Opportunistic Infections in HIV-Infected Children at Chiang Mai University Hospital, Chiang Mai, Thailand.

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Abstract

There were two hundred and thirty-two symptomatic vertical HIV-infected children admitted to Chiang Mai University Hospital from January 1989 to December 1993. They were followed up to December 1993. One hundred and eighty-three cases (79%) had 232 episodes of secondary infectious diseases. These included Pneumocystis carinii pneumonia (32%), salmonellosis (16%), bacterial pneumonia (13%), cytomegalovirus infection (10%), septicemia (other than salmonella) (7%), Cryptosporidium enteritis (5%), Penicillium marneffii infection (5%), Mycobacterium spp. infection (3%), and miscellaneous infections. (9%). Included in the miscellaneous category were soft tissue abscess (5 cases), Herpes simplex virus infection (3), Molluscum contagiosum virus infection (2), Herpes zoster infection (2), bacterial meningitis (2), severe impetigo (2), esophagial candidiasis (1), ruptured appendicitis (1), dermatophyte infection (1) and zygomycosis (1). (J Infect Dis Antimicrob Agent 1995;12:59-62)

INTRODUCTION

Chiang Mai and its 5 neighboring provinces in northern Thailand, an area with less than 10% of the total population of the country is most severely affected by the HIV/AIDS epidemic. Of the 5,990 cases of AIDS reported to the Ministry of Public Health as of April 1994. Three thousand and three cases (50.1%) were from these 6 provinces (1). A survey in December 1993 revealed that the incidence of HIV infection among women attending antenatal clinics in this area was between 2.5 and 10.65%, while the mean for all-provinces of Thailand was 1.83% (2). The rate of vertical transmission in these provinces ranged from 38.5 to 42% (3-5). The data suggest that the number of HIV-infected infants will increase rapidly in northern Thailand. Although the pathogenesis of HIV infection may be the same, the pattern of secondary opportunistic infections varies with the relative incidence and prevalence of infection with potential pathogen in a particular geographic area.

The purpose of this study is to delineate the pattern of opportunistic infections in HIV-infected children who were admitted to Chiang Mai University Hospital.

MATERIALS AND METHODS

Study group

Symptomatic vertical HIV-infected children who were admitted to Chiang Mai University Hospital from January 1989 to December 1993 were included in the study. The diagnosis of HIV infection was made by the presence of HIV-antibody in the patient with clinical manifestations of HIV infection (class P-2). They were followed up to December 1993.

Diagnosis of infectious organisms or diseases

The diagnosis for infectious organisms or diseases was made as follows.

Pneumocystis carinii pneumonia : Initially the diagnosis was made by histopathology of specimen from modified bronchial alveolar lavage (intubation...
and suction) or of lung necropsy specimen. Later the diagnosis was made by typical clinical manifestation and chest roentgenogram.

**Bacterial pneumonia**: lobar or patchy infiltrates in chest roentgenogram responding to antibiotics (cefotaxime alone or ceftriaxone alone or ampicillin plus aminoglycoside).

**Bacterial infection**: routine bacterial culture.

**Cytomegalovirus (CMV) infection**: significant increase in serum CMV-IgM and/or histopathology diagnosis of the tissue obtained by lung necropsy.

**Cryptosporidiosis**: clinical gastroenteritis with the presence of *Cryptosporidium parvum* oocyst in stool. The oocysts in stool were stained by modified Kinyoun acid-fast stain.

**Penicilliosis marneffii**: isolation of the organism from blood and/or identification of the organism in skin touch smear preparation as previously described by our group (6).

**Mycobacterium spp. infection**: clinical manifestations with positive stained smear and/or positive culture of the clinical specimens.

Minor infections such as otitis media, sinusitis, impetigo and thrush were not included in this study.

