Nontuberculous Mycobacterial Infections in King Chulalongkorn Memorial Hospital

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Background: Nontuberculous mycobacteria (NTM) can cause infections in both human immunodeficiency virus (HIV)-infected and HIV-noninfected patients. The incidence of NTM infections has been increasing since the acquired immunodeficiency syndrome (AIDS) epidemics. However, the epidemiologic and clinical data of NTM infections in Thailand are limited.

Objective: Determine the epidemiology, clinical manifestations, treatment, and outcome of NTM infections in King Chulalongkorn Memorial Hospital from January 2000 to December 2003.

Material and Method: One hundred and fourteen patients had positive NTM cultures; however, complete medical records were available in only 103 (90.3%) patients.

Results: There were 71 (68.9%) HIV-infected patients, and 38 (87%) of them had the CD4 counts of < 200 cells/ L (range 4-360). Among HIV-infected patients, the most common previous opportunistic infections included tuberculosis (36.6%), Pneumocystis jirovecii pneumonia (25.3%), cryptococcal meningitis (15.5%), penicilliosis (5.6%), and cytomegalovirus infection (5.6%). Most patients presented with prolonged fever (67%), chronic cough (54.4%), lymphadenopathy (52.4%), weight loss (50.5%), or chronic diarrhea (31%). The clinical manifestations included disseminated (17.4%) and localized (82.6%) infections. The localized infection included pulmonary infection (82.3%), followed by gastrointestinal infection (34.1%), skin infection (12.9%), lymphadenitis (8.2%), genitourinary tract infection (2.4%), central nervous system infection (2.4%), and keratitis (1.2%). Mycobacterium avium complex (MAC) was the predominant species (48.5%), followed by M. kansasii (19.4%), and rapidly growing mycobacteria (16.4%). Diffuse reticular infiltration was most commonly observed on chest radiography (53.4%). Abnormal laboratory findings included anemia (48.5%), hyponatremia (42.7%), and elevated alkaline phosphatase (39.8%). The overall mortality rate was 34.8% (45.9% and 11.1% in HIV- and HIV-noninfected patients).

Conclusion: A diagnosis of NTM infection requires a high index of suspicion in patients especially with AIDS or immunocompromised status who present with prolonged fever, with or without organ-specific symptoms and signs. Therefore, clinical specimens must be sent for mycobacterial cultures for a definite diagnosis, a determination of the species of NTM, and an appropriate management. In addition to four standard antituberculous drugs, clarithromycin should be added for the treatment of MAC in patients with AIDS who presented with disseminated opportunistic infections before obtaining the microbiologic results.

Keywords: Nontuberculous mycobacteria (NTM), HIV, AIDS, Mycobacterium avium complex, Mycobacterium kansasii, Rapidly growing mycobacteria

J Med Assoc Thai 2006; 89 (12): 2035-46
Full text. e-Journal: http://www.medassocthai.org/journal

Nontuberculous mycobacteria (NTM) include Mycobacterium species that are not M. tuberculosis complex (M. tuberculosis, M. africanum, M. bovis, M. microti, and M. canetti) and M. leprae. Earlier, the organisms carried the epithet “atypical mycobacteria” or “mycobacteria other than tuberculosis (MOTT)”\(^1\).
NTM are generally free-living organisms that are ubiquitous in the environment. They can be recovered from water, soil, aerosols, domestic, and wild animals, milk, and foods\(^3,6\). NTM can cause a wide variety of infections including pulmonary, lymphatic, skin and soft tissue, skeletal, and catheter-related infections\(^7\). Before the acquired immunodeficiency syndrome (AIDS) epidemics, the pulmonary infections caused by NTM were found predominantly in males in the sixth decade of life. Most patients have predisposing lung conditions or work under conditions where they were exposed to contaminated dusts. The major pulmonary pathogens include *M. kansasii*, *M. avium* complex (MAC), and rapidly growing mycobacteria (RGM)\(^8\). *M. scrofulaceum* is found to be the causative agent of cervical lymphadenitis in children\(^9\). *M. marinum* can cause skin and soft tissue infections, mostly associated with wound or exposed to aquarium\(^2,9\).

