Clinical, Cerebrospinal Fluid and Pathological Findings and Outcomes in HIV-Positive and HIV-Negative Patients with Tuberculous Meningitis

C.-M. Schutte

Abstract

Background: The early diagnosis of tuberculous (TB) meningitis remains difficult. In South Africa, the HIV epidemic has shifted the spectrum of meningitis towards chronic infections (mainly tuberculosis [TB] and cryptococcosis). This study aimed to analyze clinical, cerebrospinal fluid (CSF) and pathological findings and outcomes in TB meningitis to evaluate whether HIV infection significantly influences the characteristic findings.

Patients and Methods: 40 consecutive patients with TB meningitis presenting at the Pretoria Academic Hospital were evaluated clinically and chest X-rays (CXR), computerized tomography (CT) brain scans, CSF profiles, HIV and routine blood tests were analyzed. Postmortem examinations (PM) were performed in seven patients and outcomes were assessed after treatment.

Results: 20 patients were HIV-positive and 17 were negative (three not tested). History and clinical findings were similar in both groups. The mean Glasgow Coma Scale (GCS) value on admission was 13 in both groups, while CXR showed abnormalities consistent with TB in 9/17 with HIV and 7/15 without, with abnormal CT brain scans in 15/19 patients with HIV and 12/16 without. Dilated ventricles and infarcts occurred more commonly in HIV-positive patients. The CSF results showed similar results in both groups. PM in three HIV-positive patients showed weakly formed granulomas and extensive endarteritis and infarcts. Outcomes were similar in the two groups, but a low GCS value on admission was a better prognostic indicator than the CD4-count in HIV-positive patients.

Conclusion: HIV infection does not significantly alter clinical and CSF findings in TB meningitis in South Africa, but ventricular dilatation and infarcts are more frequent in HIV-positive patients. The GCS gives a better indicator of prognosis than the CD4-count.

Key Words
Tuberculous meningitis · HIV infection · Clinical findings · Outcomes

Introduction

Tuberculosis remains an endemic disease in South Africa with case notification rates of 194 per 100,000 population [1]. Diagnosing tuberculous (TB) meningitis when the patient first presents is still fraught with difficulties and patients are often treated empirically on clinical suspicion before proof of TB is obtained. Characteristically, TB meningitis develops insidiously, with CSF findings showing lymphocyte predominance, high protein and low glucose values and often elevated adenosine deaminase (ADA) levels. However, exceptions to the characteristic findings are often seen. HIV is a known risk factor for the development of CNS tuberculosis (TB) [2]. It has been shown that the HIV epidemic has shifted the spectrum of meningitis seen in South African hospitals towards chronic infections such as cryptococcosis and TB [3, 4].

The aim of this 5-year study, which is part of an ongoing meningitis study, was to analyze the clinical and CSF findings in adult HIV-positive and HIV-negative patients with TB meningitis and to compare the pathological findings and outcomes in the two groups of patients.

Patients and Methods

40 consecutive adult patients with proven or clinically probable TB meningitis presenting at the neurology ward of the Pretoria Academic Hospital from March 1994 to June 1999 were included in the study. When either CSF cultures for TB or PCR for TB were positive (n = 16), or Ziehl-Neelsen staining showed acid-fast bacilli (n = 0) or postmortem (PM) confirmed caseating granulomas with meningeal exudates (n = 8), the case was classified as definite TB meningitis. All cultured mycobacteria were Mycobacterium tuberculosis. All other patients who had TB at another site (n = 9) with characteristic clinical and CSF findings or known previous TB who improved on TB treatment coupled with characteristic clinical and CSF findings (n = 4) or showed improvement on TB treatment with characteristic clinical and CSF findings were classified as highly probable TB meningitis cases (n = 8). Five of the patients

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and HIV infection is a risk factor for specific results or

Results
Of the 40 patients included in the study over the 5-year pe-
period, 20 were HIV-positive (50%), 17 were HIV-negative
(43%) and in three no HIV test had been done because the
patients had passed away soon after admission. The three
patients in whom the HIV test had not been performed
were excluded from the reported results.

