

Four Cases of *Pneumocystis carinii* Pneumonia in Shenyang, Northeast China

CHUN-LI AN¹⁾ AND MASANOBU TANABE^{1,2)}

¹⁾Department of Parasitology, School of Basic Medicine, China Medical University, No. 92, Bei 2 Ma Ru, Heping-Qu, Shenyang City, Liaoning Province (ZIP=110001), The People's Republic of China.

²⁾Department of Tropical Medicine and Parasitology, School of Medicine, Keio University, 35 Shinanomachi, Shinjuku-ku, Tokyo 160, Japan.

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Abstract

The first four cases of *Pneumocystis carinii* pneumonia (PCP) were etiologically diagnosed from the hospitalized patients in Shenyang, northeast China. *P. carinii* was identified by Giemsa and Gomori's methenamine silver nitrate stains in the specimens obtained by transbronchial lung biopsy (TBLB) and bronchoalveolar lavage (BAL). These patients were all recipients of renal transplantation and showed clinical signs and symptoms due to interstitial pneumonia during immunosuppressive therapy. They were all cured by oral administration of trimethoprim-sulfamethoxazole, but one of them later died of aspergillosis. Background, clinical course and diagnosis of these patients are discussed with special reference to PCP cases in China.

Key words: *Pneumocystis carinii* pneumonia (PCP); Gomori's methenamine silver nitrate stain (GMS); transbronchial lung biopsy (TBLB); bronchoalveolar lavage (BAL).

Introduction

Pneumocystis carinii is an opportunistic pathogen that often causes interstitial pneumonia among the subjects who have an abnormal or altered immune status (Walzer *et al.*, 1974). Because antibacterial or anti-fungal chemotherapy has no effect on *P. carinii* pneumonia (PCP), the mortality rate for non-AIDS patients has been estimated as nearly 100% in the absence of appropriate treatment (Goldsmith, 1994). Therefore, proper diagnosis and adequate treatment in the early phase of the disease are required to lower its mortality rate.

The diagnosis of PCP is usually performed by the identification of the organisms in the clinical specimens using cytological staining (Goldsmith, 1994; Walzer, 1988) or immunohistochemistry using monoclonal antibody (Blumenfeld and Kovacs,

1988), and by the demonstration of specific DNA or RNA sequences using polymerase chain reaction (Kitada *et al.*, 1991) or *in situ* hybridization (Hayashi *et al.*, 1990). Recently, we have established a diagnostic method for PCP using cytological stains, Giemsa and Gomori's methenamine silver nitrate (GMS) stains, in our laboratory (An *et al.*, 1994). Then we have applied this method to the etiological diagnosis of the clinically suspected patients, and demonstrated the first PCP cases from the hospitalized patients in Shenyang, northeast China.

In this communication, we present the background, clinical course, diagnosis and treatment of these patients, and also summarize PCP cases reported in China until June, 1995.

Materials and Methods

During March 1994 and April 1995, clinically suspected patients with PCP were selected according to its clinical criteria (Goldsmith, 1994; Walzer, 1990) from the hospitalized patients in the Military General Hospital of Shenyang and the First Hospital of China Medical University, Shenyang City, northeast China. Five patients were clinically diagnosed

Correspondence: Chun-Li AN

安 春麗¹, 田邊將信² (¹中国医科大学基础医学部寄生虫学教研室, ²慶應義塾大学医学部熱帯医学・寄生虫学教室)

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as suspected PCP cases. They were all recipients of renal transplantation and had received immunosuppressive therapy. They showed persistent fever, some respiratory symptoms, abnormalities on chest roentgenography, and unresponsiveness to chemotherapy with antibiotics. The specimens were prepared by transbronchial lung biopsy (TBLB) and bronchoalveolar lavage (BAL), and were immediately fixed with methanol. *P. carinii* was identified according to our previous method (An *et al.*, 1994) using Giemsa and GMS stains.

