Pneumocystis carinii Colonization in the Absence of Immunosuppression

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A prospective study was undertaken to evaluate the incidence and the course of Pneumocystis carinii colonization in immunocompetent patients with severe pulmonary diseases. A further perspective was to determine the diagnostic values of different detection methods. Bronchoalveolar lavage fluid samples from 77/838 adult HIV-negative patients were examined by Diff-Quik stain, direct immunofluorescence test and polymerase chain reaction. All Diff-Quik stains were negative, but direct immunofluorescence tests and polymerase chain reactions were positive in the samples of 5 patients. The normal number of granulocytes and CD4 + T- lymphocytes (median 810 cells/µl) and normal values of immunoglobulins proved the relative competence of the immune systems of the 77 patients. Although none of these patients received any agent effective against P. carinii, none developed a P. carinii pneumonia within a 120.5-d surveillance period. Nosocomial transmission could be excluded. As the colonization with P. carinii did not result in pneumonia in immunocompetent patients, clinically silent carriers have to be assumed. In non-AIDS patients, sensitive detection methods have to be used to identify colonized persons.

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INTRODUCTION

Pneumocystis carinii pneumonia (PCP) occurs predominantly in immunocompromised patients (1, 2) and is extremely rare in immunocompetent adults (3). In those patients not suffering from the acquired immunodeficiency syndrome (AIDS), PCP has almost exclusively been described in patients receiving long-term corticosteroid therapy (4–6) and in patients with underlying malignant diseases (1, 7). Diff-Quik staining is the most effective diagnostic tool for PCP, if the number of parasites in bronchoalveolar lavage fluid (BALF) is high (8). New detection methods, such as immunofluorescence tests (DIFF) and polymerase chain reactions (PCR), have recently been described, making the detection of few numbers of the organism possible (9, 10). Low numbers of parasites may be found in clinically silent but colonized persons. Such carriers may be at risk of a reactivation or may be the source of a nosocomial transmission (11, 12). Recent reports demonstrate such a colonization in HIV-antibody negative persons (13, 14).

The aim of our prospective study was to evaluate the incidence and the course of P. carinii colonization in immunocompetent patients with primary pulmonary diseases and to describe the diagnostic value of different detection methods.

MATERIALS AND METHODS

Over an 18-month period in 1994–95, 838 HIV-antibody negative patients with acute respiratory illness underwent bronchoscopy on an outpatient basis. Inclusion criteria were normal immunological function, no immunosuppressive or cytotoxic therapy in case history and no specific therapy against P. carinii. 77 patients (44M) met these criteria. The mean age was 49.8 y (range 22–87 y). They did not receive any cytotoxic drugs or corticosteroids before and after bronchoscopy. An informed consent was obtained after the nature of the procedure had been fully explained. Bronchoscopies, processing of the BALF samples, and P. carinii PCR were performed according to methods described previously (8, 10, 15). The samples were also tested with DIFT (Cellabs Pty Ltd, Sydney, Australia). Smear staining and cultures were carried out for isolation and identification of bacteria and mycobacteria.

Each patient underwent a chest roentgenogram (postero-anterior, lateral view), and an arterial blood gas measurement (AVL 947, AVL, Graz, Austria). Measurements of immunological functions were performed by blood cell count and flowmetry (the cells were stained with fluorescein isothiocyanate and phycoerythrune, FACS Prep., Becton Dickinson, San José, CA, USA) in peripheral blood and BALF. Kinetic nephelometry (ARRAY 360 System, Beckman Instruments Inc., Fullenton, CA, USA) was performed also. The patients were followed up for a mean of 120.5 d (range 4–845 d). They were evaluated biweekly by physical examination and arterial blood gas measurement.

Mean values, medians, and standard deviations were calculated using SPSS 6.0.1 (Krankenanstalt Rudolfsstiftung, Vienna, Austria).

RESULTS

In 5/77 HIV-antibody negative and immunocompetent patients a colonization with P. carinii could be proven by corresponding positive test results in DIFT and PCR. Diff-Quik staining was negative in all cases. The characteristics of the 5 P. carinii colonized patients are listed in Table I. The patients did not receive any specific therapy against P. carinii at any time, and they did not get corticosteroids and cytotoxic drugs. During the mean 95 d of follow up none of the colonized patients developed clinical signs of PCP.