Since the AIDS epidemics, the picture of NTM infections has been radically changed. 25-50% of patients with AIDS in the United States and Europe are infected with NTM, mostly by MAC\(^10-20\).

In Thailand, the first patient with NTM infection caused by *M. kansasii* was reported in 1968\(^21\). Since then, there have been several reports of NTM infections caused by *M. scrofulaceum*, *M. gordonae*, MAC, *M. chelonae*, *M. fortuitum*, *M. szulgai*, *M. smegmatis*, *M. marinum*, and other RGM\(^22-27\).

The epidemiology of NTM infections has been changed since the first case of HIV infection was reported in Thailand. The incidence of MAC infections has been increasing in parallel with the increased incidence of patients with AIDS\(^28-32\). Furthermore, an improved technology in mycobacterial culture with the automated commercial system in fluid media and molecular microbiology has improved the yield and has reduced the time for identification of NTM. This also contributes to the changing patterns of epidemiology of NTM infections. In King Chulalongkorn Memorial Hospital (KCMH), there was only one study of NTM infections by Phowthongkum et al who described nine patients with RGM infections from 1997 to 2003\(^33\).

The present study, thus, aimed to determine the epidemiology, clinical manifestations, treatment, and outcome in the patients with NTM infections in KCMH, a medical school, Bangkok, Thailand from January 2000 to December 2003.

**Material and Method**

**Patients**

A retrospective review of the records of the patients with positive culture of NTM from the Department of Clinical Microbiology, Chulalongkorn University, Bangkok was carried out from January 2000 to December 2003. All available medical records were then carefully examined for epidemiology, clinical manifestations, treatment, and outcome.

A diagnosis of NTM pulmonary infections was based on the American Thoracic Society (ATS) criteria\(^1,34\). Other NTM infections were defined based on the compatible clinical features accompanying positive culture for the NTM from the specimens obtained from the involved organ in the absence of any other isolated pathogens. Disseminated infection was defined with the presence of one of the following: 1) multiple sites of cutaneous abscesses, 2) involvement of two or more noncontiguous extrapulmonary sites, 3) positive blood or bone marrow culture, or 4) clinical evidence of deep infection\(^29\).

**Microbiology**

Blood culture was performed using the MB/BacT mycobacteria detection system\(^35\). The inoculated bottles were placed in the CO\(_2\) incubator at 37 ± 2°C, where they were continuously monitored for the growth of mycobacteria by the MB/BacT mycobacteria detection system. Other clinical specimens were inoculated on Lowenstein-Jensen media according to the standard procedures\(^36\). The isolates were identified by the standard methods as previously described\(^36,37\).

**Statistic analysis**

The statistical analyses were performed using the SPSS software, version 13.0, for Microsoft Windows.

**Results**

There were 114 patients with NTM infections during the study period, but complete medical records were available in 103 patients.

**Epidemiology**

The demographic characteristics and associated conditions of all patients are shown in Table 1 and 2. There were 59 males and 44 females with the median age of 33 years (range 8-75 years). There were 71 (68.9%), 20 (19.4%) and 12 (11.7%) patients with, without, and unknown HIV infection, respectively. Of 32 patients without and unknown HIV infection, 15 (47%) had preexisting illness. Of 44 HIV-infected patients with known CD4 cell counts, there were 27 (61.4%) and 38 (87%) patients with CD4 cell counts of
<50 and <200 cells/L, respectively. 66 (92.9%) HIV-infected patients had previous opportunistic infections including tuberculosis (26, 36.6%), Pneumocystis jirovecii pneumonia (18, 25.3%), cryptococcal meningitis (11, 15.5%), penicilliosis (4, 5.6%), and cytomegalovirus infection (4, 5.6%) (Table 3).

