Pneumocystis carinii Pneumonia in Patients without HIV Infection

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Abstract

Background : *Pneumocystis carinii* pneumonia (PCP) can occur in immunocompromised patients without HIV infection. Risk factors, clinical features, treatment outcomes, and factors related to mortality in these patients may be useful clinical data for physicians who care for these patients.

Method : A retrospective study of PCP patients without HIV infection at Ramathibodi Hospital, from 1994 to 2001, was conducted. Only cases with microbiological and/or pathological proven were included.

Results : There were 19 patients with 42.1 per cent males and a mean age of 44.6 years. All patients had underlying immunocompromised diseases. 94.7 per cent of the cases received immunosuppressive drugs. PCP occurred at a mean duration of 26.4 months after the diagnosis and treatment of underlying diseases. Common clinical presentations of PCP were progressive dyspnea, fever, and non-productive cough. All patients had abnormal chest radiography with a majority of bilateral interstitial infiltration (63.2%). Diagnosis of PCP was confirmed with microbiological examination from bronchoalveolar larvage (84.2%) and pathological diagnosis from transbronchial biopsy (15.8%). Almost all of the cases (94.7%) were treated with co-trimoxazole. Ten patients (52.6%) had concomitant bacterial pneumonia or fungal pneumonitis. Overall mortality rate was 36.8 per cent. Mortality was significantly higher in patients who needed mechanical ventilation ($p = 0.006$). There was a trend toward a higher mortality rate in patients with concomitant pulmonary diseases ($p = 0.09$).

Conclusions : PCP may complicate a variety of immunocompromised states especially autoimmune diseases and hematologic malignancy. Patients who receive corticosteroids and/or cytotoxic drugs should receive primary PCP prophylaxis. The mortality rate is high especially in severe cases that need mechanical ventilation. Intensive care and close monitoring are needed for these patients.

Key word : *Pneumocystis carinii* Pneumonia, PCP, Non-HIV, Mortality Rate

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J Med Assoc Thai 2003; 86: 612-616**

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Pneumocystis carinii pneumonia (PCP) can occur in patients with a variety of immunocompromised states[1-9]. Cellular immunodeficiency from the disease or treatment is responsible for the risk of PCP[1,10]. In the era of HIV infection, the high rate of PCP occurs among HIV-infected patients and overshadows PCP as a cause of pneumonia in non HIV-infected patients. The studies regarding the incidence of PCP in non-HIV infected patients reveal an increasing incidence[11,12]. Mortality in non-HIV infected patients is much higher[6,12,13]. The data regarding risk factors, clinical features, and treatment outcomes in these patients may be useful for physicians who care for PCP patients without HIV infection.

MATERIAL AND METHOD

A retrospective study of PCP patients without HIV infection at Ramathibodi Hospital was conducted. Only cases with microbiological and/or pathological proven PCP, from January 1994 to December 2001, were included. HIV-infected patients were excluded. The data regarding risk factors, clinical features, treatment outcomes, and mortality rate in these patients were studied. General characteristics of patients were described using mean and standard deviation for continuous data, frequency and percentage for categorical data. Association between the mortality and related factors was determined using Fisher-exact test. Analyses were performed using STATA version 7.0[14]. P-value less than 0.05 was considered as statistically significant.

RESULTS

There were 19 patients. Eight of the 19 (42.1%) were male. The age of the patients ranged from 25-81 years. Mean age was 44.6 ± 16.1 years. The numbers of cases in each year from 1994 to 2001 were 1, 3, 3, 1, 2, 5, 3, 3 cases, respectively. All patients had underlying diseases including systemic lupus erythematosus (6 cases, 31.5%), hematologic malignancy (6 cases, 31.5%), bone marrow transplantation (3 cases, 15.8%), solid organ malignancy (1 case, 5.3%), chronic renal failure (1 case, 5.3%), renal transplantation (1 case, 5.3%), and polyarteritis nodosa (1 case, 5.3%). Eighteen patients (94.7%) received immunosuppressive drugs including high dose corticosteroids, cytotoxic drugs, or both. PCP occurred at a mean (range) duration of 26.4 (1-156) months after the diagnosis and treatment of the underlying diseases. Clinical manifestations, chest radiography, and laboratory findings are shown in Table 1. All patients had abnormal chest radiography. Diagnosis of PCP was confirmed with microbiological examination from bronchoalveolar larvage (16 cases, 84.2%) and pathological diagnosis from transbronchial biopsy (3 cases, 15.8%). Eighteen from 19 patients (94.7%) were treated with sulfamethoxazole/trimethoprim; the other was treated with clindamycin and primaquin due to hypersensitivity to sulfamethoxazole/trimethoprim. Ten patients (52.6%) had concomitant bacterial pneumonia or fungal pneumonitis. Seven patients died from respiratory failure. Overall mortality rate was 36.8 per cent. Factors related to mortality are shown in Table 2. The mortality was significantly higher in patients who needed mechanical ventilation ($p = 0.006$). The mortality rate in patients who needed mechanical ventilation was 75 per cent.