**RESULTS**

There were 232 symptomatic vertical HIV-infected children admitted to Chiang Mai University Hospital from January 1989 to December 1993. The number of cases has progressively increased every year as shown in Fig. 1. Of these 232 children, 183 were admitted at least once with documented secondary infectious diseases. Of the remaining 49 children, 20 were admitted with fever and pulmonary infiltrates of unknown etiology, 14 with chronic diarrhea in which specific pathogens were not found, 5 with lymphoid interstitial pneumonitis, and 10 with either neurologic or hematologic problems (Table 1 and 2). Of the 74 cases with the diagnosis of *Pneumocystis carinii* pneumonia (PCP), 24 had histopathology proof of the organism. In 50 later cases the diagnosis was made on typical clinical findings (including response to treatment with cotrimoxazole) and typical chest roentgenogram. The age range was 1 to 48 months with a median age of 3 months. Only one case was 48 months old, the rest were less than 12 months old. In all of them PCP was the first presenting symptom of HIV infection. Their serum lactic dehydrogenase ranged from 375 to more than 1,400 IU/L with the median value of 910 IU/L (normal value <250 IU/L). Fifty-five patients (74%) died. Of the 37 episodes of

<table>
<thead>
<tr>
<th>Medical Problems</th>
<th>Cases</th>
<th>(%)</th>
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<tbody>
<tr>
<td>Documented secondary infectious diseases</td>
<td>183</td>
<td>(78.9)</td>
</tr>
<tr>
<td>Pulmonary infiltrates of unknown etiology</td>
<td>30</td>
<td>(13)</td>
</tr>
<tr>
<td>Chronic diarrhea of unknown etiology</td>
<td>14</td>
<td>(6.0)</td>
</tr>
<tr>
<td>Neurologic or hematologic problems</td>
<td>10</td>
<td>(4.3)</td>
</tr>
<tr>
<td>Lymphoid interstitial pneumonitis</td>
<td>5</td>
<td>(2.2)</td>
</tr>
</tbody>
</table>

**Table 2. Opportunistic infections in 183 symptomatic HIV-infected children at Chiang Mai University Hospital.**

<table>
<thead>
<tr>
<th>Pathogen of Disease</th>
<th>Episodes*</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Pneumocystis carinii</em> pneumonia</td>
<td>74</td>
<td>32</td>
</tr>
<tr>
<td>Salmonellosis (Septicemia 22)</td>
<td>37</td>
<td>16</td>
</tr>
<tr>
<td>Bacterial pneumonia**</td>
<td>30</td>
<td>13</td>
</tr>
<tr>
<td>Cytomegalovirus</td>
<td>24</td>
<td>10</td>
</tr>
<tr>
<td>Septicemia (other than salmonella)</td>
<td>16</td>
<td>7</td>
</tr>
<tr>
<td>Cryptosporidium</td>
<td>12</td>
<td>5</td>
</tr>
<tr>
<td>Penicillium marneffii</td>
<td>11</td>
<td>5</td>
</tr>
<tr>
<td>Mycobacterium spp.</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>Others***</td>
<td>20</td>
<td>9</td>
</tr>
</tbody>
</table>

Total: 232 100

* Recurrent or relapse with the same pathogen was counted as one episode.

