)
Crepitations	84 (77.8)
Chest radiographs, n (%)	
Ill-defined shadows	69 (63.9)
Consolidation	39 (36.1)
Pleural effusion	11 (10.2)
Blood tests	
Sodium, mmol/L	134 (129–137)
Urea, mmol/L	7.5 (5.6–10.1)
Creatinine, µmol/L	97 (72-126)
Albumin, g/L	32 .3 (±4.8)
White cell counts, $\times 10^9/L$	12.1 (8.6–15.7)
CURB score, n (%)	
0-1	40 (37.0)
2-4	68 (63.0)
CLIRE confusion blood uses level respiratory rate and l	and his a management IOD

CURB, confusion, blood urea level, respiratory rate, and low blood pressure; IQR, interquartile range.

*Eighteen (16.7%) patients had cough longer than 2 weeks.

in this study. Clinical characteristics and investigation results of the study population are listed in Table 1.

Microbial Findings

Sputum routine and mycobacterial cultures were performed in 61 (56.5%) and 41 (38.0%) patients, respectively. NPA samples were collected in all patients for PCR tests and 101 (93.5%) patients for viral culture. A paired serology was available in 92 (85.2%) patients. Urinary antigen tests for *L. pneumophila* and *S. pneumoniae* were carried out in 94 (87.0%) patients. Blood and urine samples were collected for routine culture in 92 (85.2%) patients.

Causative factors were established in 74 (68.5%) patients. The microbial findings are summarized in Tables 2 and 3. Concomitant bacteriuria was found in 16 patients.

Pneumonia of Unknown Cause

More than 30% of the study patients belonged to a category of "pneumonia of unknown etiology." They had no pathogen identified

Summary on Bacterial Findings With Either Definitive or Probable Cause

Pathogens	Total	Sputum	Serology	Blood	NPA PCR	Urinary Antigen
Bacterial pathogens						
Streptococcus pneumoniae	16			1		16
Haemophilus influenzae	5	5				
Pseudomonas spp.	7	7				
Escherichia coli	1	1				
Serratia spp.	1	1				
Klebsiella spp.	1	1				
MRSA	3	2		1		
MAC	3	3				
Atypical pathogens						
Mycoplasma pneumoniae	6		1		5	
Chlamydophila pneumoniae	3				3	
Chlamydophila psittaci	2		2			
Coxiella burnetii	1		1			

MAC, *Mycobacterium avium* complex; MRSA, methicillin-resistant *Staphylococcus aureus*; NPA, nasopharyngeal aspirate; PCR, polymerase chain reaction.

One patient had infection with *S. pneumoniae* diagnosed by both blood culture and urinary antigen test.

despite extensive microbial investigations for respiratory and urinary pathogens. The acute inflammatory condition of the lower respiratory tract was more likely caused by aspiration pneumonitis than aspiration pneumonia. A similar percentage of patients with and without nasogastric tube feeding was represented (30.0% vs 31.8%, P = .874).

All the patients were treated with empirical antibiotics on admission. This group of patients had a lower in-hospital mortality rate than those with pathogens identified, although statistical significance was not reached (5.9% vs 18.9%, P = .077).

The presence of purulent sputum and crepitations on chest auscultation were the features that distinguished patients with and without pathogens identified, as listed in Table 4.

AP Infections and Antimicrobials

The prevalence rate of AP infections in NHAP was 10.2% (11/108). The commonest APs were *M. pneumoniae* (6) and *C. pneumoniae* (3). Coinfections with viruses or other bacteria occurred in five of them. Urinary antigen tests did not detect any *L. pneumophila*. There was no difference in the clinical characteristics of pneumonia caused by APs and other pathogens (Table 5). The atypical isolates were not clustered in time or in a specific facility.

With one exception, none of the patients with AP infection was treated with antibiotic covering APs during hospitalization. This patient was treated with levofloxacin on admission because of allergy to penicillin. The other 10 patients received penicillin antibiotics. AP

Table	3
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Summary on	Viral Findings	With	Either	Definitive	or Probable	Cause

Pathogens	Total	NPA Viral Isolation	NPA PCR	Serology
Influenza A	4	2	2	2
Influenza B	3	1	3	1
Parainfluenza virus type 1	5		5	1
Parainfluenza virus type 2	1		1	
Parainfluenza virus type 3	8	3	4	7
Parainfluenza virus type 4	1		1	
Respiratory syncytial virus	13	2	6	5
Metapneumovirus	9		9	
Enterovirus	3		3	
Coronavirus	2		2	
Rhinovirus	1		1	

NPA, nasopharyngeal aspirate; PCR, polymerase chain reaction. One infection can be detected by more than one test.

