TUBERCULOSIS

TUBERCULOSIS AND HUMAN IMMUNODEFICIENCY VIRUS (HIV) INFECTION

According to WHO estimates by the end of the year 1995, up to 10 million of African people will have been infected with HIV (Chin, 1992). In Africa, HIV infection is transmitted predominantly through heterosexual intercourse and the highest seroprevalence rates are observed among young urban adults (Lancet, 1989). On the other hand, one third of the African population had been infected with tuberculosis (Porter, 1992). More than 1 million cases of active tuberculosis occur annually in Africa which, with 220 cases of tuberculosis out of 100,000 population, has the highest incidence of tuberculosis over the world (Sudre et al., 1992).

Worldwide prevalence of tuberculosis infection, 1990

<table>
<thead>
<tr>
<th>Region</th>
<th>Prevalence %</th>
<th>Number infected (Millions)</th>
<th>Percentage of total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td>33.8</td>
<td>171</td>
<td>9.9</td>
</tr>
<tr>
<td>Americas</td>
<td>25.9</td>
<td>117</td>
<td>6.8</td>
</tr>
<tr>
<td>Eastern Mediterranean</td>
<td>19.4</td>
<td>52</td>
<td>3.0</td>
</tr>
<tr>
<td>South-East Asia</td>
<td>34.3</td>
<td>426</td>
<td>24.7</td>
</tr>
<tr>
<td>Western Pacific</td>
<td>43.8</td>
<td>195</td>
<td>11.3</td>
</tr>
<tr>
<td>China</td>
<td>33.7</td>
<td>379</td>
<td>22.0</td>
</tr>
<tr>
<td>Europe and others</td>
<td>31.6</td>
<td>382</td>
<td>22.2</td>
</tr>
<tr>
<td>All regions</td>
<td>32.8</td>
<td>1,722</td>
<td>100</td>
</tr>
</tbody>
</table>

As HIV infection is more frequent among young urban adults in whom the prevalence of tuberculosis approaches nearly 50% (Allen et al., 1992), it is easy to understand that the majority of individuals (77%) infected at the same time with HIV and tuberculosis are living in Africa (Raviglione et al., 1992).

1. Epidemiological data

Early evidence of interaction between HIV infection and tuberculosis in developing countries was suggested by high rates of tuberculosis among AIDS patients originating from Haiti and Africa (Pitchenik et al., 1984; Sonnet et al., 1987) In addition, reports from Africa have shown high levels of HIV seroprevalence in tuberculous patients, with a range from 17 to 88% (Harries, 1990; Batungwanayo et al., 1991).

Recent cohort studies carried out in USA and Africa (Braun et al., 1991; Allen et al., 1992) have shown an increased risk of tuberculosis in individuals dually infected with HIV and tuberculosis. This risk has been found to be 24 to 26 times higher in HIV-infected persons than in HIV-negative individuals. In HIV and/or AIDS patients, tuberculosis (TB) may result from reactivation of latent infection or from exogenous reinfection with rapid progression to disease. The epidemiological data are consistent with the recent resurgence of TB in many HIV-epidemic African countries. A definite increase of TB notified cases has been registered in some countries such as Burundi, Tanzania and Uganda (Standaert et al., 1989; Styblo, 1990; Goodgame, 1990).

2. Clinical pattern

The clinical presentation of HIV-associated tuberculosis is similar to the disease experienced by non-HIV-infected patients. Common symptoms are weight loss, fever, cough, chest pain and dyspnoea, also encountered in many other HIV-related pulmonary diseases such as Pneumocystis carinii pneumonia or isolated pulmonary cryptococcosis (Batungwanayo et al., 1994). Other conditions frequently diagnosed in HIV-positive patients with tuberculosis are: oral candidiasis, active or past herpes zoster, non-typhi salmonella bacteraemia and Kaposi's sarcoma (Batungwanayo et al., 1992). These manifestations are uncommon in HIV seronegative patients and are clinical markers highly predictive for concurrent HIV infection.

The radiographic pattern of HIV-associated pulmonary tuberculosis depends on the degree of immuno-suppression. At the early stage of the infection, the chest film usually reveals a post-primary pattern with upper lobe infiltrates and cavities. In more advanced HIV-disease, the radiographic pattern is similar to that of primary tuberculosis with diffuse and military infiltrates, intra-thoracic adenopathies, middle or lower lobe infiltrates, pleural effusion (Pitchenik and Rubinson, 1985; Kamamfu et al., 1990; Batungwanayo et al., 1992).

Another striking clinical manifestation of tuberculosis in patients with HIV infection is the high frequency of extra-pulmonary involvement. Data from USA have reported an extra-pulmonary involvement in 25-75% of the patients with AIDS/HIV infection (Chaisson and Slutkin, 1989). In Africa, during the pre-AIDS era, only a small proportion (10-12%) of
TB cases involved extra-pulmonary sites (Kenya, 1984; Tanzania, 1985). This distribution has dramatically changed with the advent of the HIV epidemic. For instance, in a series of 334 HIV-associated TB cases from Kigali, Rwanda 56% had at least one extra-pulmonary site of involvement (Batungwanayo et al., 1991). In another series from Malawi, 57% of HIV seropositive patients had extra-pulmonary tuberculosis compared with 20% of HIV seronegative patients (Kelly et al., 1990). The most frequent forms of extra-pulmonary tuberculosis are peripheral and/or intrathoracic lymphadenitis and mililiary forms (Barmes et al., 1991).

