CLINICAL FEATURES OF COMMUNITY-ACQUIRED PNEUMONIA TREATED AT SRINAGARIND HOSPITAL, KHON KAEN, THAILAND

Wipa Reechaipichitkul and Puntip Tantiwong

Department of Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen 40002, Thailand

Abstract. Pneumonia is a serious illness associated with significant morbidity and mortality. The interpretation guidelines for pneumonia management requires knowledge of both the clinical presentation of the disease and local epidemiology. We studied the clinical features, initial laboratory results, antibiotic sensitivities, and outcomes of patients diagnosed with acute community-acquired pneumonia between January 1999 and December 2000 at Srinagarind Hospital. The causative organisms were identified in only 52.2% patients; *Streptococcus pneumoniae* accounted for 23.1% of infections. Other common causes included *Klebsiella pneumoniae* (19.2%), *Burkholderia pseudomallei* (15.4%), *Hemophilus influenzae* (11.5%), *Mycoplasma pneumoniae* (6.2%), and *Staphylococcus aureus* (4.6%). Younger patients were more likely to be infected with *M. pneumoniae*, while the mean age of those with other types of infections was 50. Healthy adults were infected with *M. pneumoniae* and *S. pneumoniae*; specific pathogens attacked patients with certain co-morbidity : i) diabetes mellitus and ageing, ii) diabetes mellitus and renal disease, iii) cardiovascular diseases, and iv) connective tissue diseases and steroid-use; these patients were vulnerable to i) *K. pneumoniae*, ii) *B. pseudomallei*, iii) *H. influenzae*, and iv) *S. aureus* respectively. White blood cell counts were normal in *M. pneumoniae* infection. Gram-stained sputum had some limitations, especially when determining Gram-negative infections; chest x-rays could not differentiate pathogens. Bactermia was found in one half of patients infected with *B. pseudomallei* and *S. aureus*. Antibiotic-resistant organisms were not common in our study. Because morbidity and mortality were high among patients infected with *S. aureus* and *B. pseudomallei*, empirical antibiotic treatment should be considered in suspected cases, especially when patients present with acute severe community-acquired pneumonia.

INTRODUCTION

Pneumonia is the second most common infectious disease in Thailand. Whereas diarrhea is more common, pneumonia is associated with more fatalities (Ministry of Public Health, 1998). Although the mortality and morbidity of community-acquired pneumonia remain significant, both the clinical course and the outcome can be improved by the rapid and appropriate use of antibiotics. Etiology can be established by isolating the causative pathogen or by detection of a rising serological titer, but no single test can determine the cause of community-acquired pneumonia at the time of presentation. Attempts have been made to make presumptive diagnoses based on clinical, laboratory, and radiographic findings (MacFarlane *et al*, 1984; Woodhead and MacFarlane, 1987; Farr *et al*, 1989). Diagnostic guidelines developed by ATS (1993) and IDSA (2000) in western countries, in which melioidosis is not significant, must be adapted for use in Thailand. The basic clinical features and initial laboratory findings that are related to infections with common pathogens in Thailand are used to guide initial antibiotic therapy.

The aim of our study was to define the clinical features, initial laboratory findings, and antibiotic sensitivity patterns for each major pathogen; in addition, the outcome of acute community-acquired pneumonia in adults is discussed.

MATERIALS AND METHODS

The criteria for the diagnosis of acute community-acquired pneumonia were: a history of

fever with cough for ≤14 days prior to admission; abnormal infiltration shown by chest x-ray (excluding lung abscesses, bronchiectasis, and lung masses). Identification of the pathogen depended on isolation of the infective organism from sputum, blood, or pleural fluid. A four-fold increase in or a single titer of ≥1:80, by the passive hemagglutination test, was used for the diagnosis mycoplasma infections. A presumptive diagnosis of pneumococcal pneumonia was made in cases in which Gram-stained sputum showed Gram-positive diplococci and a clinical response to intravenous penicillin G was seen after a few days.

