CLINICAL FEATURES, ETIOLOGY AND SHORT TERM OUTCOMES OF INTERSTITIAL PNEUMONITIS IN HIV/AIDS PATIENTS

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Abstract. A prospective study was conducted at Bamrasnaradura Hospital, Nonthaburi Province, Thailand from November 11, 2002 to January 5, 2003. A total of 59 HIV/ AIDS patients with interstitial infiltrates on chest radiographs were included in the study. The objectives of this study were to describe the clinical manifestations and determine the etiologies of interstitial pneumonitis, assess the short-term outcomes and determine the accuracy of the clinical diagnosis of the etiologies of interstitial pneumonitis in HIV/AIDS patients at Bamrasnaradura Hospital, Nonthaburi, Thailand. Tuberculosis was the most common diagnosis (44%), followed by *Pneumocystis carinii* pneumonia (25.4%), bacterial pneumonia (20.3%) and fungal pneumonia (10.2%). In tuberculosis, compared to other diagnoses, a mild cough (p=0.031), pallor (p=0.021), lymphadenopathy (p< 0.001), absence of skin lesions (p= 0.003), higher mean body temperature (p=0.004) and an absence of dyspnoea on exertion (p=0.042) were significant findings. On multivariate analysis, however, only an absence of skin lesions (p=0.023) remained a statistically significant predictor of TB. In *Pneumocystis carinii* pneumonia compared to other diagnoses, dyspnea on exertion (p=0.014), non-purulent sputum production (p=0.047), a higher mean respiratory rate (p< 0.001), absence of lymphadenopathy (p<0.001) and lack of purulent sputum (p=0.030) were significant factors. By multivariate analysis, only an absence of lymphadenopathy were shown to be independently and statistically significantly associated (p=0.040). In bacterial pneumonia, compared to other diagnoses, production of purulent sputum (p=0.014), hemoptysis (p=0.006), pallor (p=0), skin lesions (p=0.002) and a severe cough (p=0.020) were significantly associated factors. On multivariate analysis, none of these factors were statistically significant. In fungal pneumonia, compared to other diagnoses, headache and papulonecrotic skin lesions were common findings, but no factor had a significant association. After four weeks, 59.3% of the patients were alive, 13.6% died and 27.1% were lost to follow-up. Among the alive patients 88.6% had clinically improved. On multivariate analysis, no factor was shown to be a statistically significant predictor of death. The cumulative survival after 28 days was highest among PCP patients, followed by bacterial pneumonia, tuberculosis and fungal pneumonia, but this difference was not statistically significant (p=0.0453).

INTRODUCTION

The number of patients with AIDS has increased in recent years as the epidemic of HIV/ AIDS has matured, yet few data have been reported on the clinical manifestations of AIDS in Thailand, which is experiencing one of the largest epidemics in Asia (Chariyalertsak *et al*, 2001). Pulmonary diseases are a major source of morbidity and mortality in patients living with HIV/ AIDS. The lungs of individuals infected with HIV are often affected by opportunistic infections and tumors; over two-thirds of the patients have at least one respiratory episode during the course of the disease (Millar, 1987; Miller, 1996). In most of the countries of sub-Saharan Africa and Asia, where HIV epidemic is at its peak, diagnostic facilities for AIDS-related lung diseases are scarce. Early diagnosis and rapid onset of

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therapy can substantially prolong survival and improve the quality of life of patients with HIV/AIDS.

Early in the AIDS epidemic, pulmonary diagnostic evaluations predominantly focused on *Pneumocystic carinii* pneumonia (PCP) because nearly three quarters of HIV-infected patients developed PCP at least once during the course of the disease. Advances in the identification of risk factors for PCP and the widespread use of PCP prophylaxis, however, have contributed to a decrease the incidence of PCP. Subsequently bacterial pneumonia, which occurs more frequently in HIV-infected persons than in the general population, became an increasingly frequent cause of pneumonia in HIV-infected patients, culminating with the addition of recurrent bacterial pneumonia as an AIDS-defining diagnosis in the Center for Disease Control's (CDC's) 1993 expanded has case definition for AIDS (Huang and Stansell, 1996; CDC, 1992). Tuberculosis has become an increasing cause of morbidity and mortality. Kaposi's sarcoma, the commonest HIV-associated malignancy, may affect the lungs in addition to the skin. HIV-associated pulmonary disorders range from mild abnormalities of pulmonary function unaccompanied by respiratory symptoms, to fulminating opportunistic infections, which were previously rare (Rosen, 1996).