Clinical manifestations
Most patients presented with prolonged fever (69, 67%), chronic cough (56, 54.4%), lymphadenopathy (54, 52.4%), weight loss (52, 50.5%), or...
Table 4. The clinical manifestations of all 103 patients with NTM infections, according to the HIV serostatus

<table>
<thead>
<tr>
<th>Clinical manifestations</th>
<th>HIV serostatus (No.)</th>
<th>Total No. (percent)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Disseminated infection</td>
<td>16</td>
<td>1</td>
</tr>
<tr>
<td>MAC</td>
<td>15</td>
<td>1</td>
</tr>
<tr>
<td>M. kansasii</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Localized infection</td>
<td>55</td>
<td>19</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>54</td>
<td>12</td>
</tr>
<tr>
<td>MAC</td>
<td>29</td>
<td>3</td>
</tr>
<tr>
<td>M. kansasii</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>RGM</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Other</td>
<td>9</td>
<td>4</td>
</tr>
<tr>
<td>Gastrointestinal tract infection</td>
<td>27</td>
<td>1</td>
</tr>
<tr>
<td>MAC</td>
<td>15</td>
<td>-</td>
</tr>
<tr>
<td>M. kansasii</td>
<td>4</td>
<td>-</td>
</tr>
<tr>
<td>RGM</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Other</td>
<td>5</td>
<td>-</td>
</tr>
<tr>
<td>Skin</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>MAC</td>
<td>3</td>
<td>-</td>
</tr>
<tr>
<td>RGM</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>M. kansasii</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Other</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Lymphadenitis</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>M. kansasii</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>RGM</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Other</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Genitourinary tract infection</td>
<td>-</td>
<td>2</td>
</tr>
<tr>
<td>RGM</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>MAC</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Central nervous system infection</td>
<td>-</td>
<td>2</td>
</tr>
<tr>
<td>RGM</td>
<td>-</td>
<td>2</td>
</tr>
<tr>
<td>Keratitis</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>RGM</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

MAC: *Mycobacterium avium* complex, RGM: rapidly growing mycobacteria

chronic diarrhea (32, 31%). The clinical manifestations included disseminated (18, 17.4%) and localized (85, 82.6%) infections (Table 4). Of 18 patients with disseminated infection, MAC was the predominant species (17, 94.4%), followed by *M. kansasii* (1, 5.6%). The localized infection (85, 82.6%) included pulmonary infection (70, 82.3%), gastrointestinal infection (29, 34.1%), skin infection (11, 12.9%), lymphadenitis (7, 8.2%), genitourinary tract infection (2, 2.4%), central nervous system infection (2, 2.4%), and keratitis (1, 1.2%) (Table 4). Of 70 pulmonary infections, there were MAC (32, 45.7%), *M. kansasii* (17, 24.3%), RGM (8, 11.4%), *M. flavescence* (4, 5.7%), *M. scrofulaceum* (3, 4.3%), *M. szulgai* (1, 1.4%), *M. gordonae* (1, 1.4%), and unspecified species (4, 5.7%). Of 29 gastrointestinal infections, there were MAC (16, 57.1%), *M. kansasii* (5, 17.2%), RGM (3, 11%), *M. flavescence* (1, 3.4%), *M. scrofulaceum* (1, 3.4%), and unspecified species (3, 10.3%). Of 11 skin infections, there were MAC (3, 27.2%), RGM (5, 45.5%), *M. kansasii* (2, 18.1%), and *M. szulgai* (1, 9.1%). Of seven lymphadenitis, there were *M. kansasii* (3, 42.8%), MAC (2, 28.6%), RGM (1, 14.3%), and *M. flavescence* (1, 14.3%).

**Microbiology**

The frequency of NTM infections in each
The clinical specimens recovered for 103 NTM patients year from 2000 to 2003 varied from 26, 31, 27, and 19 patients, respectively. The clinical specimens recovered for NTM included sputum (52, 50.5%), blood (12, 11.7%), stool (12, 11.7%), pus (8, 7.8%), and tissue (11, 10.7%) (Table 5). The distribution of the species of NTM is shown in Table 6. MAC was the predominant species (50, 48.5% isolates), followed by M. kansasii (20, 19.4%), RGM (17, 16.4%), and M. flavescence (5, 4.9%). Of 20 HIV-noninfected patients, there were M. kansasii (5, 25%) and RGM (5, 25%), followed by MAC (4, 20%), and M. szulgai (2, 10%). Of 71 HIV-infected patients, there were MAC (44, 62%), followed by M. kansasii (11, 15.5%), RGM (6, 8.4%), and M. flavescence (4, 5.6%).