Between January 1999 and December 2000, hospitalized patients of Srinagarind Hospital, Khon Kaen, (15 years of age or older) in whom acute community-acquired pneumonia had been diagnosed, were studied. The patient records were reviewed to obtain : age, sex, underlying diseases, symptoms and signs on admission, complete blood count, the result of sputum staining (Gram's), the chest x-ray findings, the results of sputum and blood cultures, including sensitivity patterns, clinical complications, morbidity and mortality, and the length of hospital stay. Patients with HIV infection were excluded. Comorbidities included : renal diseases (*eg* renal stones and renal failure), cardiovascular diseases (*eg* valvular and ischemic heart diseases), neurological diseases (*eg* Parkinson's disease and cerebrovascular accidents), and steroid use (>15 mg/day).

The study was approved by the Ethics Committee of the Faculty of Medicine, Khon Kaen University.

Statistical analysis

Descriptive statistics were used to describe the data. The means and standard deviations were calculated for continuous data; number and percentage were determined for categorical data.

RESULTS

During the study period, 230 patients (average age 50 yrs) were diagnosed as having acute community-acquired pneumonia; however, the causative organisms were identified in only 120 cases (52.2%) (Table 1). Ten patients were infected with two pathogens. *S. pneumoniae* accounted for 23.1% of acute-community acquired pneumonia, followed by *K. pneumoniae* (19.2%), *B. pseudomallei* (15.4%), *H. influenzae* (11.5%), *M. pneumoniae* (6.2%), and *S. aureus* (4.6%). A presumptive diagnosis of pneumococcal pneumonia was made in 5 patients. Other atypical causes of pneumonia, such as chlamydia and legionella infection, were not found because the specific serologic diagnosis was not available.

K. pneumoniae infections predominated among the older patients, while *M. pneumoniae* affected younger patients (Table 2). *M. pneumoniae* and *S. pneumoniae* infections were more likely to be associated with patients who had no co-morbidity. *B. pseudomallei* and *K. pneumoniae* were commonly associated with diabetes mellitus; *H. influenzae* infections with cardiovascular diseases; and *S. aureus* with connective tissue diseases and steroid use.

Table 1
Causative organisms.

Organism	No.	%
Streptococcus pneumoniae	30	23.1
Klebsiella pneumoniae	25	19.2
Burkholderia pseudomallei	20	15.4
Hemophilus influenzae	15	11.5
Mycoplasma pneumoniae	8	6.2
Staphylococcus aureus	6	4.6
Escherichia coli	6	4.6
Pseudomonas aeruginosa	6	4.6
Acinetobacter spp	6	4.6
Group A *Streptococcus*	3	2.3
Group B β-hemolytic *Streptococcus*	2	1.5
M. tuberculosis	1	0.8
Nocardia spp	1	0.8
Strongyloides stercoralis	1	0.8
	130	100

Notes: 10 patients were infected with two pathogens.

Table 2
Patients' characteristics.

Characteristics	*S. pneumoniae* (n=30)	*K. pneumoniae* (n=25)	*B. pseudomallei* (n=20)	*H. influenzae* (n=15)	*M. pneumoniae* (n=8)	*S. aureus* (n=6)
Age (mean, SD)	50.4 (SD=21.4)	59.2 (SD=12.5)	51.4 (SD=10.3)	54.9 (SD=19.7)	31.1 (SD=12.4)	49.8 (SD=27.1)
Male : female	2 : 1	1.1 : 1	5.7 : 1	0.9 : 1	0.3 : 1	0.5 : 1
Underlying diseases (%)						
COPD	13.3	8	0	13.3	0	0
DM	13.3	32[a]	35[a]	26.7[a]	0	0
Alcoholism	10	12	0	0	0	16.7
Cirrhosis	3.3	12	5	0	0	33.3
Renal diseases	13.3	12	20	13.3	0	0
Cardiovascular	16.7	20	0	26.7[a]	12.5	0
Neurological	6.7	0	0	20	0	0
CNT	10	0	10	0	0	50[a]
Hematologic	0	12	5	6.7	0	0
Steroid use	20	12	15	20	0	50[a]
None	23.3[a]	12	30	20	87.5[a]	16.7

COPD = chronic obstructive pulmonary disease, DM = diabetes mellitus, CNT = connective tissue diseases
[a]maximum in each group.