The objectives of this study were to describe the clinical manifestations and determine the etiologies of interstitial pneumonitis as well as to assess the short term outcomes and determine the accuracy of the clinical diagnosis of the etiologies of interstitial pneumonitis in HIV/AIDS patients at Bamrasnaradura Hospital, Nonthaburi, Thailand.

PATIENTS AND METHODS

A prospective cohort study was conducted at Bamrasnaradura Hospital, Nonthaburi from November 11, 2002 to January 5, 2003. Study participants were adult HIV/AIDS patients presenting with respiratory symptoms and signs at the outpatient clinic or admitted to the ambulatory care unit or inpatient department for the same reason. Eligible patients were those ≥13 years old, seropositive HIV status based on 2 repeated tests (ELISA, latex agglutination test) or confirmed by the Western blot test, a chest radiograph showing interstitial infiltrates or mixed interstitial plus any other infiltrates read by a radiologist or pulmonologist. Only the patients who gave informed consent were included in the study. Pregnant cases were not included in the study.

For each enrolled patient, a history, physical examination and investigation were done and documented. The HIV status of the patients was documented from previous records or screened again at Bamrasnaradura Hospital. Interstitial infiltrates on the chest radiographs were confirmed by a radiologist and/or a pulmonologist. Baseline investigations were done and patients presenting with symptoms, laboratory results and chest radiographs highly suggestive of PCP, without any other causative agent discovered, were started on treatment for PCP. Other patients received treatment according to their initial diagnosis. Mycobacterial infections were diagnosed on the basis of acid-fast bacilli (AFB) in the sputum, TTA, lymph node and/or a combination of them. In AFB sputum negative cases, clinical manifestations with radiographic findings were used to diagnose tuberculosis. Bacterial pneumonia was classified according to the result of the Gram's stain of the sputum or TTA aspirates and sputum/TTA/blood cultures. Fungal pneumonia was presumed when sputum smears, TTA aspirates, lymph nodes or skin lesions revealed fungi. Disseminated fungal disease was diagnosed when fungi were isolated from other specimens than sputum.

All patients were reassessed on day 7 and necessary adjustments in treatment/ management were made. Patients were followed at weeks 1, 2 and 4-5 to assess the outcome.

Statistical analysis

All data collected were analyzed using SPSS version 10 (SPSS Inc, 1997) and EPI INFO version 6 (WHO and CDC Atlanta). Sensitivity, specificity and Odds ratios of clinical features were also calculated to indicate the strength of association between the variables of interest. Demographic and clinical parameters were investigated for their association with each of the

different diagnostic categories by univariate and multivariate analysis. For univariate analysis parameters, $p<0.05$ was considered as statistically significant. For multivariate analysis of sex, age and other factors with $p<0.1$, these were further analyzed for their association with each of the diagnostic categories. Survival analysis for death was performed on the total cases and according to the individual diagnoses using the Kaplan-Meir survival method in order to detect time from diagnosis to death. All statistical significance was assessed at the 5% level.

RESULTS

From November 11th 2002 to January 5th 2003 a total of 61 patients presented with interstitial pneumonia to Bamrasnaradura Hospital. Two of them were excluded from the study because of a missing final diagnosis, so that a to-

Table 1
Baseline clinical features of interstitial pneumonia cases (n=59).

Symptom/sign	Number	Percent
General symptoms		
Weight loss	50	84.7
Fever	52	88.1
Diarrhea	26	44.1
Night sweats	36	61.0
Headache	28	47.5
Pulmonary symptoms		
Cough		
Mild	37	62.7
Moderate	13	22.0
Severe	6	10.2
Unknown	3	5.1
Purulent sputum	25	42.4
Nonpurulent sputum	22	37.3
Hemoptysis	4	6.8
Chest pain	34	57.6
Shortness of breath	40	67.8
Dyspnea on exertion	40	67.8
General signs		
Pallor	18	30.5
Jaundice	2	3.4
Oral thrush	22	37.3
Hepatomegaly	7	11.9
Splenomegaly	4	6.8
Lymphadenopathy	29	49.2
Skin lesions	31	52.5
Pulmonary signs		
Abnormal auscultation	27	45.8
Dyspneic appearance	18	30.5
	Median	Range
Duration of fever (days)	14	2-180
Duration of diarrhea (days)	17.5	1-90
Respiratory rate (per minute)	22	18-60
Body weight (kg)	48.3	31-56.9
Body temperature (degree Celsius)	38	36-40

Table 2
Principal diagnoses and associated Dx (in parenthesis) of the interstitial pneumonia cases (n=59).

