SEVERE COMMUNITY-ACQUIRED PNEUMONIA (CAP) TREATED AT SRINAGARIND HOSPITAL, KHON KAEN, THAILAND

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Abstract. In Thailand, the death rate from community-acquired pneumonia (CAP), especially severe CAP, has increased steadily over the past decade. To optimize the outcome, rapid start of appropriate antibiotics and supportive care are the mainstay of management. We therefore assessed the local etiology and outcome of adult patients with severe CAP admitted between January 1, 1999 and December 31, 2001. One hundred and five of 383 patients (27.4%) met the ATS criteria for severe CAP. The mean age was 56.9 (SD 18.2) years. The male to female ratio was 60:45. Duration of symptoms before admission was 5.3 (SD 4.0) days. Most of them (91.4%) had co-morbidity, diabetes mellitus being most common. A microbiological pathogen was isolated in 62 patients (59%). The pathogens most commonly isolated were *B. pseudomallei* (29.4%), *S. pneumoniae* (20.6%), *K. pneumoniae* (19.1%), and *H. influenzae* (11.8%). Other less common pathogens were *E. coli* (5.9%), *S. aureus* (5.9%), *M. pneumoniae* (1.5%), *M. catarrhalis* (1.5%), *P. aeruginosa* (1.5%), *P. fluorescens* (1.5%), and *S. stercoralis* (1.5%). Hospitalization averaged 14.7 (SD 14.3) days and mortality was 21%. Clinicals in 17.1% of patients did not improve and they transferred home. Most (81.9%) patients required mechanical ventilation, while 60 (57.1%) developed septic shock, and 13 (12.3%) acute renal failure. Severe CAP carried high mortality, despite intensive care. Empirical therapy for *B. pseudomallei* should be considered, where endemic, and for patients with diabetes mellitus or chronic renal failure.

INTRODUCTION

In Thailand, community-acquired pneumonia (CAP) is the most common cause of death from infectious disease (Ministry of Public Health, 1998). In the United States, approximately 4 million adults are diagnosed with CAP annually, of whom >600,000 (15%) are hospitalized and 45,000 die (Marston *et al*, 1997). About 10% of all hospitalized CAP patients are severe and require intensive care (ICU) (Torres *et al*, 1996); mortality among these patients is between 20-50% (Fine *et al*, 1996; Ewig *et al*, 1998; Ruiz *et al*, 1999). Rapid initiation of appropriate antimicrobials, based on local epidemiology, is crucial for a favorable outcome. We therefore conducted a study of the local epidemiology, microbial agents, clinical features, and outcome of severe CAP in our 800-bed teaching hospital.

MATERIALS AND METHODS

A cross-sectional study was carried out between January 1, 1999 and December 31, 2001 at Srinagarind Hospital, Khon Kaen University, Khon Kaen, Thailand. Patients aged ≥15 years with severe CAP were included. The diagnosis of CAP was made according to the presence of infiltrate on a chest radiograph with acute onset (≤2 weeks) of symptoms suggestive of a lower respiratory tract infection (Thai Thoracic Society, 2001). Patients had (three of the five): fever, cough with or without productive sputum, dyspnea, pleuritic chest pain, and consolidation or crackles on physical examination. Severe CAP, according to the criteria (sensitivity 78%; specificity 94%) set by the American Thoracic Society (ATS) (Ewig *et al*, 1998; Niederman *et al*, 2001). These criteria were the presence of either one of two major criteria, or the presence of two of three minor criteria. The major criteria include need for mechanical ventilation and septic shock; the minor criteria include systolic blood pressure < 90 mmHg, multilobar involvement, and $Pao_2/Fio_2 < 250$.