Table 1. Clinical manifestations of 19 PCP patients without HIV infection.

Clinical characteristics	Cases	%
Clinical manifestations		
Fever	17	89.5
Progressive dyspnea	18	94.7
Nonproductive cough	13	68.4
Productive cough	6	31.6
Crackles	9	47.4
Wheezing	2	10.5
Chest radiography		
Interstitial infiltration	12	63.2
Interstitial and alveolar infiltration	4	21.1
Alveolar infiltration	4	21.1
Ground-glass appearance	3	15.8
Laboratory findings		
Hypoxemia (PaO_2 < 60 mmHg)	9	47.4
Elevated LDH (> 310 U/L)	12	63.2
Hypoalbuminemia (< 30 g/L)	10	52.6

DISCUSSION

The present study showed a higher incidence of PCP in patients without HIV infection in the recent years. More than half of the cases occurred in the last 3 years of the study. More potent immunosuppressive therapy given for a wider array of diseases and the higher incidence of transplantation may be the explanation for this finding[15]. Almost all of the patients (94.7%) in the present study received immunosuppressive drugs. A variety of underlying diseases also reflect the various immunocompromised states in clinical practice-systemic lupus erythematosus and hematologic malignancy.

Table 2. Factors related to mortality in 19 PCP patients without HIV infection.

Factors	Cases of nonsurvivors (n = 7)	%	Cases of survivors (n = 12)	%	Relative risk (95% CI)	P-value
Renal or bone marrow transplantation	1	14.3	3	25.0	0.5 (0.42-6.02)	0.30
Previous chemotherapy	6	85.7	9	75.0	2.0 (0.17-24.07)	0.30
Previous corticosteroid therapy	6	85.7	9	75.0	2.0 (0.17-24.07)	0.30
Previous chemotherapy and corticosteroid therapy	5	71.4	7	58.3	1.79 (0.24-13.21)	0.32
Concomittant pulmonary infection	4	57.1	6	50.0	1.33 (0.20-8.71)	0.09
Mechanical ventilation	6	85.7	2	16.7	30.0 (4.5-90.3)	0.006

A wide range (1-156 months) of the duration after the diagnosis and treatment of the underlying diseases and PCP demonstrates that there is no specific time for the PCP occurrence. Common clinical presentations of the patients were progressive dyspnea, fever, and non-productive cough, all of which were not different from HIV-infected patients[1]. However, the clinical course of PCP in patients without HIV progresses rapidly[11,16]. A study of the role of hospital experience in the diagnosis of PCP showed that a hospital's prior experience with patients with PCP is associated with an early and correct diagnosis[17]. Hence, awareness of PCP is needed for the early diagnosis in patients without HIV infection. Chest radiography in the presented patients showed a distribution of abnormalities as seen in previous studies in both HIV and non-HIV infected patients [1,11]. The diagnosis in the majority of the patients (84.2%) was confirmed with microbiological examination from bronchoalveolar larvage. In addition, many studies showed the effectiveness of this diagnostic procedure in both HIV and non-HIV infected patients [18-23]. Bronchoscopy and bronchoalveolar larvage should be performed in patients without HIV infection who were suspected for PCP. Sputum induction was inferior since only 6.9 per cent had a positive result from a comparative study[20].

Overall mortality rate in the present study was similar to previous studies (36.8% and 35-50%) [6,11-13]. However, mortality rate in patients who needed mechanical ventilation in our study was higher than a previous study (75% *versus* 59%)[13]. Intensive ventilator care and early ventilation support may minimize the mortality. Mechanical ventilation is the only significant factor related to the mortality ($p = 0.006$). There was a trend toward a higher mortality in patients with concomitant pulmonary diseases ($p = 0.09$).

In conclusion, PCP is another important cause of pneumonia in a variety of immunocompromised patients other than HIV infection. Clinical suspicion of PCP is needed for an early diagnosis. Primary PCP prophylaxis should be given in patients with autoimmune diseases or hematologic malignancy and they should receive chemotherapy and/or corticosteroids therapy. According to the high mortality, intensive care and close monitoring should be provided for severe cases that need mechanical ventilation.