### Table 5. The clinical specimens recovered for 103 NTM

<table>
<thead>
<tr>
<th>Specimen</th>
<th>No. (percent)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sputum</td>
<td>52 (50.5)</td>
</tr>
<tr>
<td>Blood</td>
<td>12 (11.7)</td>
</tr>
<tr>
<td>Stool</td>
<td>12 (11.7)</td>
</tr>
<tr>
<td>Tissue</td>
<td>11 (10.7)</td>
</tr>
<tr>
<td>Pus</td>
<td>8 (7.8)</td>
</tr>
<tr>
<td>Bone marrow</td>
<td>3 (2.9)</td>
</tr>
<tr>
<td>Cerebrospinal fluid</td>
<td>2 (1.9)</td>
</tr>
<tr>
<td>Ascitic fluid</td>
<td>2 (1.9)</td>
</tr>
<tr>
<td>Urine</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Total</td>
<td>103 (100)</td>
</tr>
</tbody>
</table>

### Table 6. The distribution of the species of 103 NTM, according to the HIV serostatus

<table>
<thead>
<tr>
<th>Species of NTM</th>
<th>HIV serostatus No. (percent)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>MAC</td>
<td>44 (61.9)</td>
<td>4 (20)</td>
</tr>
<tr>
<td>M. kansasii</td>
<td>11 (15.5)</td>
<td>5 (25)</td>
</tr>
<tr>
<td>RGM</td>
<td>6 (8.4)</td>
<td>5 (25)</td>
</tr>
<tr>
<td>M. flavescence</td>
<td>4 (5.6)</td>
<td>1 (5)</td>
</tr>
<tr>
<td>M. szulgai</td>
<td>2 (2.8)</td>
<td>1 (5)</td>
</tr>
<tr>
<td>M. gordonae</td>
<td>0</td>
<td>2 (10)</td>
</tr>
<tr>
<td>Unspecified species</td>
<td>4 (5.6)</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Total</td>
<td>71 (68.9)</td>
<td>20 (27.4)</td>
</tr>
</tbody>
</table>

MAC: Mycobacterium avium complex, RGM: rapidly growing mycobacteria including M. fortuitum, M. chelonae, and M. abscessus

### Table 7. The pattern of infiltration on chest radiography of 103 NTM infections, according to the HIV serostatus

<table>
<thead>
<tr>
<th>Pattern of infiltration</th>
<th>HIV serostatus (No.)</th>
<th>Total No. (percent)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Diffuse reticular infiltration</td>
<td>41</td>
<td>8</td>
</tr>
<tr>
<td>Alveolar infiltration</td>
<td>13</td>
<td>3</td>
</tr>
<tr>
<td>Normal</td>
<td>13</td>
<td>3</td>
</tr>
<tr>
<td>Bronchiectasis</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>No available chest radiography</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>71</td>
<td>20</td>
</tr>
</tbody>
</table>

* The patients with no available chest radiography were not included in the calculation of percentage
Other laboratory data

Diffuse reticular (55, 60.4%) infiltrations were most commonly observed on chest radiography (Table 7). Of 55 diffuse reticular infiltrations, there were MAC (24, 43.6%), *M. kansasii* (12, 21.8%), RGM (10, 8.2%), *M. scrofulaceum* (3, 5.4%), *M. flavescence* (2, 3.6%), *M. szulgai* (1, 1.8%), and unspecified species (3, 5.4%). Of 76 alveolar infiltrations, there were MAC (11, 68.6%), *M. kansasii* (2, 12.5%), RGM (1, 6.3%), *M. flavescence* (1, 6.3%), and *M. gordonae* (1, 6.3%). Other abnormal laboratory findings included anemia (50, 48.5%), hyponatremia (44, 42.7%), and elevated alkaline phosphatase (41, 39.8%).