The respiratory symptoms of the 77 patients did not meet the Centers for Disease Control (CDC) criteria for a pre-
Table I. Characteristics of the 5 patients with *P. carinii* colonization

<table>
<thead>
<tr>
<th>No.</th>
<th>Sex</th>
<th>Chest roentgenogram</th>
<th>PaO₂/PaCO₂ (kPa)</th>
<th>Results of CD4+ / CD8+ cells/µl</th>
<th>Pulmonary disease</th>
<th>Follow-up in days/alive/outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>bilateral consolidation</td>
<td>11.30/5.32</td>
<td>Diff-Quik ++</td>
<td>1600/600</td>
<td>tuberculosis</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>bilateral consolidation</td>
<td>9.38/5.03</td>
<td>DIFT ++</td>
<td>1390/600</td>
<td>bronchogenic carcinoma</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>unilateral pleural effusion</td>
<td>10.50/4.12</td>
<td>PCR ++</td>
<td>850/300</td>
<td>pleuritis (Mycobacterium tuberculosis)</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>unilateral consolidation</td>
<td>10.24/5.19</td>
<td></td>
<td>1510/520</td>
<td>tuberculosis</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>unilateral consolidation</td>
<td>10.51/5.05</td>
<td></td>
<td>nd</td>
<td>bacterial pneumonia</td>
</tr>
</tbody>
</table>

**nd,** Not done.

**DISCUSSION**

Recent studies have pointed out that *P. carinii* is an ubiquitous parasitic fungus (18, 19), but it is still a major point of discussion whether acute *P. carinii* infection occurs as a combination of both (1,5,6,11,19). It has been suggested that the healthy host is not colonized by *P. carinii*; however, healthy individuals are not colonized by *P. carinii*. It has been suggested that the healthy host is not colonized by *P. carinii*. It has been suggested that the healthy host is not colonized by *P. carinii*.

In 577 patients (6.5%), *P. carinii* was identified in BALF. This value corresponds closely with recent findings in Spanish HLV-infected patients with chronic pulmonary disease.

**Table II. Underlying pulmonary disease (n = 77)**

<table>
<thead>
<tr>
<th>No.</th>
<th>Underlying pulmonary disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>Lung edema</td>
</tr>
<tr>
<td>13</td>
<td>Mycobacterium tuberculosis</td>
</tr>
<tr>
<td>19</td>
<td>Bronchogenic carcinoma</td>
</tr>
<tr>
<td>13</td>
<td>Acute bronchiectasis</td>
</tr>
<tr>
<td>13</td>
<td>Bacterial pneumonia</td>
</tr>
<tr>
<td>13</td>
<td>Bacterial pneumonia + pleural effusion</td>
</tr>
<tr>
<td>14</td>
<td></td>
</tr>
</tbody>
</table>

The occurrence of a nosocomial transmission was observed as patients suffering from PCP were not treated or transferred on the same day. Decompression of the endoscopes was strictly performed according to Bailey and Bradley (2).
bronchial diseases (10%) (14), but it contradicts results of PCR examinations of immunocompetent persons in Germany (0%) (23).

The pathogenicity of P. carinii in immunocompetent patients is still unclear (14). There is no evidence that bacterial pneumonia, tuberculosis and bronchogenic carcinoma are predisposing factors for PCP (24, 25). In contrast, therapy with corticosteroids seems to constitute a risk factor (4–6). Recently data have been published that give considerable evidence for an air-borne route of P. carinii infection (26).

A preliminary study at our department proved Diff-Quik stain, DIFT, and PCR to be equally effective methods to diagnose PCP. In samples of 217 AIDS patients the sensitivity was 99.2, 97.3 and 98.2%, respectively, the specificity was 79.1, 56.1, and 65.9%, respectively (unpublished data). In contrast, based on our results, Diff-Quik stain fails to uncover immunocompetent, low amount carriers. We conclude that P. carinii is not a pathogen in the lungs of immunocompetent individuals and the colonization does not warrant a specific therapy.

REFERENCES


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