** Eight cases had bacteremia and were also counted as septicemia episodes.

*** Others include; soft tissue abscess 5, *Herpes simplex* virus 3, *Molluscum contagiosum* virus 2, *Herpes zoster* 2, bacterial meningitis 2, severe impetigo 2, esophageal candidiasis 1, ruptured appendix 1, dermatophyte 1, zygomycosis 1
salmonellosis, the bacteria were isolated from blood in 22 and from stool in 15 episodes. The age range was 1-64 months with the median age of 11 months. *S. enteritidis* was found in 84 percent and *S. cholerasuis* in 16 percent of cases. Fifty-eight percent had at least one episode of recurrence. Salmonellosis is not the direct cause of death in any of our patients. Of the 30 patients with bacterial pneumonia hemoculture was positive in 8 (*Streptococcus pneumoniae* 6 cases, *Salmonella enteritidis* 1 case and *Proteus vulgaris* 1 case). The age range was 2-22 months with the median age of 10 months. Empyema thoracis was presented in 3 cases. Clinical manifestations of CMV infection included severe pneumonia in 18 cases, sepsis with mild pneumonitis in 3 cases, myocarditis in 1 case, hepatitis in 1 case, and central nervous system involvement with retinitis and pneumonia in 1 case. The pathogens causing 16 episodes of septicemia other than salmonella were *Streptococcus pneumoniae* (9), *Escherichia coli* (2), *Haemophilus influenzae* (1), *Enterococcus* spp. (1), *Enterobacter aerogenes* (1), *Pseudomonas aeruginosa* (1) and Proteus vulgaris (1). E. aerogenes, Ps. aeruginosa and *P. vulgaris* were acquired nosocomially. Disseminated *Penicillium marneffii* infection was diagnosed in 11 patients. Their ages ranged from 4 to 64 months. These children presented with fever, generalized lymphadenopathies, hepatosplenomegaly, papular skin lesions, severe anemia, thrombocytopenia, and osteolytic bone lesions (6). Of the 8 episodes of infection with *Mycobacterium* spp., 3 were *Mycobacterium tuberculosis* infection and 5 were *Mycobacterium bovis*, Bacille Calmette-Guerin (BCG) strain infection. Case with *Mycobacterium tuberculosis* infection exhibited pulmonary tuberculosis in 2 cases and miliary tuberculosis with meningitis in 1 case. The age of 5 cases with *Mycobacterium bovis*, Bacille Calmette-Guerin (BCG) strain, ranged from 7 to 21 months (median 11 months). They presented with inflammation of the previously healed BCG scar, enlarged ipsilateral axillary lymph nodes and pulmonary lesions.

**DISCUSSION**

Seventy-nine percent (183/232 cases) of symptomatic vertical HIV-infected children who were admitted to Chiang Mai University Hospital had at least one episode of opportunistic infection. This finding is not surprising when the well known immunologic compromise of HIV-infected persons was considered. Most of the pathogens or diseases reported have been described in the current literature as had been found in HIV-infected patients. This finding demonstrated that most of HIV-infected children sought medical attention because of their opportunistic infections. To prepare for the expected AIDS epidemic in children, pediatricians and general practitioners in Thailand need knowledge of these infectious diseases.

PCP was the leading disease found in this group of patients. This finding is similar to report cases to Center for Disease Control where PCP was found in 39 percent (7). Most of the studies (7-9) including this one emphasized the highest incidence of this disease in the first year of life. The death rate in PCP patients in this study (74%) is higher than in other studies (35, 50 and 70%) from the Western world (7-9). This may be due to delay in diagnosis and/or lack of sophisticated life-supporting equipment which is common in developing countries.

The second leading opportunistic infection in this study was salmonellosis. The incidence of salmonella septicemia in salmonellosis cases was more than half in this study (60%) and in the review in HIV-infected adults (78%) (10). Salmonella species was the most common blood isolates associated with disease in HIV-infected children in this study and in the study in Rwanda HIV-infected children (11, 12), but it was the second most common following *Streptococcus pneumoniae* in studies from the Western world (13).

The overall incidence of bacteremia in this study was 16 percent (22 salmonella species and 16 others in 232 episodes), similar to the 20 percent in a retrospective review in Rwanda HIV-infected children (12).

Pneumonia attributed to CMV is considered to result in a diffuse interstitial process which is impossible to differentiate from PCP. Finding CMV in lung necropsy specimens in HIV-infected infants who were treated as PCP was not uncommon, but the true pathogenic role of CMV in this setting is unclear. The overall incidence of CMV retinitis in the pediatric HIV-infected population (1.6%) appears to be much lower than in adults (20%) (14). In this study there was only one case. Because the symptoms are so rare and nonspecific the low incidence in both studies may due to inadequate screening by physicians. *Penicillium marneffii* infection, which was the third most common opportunistic infection in northern Thai HIV-infected adults (15), caused only 5 percent of infection in this...
study. This opportunistic infection usually occurred in the later stage of HIV-infected patients. Physicians in endemic area (Southeast Asia and south China) should be aware of this disease. The true incidence of some pathogens, such as *Mycobacterium avium* complex, *Toxoplasma gondii* might be underestimated, due to our limited laboratory resources.

References