Treatment and outcome

Twenty-three (22.3%) patients did not receive antimycobacterial agents (Table 8) because they were during the investigation period, died, or lost to follow-up before obtaining the culture results (Table 9). Most patients were empirically treated as tuberculosis (patients with, without, and unknown HIV infection) or tuberculosis and MAC (HIV-infected patients) due to positive acid-fast-bacilli (AFB) staining of clinical specimens or compatible clinical features, and eventually the regimen was modified after obtaining the species identification of NTM and the susceptibility results. The overall mortality was 34.8% (45.9% and 11.1% in HIV-infected and HIV-noninfected patients). The highest mortality rate was observed in infections caused by MAC (18, 36%), followed by *M. kansasii* (6, 30%), RGM (2, 11.8%), *M. flavescence* (1, 20%), and unspecified species (4, 80%). These rates of disseminated, pulmonary, and gastrointestinal infection were 22.2%, 32.9%, and 51.7%, respectively.

All data of each patient are summarized in Table 10.

Discussion

From January 2000 to December 2003, 103 patients with NTM infections had complete medical records. Most patients had associated HIV infection or other immunocompromised condition. In the present study, there were 17 (16.5%) patients without preexisting condition. Surprisingly, only one case with pulmonary infection by MAC had preexisting chronic obstructive pulmonary disease (COPD). This is in contrast to the literature. It describes the most important

### Table 8. Initial antimycobacterial regimens for treatment of 103 NTM infections

<table>
<thead>
<tr>
<th>Drug</th>
<th>Patients No. (percent)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>No treatment</td>
<td>23 (22.3)</td>
<td></td>
</tr>
<tr>
<td>HRZE</td>
<td>31 (30.1)</td>
<td></td>
</tr>
<tr>
<td>HRZEK</td>
<td>21 (20.4)</td>
<td></td>
</tr>
<tr>
<td>HRZEKO</td>
<td>11 (10.7)</td>
<td></td>
</tr>
<tr>
<td>HREOS</td>
<td>3 (2.9)</td>
<td></td>
</tr>
<tr>
<td>HRZEO</td>
<td>3 (2.9)</td>
<td></td>
</tr>
<tr>
<td>HRZESC</td>
<td>2 (1.9)</td>
<td></td>
</tr>
<tr>
<td>HR</td>
<td>2 (1.9)</td>
<td></td>
</tr>
<tr>
<td>REKA</td>
<td>2 (1.9)</td>
<td></td>
</tr>
<tr>
<td>HRE</td>
<td>2 (1.9)</td>
<td></td>
</tr>
<tr>
<td>Minocycline</td>
<td>2 (1.9)</td>
<td></td>
</tr>
<tr>
<td>KC</td>
<td>1 (1)</td>
<td></td>
</tr>
<tr>
<td>HREK</td>
<td>1 (1)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>103 (100)</td>
<td></td>
</tr>
</tbody>
</table>


### Table 9. The outcome after discharging from the hospital in 103 patients with NTM infections

<table>
<thead>
<tr>
<th>Outcome</th>
<th>HIV serostatus (No.)</th>
<th>Total No. (percent)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Improved</td>
<td>33</td>
<td>16</td>
</tr>
<tr>
<td>Dead</td>
<td>28</td>
<td>2</td>
</tr>
<tr>
<td>Referred</td>
<td>10</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>71 (68.9)</td>
<td>20 (19.4)</td>
</tr>
</tbody>
</table>

* The referred patients were not included in the calculation of percentage
Table 10. A summary of 103 patients with NTM infections

