Original article

Clinical and microbiological characteristics of community-acquired pneumonia among HIV-infected patients in northern Thailand

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ABSTRACT

Human immunodeficiency virus (HIV) infections are prevalent in Thailand. However, the clinical and microbiological characteristics of community-acquired pneumonia (CAP) in such patients are not completely clear at present. In the present study, we analyzed the characteristics of CAP in 191 HIV-infected patients (192 episodes, 130 males and 61 females, mean age 32.9 years, range:20-62) who had been admitted to Nakornping Hospital in northern Thailand between December 1996 and January 2002. The mean peripheral blood CD4 lymphocyte count was 68.5/mm^3 (range:0-791). The most common organisms detected in the blood of the subjects were as follows: *Penicillium marneffei*, 13, *Salmonella spp.*, 5, *Cryptococcus neoformans*, 4, *Staphylococcus aureus*, 3 and *Rhodococcus equi*, 3, and the most common organisms detected in sputum included *Haemophilus influenzae*, 38, *P. marneffei*, 10, *Streptococcus pneumoniae*, 10, *R. equi*, 9, and *S. aureus*, 9. Life-threatening meningitis in 5 (cryptococcal in 3 and tuberculous in 2), pneumothorax in 2 and tuberculous lymphadinitis in 1 were also noted, resulting in 21 fatalities (10.9%). The mean peripheral blood CD4 lymphocyte count for cases in which the subject died was 74.8/mm^3 (range:0-340). Logstic regression analysis demonstrate that high age (odds ratio of over 40 y.o.: 15.62) and *R. equi* infection (odds ratio: 8.14) are related to death of HIV- infected patients with CAP. The above findings indicate that various types of organisms, including mixed organisms, cause CAP in HIV-infected patients in northern Thailand, and high age and *R. equi* infection

seem to be risk factor for the death.

Key words: community-acquired pneumonia, human immunodeficiency virus, HIV, AIDS, Thailand

INTRODUCTION

Pulmonary infections are common complications and a major cause of mortality in human immunodeficiency virus (HIV) infected individuals[1-3]. They significantly reduce the quality of life and longevity, and exert a great influence on the cost of medical care. In countries where the majority of the population have access to highly active antiretroviral therapy (HAART), a dramatic decrease in morbidity and mortality in HIV-infected persons has already been reported[4,5]. However, Thailand has not yet achieved that status during the period of this study, although HAART procedures have recently initiated[6]. The proportion of HIV-infected patients continues to be high at present[7], and it has been reported that Thailand has an estimated number of people living with HIV/AIDS of approximately 600,000[6]. Prophylaxis and the treatment of pulmonary infections complicating HIV-infected patients are very important in their overall management, but the clinical and microbiological characteristics of pulmonary infections among such patients have not been carefully evaluated in Thailand. The aim of the present clinical study was to investigate the state of community-acquired pneumonia (CAP) complicating HIV-infections in Thailand.

METHODS

All studies described herein were approved by the Human Ethics Review Boards of our institutions, and a informed consent was obtained from each subject.

Patients. This study was performed in HIV-infected patients who had been admitted to Nakornping Hospital, which is major community hospital and the center of HIV infected patients in northern Thailand between December 1996 and January 2002. CAP was diagnosed by new abnormal shadow likely infiltration on a chest roentgenogram with at least two of the following clinical and laboratory findings: fever (temperature, >37.8° C), cough, the production of purulent sputum, dyspnea and leukocytosis (WBC count, >10,000/μL). Although a few patients in this study had such chronic lower respiratory tract diseases as chronic bronchitis or bronchiectasis, most cases did not have such underlying diseases. Also, no cases in this study receive HAART. Patients were excluded from the study when the abnormal shadow on a chest roentgenogram was due to other causes such as congestive heart failure, pulmonary infarction or lung cancer.

