

Pneumocystis carinii Pneumonia : Clinical Presentations, Chest Radiographs, and Outcomes

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Abstract

We retrospectively reviewed clinical presentations, laboratory findings, and chest radiographs of 25 HIV infected patients with *Pneumocystis carinii* pneumonia (PCP), diagnosed at Srinagarind Hospital between April 1992 and April 1994. The most common presentations were fever (100%), dyspnea (100%), nonproductive cough (84%), and tachypnea (100%). Normal leukocyte count, elevated serum lactate dehydrogenase, and hypoxemia were found in 92, 100, and 100 percent respectively. Bilateral diffuse interstitial (28%), perihilar (28%), mixed interstitial/alveolar (36%) were also found. Twenty of 24 cases (83.3%) responded to treatment with trimetoprim/ sulfamethoxazole (TMX/SMZ). A shorter course of steroid (7 days) was as effective as a longer course (>7 days). All patients who received secondary prophylaxis with TMX/SMZ did not relapse during follow-up. Coexisting infections were found in 24 percent, mostly with cryptococcosis. Mortality rate was 16 percent, all of them received mechanical ventilation. (*J Infect Dis Antimicrob Agents* 1996;13:83-8.)

INTRODUCTION

Pneumocystis carinii pneumonia (PCP) is one of the most common pulmonary infections in HIV infected patients, and also a common acquired immunodeficiency syndrome (AIDS) defining criteria (1-6). The prevalence rate of PCP is different among various geographical areas (7-11). Although the clinical presentations, laboratory findings, chest radiographs of PCP are well described in western countries (1-3,5-6,12), there has been no well defined study in Thailand so far because of the lacking of bronchoscopic results for definite PCP diagnosis. Furthermore, pulmonary coinfections with PCP are also common (13). The prevalence of opportunistic infections in Thailand also differ from other countries. Thus, clinical findings and chest radiographs of PCP may be modified or mimicked by other infections.

We retrospectively reviewed clinical presentations, laboratory findings, and chest radiographs of patients with PCP at Srinagarind Hospital, which is located in the northeastern part of Thailand. All of them were definitely diagnosed by bronchoscopy. We also evaluated the efficacy of a short course of steroid treatment for PCP.

MATERIALS AND METHODS

Medical records and chest radiographs of HIV infected patients who were diagnosed and followed up at Srinagarind Hospital, Khon Kaen, between April 1992-April 1994 were reviewed. The inclusion criteria were

1. Patients who were older than 15 years old,
2. PCP was definitely diagnosed by detection of

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Pneumocystis carinii in clinical specimens such as bronchoalveolar lavage fluid or lung tissue using Giemsa or Gomori methenamine silver staining (GMS).

Coexisting pulmonary infections were diagnosed by either a culture confirmation or histologically proven. Chest radiographs were reviewed independently by two authors who were unaware of the clinical diagnosis.

RESULTS

There were 202 HIV infected patients admitted to the hospital during the same period. PCP was clinically suspected in 22 cases (10.9%) and was definitely diagnosed in 25 cases (12.4%). All had history of heterosexual contact with HIV. Patients' age ranged between 20-57 years with a mean of 29.9 years, CD₄ cell count was less than 200/mm³ in all 20 patients who had been tested (mean 152 ± 28/mm³). PCP was the initial AIDS defining illness in 20 patients. The other 5 cases had tuberculosis recently (2 tuberculous lymphadenitis, 2 pulmonary tuberculosis and 1 disseminated tuberculosis).

Duration of the respiratory symptoms was less than 1 week in 5 cases (20%), between 1-2 weeks in 7 cases (28%), and more than 2 weeks in 13 cases (52%). The mean duration of symptoms was 21 days.

The clinical symptoms and signs are shown in Table 1. All patients presented with fever, dyspnea, and mostly non-productive cough. Physical examination of the chest was usually normal; only 20 percent of them had crepitations (rales).

Leukocyte count was usually normal. Only 2 patients (8%) had leukocytosis and both of them had concomitant cryptococcal infection. Arterial blood gas analysis performed in all patients showed that arterial oxygen tension at room air or equivalent was less than 70 mmHg in all cases. Elevated serum lactate dehydrogenase (LDH) level more than 250 unit/L was seen in all patients.

Chest radiographic patterns are summarized in Table 2. All of PCP cases had bilateral diseases. Twenty-eight percent of cases had diffuse interstitial infiltrates. Predominant interstitial infiltrates with a significant alveolar component were also seen in 9 cases (36%). Perihilar infiltrates were found in a similar proportion (28%). Reticulonodular or bilateral upper lobe or lower lobe infiltrates were rarely found. One patient who had diffuse infiltrate developed spontaneous pneumothorax, which needed intercostal drainage and mechanical ventilation.

Table 1. Clinical and laboratory features at presentation in 25 patients with *Pneumocystis carinii* pneumonia.