Charts of diagnosed CAP-patients were retrieved and reviewed for age, sex, underlying diseases, incubation period, symptoms and signs on admission, the result of sputum and blood cultures, the result of cultures from sterile sites, serology titer for *M. pneumoniae*, chest x-ray find-

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ing, outcome of treatment, clinical complications, morbidity and mortality, and length of hospital stay. The microbial etiology was identified by isolation of the infective organism in the sputum, blood, pleural fluid or sterile sites. A four-fold increase in titer by the passive hemagglutination test indicated mycoplasma infection.

Ethics

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

Statistical analysis

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

RESULTS

Over the three-year study period, 383 patients were diagnosed with CAP and of these 105 (27.4%) met the criteria for severe CAP (Table 1). The average age, among the 60 male and 45 female patients with severe CAP, was 56.9 (SD 18.2) years. Farming was the most common occupation (31.4%).

The mean incubation period was 5.3 (SD 4.0) days. Most (91.4% or 96/105) patients had one or more co-morbidities. Underlying diseases included diabetes mellitus (27 cases), cardiovascular (16), hematologic (15), chronic renal failure (14), connective tissue (14), and neurological (13) (Table 2).

Causative organisms were identified in 62 patients (59.0%); six were infected with two pathogens, namely: *B. pseudomallei* and *K. pneumoniae* (1), *S. pneumoniae* and *K. pneumoniae* (1), *S. pneumoniae* and *M. catarrhalis* (1), *B. pseudomallei* and *E. coli* (1), and *K. pneumoniae* and *E. coli* (2). *B. pseudomallei* was found in 29.4% of the isolates and was the predominant pathogen among patients with severe CAP (Table 3), followed by *S. pneumoniae* (20.6%), *K. pneumoniae* (19.1%), *H. influenzae* (11.8%), *E. coli* (5.9%), and *S. aureus* (5.9%). Severe CAP was caused in one case each (1.5%) of *M. pneumoniae*, *M. catarrhalis*, *P. aeruginosa*, *P. fluorescens*, and *S. stercoralis*.

Hospitalization averaged 14.7 (SD 14.3) days (*ie* 36.2% ≤7 days and 13.3% ≥28 days). Overall, 61.9% of patients improved with treat-

Table 1
Patient characteristics.

Patient characteristic	N = 105
Age, years (mean, SD)	56.9 (18.2)
Male:female ratio	60:45
Incubation, days (mean, SD)	5.3 (4.0)
Occupation (%)	
Farmer	31.4
Civil servant	19.0
Underlying disease (%)	
Yes	91.4
No	8.6

Table 2
Underlying diseases of the patients.

Underlying diseases[a] (N = 105)	No (%)
Diabetes mellitus	27 (25.7)
Cardiovascular disease	16 (15.2)
Hematologic disease	15 (14.3)
Chronic renal failure	14 (13.3)
Connective tissue disease	14 (13.3)
Neurological disease	13 (12.4)
Chronic obstructive pulmonary disease	10 (9.5)
Malignancy	5 (4.8)
Old pulmonary tuberculosis	5 (4.8)
Chronic liver disease	3 (2.9)
Other	5 (4.8)

[a]Some patients had more than one underlying disease

Table 3
Organisms identified as causative of severe CAP in 62 patients.

Organism	No.	%
Burkholderia pseudomallei	20	29.4
Streptococcus pneumoniae	14	20.6
Klebsiella pneumoniae	13	19.1
Hemophilus influenzae	8	11.8
Escherichia coli	4	5.9
Staphylococcus aureus	4	5.9
Mycoplasma pneumoniae	1	1.5
Moraxella catarrhalis	1	1.5
Pseudomonas aeruginosa	1	1.5
Pseudomonas fluorescens	1	1.5
Strongyloides stercoralis	1	1.5
Total	68	100

Note: Six patients were infected with two pathogens

Table 4
Outcome of treatment.

