Extrapulmonary tuberculosis among adults:
Experience at Chris Hani Baragwanath Academic Hospital, Johannesburg, South Africa

A S Karstaedt, MB ChB, MMed

Division of Infectious Diseases, Department of Medicine, Chris Hani Baragwanath Hospital and University of the Witwatersrand, Johannesburg, South Africa

Background. Extrapulmonary tuberculosis (EPTB) occurs in 15 - 20% of immunocompetent and 20 - 70% of HIV-infected patients with tuberculosis. There are few recent incidence data for EPTB.

Methods. Adults (N=2 963) with culture-proven EPTB seen over 2 years at Chris Hani Baragwanath Academic Hospital, the main referral hospital serving Soweto, Johannesburg, South Africa, were retrospectively studied for pattern and incidence.

Results. The commonest sites of EPTB were the pleura (39.1%), lymph nodes (31.0%), blood (21.8%), meninges (7.3%), and peritoneum (2.9%). Disseminated tuberculosis occurred in 25.0%. The median age was 33 years (range 18 - 87 years). Males comprised 53.2% overall, with a female majority in the peritonitis group. For Soweto, the incidence of adult EPTB was 88.6/100 000 population, rising to 139.4/100 000 and 125.7/100 000 in the 25 - 34-year and 35 - 44-year age groups, respectively. There was no secondary peak in the elderly (17.9/100 000).

Conclusions. This retrospective cohort showed a high incidence of EPTB, most marked in the 25 - 44-year age group. Culture of extrapulmonary sites is of importance to confirm diagnosis of tuberculosis and to ensure antimycobacterial drug susceptibility testing.


Microbiology

The central TB laboratory of the National Health Laboratory Service, Johannesburg, utilised liquid culture media, namely BACTEC 13A or BACTEC MYCO/F Lytic (Becton Dickinson), or solid media (Lowenstein-Jensen), depending on the source of the specimen.

Ethics

The study was approved by the Committee for Research on Human Subjects of the University of the Witwatersrand, Johannesburg.

Results

Over the 2-year period of the study, 2 963 adults had Mycobacterium tuberculosis cultured from 3 166 extrapulmonary sites (Table 1). The commonest sites were the lymph nodes and pleura, which together accounted for nearly 70% of specimens. A positive TB smear was documented in 370 lymph nodes (40.3%). Disseminated disease (bacteraemia or >1 extrapulmonary organ) was present in 742 patients (25.0%). The site of origin in the ‘pus’ group was not specified and probably comprised lymph nodes, superficial skin and soft tissue and deep organ abscesses, and empyema. Males predominated, with gender parity among patients with lymphadenitis and a female preponderance in those with peritonitis. The median age of 33 years was similar across all disease groups. Of the 217 patients with meningitis, 127 (58.5%) were HIV-infected (12 were not tested). Of patients with TB bacteraemia for whom hospital records were available, HIV infection was established in 227 (35%); only 1 patient...
was known not to be infected with HIV. (It should be noted that while
many more had been tested for HIV, the results had in many cases not
been documented and had been deleted from the laboratory database.)
There were 37 patients aged ≥65 years (of whom 25 (67.6%) were male);
pleural involvement was evident in 22 specimens (59.5%), bacteraemia
in 8, lymphadenopathy in 6, and liver involvement, abscess and urinary
tract infection in 1 each (2 patients had 2 specimens).

The annual incidence of EPTB by age is presented in Table 2. Of the
2 963 patients, 1 283 (43.3%) were documented to have addresses in
Soweto and 915 (30.9%) had no address available; the remaining
patients had been referred to Chris Hani Baragwanath Academic
Hospital for diagnostic work-up. The incidence of EPTB in adults
based on culture was 88.6/100 000 population, reaching 139.4 and
125.7/100 000, respectively, for 25 - 34-year-olds and 35 - 44-year-
olds. There was no secondary peak in the elderly.

Discussion
In this study in a large urban referral hospital with high tuberculosis
and HIV prevalence rates, there was an incidence of EPTB of
88.6/100 000 population based on positive TB culture obtained
from extrapulmonary sources. This is a minimum estimate of the
incidence of EPTB. It would have excluded patients with EPTB in
whom the TB diagnosis was made by other diagnostic criteria, from
whom an extrapulmonary specimen was not obtained, or in whom
the diagnosis was not suspected. Moreover, culture positivity would
have varied according to bacillary load. Rates of EPTB were especially
high in the 25 - 44-year age group, in which the highest HIV
population rates would be expected. The incidence of EPTB in adults
†Number of patients with known Soweto addresses over the 2-year study period.

Table 1. Frequency of organ involvement, gender and age of adults with extrapulmonary tuberculosis

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>EPTB</th>
<th>Pleural</th>
<th>Lymph node</th>
<th>Bacteraemia</th>
<th>Meningitis</th>
<th>Pus</th>
<th>Peritonitis</th>
<th>Other*</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>2 963</td>
<td>1 160</td>
<td>919</td>
<td>646</td>
<td>217</td>
<td>89</td>
<td>87</td>
<td>48</td>
</tr>
<tr>
<td>%</td>
<td>100</td>
<td>39.1</td>
<td>31.0</td>
<td>21.8</td>
<td>7.3</td>
<td>3.0</td>
<td>2.9</td>
<td>1.6</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>1 576 (53.2)</td>
<td>646 (55.7)</td>
<td>465 (50.6)</td>
<td>357 (53.3)</td>
<td>316 (53.5)</td>
<td>50 (57.5)</td>
<td>31 (35.6)</td>
<td>28 (58.3)</td>
</tr>
<tr>
<td>Median age (years)</td>
<td>33</td>
<td>32</td>
<td>32</td>
<td>32</td>
<td>33</td>
<td>33</td>
<td>33</td>
<td>34</td>
</tr>
<tr>
<td>Age range (years)</td>
<td>18 - 87</td>
<td>18 - 87</td>
<td>18 - 83</td>
<td>18 - 77</td>
<td>19 - 60</td>
<td>18 - 86</td>
<td>18 - 59</td>
<td>20 - 82</td>
</tr>
<tr>
<td>&gt;1 site, n (%)</td>
<td>207 (7)</td>
<td>86 (7)</td>
<td>104 (11)</td>
<td>119 (18)</td>
<td>28 (13)</td>
<td>11 (12)</td>
<td>18 (21)</td>
<td>13 (27)</td>
</tr>
</tbody>
</table>