<table>
<thead>
<tr>
<th>No.</th>
<th>Sex</th>
<th>Age (yrs)</th>
<th>Year</th>
<th>Associated condition</th>
<th>CD4 (cells / L)</th>
<th>Species</th>
<th>Infection</th>
<th>Specimen</th>
<th>Chest X-ray</th>
<th>Treatment regimen</th>
<th>Outcome</th>
<th>FU</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>24</td>
<td>2000</td>
<td>No</td>
<td>NA</td>
<td>M. fortuitum</td>
<td>Disseminated, GI</td>
<td>Blood</td>
<td>Normal</td>
<td>Minocycline</td>
<td>Improved</td>
<td>FU</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>31</td>
<td>2000</td>
<td>HIV, TB, Toxoplasmosis</td>
<td>30</td>
<td>MAC</td>
<td>Disseminated, lung</td>
<td>Blood</td>
<td>Normal</td>
<td>HRZEK</td>
<td>Referred</td>
<td>Loss</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>35</td>
<td>2000</td>
<td>HIV, PCP</td>
<td>NA</td>
<td>MAC</td>
<td>Lymph node</td>
<td>Tissue</td>
<td>Reticular</td>
<td>HRE</td>
<td>No</td>
<td>Improved Loss</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>42</td>
<td>2000</td>
<td>No</td>
<td>NA</td>
<td>M. kansasii</td>
<td>Lung</td>
<td>Sputum</td>
<td>Reticular</td>
<td>HRZE</td>
<td>Improved</td>
<td>FU</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>35</td>
<td>2000</td>
<td>HIV, CMV</td>
<td>4</td>
<td>MAC</td>
<td>Disseminated, skin</td>
<td>Blood</td>
<td>Normal</td>
<td>HRZEK</td>
<td>Improved</td>
<td>FU</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>34</td>
<td>2000</td>
<td>HIV, CMV</td>
<td>16</td>
<td>MAC</td>
<td>Disseminated, GI</td>
<td>Stool</td>
<td>Reticular</td>
<td>HRZEK</td>
<td>Dead</td>
<td>Loss</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>57</td>
<td>2000</td>
<td>HIV, CMV, VZV</td>
<td>24</td>
<td>MAC</td>
<td>Disseminated, GI</td>
<td>Blood</td>
<td>Bronchiectasis</td>
<td>HRZE</td>
<td>Improved</td>
<td>Loss</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>34</td>
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### Table 10. A summary of 103 patients with NTM infections (Cont.)

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**Toxoplasmosis**

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**HIV:** human immunodeficiency virus, **DM:** diabetes mellitus, **HT:** hypertension, **RA:** rheumatoid arthritis, **NHL:** non-Hodgkin lymphoma, **COPD:** chronic obstructive pulmonary disease, **AML:** acute myeloid leukemia, **CIR:** cirrhosis, **HYD:** hydrocephalus, **DYS:** dyslipidemia, **CAR:** cardiomyopathy, **HEP:** hepatitis, **TB:** tuberculosis, **PCP:** Pneumocystis jirovecii pneumonia, **CRY:** cryptosporidial meningitis, **PEN:** penicilliosis, **CMV:** cytomegalovirus infection, **TOX:** toxoplasmosis, **HIS:** histoplasmosis, **GI:** gastrointestinal tract, **GU:** genitourinary tract, **CNS:** central nervous system, **H:** ionizad, **R:** rifampin, **Z:** pyrazamide, **E:** ethambutol, **K:** clarithromycin, **O:** ofloxacin, **C:** ciprofloxacin, **A:** amikacin, **S:** streptomycin, **NA:** not applicable, **BM:** bone marrow, **CSF:** cerebrospinal fluid, **FU:** follow up
risk factor for acquisition of NTM pulmonary disease is the presence of underlying chronic lung disease, especially COPD(2,38,39). Most patients in the present study had symptomatic HIV infection with CD4 cell counts of < 200 cells/ L. This is consistent with previous studies(18,40-43). In the present study, the number of NTM cases each year from 2000 to 2003 had not increased despite the increasing number of HIV-infected patients and the improvement of diagnostic methods for NTM infections. This is probably due to most patients being HIV-infected patients, and there has been an increasing use of antiretroviral drugs resulting in a restoration of the immune response.