Diagnosis	Number	Percent
PCP	13	
PC (+TB)	2	
Sub-total PCP	15	25.4
Pulmonary tuberculosis	5	
Pulmonary TB (+ Nocardiosis)	1	
Pulmonary TB (+ Bacterial pneumoniae)	1	
Pulmonary TB (+ Cryptococcal meningitis)	2	
Pulmonary TB (+ Cryptosporodiosis)	1	
Sub-total pulmonary TB	10	16.9
Disseminated tuberculosis	12	
Disseminated TB (+ Cryptococcal meningitis)	1	
Disseminated TB (+ PCP+ Bacterial pneumonia)	1	
Disseminated TB (+ VZV+PID)	1	
Disseminated TB (+ Facial palsy)	1	
Sub-total disseminated TB	16	27.1
Bacterial pneumonia	8	
Bacterial pneumonia (+TB)	1	
Bacterial pneumonia (+ Exfoliative dermatitis)	1	
Bacterial pneumonia (+ Cystic beinchiectasis)	1	
Bacterial pneumonia (+ Kaposi's sarcoma)	1	
Sub-total bacterial pneumonia	12	20.3
Disseminated cryptococcosis	4	
Disseminated cryptococcosis (+CMV)	1	
Sub-total disseminated cryptococcosis	5	8.5
Disseminated histoplasmosis	1	1.7
Grand total	59	100

tal of 59 patients were finally included in our study.

Demographic characteristics

Among the 59 patients in our study, 40 were male (67.8%) with a mean age of 34 years ±8.44. The main reported mode of transmission for HIV infection was heterosexual contact (43 patients, 72.9%), followed by intravenous drug usage (7 patients, 11.9%), homosexual contact (5 patients, 8.5%) and other or unknown risk factors (4 patients, 6.8%). The mean duration of HIV diagnosis was 3.13 years (SD 3.29). Eight participants received antiretroviral treatment (13.6%), 24 were on OI prophylaxis (40.7%) and 25 had a history of previous opportunistic infections (42.2%).

The clinical features are summarized in Table 1. Weight loss (84.7%) and fever (88.1%) were the commonest general symptoms. Cough, shortness of breathe (67.8%) and dyspnea on exertion (67.8%) were the commonest pulmonary symptoms. Skin lesions (52.5%) and lymphadenopathy (49.2%) were the commonest signs noted.

The etiologies of interstitial pneumonitis in the cases are summarized in Table 2.

Tuberculosis was the most common diagnosis among the 59 patients with interstitial pneumonia (pulmonary TB in 10 patients, 16.9%, and disseminated TB in 16 patients, 27.1%). PCP was diagnosed in 15 patients (25.4%), bacterial pneumonia was seen in 12 (20.3%) and fungal pneumonia in 6 participants [5 (8.5%) patients with disseminated cryptococcosis and 1 (1.7%) with disseminated histoplasmosis].

Among the laboratory parameters, only the mean hemoglobin concentration was significantly different between the different diagnostic categories (p=0.001); it was lowest in TB.

The radiological findings according to the diagnostic categories are shown in Table 3. In each category bilateral interstitial infiltrates present the major radiological findings. Nodular infiltrates were only seen in TB (11.4%), whereas cavitary infiltrates were only seen in bacterial pneumonia (8.3%).

Table 4 summarizes the agents identified from the interstitial pneumonia cases. Acid-fast

Table 3
Radiological findings according to diagnostic category (n=59).

Radiological findings	PCP N (%)	TB N (%)	Bacterial N (%)	Fungal N (%)
Interstitial infiltrates				
Unilateral	1 (6.7)	7 (26.9)	3 (25)	1 (16.7)
Bilateral	13 (86.7)	15 (57.7)	8 (66.7)	4 (66.7)
Nodular		1 (3.8)		
Mixed	1 (6.7)		1 (8.3)	1 (16.7)
Patchy		1 (3.8)		
Interstitial thickening		1 (3.8)		
Miliary		1 (3.8)		
Other infiltrates				
Diffuse	3 (20)	1 (3.8)	1 (8.3)	2 (33.3)
Hilar adenopathy	1 (6.7)	5 (19.2)		1 (16.7)
Alveolar	3 (20)	1 (3.8)		
Nodular		2 (7.6)		
Cavitary			1 (8.3)	
Pleural effusion		2 (7.6)		
Patchy		3 (11.5)		
Peribronchial thickening			1 (8.3)	

Table 4
Identified agents from the interstitial pneumonia cases (n=59).