ACKNOWLEDGEMENTS

The authors wish to thank all the attending staff and residents who cared for the patients in this study and all the staff in the tuberculosis section of the microbiology laboratory.

(Received for publication on September 28, 2002)

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โรคปอดอักเสบจากเชื้อ *นิวโมซิสติส คารินิไอ* ในผู้ป่วยที่ไม่ติดเชื้อเอ็ชไอวี

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ที่มา : ปอดอักเสบจากเชื้อ*นิวโมซิสติส คารินิไอ* (พีซีพี) พบได้ในผู้ป่วยที่มีภูมิคุ้มกันบกพร่องที่ไม่ได้เกิดจากการติดเชื้อเอ็ชไอวี การศึกษาปัจจัยเสี่ยง ลักษณะทางคลินิก ผลการรักษา และปัจจัยที่มีผลต่ออัตราการตายน่าจะเป็นประโยชน์ต่อการดูแลรักษาผู้ป่วยเหล่านี้

วิธีศึกษา : เป็นการศึกษาแบบย้อนหลังในผู้ป่วยโรคพีซีพีที่ไม่ติดเชื้อเอ็ชไอวีในโรงพยาบาลรามาธิบดี โดยรวบรวมผู้ป่วยในปีพ.ศ. 2537-2544 คัดเลือกผู้ป่วยที่ได้รับการยืนยันการวินิจฉัยโดยการพบเชื้อจากการตรวจทางจุลชีววิทยา และ/หรือทางพยาธิวิทยา

ผลการศึกษา : มีผู้ป่วยจำนวน 19 ราย เป็นเพศชายร้อยละ 42.1 และผู้ป่วยมีอายุเฉลี่ย 44.6 ปี ผู้ป่วยทุกรายมีโรคประจำตัวที่ทำให้ระบบภูมิคุ้มกันพกพร่อง ร้อยละ 94.7 เคยได้รับยากดภูมิคุ้มกันมาก่อน โรคพีซีพีเกิดขึ้นในระยะเวลาเฉลี่ย 26.4 เดือนหลังได้รับการวินิจฉัยและรักษาโรคประจำตัว อาการนำที่พบบ่อยคือเหนื่อย ไข้ และไอแห้ง ๆ ผู้ป่วยทุกรายมีภาพถ่ายรังสีปอกผิดปกติ ส่วนใหญ่ร้อยละ 63.2 เป็นแบบ bilateral interstitial infiltration การวินิจฉัยได้รับการยืนยันโดยการพบเชื้อจากการตรวจทางจุลชีววิทยาร้อยละ 84.2 และทางพยาธิวิทยาจากการตรวจชิ้นเนื้อปอดร้อยละ 15.8 ผู้ป่วยเกือบทุกราย (ร้อยละ 94.7) ได้รับการรักษาด้วยโคไตรม็อกซาโซล มีผู้ป่วย 10 ราย (ร้อยละ 52.6) ที่มีการติดเชื้ออื่นที่ปอดร่วมด้วย อัตราการตายเท่ากับร้อยละ 36.8 ผู้ป่วยที่ต้องใช้เครื่องช่วยหายใจจะมีอัตราการตายสูงกว่าอย่างมีนัยสำคัญทางสถิติ ($p = 0.006$) และมีแนวโน้มของอัตราการตายที่สูงขึ้นในผู้ป่วยที่มีการติดเชื้ออื่นที่ปอดร่วมด้วย ($p = 0.09$)

สรุป : โรคพีซีพีเป็นโรคแทรกซ้อนที่พบได้ในผู้ป่วยที่มีระบบภูมิคุ้มกันพกพร่องชนิดต่าง ๆ โดยเฉพาะผู้ป่วยที่เป็นโรค autoimmune และโรคมะเร็งทางระบบโลหิต ในผู้ป่วยที่ได้รับยากดระบบภูมิคุ้มกันควรได้รับยาป้องกันโรคพีซีพีชนิดปฐมภูมิ ในผู้ป่วยที่ต้องใช้เครื่องช่วยหายใจมีอัตราการตายสูง ควรได้รับการดูแลอย่างใกล้ชิด

คำสำคัญ : ปอดอักเสบจากเชื้อ*นิวโมซิสติส คารินิไอ*, PCP, ไม่ติดเชื้อเอ็ชไอวี, อัตราการตาย

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จดหมายเหตุทางแพทย์ ฯ 2546; 86: 612-616

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