Comparison of Nursing Home-Acquired Pneumonia With and Without Pathogen Identified

Characteristics With Pathogen Without Pathogen Р (n = 74) (n = 34) Demographics Age, y 86.6 (±9.2) 83.3 (±9.0) .084 Male sex, n (%) 31 (41.9) 19 (55.9) .176 MMSE 15.7 (±6.4) 15.8 (±6.0) .996 CCI 3(1-4)3(2-4).361 4 (2-11) BI 4(2-10).644 Comorbidities, n (%) 34 (45.9) 18 (52.9) .499 CVA Dementia 40 (54.1) 19 (55.9) 859 Diabetes 15 (20.3) 11 (32.4) .173 IHD 8 (23.5) .132 9(12.2) CHF 14 (18.9) 4(11.8).354 COPD 14 (18.9) 7 (20.6) .839 CKD 12 (16.2) 6(17.6) .853 CLD 2 (2.7) .944 1(2.9)Active malignancy 4 (5.4) 2 (5.9) .920 Respiratory symptoms, n (%) 68 (91.9) 30 (88.2) .722 Fever Shortness of breath 54 (73.0) 27 (79.4) .473 67 (90.5) 32 (94.1) .717 Cough Mucoid sputum 31 (41.9) 14 (41.2) .944 Purulent sputum 8 (23.5) .005 39(52.7)Hemoptysis 2 (2.7) 1 (2.9) .944 Respiratory signs, n (%) Rhonchi 14 (18.9) 7 (20.6) .839 Bronchial breath sounds 7 (9.5) 1(2.9).431 Crepitations 63 (85.1) 21 (61.8) .007 Chest radiographs, n (%) 46 (62.6) 23 (67.6) .582 Ill-defined shadows Consolidation 28 (37.8) 11 (32.4) 582 4 (11.8) Pleural effusion 7 (9.5) .739 Blood tests Sodium mmol/L 133(131 - 135)135(133 - 136)844 Urea, mmol/L 9.0 (5.5-10.0) 7.0 (6.2-10.8) .300 95 (73-128) Creatinine, µmol/L 98 (71-126) .863 32.3(+5.0)32.4(+4.4).977 Albumin, g/L White cell counts, $\times 10^9/L$ 12.3 (8.6-15.6) 11.3 (8.4-17.4) 953 CURB score, n (%) 0 - 129 (39.2) 11 (32.4) 2 - 445(608)23 (67 6) 494 Length of stay, d 11(6-18)11 (6-19) .992 2 (5.9) In-hospital mortality, n (%) 14 (18.9) .077

BI, Barthel index; CCI, Charlson comorbidity index; CHF, congestive heart failure; CKD, chronic kidney diseases; CLD, chronic liver diseases; COPD, chronic obstructive pulmonary diseases; CURB, confusion, blood urea level, respiratory rate, and low blood pressure; CVA, cerebrovascular accident; IHD, ischemic heart disease; MMSE, Mini-Mental State Examination.

Numerical ranges indicate interquartile range.

infection did not result in any death. The overall in-hospital mortality rate of the study population was 14.8%.

Discussion

Our study demonstrated that APs are not an important cause of NHAP, as reflected by the low prevalence and the lack of antibiotic treatment with atypical coverage not resulting in mortality. Despite some advances in technology with availability of multiplex PCR for detection of common pathogens in the NPA specimen, the cause of NHAP could not be identified in 31.5% of cases. Aspiration pneumonitis presumably accounted for some of these cases.

The prevalence rate of AP infections in this study was 10.2% (11/ 108), which was greater than the findings (<5%) of previous studies.^{13,14} There was no reliable clinical characteristic to differentiate between NAHP caused by APs and other pathogens. The combined use of NPA PCR tests and traditional serology likely had contributed to a greater prevalence of AP infections in our study. *M. pneumoniae* and *C. pneumoniae* infections were diagnosed

Table 5

Comparison of Nursing Home-Acquired Pneumonia Caused by Atypical Pathogens and Other Pathogens

Characteristics	Atypical Pathogens $(n = 11)$	Other Pathogens $(n = 63)$	Р
Demographics			
Age, v	88 (75-99)	89 (81-92)	.945
Male sex, n (%)	6 (54.5)	25 (39.7)	.510
MMSE	19 (13-22)	12 (10-19)	.281
CCI	2 (0-4)	3 (1-4)	.371
BI	4 (3-7)	4 (2-10)	.605
Comorbidities, n (%)	- ()	- ()	
CVA	4 (36.4)	30 (47.6)	.489
Dementia	5 (45.5)	35 (55.6)	.535
Diabetes	3 (27.3)	12 (19.0)	.684
IHD	1 (9.1)	8 (12.7)	.736
CHF	3 (27.3)	11 (17.5)	.426
COPD	2 (18.2)	12 (19.0)	.946
CKD	2 (18.2)	10 (15.9)	.848
CLD	0(0)	2 (3.2)	NC
Active malignancy	1 (9.1)	3 (4.8)	.482
Respiratory symptom, n (%)			
Fever	1 (9.1)	5 (7.9)	.897
Shortness of breath	8 (72.7)	46 (73.0)	.984
Cough	10 (90.9)	57 (90.5)	.964
Mucoid sputum	6 (54.5)	25 (39.7)	.510
Purulent sputum	4 (36.4)	35 (55.6)	.239
Hemoptysis	0(0)	2 (3.2)	NC
Respiratory signs, n (%)			
Rhonchi	3 (27.3)	11 (17.5)	.443
Bronchial breath sounds	1 (9.1)	6 (9.5)	.964
Crepitations	8 (72.7)	55 (87.3)	.352
Chest radiographs, n (%)			
Ill-defined shadows	6 (54.5)	40 (63.5)	.738
Consolidation	5 (45.5)	23 (36.5)	.738
Pleural effusion	1 (9.1)	6 (9.5)	.964
Blood tests			
Sodium, mmol/L	132 (128–137)	133 (129–136)	.834
Urea, mmol/L	6.5 (5.5-8.3)	7.5 (5.4–10.6)	.301
Creatinine, µmol/L	97 (75-105)	100 (70-131)	.399
Albumin, g/L	34 (29-37)	33 (29-36)	.356
White cell counts, $\times 10^9/L$	13.4 (7.6–22.6)	12.1 (8.6–15.5)	.710
CURB score, n (%)			
0-1	6 (54.5)	23 (36.5)	
2-4	5 (45.5)	40 (63.5)	.322
Length of stay, d	7 (5–15)	11 (7–21)	.155