Microbiological studies. On admission, two sets of blood cultures using BACTEC Plus Aerobic and BACTEC Myco/F lytic medium (Becton Dickinson Microbiology Systems, MD, USA) were obtained, and when good-quality sputum, based on the criteria of Bartlett[8] was available, acid-fast staining, Gram staining and a sputum culture using blood agar and chocolate agar for bacteria, Sabouraud dextrose agar for fungi, and a Lowenstein-Jensen medium for

mycobacterium were performed using standard methods.

Clinical study. Serum samples were collected on admission and/or subsequently, to determine the CD4 lymphocyte count[9] and other laboratory tests. Cases with CAP were analyzed for differences in age, sex, microbiological results, treatment, clinical outcome and complications.

Statistical analysis. Logistic regression analysis was performed by SYSTAT 10.2 (HULINKS Inc., Tokyo, Japan).

RESULTS

Patients characteristics. A total of 191 patients, including 130 males and 61 females, with a mean age of 32.9 years (range:20-62), and a total of 192 episodes of CAP were enrolled in the present study. The mean peripheral blood CD4 lymphocyte count was 68.5/mm^3 (range:0-791).

Microbiological results. Although approximately 10% of patients already received antibiotics such as penicillin before admission, blood and sputum culture were done in most cases. The most common organisms detected in the blood of the subjects were as follows: *Penicillium marneffei*, 13, *Salmonella spp.*, 5, *Cryptococcus neoformans*, 4, *Staphylococcus aureus*, 3 and *Rhodococcus equi*, 3, and the most common organisms detected in the sputum were as follows: *Haemophilus influenzae*, 38, *P. marneffei*, 10, *Streptococcus pneumoniae*, 10, *R. equi*, 9, and *S. aureus*, 9 (Table 1). No significant organism could not be detected in the 161 episodes (83.9%) from blood cultures and the 115 episodes (59.9%)

from sputum cultures.

Complication and clinical outcome. Life-threatening meningitis in 5 (cryptococcal in 3 and tuberculous in 2), pneumothorax in 2 and tuberculous lymphadinitis in 1 were noted. One hundred-fifty patients (78.1%) improved and could be discharged, 21 patients (10.9%) failed to improve (i.e. transfer, discharge against advice, escape) and 21 patients (10.9%) died. The mean peripheral blood CD4 lymphocyte count for cases of patients who died was 74.8/mm^3 (range:0-340) and the admission period was 1-52 (mean 12.0) days. The organisms isolated from cases of death were *H. influenzae* from the sputum, 5, *R. equi* from sputum, 3, *P. marneffei* from sputum, 3, *S. aureus* from sputum, 1, and sputum and blood, 1, *Klebsiella pneumoniae* from sputum, 2, *S. pneumoniae* from sputum, 1, and blood, 1, *Moraxella catarrhalis* from sputum, 1, and *Nocardia spp.* from sputum, 1.

Characteristics of CAP caused by various organisms. CAP caused by *H. influenzae* in 38 *P. marneffei* in 18, *S. pneumoniae* in 11, *R. equi* in 10, and *S. aureus* in 10 patients were compared (Table 2). The mean age were almost similar. The ratio male to female in CAP caused by *S. pneumoniae* seems to be lower, and mixed infections could occasionally be seen in each groups (data not shown). The mean peripheral blood CD4 lymphocyte count for CAP caused by *R. equi* (7.9) was lower than those by another kind of organisms, and the mortality rate of CAP caused by *R. equi* (30.0%) tended to be higher compared to other types of infections.

Statistical analysis concerning death. Some kinds of factors were compared between survivor and dead cases with CAP (Table 3). The mean CD4, prevalence of septicemia seems to be similar between these 2 groups, but ratio male to female, high age and *R. equi* infection look higher in dead cases. Logstic regression analysis demonstrate that high age (odds ratio of over 40 y.o.: 15.62) and *R. equi* infection (odds ratio: 8.14) are related to death, but septicemia (odds ratio: 0.83) and CD4 (odds ratio of below 50.: 0.14) are not concerned with death in our study (Table 4).