The predominant clinical presentations of the presented patients were prolonged fever, chronic cough, lymphadenopathy, weight loss, and chronic diarrhea. As described elsewhere(10-12), these features accompanying with anemia and elevated serum alkaline phosphatase suggest the disseminated infection, commonly caused by MAC in HIV-infected patients. As seen worldwide, the pulmonary infection in HIV-noninfected patients without HIV infection. The commonest NTM pulmonary pathogens in the present study were MAC (53.7% and 25% in HIV-infected and HIV-noninfected patients), consistent with previous studies(2,7,44,45). The presented rates of M. kansasii in pulmonary infection were 18.5% and 25% in HIV-infected and HIV-noninfected patients, respectively. These high rates are consistent with several reports in America(48), the United Kingdom(46), Japan(47), and Switzerland(48) as well as Thailand(23,28). However, there was little or no pulmonary infection caused by M. kansasii in Australia(49), Hong Kong(50), Canada(50), and Sweden(50) where the predominant pathogen was MAC. One study of NTM pulmonary infection in Thailand during 1969 and 1978 reported only one patient with M. kansasii infection(52). This discrepancy may be due to the difference in geographic distribution and study period. RGM are also recognized as common etiologic pathogens of pulmonary disease, occurring mostly in elderly patients without preexisting lung disease(44,53). In the present study, RGM accounted for 11.4% of all patients with pulmonary infections, consistent with the authors’ previous report in KCMH(33).

Most patients especially with AIDS in the present study who presented with prolonged fever and watery diarrhea had MAC infection, and AFB staining was positive in most stool specimens. The authors recommend routine AFB staining of stool specimens in all patients with AIDS who presented with chronic diarrhea.

In the present study, RGM and MAC are the species of NTM that most commonly cause skin and soft-tissue infections. MAC infections occurred only in patients with AIDS, when RGM could cause infections in both HIV-infected and HIV-noninfected patients. Both direct skin infection and reactive skin lesions like Sweet’s syndrome were observed in the presented patients without HIV infection, consistent with a previous report by Chetchotisakd et al(56).

Chest radiographic changes in patients with and without HIV infection were similar to those observed with tuberculosis, both localized and disseminated forms with alveolar infiltration involving the upper lobe and with diffuse reticular infiltrations involving the lower lobes, respectively. Most patients in the present study had diffuse reticular pulmonary infiltrations because most had symptomatic HIV infection or immunocompromised condition.

In the present study, most patients especially with AIDS received an empirical treatment with four standard antituberculous drugs (isoniazid, rifampin, ethambutol, and pyrazinamide) with or without anti-MAC agents (clarithromycin in addition to ethambutol and rifampin). Nearly one-fourth of the patients did not receive specific antituberculous agents because they were during the investigation period, died, or lost to follow-up before a definite diagnosis of NTM infection could be made. The outcome of disseminated MAC infection especially in patients with AIDS was poor in the present study, compared to those without HIV infection. This observation is consistent with previous studies(10-12,16,44). Restoration of immune response with highly active antiretroviral therapy after some control of mycobacterial infection may be the most important factor to improve the outcome of treatment in those patients.

In conclusion, a diagnosis of NTM infection requires a high index of suspicion in patients especially with AIDS or immunocompromised status who present with prolonged fever, with or without organ-specific symptoms and signs. Thus, clinical specimens must be sent for mycobacterial cultures for a definite diagnosis, a determination of the species of NTM, and an appropriate management. In addition to four standard antituberculous drugs, clarithromycin should be added for the treatment of MAC in patients with AIDS who present with disseminated opportunistic infections before obtaining microbiologic results.
References


49. Hosker HS, Lan CW, Ng TK, Ma HK, Chan SL. The prevalence and clinical significance of pulmonary infection due to non-tuberculous mycobacteria in Hong Kong. Respir Med 1995; 89: 3-8.