Agent	Number	Percent
Acid-fast bacilli	22	37.3
Bacteria	15	25.4
Acinetobacter spp (1)		
Escherichia coli + MRSA (1)		
Haemophilus influenzae (1)		
Haemophilus influenzae+Streptococcus pneumoniae (1)		
Haemophilus influenzae+Streptococcus viridans (2)		
Streptococcus pneumoniae (1)		
Streptococcus pneumoniae + *Klebsiella pneumoniae* (1)		
Nocardia asteroides (1)		
Pseudomonas aeruginosa (2)		
Staphylococcus aureus + *Bacillus* spp (1)		
Klebsiella pneumoniae + *Streptococcus viridans* (1)		
Other gram-negative bacilli (2)		
Fungi	9	15.3
Cryptococcus neoformans (8)		
Histoplasma capsulatum (1)		
Total	46	78

More than one organism were isolated from some patients

Table 5
Outcome of the interstitial pneumonia cases after 4 weeks of follow-up.

	Number	Percent
Outcome (n=59)		
Alive	35	59.3
Death	8	13.6
Lost to follow-up	16	27.1
Clinical outcome of alive patients (n=35)		
Improved	31	88.6
Not improved	0	0
Deteriorated	4	11.4
Time when lost to follow-up (n=16)		
Week 1	7	43.8
Week 2	9	56.3

bacilli were found in 22 patients (37.3%), bacteria in 15 patients (25.4%) and fungi in 9 patients (15.3%). More than one organism was isolated from some patients. Some organisms were found in association with other agents, but they were not considered to be the causative agents of bacterial pneumonia.

Table 5 summarizes the outcomes of the interstitial pneumonia cases. After four weeks of follow-up, 59.3% of the included patients were alive, 13.6% had died (after 28 days of follow-up) and 27.1% were lost to follow-up, 88.6% of the alive patients had clinically improved, and the rest had deteriorated. The mean survival time (Kaplan Meir) was estimated to be 26 days out of the 28 days (SE 1, 95% CI 24-27) (Fig 1). Log rank analysis of survival distribution for the four different diagnostic categories showed that the cumulative survival was highest among PCP patients, followed by bacterial pneumonia, tuberculosis and fungal pneumonia, but this difference was not statistically significant (p= 0.453) (Fig 2).

Demographic, clinical and laboratory parameters were investigated for their association with death by univariate and multivariate analysis. On univariate analysis a history of previous opportunistic infection (p=0.019), diagnosis of an associated disease (p=0.001), pallor (p=0.003), abnormal lung auscultation (p=0.027) and a higher median BUN (p=0.038) were shown to be strongly associated with death. On multivariate analysis, no factor was found to be an

Table 6
Outcome of the interstitial pneumonia cases according to diagnosis.

Diagnosis	Alive N (%)	Death N (%)	LFU N (%)	p[a]
PCP (n=15)	12 (80)	1 (6.7)	2 (13.3)	0.168
TB (n=26)	13 (50)	4 (15.4)	9 (34.6)	0.415
Bacterial pneumonia (n=12)	6 (50)	2 (16.7)	4 (33.3)	0.762
Fungal pneumonia (n=6)	4 (66.7)	1 (16.7)	1 (16.7)	0.828

[a]p-value is from the chi-square test when PCP was compared with other diagnoses together, TB with others, bacterial pneumonia with others and fungal with all others together.

independent, statistically significant predictor of death.

By comparing the outcomes for each diagnostic category with each of the others, no statistically significant difference was found. The outcomes according to the diagnostic category are summarized in Table 6. In the comparison of PCP with other diagnosis by univariate analysis, non-purulent sputum (sensitivity 60%, specificity 69%, p=0.047), dyspnea on exertion (sensitivity 93%, specificity 41%, p=0.014) and a higher mean respiratory rate (p=0.000) were shown to be strongly associated with PCP. The absence of OI prophylaxis (sensitivity 20%, specificity 48%, p=0.030), of purulent sputum (sensitivity 20%, specificity 48%, p=0.030) and of lymphadenopathy (sensitivity 13%, specificity 37%, p=0.001) showed a statistically significant association. On multivariate analysis, however, only the absence of lymphadenopathy was found to be an independent, statistically significant factor (p=0.040).