Table 3
Initial symptoms and signs.

Symptoms and signs	*S. pneumoniae* (n=30)	*K. pneumoniae* (n=25)	*B. pseudomallei* (n=20)	*H. influenzae* (n=15)	*M. pneumoniae* (n=8)	*S. aureus* (n=6)
Duration of symptoms (mean,SD)	3.7 (SD=3.3)	5.3 (SD=4.2)	7.0 (SD=4.0)	5.3 (SD=3.8)	6.5 (SD=3.6)	4.3 (SD=2.4)
Sputum characteristic (%)						
no sputum	23.3	24	45	26.7	37.5	0
purulent	43.3	32	25	46.7	12.5	66.7
mucoid	30	36	20	20	37.5	33.3
rusty	3.3	0	0	0	0	0
bloody	0	8	10	6.7	12.5	0
Dyspnea (%)	73.3	68	20	66.7	37.5	33.3
Pleuritic chest pain (%)	13.3	24	20	0	0	16.7
Temperature on admission (%)						
<36.5ºC	0	0	15	13.3	0	0
36.5ºC - 37.8ºC	40	48	10	53.3	50	16.7
37.9ºC - 38.5ºC	23.3	20	30	6.7	0	50
38.6ºC - 39.5ºC	13.3	28	25	26.7	50	33.3
>39.5ºC	23.3	4	20	0	0	0

Patients with pneumococcal infections experienced shorter-lived symptoms (Table 3), whereas symptoms in patients with *B. pseudomallei* lasted longer. Purulent and mucoid were the common characteristics of the sputum specimens. Forty-five percent of patients infected

Table 4
Laboratory results.

Laboratory results	*S. pneumoniae* (n=30)	*K. pneumoniae* (n=25)	*B. pseudomallei* (n=20)	*H. influenzae* (n=15)	*M. pneumoniae* (n=8)	*S. aureus* (n=6)
White blood cell count (%)						
<5,000	10.3	16	11.1	0	14.3	16.7
5,000-10,000	20.7	28	22.2	13.3	57.1	50
10,001-15,000	41.4	32	22.2	60	28.6	16.7
15,001-20,000	10.3	16	11.1	20	0	16.7
20,001-25,000	10.3	8	22.2	0	0	0
>25,000	6.9	0	11.1	6.7	0	0
Polymorphonuclear cells (%)						
<80%	53.6	52	41.2	60	71.4	50
80-90%	39.3	44	47.1	40	28.6	16.7
>90%	7.1	4	11.7	0	0	33.3
Gram-stained sputum (%)[a]						
GPDC	85.7	27.3	31.2	36.4	12.5	33.3
GPC in cluster	0	0	0	0	0	33.3
GNR	3.5	27.3	31.2	36.4	0	0
GNCB	0	0	0	18.2	0	0
GNR safety pin	0	0	6.4	0	0	0
Not found	10.8	45.4	31.2	5	87.5	33.3
Chest x-rays (%)						
Lobar infiltration	10	4	5	0	37.5	0
Localized patchy infiltration	73.3	56	40	53.3	37.5	33.3
Interstitial infiltration	6.7	4	0	6.7	25	16.7
Bilateral alveolar or multilobar infiltration	10	36	55	40	0	50
Positive sputum culture (%)	65.5	95.8	90	100	0	83.3
Positive hemoculture (%)	28	17.4	57.9	8.3	0	50