Outcome	N = 105
Hospital stay, days (mean, SD)	14.7 (14.3)
Outcome (n, %)	
Improvement	65 (61.9)
No improvement	18 (17.1)
Death	22 (21.0)
Complication	
Mechanical ventilation	86 (81.9)
Septic shock	60 (57.1)
Acute renal failure	13 (12.3)
Parapneumonic effusion or empyema thoracis	8 (7.6)
Extrapulmonary infection	6 (5.7)
Pneumothorax	2 (1.9)

ment, 17.1% did not, and 21.0% died (Table 4). Most (81.9%, 86/105) of severe CAP-patients required mechanical ventilation because of acute respiratory failure. Septic shock occurred in 60 (57.1%) patients and 13 (12.3%) developed acute renal failure. Parapneumonic effusion or empyema thoracis, extrapulmonary infection and pneumothorax caused high morbidity and prolonged hospitalization in 7.6, 5.7 and 1.9% of cases. Sites of extrapulmonary infection were the liver, spleen, joint and central nervous system.

DISCUSSION

In our study, 27.4% of hospitalized severe CAP patients required ICU admission, which is significantly higher than in other series (Leeper, 1996; Torres *et al*, 1996; Ewig *et al*, 1999). Early recognition of severe CAP would enable prompt, direct therapy. Patients with severe CAP have a distinct spectrum of etiologic agents. In western countries, *S. pneumoniae* and *L. pneumophila* are the most common causative pathogens (Ewig *et al*, 1999); in our hospital, in northeast Thailand, *S. pneumoniae* (23.1%), *K. pneumoniae* (19.2%) and *B. pseudomallei* (15.4%) were previously identified pathogens of hospitalized CAP (Reechaipichitkul and Tantiwong, 2002). In the current study, patients with severe CAP had *B. pseudomallei* (29.4%), *S. pneumoniae* (20.6%), and *K. pneumoniae* (19.1%). *L. pneumophila*, common in severe Western CAP (Pachon *et al*, 1990; Hubbard *et al*, 1993; Hirani and MacFarlane, 1997), was documented in 2.7% of hospitalized CAP in Thailand (Wattanathum, 2000). The Thai microbial spectrum is, therefore, comparable to that found in Singapore, where *B. pseudomallei* was the most common pathogen (Tan *et al*, 1998).

The majority of patients with severe CAP had co-morbidities and one-third in various studies were previously healthy (Torres *et al*, 1991; Rello *et al*, 1993; Moine *et al*, 1994). The most common co-morbidity was chronic obstructive pulmonary disease (COPD), present in one-third to one-half of patients, followed by alcoholism, chronic heart disease, and diabetes mellitus. In our study, about 90% of severe CAP-patients had at least one co-morbidity, the most common being diabetes mellitus, which was present in one-fourth of our patients, followed by cardiovascular disease, hematologic disease, chronic renal failure, and connective tissue disease. In a case-control study, diabetes mellitus, renal disease, and thalassemia were risk factors for melioidosis infection (Suputtamongkol *et al*, 1999). Patients in our area, especially farmers, with underlying diabetes mellitus are susceptible to *B. pseudomallei* infection.

Hospitalization averaged about 2 weeks; however, one-third of severe CAP-patients were admitted for ≤1 week because of a rapid deterioration to severe illness. About 13% had long hospitalization because of complications. ICU admission was required because of acute respiratory failure, hemodynamic monitoring, and septic shock (Restrepo *et al*, 2001). Eighty percent of our patients required mechanical ventilation and half developed septic shock; these two complications were the major causes of morbidity and mortality. Overall mortality was similar to other studies (Leroy *et al*, 1995; Ewig *et al*, 1998; Ruiz *et al*, 1999).

In conclusion, despite advances in antimicrobial therapy and supportive measures, mortality remains high among patients with severe CAP requiring ICU admission. According to our bacteriological data, and since *B. pseudomallei* is endemic, an initial, empirical, high dose of ceftazidime (2 g intravenous every 8 hours) (White *et al*, 1989) and other antimicrobials, such as advanced generation macrolides or antipneumococcal fluoroquinolones to cover other pathogens should be considered. An-

timicrobials can be adjusted once the specific pathogens are identified.

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