In the comparison of tuberculosis with other diagnoses, mild cough (sensitivity 81%, specificity 47%, p=0.031), pallor (sensitivity 46%, specificity 82%, p=0.021), lymphadenopathy (sensitivity 80%, specificity 77%, p=0.000), a higher mean body temperature (p=0.004) and the absence of dyspnea on exertion (sensitivity 54%, specificity 21%, p=0.042) and of skin lesions (sensitivity 31%, specificity 30%, p=0.003) showed a statistically significant association on univariate analysis. Adding hemoglobin as an associated factor on multivariate analysis, we found that only the absence of skin lesions (p= 0.023) remained an independent, statistically significant predictor of TB.

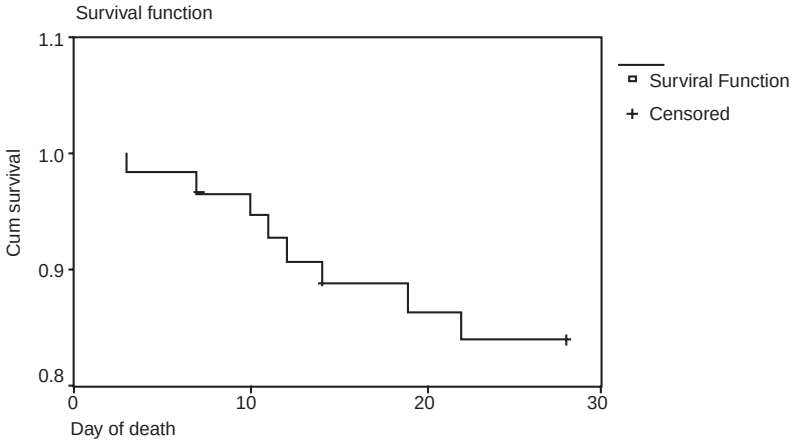
With the comparison of bacterial pneumonia with other diagnoses, by univariate analysis ARV treatment (sensitivity 33%, specificity 91%, p=0.028), OI prophylaxis (sensitivity 75%, specificity 65%, p=0.013), purulent sputum (sensitivity 75%, specificity 64%, p=0.014), hemoptysis (sensitivity 25%, specificity 98%, p=0.006), skin lesions (sensitivity 92%, specificity 57%, p=0.002), and moderate/ severe cough (sensitivity 58%, specificity 73%, p=0.020), were associated with bacterial pneumonia. On multivariate analysis, none of these factors was found to be statistically significant associated factors.

No factor showed a statistically significant association with fungal pneumonia on univariate or multivariate analysis.

DISCUSSION

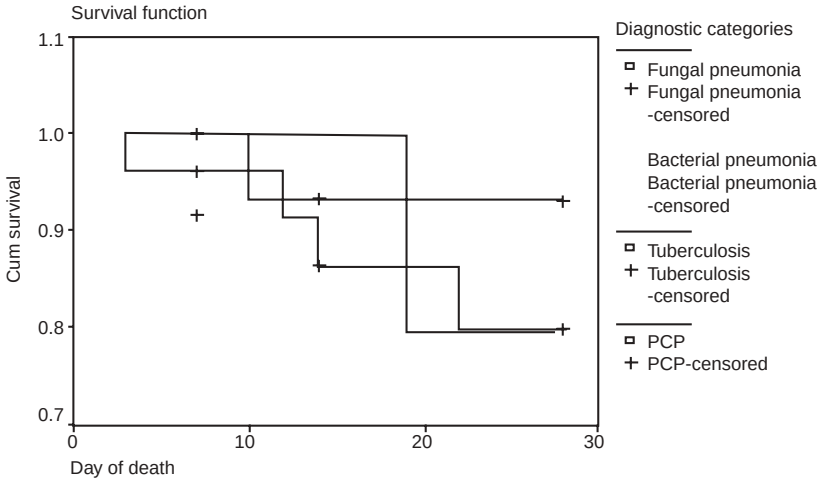
The findings of our study of 59 patients presenting with interstitial pneumonitis revealed that the most common diagnosis was tuberculosis in 44%, which is in accordance with previous studies identifying tuberculosis (pulmonary and extrapulmonary) as the most common opportunistic infection in Thailand as well as in other developing countries (WHO, 1994; Burwen *et al*, 1995; Raviglione *et al*, 1995; Kitayaporn *et al*, 1996; Tansuphasawadikul *et al*, 1998; Zumla *et al*, 1999; Chariyalertsak *et al*, 2001; Putong *et al*, 2002).