การติดเชื้อมัยโคแบคทีเรียที่ไม่ใช่เชื้อวัณโรคในโรงพยาบาลจุฬาลงกรณ์

สุธี สุกิจวิช, นิพนธ์ อุดมสันติสุข, ชุษณา สวนกระต่าย

เชื้อมัยโคแบคทีเรียที่ไม่ใช่เชื้อวัณโรค (nontuberculous mycobacteria, NTM) สามารถติดเชื้อได้ทั้งผู้ป่วยติดเชื้อเอชไอวีและผู้ป่วยไม่ติดเชื้อเอชไอวี อุบัติการณ์ของการติดเชื้อ NTM เพิ่มขึ้นในช่วงที่มีการระบาดของโรคเอดส์ อย่างไรก็ตามระบบบริการและข้อมูลทางคลินิกของการติดเชื้อ NTM ในประเทศไทยยังจำกัด การศึกษาที่มีวัตถุประสงค์เพื่ศึกษาการระบาด, ลักษณะทางคลินิก, การรักษา, และผลของการรักษาการติดเชื้อ NTM ในโรงพยาบาลจุฬาลงกรณ์ตั้งแต่เดือนมกราคม พ.ศ. 2543 ถึง ธันวาคม พ.ศ. 2546 มีผู้ป่วย 114 ราย ที่ผลเพาะเชื้อ NTM แต่เวชระเบียนที่สมบูรณ์มีเพียง 103 ราย (90.3%) มีผู้ป่วย 71 ราย (68.9%) ที่ติดเชื้อเอชไอวี และ 38 ราย (37.5%) ที่มีระดับ CD4 น้อยกว่า 200 เซลล์ต่อไมโครลิตร (พิสัย 4-360) ในผู้ป่วยติดเชื้อเอชไอวี การติดเชื้อจะมีโอกาสที่พบบ่อยได้แก่ วัณโรค (36.6%), Pneumocystis jirovecii pneumonia (25.3%), cryptococcal meningitis (15.5%), penicilliosis (5.6%) และ cytomegalovirus infection (5.6%). ผู้ติดเชื้อเอชไอวีและไม่ติดเชื้อเอชไอวี ส่วนใหญ่มาพบแพทย์ด้วยอาการนำคือ ไข้เรื้อรัง (67%) ไอเรื้อรัง (54.4%) ต่อมน้ำเหลืองโต (52.4%) น้ำหนักลด (50.5%) หรือ ท้องเสียเรื้อรัง (31%) สำหรับลักษณะทางคลินิกของการติดเชื้อได้แก่ การติดเชื้อแบบแพร่กระจาย (17.4%) และการติดเชื้อแบบเฉพาะที่ (82.6%) การติดเชื้อที่พบบ่อยที่สุด คือ การติดเชื้อในปอด (82.3%) ตามด้วยการติดเชื้อแบบเฉพาะที่ที่พบบ่อยที่สุด (34.1%) การติดเชื้อที่พบบ่อยที่สุดในผู้ป่วยติดเชื้อเอชไอวี (82.3%) การติดเชื้อแบบแพร่กระจาย (2.4%) การติดเชื้อแบบเฉพาะที่ (2.4%) และการขาดทักษะที่น้อย (1.2%) พบการติดเชื้อ Mycobacterium avium complex (MAC) มากที่สุด (48.5%) ตามมาด้วย M. kansasii (19.4%) และ Mycobacterium intracellulare (16.4%) พบการติดเชื้อของปอดพบมากเป็น diffuse reticular infiltration มากที่สุด (53.4%) ความผิดปกติของผลตรวจทางห้องปฏิบัติการที่พบคือ ซีด (48.5%) ปริมาณโซเดียมในเลือดต่ำ (42.7%) และ alkaline phosphatase สูง (39.8%) อีกทั้งการตายโดยรวมสูงถึง 34.8% ของผู้ป่วยเอดส์ และ 11.1% ในผู้ไม่ติดเชื้อเอชไอวี

โดยสรุป การวินิจฉัยการติดเชื้อ NTM ต้องอาศัยความสงสัยเป็นอย่างสูงในผู้ป่วยที่มีอาการไข้เรื้อรังอาจร่วมหรือไม่ร่วมกับอาการและอาการแสดงที่จำเป็นข้างต้นเพื่อประกอบการวินิจฉัย การหา species ของ NTM และการรักษาที่เหมาะสม นอกเหนือจากการใช้ยาต้านวัณโรคมาตรฐาน 4 ชนิด ควรเพิ่มclarithromycin เพื่อใช้ในการติดเชื้อ MAC ในผู้ป่วยแอลอีที่มีอาการและอาการแสดงของการติดเชื้อแบบเฉพาะที่กระจาย ก่อนทราบผลการตรวจทางจุลชีววิทยา.