DISCUSSION

The incidence of specific opportunistic infections in HIV-infected individuals vary in different countries, since the prevalence of microorganisms in a given environment determines the patterns of the invading pathogens. In the United States, disseminated *Mycobacterium avium* complex disease was reported to be the most common opportunistic infection in homosexual patients with acquired immunodeficiency syndrome (AIDS)[10]. On the other hand, in South Korea, tuberculosis was the most frequent opportunistic infection in HIV-infected subjects[11]. Thailand has one of the most explosive HIV/AIDS epidemics in the world. Penicilliosis due to *P. marneffei* was the third most frequent AIDS-defining infection after tuberculosis and cryptococcosis in northern Thailand prior to the introduction of HAART, and is endemic in Southeast Asia[12]. In our study, CAP caused by *P. marneffei* in HIV-infected patients was frequent,

different from other countries. CAP caused by *R. equi* was also frequently seen in our study, which tended to appear in the later stages of HIV infections and was fatal compared to other types of infections. In fact, the CD4 count of patients with CAP caused by *R. equi* was lower than those of other types of infection and the mortality rate was significantly high compared to another kinds of infection in our study. A marked increase in the incidence of infections caused by *R. equi* has been reported since the start of the HIV epidemic in 1981[13,14], and the outcome has been reported to be fatal in 60% of HIV-infected patients and in 28% of HIV-negative individuals[15]. Recent studies indicate that pulmonary infections caused by *R .equi* are not uncommon in HIV-infected patients in northern Thailand[16]. Since Chiang Mai is surrounded by many farmland in northern Thailand, many farmers were involved in our study. It may be one reason that the rate of *R. equi* infection as zoonosis was relatively high. In pulmonary nocardiosis and CAP caused by *R. equi*, cavitary pulmonary lesions, similar to pulmonary tuberculosis were noted[17]. Therefore, a misdiagnosis of pulmonary tuberculosis should be avoided by a careful examination, laboratory tests and a radiological work-up. Other common pathogens causing CAP in our study were *H. influenzae*, *S. pneumoniae* and *S. aureus*, and these organisms are similar to those reported in previous reports on non HIV-infected[18,19] and HIV-infected patients[1,2]. In addition to differences in pathogenic microorganisms and the proportion of mixed infection between deceased cases in the present study and survivors, we should also recognize differences in the general

condition of a patient and accompanying socioeconomic problems. Although high age was significantly related to death among HIV-infected patients with CAP, CD4 was not concerned with the mortality. Since the CD4 was already low in most patients of our study and that means most cases were already later stages of HIV infections, it might influence the result. Although HAART has recently been started[7], its effect has not been fully evaluated in Thailand. In such situations, immunization and prophylaxis defined in a number of studies should be considered[20-22].

In conclusion, various types of organisms, including mixed organisms, cause CAP in HIV-positive patients in northern Thailand.

Conflict of interests statement

We declare that we have no conflict of interest.

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Table 1. Pathogens isolated from blood and sputum from HIV-infected subjects with community-acquired pneumonia