A study in Thailand showed that PCP was the fourth most common AIDS-defining condition (Tansuphasawadikul *et al*, 1999). In our study, PCP was the second most common diagnosis of interstitial pneumonitis cases after TB (25.4%). In contrast to these findings, clinicians,



Number of cases: 59 Censored: 51 (86.44%); Events: 8
Survival time: Mean (SE) 26 (1) 95% confidence interval 24-27

Fig 1–Kaplan Meier survival plot of the interstitial pneumonia cases.



Log rank analysis for the equality of survival distribution for different diagnostic categories
Statistic 0.61 df 1 significance 0.453

Fig 2–Kaplan Meir survival plot for 4 different diagnostic categories.

in some developing countries in Africa, report that PCP infection is rare among AIDS patients in their countries. This suggests that there might be significant geographic variation in regards to environmental exposure to this organism, or that early AIDS related mortality due to other causes may reduce the rates of PCP infection among African patients (Chariyalertsak *et al*, 2001).

In contrast to other reports showing that bacterial pneumonia appears to occur more frequently than PCP among HIV-1 infected persons (Noskin and Glassroth, 1996), bacterial pneumonia was the third most common diagnosis after TB and PCP in our study (20.3% of the cases).

Fungal pneumonia due to disseminated cryptococcosis and disseminated histoplasmosis was noted in 10.2% of our study participants. Systemic fungal infections are common among patients with AIDS in Thailand and the frequency of cryptococcosis among AIDS patients in Thailand is significantly higher than that in similar populations in Australia or the USA (Chariyalertsak *et al*, 2001).

Disseminated TB was diagnosed in 61.5% and pulmonary TB in 38.5% of a total of 26 patients with tuberculosis. Previous studies show that evidence for disseminated TB exists in nearly half of the subjects (Alpert *et al*, 1997; Garrait *et al*, 1997; Putong *et al*, 2002). A possible explanation for this is that extensive CD4 cell depletion in HIV infection results in impaired immunity against TB, leading to the development and dissemination of active TB, and that treatment is often delayed (Putong *et al*, 2002). Previous studies in Thailand seem to indicate that fewer than half of all the cases are purely pulmonary (Putong *et al*, 2002). This difference between Thailand and Western countries may be attributed to many factors, including the fact that Western patients are less likely to be significantly immunocompromized, and more likely to have access to antiretroviral therapy. In these circum-

stances, a more typical picture of TB can be expected (Shafer *et al*, 1996, Putong *et al*, 2002).

Analysis of the clinical manifestations of TB-HIV/AIDS patients shows the findings are consistent with other studies. The frequent occurrence of lymphadenopathy is also noted by many researchers and is probably due to the pathological process of clearance of infected macrophages (Shafer and Edlin, 1996; Putong *et al*, 2002). Hematological abnormalities, such as lower mean hemoglobin levels are another finding consistent with previous studies (Sacks and Pendle, 1998; Tansuphasawadikul *et al*, 1999; Putong *et al*, 2002).

Although it has been reported that sputum is more frequently negative than in HIV negative individuals (Helbert *et al*, 1990; Huang and Stansell, 1996; Sacks and Pendle, 1998), this finding could not be confirmed in our study. Almost all the patients diagnosed with tuberculosis were sputum AFB positive in our study. Several reported series indicate that the prevalence of positive sputum smears and cultures in patients with pulmonary TB is approximately the same in HIV-infected and non-infected persons, although this finding has not been universal (Pitchenick *et al*, 1987; Theuer *et al*, 1990; Chin and Hopewell, 1996). On the radiological findings, cavitary infiltrates, while specific, were not seen among the TB patients of our study group. These results are in accordance with previous studies in developed and developing countries (Pitchenick and Rubunson, 1984; Raviglione *et al*, 1992; Shafer and Edlin, 1996; Alpert *et al*, 1997; Sacks and Pendle, 1998; Putong *et al*, 2002), signifying that advanced immunosuppression is associated with a poor granulomatous response.

Analysis of the clinical manifestations of PCP-HIV/AIDS patients shows that these findings are in accordance with previous studies showing that presenting symptoms in HIV-infected patients with PCP are non-specific and include fever, dyspnea on exertion or at rest and cough (Levine *et al*, 1996).