Results

By parasitological examinations, *P. carinii* could be identified in the specimens prepared by TBLB and BAL from 4 out of 5 clinically suspected patients. The clinical progress of these 4 patients are summarized in Table 1. The mean age (range) of these patients was 42.8 (28–51) years old. The signs of pneumonia appeared during the immunosuppressive therapy for the management of organ transplants, with a mean latent period (range) of 4.3 (2–9) months after renal transplantation. They showed persistent high fever and bilateral diffuse infiltrations on chest roentgenography with or without respiratory symptoms such as nonproductive dry

cough, tachypnea and dyspnea. Anti-bacterial chemotherapy had no effect on these patients. They were all cured by oral administration of trimethoprim (TMP)-sulfamethoxazole (SMX) for two weeks in a dose of 20 mg TMP and 100 mg SMX per kg of body weight per day in four divided doses. However, one patient later died of aspergillosis.

It is summarized in Table 2 that 55 PCP cases, 38 males and 17 females, have been reported in China as of June, 1995. The first report of two infantile cases was published in 1959. The number of cases reported from Beijing and Shanghai was greater than those from other cities. Out of these 55, 13 patients (23.6%) were infants in the 0–1 year age group. Eighteen patients (32.7%) were children in the 2–16 year age group, and 24 subjects (43.6%) were adults over 18 years old. The most prevalent underlying disease predisposing to the development of PCP was hematopathy (27 cases), followed by renal transplantation (9 cases), congenital immunodeficiency (5 cases), lung cancer (5 cases), immature fetus (2 cases), lung diseases (2 cases), AIDS (one case), severe senile hepatitis (one case), *Legionella pneumophila* pneumonia (one case), neurodermatitis (one case), and unidentified patient (one case). Of these 55, 20 cases (36.4%) were pathologically diagnosed by post-mortem autopsy.

Table 1 Age, sex and clinical progress in four cases of *Pneumocystis carinii* pneumonia in Shenyang, China

Cases	Age (year)	Sex	Latent period (months)	Underlying disease	Symptoms	Chest roentgenography	Diagnosis	Treatment and outcome
1	49	Female	2	Renal transplantation/steroid therapy	Fever (39°C), tachypnea	Bilateral diffuse infiltrates, blot-like shadow	TBLB	Recovered, but died of aspergillosis
2	51	Female	3	Renal transplantation/steroid therapy	Fever (39.8°C), dyspnea, non-productive cough	Bilateral diffuse infiltrates, thin piece-like shadow	TBLB	Recovered
3	28	Male	3	Renal transplantation/steroid therapy	Fever (41°C)	Bilateral diffuse infiltrates, thin piece-like shadow	TBLB BAL	Recovered
4	43	Male	9	Renal transplantation/steroid therapy	Fever (39–40°C)	Bilateral diffuse infiltrates, tiny node-like shadow	TBLB	Recovered

Table 2 List of 55 cases with *Pneumocystis carinii* pneumonia reported in China until June, 1995

Number of report	Age (year)	Sex	Number of patients	Underlying disease	Diagnosis	Reported area	References
1	<1	Male Female	1 1	Immature fetus	Autopsy	Beijing	Jirovec (1959)
2	36	Male	1	Renal transplantation	Open lung biopsy	Shanghai	Xu <i>et al.</i> (1979)
3	<1	Female	1	Congenital immunodeficiency	Autopsy	Shanghai	Chen & Xu (1981)
4	48, 50	Male	2	Renal transplantation	Autopsy	Beijing	Yu & Wang (1982)
5	<1	Male	1	Congenital immunodeficiency	Autopsy	Sichuan	Xiang (1984)
6	<1	Male	1	Congenital immunodeficiency	Autopsy	Shanghai	Zhao & Wang (1985)
7	34	Male	1	AIDS	Autopsy	Beijing	Hong (1986)
8	<1	Male	1	Congenital immunodeficiency	Autopsy	Sichuan	Wu & Zheng (1986)
9	1-16	Male Female	10 6	Leukemia (16)	Autopsy (2) Clinical (14)	Beijing	Yang <i>et al.</i> (1987)
10	42	Male	1	Renal transplantation	Autopsy	Sichuan	Liu <i>et al.</i> (1988)
11	14	Male	1	Leukemia	Autopsy	Beijing	Ma (1988)
12	63	Male	1	Neurodermatitis	Autopsy	Shanghai	He <i>et al.</i> (1991)
13	<1	Male	1	Congenital immunodeficiency	Autopsy	Beijing	Wang <i>et al.</i> (1991)
14	40, 54	Male Female	1 1	Renal transplantation	Autopsy	Beijing	Xing <i>et al.</i> (1993)
15	40	Male	1	<i>Legionella pneumophila</i> pneumonia	BAL	Beijing	Lin <i>et al.</i> (1993)
16	70	Male	1	Severe senile hepatitis	Autopsy	Beijing	Huang <i>et al.</i> (1994)
17	4-11	Male Female	3 2	Leukemia (5)	Clinical (5)	Beijing	Hu & Tan (1994)