Symptoms	Percent
Fever	100
Dyspnea	100
Respiratory rate > 30/min	100
Non-productive cough	84
Productive cough	16
Cyanosis	20
Rales	20
PaO ₂ room air < 70 mmHg	100
LDH > 250 unit/L	100
WBC > 10,000/mm ³	8

LDH : lactate dehydrogenase enzyme, WBC : white blood count

Table 2. Chest radiograph findings in *Pneumocystis carinii* pneumonia.

Radiograph finding	No of cases
Bilateral involvement	25
Interstitial/alveolar infiltration	9
Diffuse interstitial infiltration	7
Perihilar infiltration	7
Reticulonodular infiltration	1
Upper/lower lobes infiltration	1
Spontaneous pneumothorax	1

Sputum was obtained by spontaneous cough in 5 cases, and by induction in 10 cases. Bronchoscopy was performed in all cases for the definite diagnosis of *Pneumocystis carinii* infection.

The fluid and sputum were stained by Giemsa and Gomori methenamine silver stain (GMS). *Pneumocystis carinii* was found by both stainings in only bronchoalveolar fluid but not in sputum.

Concomitant pulmonary infections were detected in 6 cases, 5 with *Cryptococcus neoformans*, and 1 with cytomegalovirus infection (Table 3). Two more patients had pulmonary tuberculosis 2 weeks before PCP infection was diagnosed. One patient developed cutaneous dissemination of *Herpes simplex* infection during the treatment of PCP.

Twenty-four patients were treated with trimetoprim/sulfamethoxazole (TMX/SMZ). One patient was treated with intravenous pentamidine because he was allergic to TMX/SMZ. Outcomes of the treatment are summarized in Table 3. Twenty of 24 cases (83.3%) had a successful response (absence of clinical symptoms and evidence of chest radiographic resolution) after 21 days of TMX/SMZ

Table 3. Outcomes of treatment of *Pneumocystis carinii* pneumonia.

Regimen	No of response/ total case	Percent
Trimethoprim/Sulfamethoxazole	20/24	(83.3)
Parenteral pentamidine	1/1	(100)
Prednisolone		
Short course (< 7 days)	17/20	(85)
Long course (> 7 days)	3/4	(75)

treatment.

Most of our patients (17 cases) received a short course of steroid therapy prednisolone 1 mg/kg/day for 7 days. Of these, 85 percent successfully responded as compared to 75 percent of those who received a longer course of steroid (>7 days). The patient who was treated with pentamidine was also fully recovered from the infection.

Four patients expired during the treatment. Two of them also had pulmonary cryptococcal infection. One patient had concomitant pulmonary tuberculosis. He was intubated due to severe respiratory failure and developed pneumothorax during the mechanical ventilatory support. No concomitant opportunistic infection was found in one patient who expired because of severe respiratory failure. This patient did not respond to TMX/SMZ and steroid treatment. Seventeen patients who survived were followed, all but one received TMX/SMZ for secondary PCP prophylaxis, while one received dapson. No PCP relapses occurred during follow up of at least 6 months. Four patients developed cryptococcal meningitis. Three patients expired due to severe sepsis and pneumonia (n=1), and undefined CNS diseases (n=2) after a period of 12-month follow up.

DISCUSSION

PCP is the most common pulmonary infection in HIV infected patients, occurring in 60-80 percent of cases (1-4). The prevalence of PCP is recently declining (8-9). The prevalence of PCP varied in tropical countries (7,8,14). At Srinagarind Hospital, PCP was the second most common pulmonary infection ranked after pulmonary tuberculosis (15). This prevalence differs from other regions of Thailand according to the different prevalence of opportunistic infection. A greater prevalence of tuberculosis and other fungal infections accounted for a lower prevalence of PCP in the tropics and in our

hospital than in western countries (7,8,15).

Clinical presentations of PCP have been reviewed in many papers (1-6). The course of illness had been shown to be more prolonged in HIV infected patients than in other groups (16), but the onset of symptoms may be acute with fulminant respiratory failure without prior history of HIV infection. Physicians may misdiagnose as acute bacterial pneumonia with acute respiratory distress syndrome (ARDS), and appropriate treatment may be delayed (5,16). In this study there were 3 patients who presented as ARDS and received treatment as bacterial sepsis initially. The majority of our cases had an indolent course and presented with more than 2 weeks of symptoms.

Fever, cough, and dyspnea were the main symptoms in our patients similar to the others (1-6,16). Nonproductive cough is common in PCP but productive cough can be seen when other infections superimpose. All of our patients who presented with productive cough had concomitant cryptococcal infection. Physical examination in PCP is nonspecific. Auscultation of lungs tends to give minimal findings. We found rales in only 20 percent of cases and all of them had diffuse interstitial/alveolar infiltrates.

Laboratory studies were also nonspecific (1-6,16). The majority of our patients had a normal leukocyte count in peripheral blood. Serum lactate dehydrogenase (LDH) was elevated in every patient but did not exceed 1,000 unit/L. This elevation of LDH level can be found in up to 90 percent of patients with PCP although other pulmonary diseases can increase it as well (17). Normal LDH level represents compelling evidence against PCP. Hypoxemia, manifested by a decrease in arterial oxygen tension and/or an elevation of arterial and alveolar oxygen gradient, is the rule in PCP although the degree of abnormalities varies according to duration of symptoms and severity of illness (18). Most of our patients also had hypoxemia with PaO₂ less than 70 mmHg and 28 percent of them needed mechanical ventilation. The elevated LDH level, hypoxemia and the requirement of mechanical support are all poor prognostic factors (18).