The clinical features of bacterial pneumonia in HIV-infected patients are similar to those of other pneumonia patients. Acute onset of fever, chest pain and a productive cough initially are suggestive of bacterial pneumonia (Noskin and Glassroth, 1996). Our findings of *Streptococcus pneumoniae* and *Haemophilus influenzae* as the most common causes of bacterial pneumonia coincide with the findings of previous studies (Janoff *et al*, 1992; Noskin and Glassroth, 1996; Afessa and Green, 2000). Because of limited diagnostic facilities, atypical bacterial pneumonia due to *Chlamydia pneumoniae*, *Mycoplasma pneumoniae* and *Legionella* spp could not be diagnosed in our study.

Cryptococcal infection may be limited to the lungs in immunocompetent hosts, whereas disseminated disease and meningitis are more common in immunocompromized hosts (Littman and Limmerman, 1956; Kerkering *et al*, 1981; Cameron *et al*, 1991). In our study, disseminated cryptococcosis was diagnosed in 8.5% of the cases, whereas Cryptococcal infection limited to the lungs was not found. Histoplasmosis in patients with AIDS is almost always disseminated (Davies and Sarosi, 1996). One patient with disseminated histoplasmosis was found in our study. Analysis of the clinical manifestations of fungal pneumonia in our cases did not show any factor with a statistically significant association to fungal pneumonia, either on univariate or in multivariate analysis. These findings are similar to those at of other studies (Cameron *et al*, 1991; Meyohas *et al*, 1995; Davies and Sarosi 1996). The manifestations of fungal pneumonia are non-specific and may be mistaken for those of other opportunistic infections, particularly PCP (Cameron *et al*, 1991).

There was no statistically significant difference in outcomes among the different diagnostic categories. In one study, survival was associated with the clinical presentation of TB and the CD4 count, but on multivariate analysis, the CD4 count was the only independent predictor of survival (Shafer *et al*, 1996). We could not analyze the association between the CD4 count and survival because it was not systematically performed. Although not directly comparable, our study showed that on univariate analysis, a history of previous opportunistic infection, the diagnosis of an associated disease, pallor, abnormal auscultation and a higher median BUN

were strongly associated with death in interstitial pneumonia patients. However, on multivariate analysis, no factor was found to be an independent, statistically significant predictor of death. The log rank analysis or the survival distribution for the four different diagnostic categories showed that the cumulative survival after 28 days of follow-up was highest among PCP patients, followed by bacterial pneumonia, tuberculosis and fungal pneumonia, this difference was not statistically significant in the present study. It should be noted that no baseline information was taken into consideration when calculating the time to death. Moreover, the initial date was the date of enrolment, not the date of true first diagnosis.

Our study had several limitations, such as short duration, small sample size, lack of regularity in CD4 counts, limited of laboratory tests and loss of patients to follow-up. However, it sheds light on some important aspects of the interstitial pneumonitis in HIV/AIDS patients.

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REFERENCES

Afessa B, Green B. Bacterial pneumonia in hospitalised patients with HIV Infection. *Chest* 2000; 117: 1017-22.

Alpert PA, Munsiff SS, Gourevitch MN, *et al*. A prospective study of tuberculosis and human immunodeficiency virus infection: clinical manifestations and factors associated with survival. *Clin Infect Dis* 1997; 24: 661-8.

Burwen DR, Bloch AB, Griffin LD, *et al*. National Trends in the occurrence of tuberculosis and acquired immunodeficiency syndrome. *Arch Intern Med* 1995; 155: 1281-6.

Cameron ML, Bartlett JA, Gallis HA, Waskin HA. Manifestations of pulmonary cryptococcosis in patients with acquired immunodeficiency syndrome. *Rev Infect Dis* 1991; 13: 64-7.

Center for Disease Control (CDC). 1993 Revised classification system for HIV infection and expanded surveillance of definition for AIDS among adolescents and adults. *MMWR* 1992; 41 (RR-17):1.

Chariyalertsak S, Sirisanthane T, Saengwonkey O, Nelson KE. Clinical presentation and risk behaviour of patients with AIDS in Thailand, 1994-1998: Regional variation and temporal trend. *Clin Infect Dis* 2001; 32: 955-62.

Chin DP, Hopewell PC. Mycobacterial complications of HIV infection. *Clin Chest Med* 1996; 17: 697-771.

Davies SF, Sarosi GA. Pulmonary complications of HIV infection. Fungal pulmonary complications. *Clinics Chest Med* 1996; 17: 725-44.

Garrait V, Cadranel J, Mayaud H, *et al*. Tuberculosis generates a microenvironment enhancing the productive infection of local lymphocytes by HIV. *J Immunol* 1997; 159: 2824-30.