[a]% detection in cases who gave initial sputum for examination.
GPDC = Gram-positive diplococci, GPC = Gram-positive cocci, GNR = Gram-negative rod, GNCB = Gram-negative coccobacilli.

with *B. pseudomallei* did not submit initial sputum for examination. Dyspnea frequently occurred in pneumococcal infections; pleuritic chest pain was a feature of *K. pneumoniae* infections. Most patients had a fever ranging from 36.5ºC to 37.8ºC and 37.9ºC to 38.5ºC. Leukocytosis was a common finding in infections caused by *S. pneumoniae, K. pneumoniae, B. pseudomallei,* and *H. influenzae* (Table 4), while the leukocyte count was 5,000-10,000 in *M. pneumoniae* and *S. aureus* infections. Gram-positive diplococci were identified in 85.7% of pneumococcal infections but because the test was not specific, patients with other infections may also have produced this result on the Gram-staining of sputum. In only one-third of patients with Gram-negative infections the stained sputum show Gram-negative rods (Table 4). When a causative organism could not be identified, even in an adequate sputum sample, *M. pneumoniae* was tentatively diagnosed. Localized patchy infiltration was the commonest radiographic finding, except in cases of infection with *B. pseudomallei* and *S. aureus*, in which half of the chest x-rays showed bilateral alveolar or multilobar infiltration. Interstitial

Table 5
outcome of community-acquired pneumonia.

Outcome	*S. pneumoniae* (n=30)	*K. pneumoniae* (n=25)	*B. pseudomallei* (n=20)	*H. influenzae* (n=15)	*M. pneumoniae* (n=8)	*S. aureus* (n=6)
Complication (%)						
Septic shock	20	20	30	20	12.5	33.3
Respiratory failure	20	24	50	46.7	0	50
Parapneumonic effusion	0	12	20	0	0	16.7
Extrapulmonary infection	0	0	20	0	0	0
Mortality rate (%)	0	12	20	13.3	0	33.3
Hospital stay (%)						
≤7 days	66.7	64	25	46.7	50	33.3
8-14 days	10	28	35	20	37.5	66.7
15-21 days	6.7	0	25	20	12.5	0
22-28 days	3.3	0	5	13.3	0	0
≥29 days	13.3	8	10	0	0	0

infiltration was not a common finding in *M. pneumoniae* infection, although we found lobar infiltration and localized patchy infiltration.

In pneumococcal infections, positive sputum cultures (65.5%) and positive blood cultures (28%) were found (Table 4). Half of the patients infected by *B. pseudomallei* and *S. aureus* had positive blood cultures. Ninety percent of the patients infected with *B. pseudomallei* had positive sputum cultures for the organism, although initially most of the Gram-stained sputum from these patients did not show Gram-negative rods. The melioid titers of each patient who had melioidosis pneumonia were reviewed: the initial single titers, by indirect hemagglutination (IHA), varied between 1:10 and ≥ 1:5,120.

Gram-negative rods and *S. aureus* infections were associated with higher morbidity and mortality (Table 5). *B. pseudomallei* caused extrapulmonary infections, such as septic arthritis and pericardial effusion. Patients with either *S. pneumoniae* or *M. pneumoniae* infections had shorter hospital stays (≤ 7 days), lower morbidity, and lower mortality; on the other hand, patients infected with *K. pneumoniae* had shorter hospital stays (≤ 7 days), refused treatment more often, and had a higher mortality rate. Patients infected with *B. pseudomallei* and *S. aureus* usually stayed in hospital for 8-14 days.