*Other comprised bone and joint (21), urogenital (12), pericardial (8), breast (2), miscellaneous and tissue (5).

Table 2. Incidence rate (/100 000 population/year) by age of adults with extrapulmonary tuberculosis in Soweto

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Population*</th>
<th>EPTB</th>
<th>Pleural</th>
<th>Lymph node</th>
<th>Bacteraemia</th>
<th>Meningitis</th>
<th>Peritonitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>EPTB Rate</td>
<td>Pleural Rate</td>
<td>Lymph node Rate</td>
<td>Bacteraemia Rate</td>
<td>Meningitis Rate</td>
<td>Peritonitis Rate</td>
<td></td>
</tr>
<tr>
<td>15 - 24</td>
<td>723 839</td>
<td>641.5</td>
<td>88.6</td>
<td>270</td>
<td>37.3</td>
<td>189.5</td>
<td>26.2</td>
</tr>
<tr>
<td>25 - 34</td>
<td>199 091</td>
<td>57.5</td>
<td>28.9</td>
<td>20</td>
<td>10.0</td>
<td>22</td>
<td>11.1</td>
</tr>
<tr>
<td>45 - 54</td>
<td>89 212</td>
<td>63.5</td>
<td>71.2</td>
<td>27.5</td>
<td>30.8</td>
<td>16.5</td>
<td>18.4</td>
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<tr>
<td>55 - 64</td>
<td>45 647</td>
<td>14.5</td>
<td>31.8</td>
<td>5.5</td>
<td>12.0</td>
<td>3.5</td>
<td>7.7</td>
</tr>
<tr>
<td>≥65</td>
<td>42 004</td>
<td>7.5</td>
<td>17.9</td>
<td>6</td>
<td>14.3</td>
<td>0.5</td>
<td>1.2</td>
</tr>
<tr>
<td>Unknown</td>
<td>33.5</td>
<td>24</td>
<td>1</td>
<td>4.5</td>
<td>0.5</td>
<td>1.5</td>
<td></td>
</tr>
</tbody>
</table>

EPTB = extrapulmonary tuberculosis
1Number of patients with known Soweto addresses over the 2-year study period.

Culture, the most reliable method of diagnosis, depends on specimens being taken. Histological examination is helpful, but there is a wide differential diagnosis for granulomatous disease. These alternatives are often ignored in an endemic TB area. Clinical insight may be flawed and influenced by clinical context and resource restraints, as evidenced in autopsy studies.[9]

In this study, pleural and lymph node tuberculosis rates were similar to those reported from Hong Kong, where 42% had pleural and 37% lymph node tuberculosis.[10] In a composite of several studies of EPTB, lymph node tuberculosis (35%) and pleural tuberculosis (20%) were commonest.[10] Among Somalis in Minnesota, lymph node tuberculosis caused 30% and pleural disease 9% of cases of EPTB. In reports from the USA, TB adenopathy occurred in 40% and pleural disease in 20%, while bacteraemia was the sole proof of disease in 18%.[11,12] The presence of TB bacteraemia has been shown to be an important test in HIV-infected patients, especially those with CD4 counts <100 cells/μl.[13] In a retrospective survey of unselected patients in Soweto who were investigated with mycobacterial blood culture, 19% had TB bacteraemia.[10] HIV infection has been negatively associated with a pleural site of EPTB.[11,12] The lack of documentation of HIV status for the group with pleural disease did not allow us to assess this in the study cohort. The slight male predominance found is similar to that in the USA.[10] There was, however, a marked female predominance in patients with tuberculous peritonitis. Abdominal tuberculosis generally occurs equally in both sexes, although some studies report a higher incidence in women.[13]
Limitations of the study include its retrospective nature, and the fact that resistance to anti-TB therapy and HIV status, other than in patients with meningitis and to a lesser extent bacteraemia, were not available. The results of HIV tests, among others, for the period of the study were removed from the laboratory database (and the archived discs proved unreadable). Some organ systems that rely largely on histology or clinical criteria for diagnosis would have been under-represented, including bone and joint, pericardial, gastrointestinal and genitourinary TB.

Although the data are a decade old, they do provide a baseline prior to the advent of widespread provision of antiretroviral therapy at the time of the penultimate published census for South Africa. Furthermore, the numbers of patients with EPTB were similar to those at the hospital in 2006. The high incidence of EPTB, based on culture results, persists.

The importance of culture of material or tissue obtained from extrapulmonary disease sites to confirm diagnosis and ensure anti-TB drug susceptibility testing is emphasised, at least until molecular techniques are validated and widely available.

Acknowledgements. I thank Mani Khoosal and Xoliswa Poswa of the National Health Laboratory Service for provision of culture results and Vanessa Quan of GERMS-SA for assistance with data.

References


Accepted 24 April 2013.