18	<1	Male	1	Essential thrombopenia	Autopsy	Haerbin	Huang <i>et al.</i> (1994)
19	18–53	Male Female	1 3	Leukemia (3) Essential thrombopenia (1)	Clinical (4)	Shanghai	Yuan (1994)
20	40	Male	1	Unidentified	Autopsy	Beijing	Jiang (1994)
21	36–42	Male	3	Renal transplantation (3)	TBLB (2) BAL (1)	Shanghai	Ju (1995)
22	58–66	Male Female	4 3	Lung cancer (5) Lung diseases (2)	Tracheal smear (7)	Guiyang	Chen (1995)

Twenty-three cases (41.8%) were clinically diagnosed, and the remainder, 12 cases (21.8%), were etiologically diagnosed by the identification of *P. carinii* in the specimens obtained by tracheal smear (7 cases), TBLB (2 cases), BAL (2 cases), and open lung biopsy (one case). Eighteen cases were cured by chemotherapy, but 17 patients died as a result of PCP (8 cases), or primary or secondary diseases (9 cases).

Discussion

In the present study, *P. carinii* was demonstrated by the cytological stains using Giemsa and GMS in the specimens obtained by BAL and TBLB from 4 out of 5 patients clinically suspected of having PCP. This suggests that our employed method has a sufficient sensitivity for the diagnosis of symptomatic PCP cases, and is consistent with previous findings (Flick *et al.*, 1986; Leibovitz *et al.*, 1995). The preparative methods of clinical specimens have been known to affect seriously the efficiency of PCP diagnosis. BAL and TBLB are regarded as the most valuable method for the PCP diagnosis today, because these methods have a high diagnostic sensitivity and relatively low invasiveness (Flick *et al.*, 1986; Leibovitz *et al.*, 1995; Walzer, 1988). Moreover, recent studies indicate that cytological staining techniques are as informative as polymerase chain reaction for the PCP diagnosis, when the specimens obtained by BAL are utilized (Leibovitz *et al.*, 1995;

Armbruster *et al.*, 1995). The high diagnostic efficiency in our study owes to the utilization of BAL or TBLB for the preparation of the specimens. However, cytological staining is not sufficiently sensitive for the identification of organisms in the expectorated or induced sputum (Leibovitz *et al.*, 1995; Armbruster *et al.*, 1995). Therefore, in these cases more sensitive methods such as immunohistochemistry using a monoclonal antibody (Blumenfeld and Kovacs, 1988), polymerase chain reaction (Wakefield *et al.*, 1991; Kitada *et al.*, 1991) and *in situ* hybridization of ribosomal RNA with a biotinylated oligonucleotide probe (Hayashi *et al.*, 1990) are recommended.

The present study also indicates that proper diagnosis and treatment in the early phase of the disease are efficacious for lowering the mortality rate of PCP patients. Without adequate treatment, the fatality rate for non-AIDS patients has been estimated as nearly 100% (Goldsmith, 1994). Accordingly, it seems to be important to diagnose PCP patients properly. However, as shown in Table 2, only 55 cases have been reported in China as of June, 1995. Moreover, only 12 cases (21.8%) of them have been etiologically diagnosed by the identification of *P. carinii* during the progress of the disease. Furthermore, the reported cases showed a concentration in the big cities such as Beijing and Shanghai. These evidences probably suggest that the clinical doctors in China have insufficient knowledge on PCP. PCP cases are expected to increase with the growing

number of patients with AIDS, organ transplantation and various diseases accompanying immunodeficiency in China. Therefore, awareness of this disease, and establishment of diagnostic methods and adequate treatment are truly required for the management of these immunocompromised hosts. Accordingly, dissemination of knowledge concerning PCP, and its diagnosis and treatment in China is an urgent issue.

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