When we reviewed the sensitivity pattern of each pathogen, we found that resistant organisms were not a common problem in the hospital. Penicillin-resistant *S. pneumoniae* was detected in only 4 isolates (13.3%); all *S. pneumoniae* isolates were sensitive to first generation cephalosporins. Isolates of *B. pseudomallei* were sensitive to ceftazidime, cotrimoxazole, chloramphenicol, and sulperazon. All *K. pneumoniae* isolates were sensitive to third generation cephalosporins, gentamicin, amikacin, and netilmicin; only one isolate (4%) of *K. pneumoniae* was resistant to cefalothin. Four isolates (26.7%) of *H. influenzae* were of intermediate sensitivity to erythromycin, while one (6.7%) was resistant to erythromycin; five (33.3%) were resistant to ampicillin, and seven (46.7%) were resistant to cotrimoxazole. All isolates of *H. influenzae* were sensitive to chloramphenicol, cefuroxime, and clarithromycin. One isolate (16.7%) of *S. aureus* was resistant to oxacillin; all isolates of *S. aureus* were sensitive to cefalothin, fosfomycin, and vancomycin.

DISCUSSION

The selection of initial antimicrobial therapy in patients with community-acquired pneumonia is usually made before the results of microbiological tests are available. We attempted to determine whether the presenting clinical features and initial laboratory results indicate etiology. Specific pathogens can be determined in only one half of the patients admitted to hospital with acute community-acquired pneumonia (Torres *et al*, 1991; Marston *et al*, 1997). Pneumococcal pneumonia accounted for the most of the infections, as in previous reports (Bohte *et al*, 1995 ; Bartlett and Mundy, 1995; Brown and Lenner, 1998). Our second and third most common organisms (*K. pneumoniae* and *B. pseudomallei*, respectively) were different to those isolated in the previous studies cited. In younger adults, *M. pneumoniae* was the most frequently identified causative agent (Lieberman and Schlaeffer, 1996). Pneumococcal pneumonia had the shortest incubation period, whereas meliodosis pneumonia had the longest; the duration of symptoms in *M. pneumonia* infection was also long (6.5 days).

Healthy adults were prone to *M. pneumoniae* and *S. pneumoniae* (Bohte *et al*, 1995; Mandell, 1995; Lieberman and Schlaeffer, 1996). Some underlying diseases and other factors made patients particularly vulnerable to specific pathogens: ageing (*K. pneumoniae*), diabetes mellitus (*B. pseudomallei, K. pneumoniae*), renal diseases (*B. pseudomallei*), cardiovascular diseases (*H. influenzae*), connective tissue diseases and steroid use (*S. aureus*).

The degree of fever and the characteristics of sputum could not differentiate common pathogens. Dyspnea was found most commonly in those with pneumococcal pneumonia; pleuritic chest pain affected those with *K. pneumoniae*. Patients infected with *M. pneumoniae* had no detectable rise in their white blood cell counts and their Gram-stained sputum showed no organisms, as Luby (1991) has reported. Gram-stain sputum did have some limited use in the diagnosis of *K. pneumoniae, B. pseudomallei, H. influenzae,* and *S. aureus*.

Chest X-rays had no typical pattern for any pathogen (Ruiz *et al*, 1999); however, chest X-rays were used to confirm the clinical diagnosis of pneumonia, characterize the extent and severity of disease, search for complications, and monitor the response to therapy. Bacteremia was common in *B. pseudomallei* and *S. aureus* infections (Boonsawat *et al*, 1990).

During the study period, antibiotic-resistant organisms were not a serious problem, despite reports of penicillin-resistant strains of *S. pneumoniae.* The odds ratio for mortality in patients with penicillin-resistant strains was 1.0 (95% confidence interval 0.5 to 1.9) and therefore penicillin remains the therapy of choice (Pallares *et al*, 1995). However, because of the high mortality and morbidity among patients with *S. aureus* and *B. pseudomallei* infections, empirical therapy is recommended in cases in which these organisms are suspected (Boonsawat *et al*, 1990).

In summary, specific clinical features or initial laboratory results that indicated any particular pathogen were not found. In acute severe pneumonic infections, especially in patients with co-morbidity, empirical antimicrobial therapy should be used until the specific causative agent is identified.

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