BI, Barthel index; CCI, Charlson comorbidity index; CHF, congestive heart failure; CKD, chronic kidney diseases; CLD, chronic liver diseases; COPD, chronic obstructive pulmonary diseases; CURB, confusion, blood urea level, respiratory rate, and low blood pressure; CVA, cerebrovascular accident; IHD, ischemic heart disease; MMSE, Mini-Mental State Examination; NC, noncalculable. Numerical ranges indicate interquartile range.

exclusively by NPA PCR tests, but not serology. Meanwhile, *Chlamy-dophila* and *C. burnetii* can be detected only by serology. All the patients with AP infection survived, whereas only one of them had received antibiotic covering APs. Another study also showed that AP infection resulted in a lower 30-day mortality than other pathogens, although the difference was not statistically significant (2.2% vs 6.0%, P = .09).⁷ It is hypothesized that APs cause pneumonia of milder severity, and its clinical course is usually self-limiting without antibiotic therapy, even in older people of lower immunity. Thus, we recommend that antibiotics with atypical coverage should not be used empirically for NHAP.

Legionella infection is acquired by inhalation of contaminated aerosols produced by water systems, such as cooling towers, showers, and hot water distributing systems. Aspiration of contaminated water is another route of transmission. Hot and humid environment facilitates the formation of biofilm and the subsequent growth of *L. pneumophila* in water tanks and pipes.¹⁵ Such environments, which predispose to the proliferation of this bacterium, are commonly encountered in Hong Kong, especially in nursing home settings. However, previous studies showed that *L. pneumophila* was a rare

(<5%) pathogen in NHAP.^{8,9,13,14} Our study has confirmed the rarity of *Legionella* infection in NHAP, based on the result of urinary antigen tests that were performed in nearly 90% of the study patients. This finding further supports our recommendation that empirical antibiotic with atypical coverage is not indicated routinely for NHAP. On the basis of our local data, urinary antigen test for *L. pneumophila* would not be a part of routine workup for NHAP because of low cost-effectiveness.

Aspiration pneumonitis, which is a clinical diagnosis by exclusion, is a significant cause of NHAP. Our study suggested that those nursing home residents with pneumonia who had no pathogens identified did not have purulent sputum and chest crepitations on examination. Some of these cases could be caused by aspiration pneumonitis. Because it is difficult to clinically distinguish between aspiration pneumonitis and aspiration pneumonia, especially on initial assessment,¹⁶ it is advisable to adopt a "de-escalation" approach and refrain from prescribing prolonged empirical antibiotics in patients with bulbar dysfunction and aspiration pneumonitis. This would help to reduce antibiotic resistance and the cost of unnecessary antibiotics.

This study had some limitations. First, the 4 nursing homes were chosen because they were close to the Prince of Wales Hospital for easy and quick transportation of specimens. Second, the incidence of atypical infections may vary in time and place. Our experience may not be applicable in other settings. Legionnaires' disease may be endemic in some facilities where the water supply is colonized. Chlamydophila infection may cause local outbreaks. Third, we did not examine the relationship between patients' swallowing ability and aspiration pneumonitis. Fourth, the definition of aspiration pneumonitis was arbitrary in this study. Our patients without pathogens identified did not necessarily meet the classical definition of aspiration pneumonitis, that is, sudden onset of choking after vomiting.^{2,16} Fifth, although NPA and blood serology were collected from the majority of patients, only 57% and 38% of the patients could cough up sputum suitable for routine culture and mycobacterial culture, respectively.

Conclusions

This study has shown that the overall in-hospital mortality rate of the study population with NHAP was 14.8%, whereas APs were neither a common cause of NHAP nor a significant cause of mortality. Most of the patients with APs isolated had not received antibiotics that covered the APs. Thus, patients with NHAP should not require empirical antibiotic treatment with atypical coverage.

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