However, reports from Africa have showed that pleural and pericardial tuberculosis are extremely frequent in HIV-infected patients with tuberculosis (Taelman et al., 1990; Batungwanayo et al., 1991). Tuberculous meningitis is however less frequent in Kigali, Rwanda (Taelman et al., 1992).

3. Diagnosis of HIV-associated tuberculosis

In many developing countries, diagnosis of pulmonary TB relies on microscopic detection of acid fast bacilli on sputum smear specimens. Some authors (Klein et al., 1989; Long et al., 1991) have reported a decrease in sensitivity of sputum examination in HIV-seropositive patients with pulmonary TB.

Negative sputum smear examination usually requires the use of flexible fiber-optic bronchoscopy which allows bronchial aspiration, broncho-alveolar lavage and transbronchial biopsies. Microbiological and histological examination of these respiratory samples may provide diagnosis of pulmonary TB and therefore differentiate it from other clinically similar conditions such as Pneumocystis carinii pneumonia, primary pulmonary cryptococcosis, non-specific interstitial pneumonitis (Stoven et al., 1984; Batungwanayo et al., 1991).

Unfortunately, fiber-optic bronchoscopy is unavailable in most African settings. Furthermore, the diagnosis of extra-pulmonary tuberculosis depends also on available diagnostic procedures allowing examination of tissue and fluid samples. When these facilities are unavailable, physicians have to rely on clinical and radiological findings to establish a diagnosis of tuberculosis.

4. Prognosis

Mortality is high among the HIV/AIDS patients with tuberculosis. In post-mortem studies, TB was diagnosed in 31% of Zairean AIDS cases and in 42% of Ivorian cases dying in a chest Department (Nelson et al., 1990; Abouya et al., 1992). Cohort studies have also recorded a higher mortality among HIV-infected patients.

In Nairobi, Kenya, Nunn et al. (1992) have recently reported a mortality rate four times higher in the HIV-seropositive group at the end of a 6 months treatment.

Perriens et al. in Zaire (1991) have reported after one year of follow-up, a mortality rate of 31.5% and 4.4% among respectively HIV-seropositive and HIV-seronegative patients with pulmonary TB. During the first month, mortality is likely to be related to advanced tuberculosis and occurs at the same rate among HIV-seropositive and negative patients with tuberculosis. Thereafter, deaths are due to other AIDS/HIV-associated diseases which in Africa are mainly non-AIDS-defining bacterial infections such as pneumococcal and non-typhi Salmonella bacteraemia (Taelman et al., 1990).

5. Treatment

Patients with HIV-associated tuberculosis appear to respond well to anti-tuberculous treatment (Small et al., 1991). Conversion of sputum culture to negativity occurs nearly 3 months after the start of the treatment.

Some cohort studies have stressed a high rate of relapses among HIV-positive patients treated with long regimens containing thiacetazone. This recurrence rate was found 34 times greater in HIV-1 positive patients than in HIV-1 negative patients (Hawken et al., 1993). Factors associated with relapses were cutaneous thiacetazone-induced hypersensitivity and a smaller number of lung zones affected. A study from Zaire by Perriens et al. (1991) has found a recurrence rate of 18.1 per 100 persons per year of observation (PYO) in HIV-positive patients (where dual HIV and TB infection is highly prevalent) compared with 6.1 per 100 persons per year among HIV-negative patients.

By contrast, short-course rifampicin-containing regimens evaluated in Zaire (Mukadi et al., 1991) appear to be more effective. One hundred fifty-eight HIV-seropositive patients and 192 HIV-negative patients with pulmonary tuberculosis were offered 2 months of treatment with rifampicin, isoniazide, pyrazinamide and ethambutol, followed by isoniazide-rifampicin twice weekly for 4 months. Relapse rates were 9% and 6% 6 months after the end of the treatment in HIV-positive and HIV-negative patients respectively. Such short-course chemotherapy should be recommended in geographical areas where HIV and
Mycobacterium tuberculosis infection are highly endemic, especially in Central Africa.

6. Implications for tuberculosis control programmes

It is now well established that HIV infection is the most potent factor favouring reactivation of latent tuberculosis infections. Nearly 80% of newly infected patients with HIV and tuberculosis are now living in Africa. These persons will experience a 5 to 10% annual incidence of tuberculosis (Selwyn et al., 1989; Allen et al., 1992). This will enormously increase the burden of TB cases on the already overwhelmed national tuberculosis programme. So far, preventive chemotherapy is not as yet an integral part of TB national control programmes in developing countries. The increased burden of TB cases may require preventive chemotherapy to lower the incidence of active tuberculosis among HIV-infected individuals. The efficacy of isoniazid in preventing TB in dually infected persons has been recently assessed in Haiti and Zambia: this drug was found to successfully decrease the incidence of TB and to delay the onset of other HIV-associated diseases (Wadhavan et al., 1990; Pape et al., 1993).

However, before implementing anti-TB preventive chemotherapy in Africa, further studies evaluating the cost-efficacy of various preventive anti-tuberculosis regimens are necessary.

J. Batungwanayo, H. Taelman and J. Clerinx

BIBLIOGRAPHY


HARRIES AD. (1990), Tuberculosis and human immunodeficiency virus infection in developing countries, – Lancet, ii, pp. 387-390.


TAELMAN H., KAGAME A., BATUNGWANAYO J. et al. (1990), Pericardial effusion and HIV infection, – Lancet, i, p. 924.