Blood culture:	***Penicillium marneffei***	**11**	**Sputum culture:**	***Haemophilus influenzae***	**27**
	P. marneffei + R. equi	**1**		***H. influenzae + Moraxella catarrhalis***	**1**
	P. marneffei + C. neoformans	**1**		***H. influenzae + K. pneumoniae***	**1**
	Salmonella spp.	**5**		***H. influenzae + S. aureus***	**1**
	Cryptococcus neoformans	**3**		***Rhodococcus equi***	**6**
	Staphylococcus aureus	**3**		***R. equi+S. enteritidis***	**1**
	Rodococcus equi	**2**		***R. equi + E. coli***	**1**
	Pseudomonas aeruginosa	**2**		***R. equi + P. marneffei***	**1**
	Streptococcus pneumoniae	**1**		***Penicillium marneffei***	**4**
	Enterobacter cloacae	**1**		***P. marneffei + H. influenzae***	**2**
	Mycobacterium tuberculosis	**1**		***P. marneffei + K. pneumoniae***	**1**
	Negative	**161 (83.9%)**		***P. marneffei + Cryptococcus neoformans***	**1**
				P. marneffei + H. influenzae+S. pneumoniae+K. pneumoniae	**1**
				Streptococcus pneumoniae	**4**
				S. pneumoniae + H. influenzae	**1**
				S. pneumoniae + P. aeruginosa	**1**
				S. pneumoniae + H. influenzae + S. aureus	**1**
				S. pneumoniae + H. influenzae + S. aureus + K. pneumoniae	**1**
				Staphylococcus. aureus	**6**
				Escherichia coli	**3**
				Mycobacterium tuberculosis	**2**
				M. tuberculosis + S. pneumoniae	**1**
				M. tuberculosis + H. influenzae	**1**
				Pseudomonas aeruginosa	**2**
				P. aeruginosa + M. catarrhalis	**1**
				Nocardia spp.	**2**
				Nocardia spp. + H. influenzae	**1**
				Salmonella enteritidis	**1**
				Klebsiella pneumoniae	**1**
				Negative	**115 (59.9%)**

Table 2. Comparison of characteristics among community-acquired pneumonia caused by various organisms

	Haemophilus influenzae (n=38)	*Penicillium marneffei* (n=18)	*Streptococcus pneumoniae* (n=11)	*Rhodococcus equi* (n=10)	*Staphylococcus aureus* (n=10)
Age distribution (mean)	**20 – 48y.o. (30.2)**	**24 – 44 y.o. (33.5)**	**23 – 38 y.o. (31.4)**	**21 – 42 y.o. (31.6)**	**25 – 35y.o. (29.6)**
Male / Female	**24 / 14**	**15 / 3**	**5 / 6**	**9 / 1**	**7 / 3**
Detection site					
sputum and blood	**0**	**5**	**0**	**2**	**2**
sputum	**38**	**4**	**10**	**7**	**7**
blood	**0**	**4**	**1**	**1**	**1**
others	**0**	**5** *	**0**	**0**	**0**
CD4 distribution (mean)	**0 – 708 (84.2)**	**0 – 114 (37.9)**	**0 – 114 (30.9)**	**0 – 21 (7.9)**	**6 – 431 (84.5)**
Dead cases (%)	**5 (13.2%)**	**3 (16.7%)**	**2 (18.2%)**	**3 (30.0%)**	**2 (20.0%)**

* **3 from blood and skin, 1 from skin, and 1 from sputum, blood and skin**

Table 3. Comparison of characteristics between survivor and dead cases of HIV-infected subjects with community-acquired pneumonia

	Survivor (n = 171)	Dead cases (n = 21)
Mean CD4	**67.9**	**74.8**
Ratio male to female	**1.9**	**6.0**
Age, %		
20 - 29	**38.2**	**19.0**
30 - 39	**45.3**	**47.6**
over 40	**16.5**	**33.3**
Septicemia	**29**	**2**
***Rhodococcus equi* infection**	**7**	**3**

Table 4. Logistic regression analysis to predict death in HIV-infected subjects with community-acquired pneumonia

	Odds Ratio	95% Confidence Interval
Age group (y.o.)		
20-29	**1.0**	**–**
30-39	**5.48**	**0.55 – 55.04**
over 40	**15.63**	**1.31 – 186.1**
***Rhodococcus equi* infection**	**8.14**	**1.02 – 65.06**
Male	**1.76**	**0.32 – 9.71**
Septicemia	**0.83**	**0.14 – 4.92**
CD4		
below 50	**0.14**	**0.01 – 1.89**
50 - 199	**0.59**	**0.05 – 7.49**
over 200	**1.0**	**–**