Helbert M, Robinson, Buchanan D, *et al*. Mycobacterial infection in patients with the human immunodeficiency virus. *Thorax* 1990; 45: 45-8.

Huang L, Stansell JD. AIDS and the lung. *Med clin North Am* 1996; 80: 775-801.

Janoff EN, Breimann RF, Daley CL, Hopewell PC. Pneumococcal disease during HIV infection. *Ann Intern Med* 1992; 117: 314-24.

Kerkering TM, Duma RJ, Shadomy S. Evolution of pulmonary cryptococcosis. Clinical implications from a study of 41 patients with and without compromising host factors. *Ann Intern Med* 1981; 94: 611-6.

Kitayaporn D, Tansuphasawadikul S, Lohsomboon P, *et al*. Survival of AIDS patients in the emerging epidemic in Bangkok, Thailand. *J Acquir Immune Defic Syndr Hum Retrovirol* 1996; 11: 77-82.

Levine SJ, White DA, Fels AOS. The incidence and significance of *Staphylococcus aureus* in respiratory cultures from patients with HIV. *Am Rev Resp Dis* 1990; 141: 89-93.

Littman ML, Zimmerman LE. Cryptocossis, torulosis or European blastomycosis. New York: Grune and Stratton, 1956.

Meyohas MC, Roux P, Bollens D, *et al*. Pulmonary cryptococcosis: localized and disseminated infections in 27 patients with AIDS. *Clin Infect Dis* 1995; 21: 628-33.

Millar A. AIDS and the lung. *BMJ* 1987; 294: 1334-7.

Miller R. HIV-associated and respiratory diseases. *Lancet* 1996; 348: 307-12.

Noskin GA, Glassroth J. Bacterial pneumonia associated with HIV-1 infection. *Clin Chest Med* 1996; 17: 713-23.

Pitchenick AE, Rubunson HA. The radiographic ap-

pearance of TB in patients with AIDS and pre-AIDS. *Am Rev Respir Dis* 1984; 13: 393-6.

Pitchenick AE, Burr J, Suarez M, *et al*. Human T-cell lymphotropic virus III (HTLV III) seropositivity and related disease among 71 consecutive patients in whom tuberculosis was diagnosed. *Am Rev Respir Dis* 1987; 135: 875-9.

Putong NM, Pitisuttithum P, Supanaranond W, *et al*. Mycobacterium tuberculosis infection among HIV/ AIDS patients in Thailand: clinical manifestations and outcomes. *Southeast Asian J Trop Med Public Health* 2002; 33: 346-51.

Raviglione MC, Narain JP, Kochi A. HIV- associated tuberculosis in developing countries: clinical feature, diagnosis and treatment. *Bull World Health Organ* 1992; 70: 515-26.

Raviglione MC, Snider DE, Kochli A. Global epidemiology of tuberculosis: morbidity and mortality of a worldwide epidemic. *J Am Med Assoc* 1995; 273: 220-6.

Rosen MJ. Pulmonary complications of HIV infection: overview of pulmonary complications. *Clin Chest Med* 1996; 17: 621-31.

Sacks LV, Pendle S. Factors related to in-hospital deaths in patients with tuberculosis. *Arch Intern Med* 1998; 158: 1916-22.

Shafer RW, Bloch AB, Larkin C, *et al*. Predictors of survival in HIV-infected tuberculosis patients. *AIDS* 1996; 10: 269-72.

Shafer RW, Edlin BR. TB in patients infected with HIV perspective in the past decade. *Clin Infect Dis* 1996; 22: 683-704.

Tansuphasawadikul S, Amornkul PN, Tanchanpong C, *et al*. Clinical presentation of hospitalised adult patients with HIV infection and AIDS in Bangkok, Thailand. *J AIDS* 1999; 21: 326-32.

Tansuphasawadikul S, Poprawski DM, Pitisuttithum P, Phonrat B. Nonadherence in tuberculosis treatment among HIV patients attending Bamrasnaradura Hospital, Nonthaburi. *J Med Assoc Thai* 1998; 81: 964-69.

Theuer CP, Hopewell PC, Elias D, *et al*. Human immunodeficiency virus infection in tuberculosis patients. *J Infect Dis* 1990; 162: 8-12.

World Health Organisation (TB Programme). TB, a global emergency: WHO report on the TB epidemic. Geneva: WHO. WHO/TB/94.177, 1994.

Zumla A, Bertel S, Chintu C, Grange JM. The tuberculosis pandemic: implications for health in the tropics. *Trans R Soc Trop Med Hyg* 1999; 93: 113-1.