The degree of immunosuppression as estimated by CD₄ cell count is related to the susceptibility of developing PCP. In a prospective study (19) Phair et al found that PCP was unusual in individuals with CD₄ cell count greater than 200/mm³. Patients with PCP usually have oral thrush and antecedent fever.

In our study, all patients had CD₄ cell count less than 200/mm³ as previous studies (19-21). This can be used as a diagnostic clue in patients who have known status of CD₄ cell count who present with pulmonary infiltration.

The chest roentgenograms were abnormal in at least 95 percent of patients with PCP. Normal radiographs have been described in patients at a very early stage of infection (12,22,23). Classical PCP presents as bilateral perihilar or diffuse interstitial infiltrates. Atypical findings are lobar, reticulonodular, localized infiltration or cavitation (12,24,25). Upper lobe infiltrates predominantly occur in patients who previously used aerosolized pentamidine (24-26). In our series, all had bilateral pulmonary infiltrates, mostly diffuse interstitial (28%), or mixed interstitial/alveolar (36%). One of our patients had predominantly upper lobes infiltrates without prior use of aerosolized pentamidine. The diffuse infiltrates correlated with severe hypoxemia in our patients. We did not see pleural effusion or intrathoracic lymphadenopathy in our patients. These two findings are very rare in literature (12,22,23). Spontaneous pneumothorax is seen in 6-9 percent of PCP cases (27,28). *P. carinii* may cause cystic bullae in the lung parenchyma (29,30). One patient in this study also had spontaneous pneumothorax at initial presentation with diffuse infiltrates.

The concomitant pulmonary infections are also common with PCP (13), since patients with PCP usually have low CD₄ count less than 200/mm³. Cryptococcosis was the most common coexisting pulmonary infection in our study (20%). The prevalence rate of cryptococcosis associated with PCP in the Yinnon study is only 2.3-6.9 percent (13). This can be explained by a high incidence of cryptococcosis in our region.

In our series, PCP was definitely diagnosed only by bronchoalveolar lavage fluid examination. *P. carinii* was not found in expectorated or induced sputum examination stained either by Giemsa or GMS. Many reports suggest that induced sputum gives a high yield of PCP diagnosis (31,32) but we could not confirm this recommendation. This can be partly explained by ineffective induction of sputum due to the lacking of experience. The other reason might be the severe hypoxemia in most of our patients and they could not tolerate the procedure.

Many authorities suggest that patients who present with bilateral interstitial or perihilar infiltrates with hypoxemia should receive empirical therapy for PCP and bronchoscopy can be postponed unless the patients

deteriorate (33). However, in this study, there was a high rate of coexisting infection in PCP (24%), therefore bronchoscopy is recommended in institutes with available facilities. Early and definite diagnosis should be obtained (34) because the clinical manifestation of PCP is nonspecific (1-3,35), and early treatment with steroid in patients who is hypoxic is widely accepted. This can increase the potential for delayed treatment or increasing severity of mimicked or concomitant infections. The major disadvantage of bronchoscopy is pneumothorax, but its incidence has now declined because transbronchial biopsy is rarely performed.

Response rate in our patients to treatment with TMX/SMZ was 83.3 percent which is comparable to the other series (36,37). Trimetoprim/sulfamethoxazole is the most effective drug use for PCP treatment although a side effect is common (36,37). There was not major side effects found in this study but this can be expected when we have more PCP cases in the future. The other explanation is that because we used steroids in all of our cases, it can reduce the incidence of rash as mentioned in some studies (38-40). Steroid was shown to reduce early mortality and respiratory failure (38-40) with a 21 days tapering course.

The response rate of a 7 days prednisolone (1 mg/kg/day) treatment in our patients was 85 percent, which was comparable to those who received the conventional longer course (75%). So we recommend that in a patient who has a clinical improvement without respiratory failure during the first 7 days treatment, this shorter course of steroid should be sufficient.

TMX/SMZ was shown to be the most effective drug for PCP prophylaxis (41,42). No relapse was found in our patients who received TMX/SMZ for PCP prophylaxis.

The mortality rate in our patients was 16 percent. Mechanical ventilatory requirement is associated with high mortality rate (43). All of them received mechanical ventilation and expired within 7 days of treatment. We did not evaluate the correlation of clinical parameters and mortality in our study.

In conclusion, of the clinical presentations and laboratory findings PCP in HIV infected patients seen at our hospital is similar to other series. However our patients had more severe hypoxemia and pulmonary infiltrates than PCP patients in the western countries. Sputum examination is not useful for the diagnosis in our experience. Bronchoscopy with bronchoalveolar lavage

examination is diagnostic procedure. We recommend performing bronchoscopy in institutes with available facilities. TMX/SMZ is an effective drug in our series, both for the treatment and secondary prevention. A short course of steroid is also beneficial in patients who have initially responded.

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