Clinical Findings
According to the history, most patients had been unwell for
almost 2 weeks (range: 2 days to 3 weeks), with an average
of 9 days in the HIV-positive group and 11 days in the HIV-
negative group. All patients with known history had com-
plained of headache (34/34), and neck stiffness was a uni-
versonal finding. In both the HIV-positive and HIV-negative
groups, 75% of patients were febrile on admission. Two pa-
tients had a temperature of < 36 °C, both of whom passed
away. On clinical examination, the level of consciousness of
the patients was graded according to the Glasgow Coma
Scale (GCS) on admission. The values ranged from three
to 15 with a mean of 13/15 in both groups.

CXR were abnormal and in keeping with TB (either
old or active) in 16/32 patients (50%), of whom nine were
HIV-positive and seven were HIV-negative. Thus, HIV-pos-
itive and HIV-negative patients were equally likely to have
an abnormal CXR (9/17 or 53% HIV-positive abnormal; 7/15
or 47% HIV-negative abnormal (p = 0.72, Chi-square;
OR 1.29 (0.26–6.53)). The detailed results of the CXR il-
ustrating the different patterns of radiological involvement
are shown in table 1.

CT brain scans were abnormal in 27/35 patients (77%); 15/19
(79%) abnormal in the HIV-positive group and 12/16
(75%) abnormal in the HIV-negative group (p = 0.78,
Chi-square; OR 1.25 (0.2–7.8)). The detailed results of the CT
brain scans are shown in table 2. Hydrocephalus/enlarged
ventricles were the most common findings with 16 patients
showing a degree of ventricular dilatation. 50% of HIV-pos-
itive and 35% of HIV-negative patients showed ventricu-
dilatation (p = 0.37, Chi-square; OR 1.83 (0.4–8.56)). In-
facts also occurred in a much higher proportion of HIV-
positive patients (40% infarcts in HIV-positive patients vs
6% in HIV-negative patients (p = 0.01, uncorrected Chi-
square; Fisher’s exact 2-tailed test, p = 0.02).

The CD4-counts were performed only in HIV-positive
patients, ranging from 6.6 to 473 × 10^9/l (mean 180 × 10^9/l).
Thus, all of the patients showed evidence of immunodefi-
ciency when the lowest value for a normal CD4-count is
taken as 600 × 10^9/l. 13 patients (76%) had CD4-counts of
< 200 × 10^9/l. The serum white cell counts (sWCC) ranged
between 2.2 × 10^9/l and 16.4 × 10^9/l in the HIV-positive
group (mean 6.2 × 10^9/l), and 1.6 to 14.4 (mean 8.2 × 10^9/l)
in the HIV-negative group. The sWCC was < 11 × 10^9/l in
19/20 (95%) and 14/17 (82%) of HIV-positive and HIV-
negative patients, respectively (p = 0.21, Chi-square; OR
4.07 (0.31–113.7)).

CSF Findings
The results of the CSF analyses are given in table 3. In com-
paring CSF parameters among HIV-positive and HIV-neg-
avative patients, the two groups were similar with respect to
CSF lymphocyte counts, neutrophil counts, protein and glu-
cose levels, and ADA values (unpaired t-test; Welch cor-
rection). The HIV-positive group did show a trend towards
higher CSF lymphocyte counts (mean 164 in HIV-positive

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Results of chest X-ray findings in patients with tuberculous meningitis.</th>
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<tbody>
<tr>
<td></td>
<td>HIV-positive (N = 17)</td>
</tr>
<tr>
<td>Military TB</td>
<td>3</td>
</tr>
<tr>
<td>Infiltrate</td>
<td>4</td>
</tr>
<tr>
<td>Effusion</td>
<td>1</td>
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<tr>
<td>Bronchopneumonia</td>
<td>1</td>
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<tr>
<td>Old TB/pleural thickening</td>
<td>–</td>
</tr>
<tr>
<td>Normal</td>
<td>8</td>
</tr>
</tbody>
</table>

TB: tuberculosis; some patients had more than one abnormality on chest X-ray

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Results of CT brain scans in patients with tuberculous meningitis.</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>HIV-positive (n = 19)</td>
</tr>
<tr>
<td>Hydrocephalus/enlarged ventricles</td>
<td>10</td>
</tr>
<tr>
<td>Meningeal enhancement</td>
<td>3</td>
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<tr>
<td>Infarction</td>
<td>8</td>
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<tr>
<td>Granuloma</td>
<td>2</td>
</tr>
<tr>
<td>Edema</td>
<td>1</td>
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<tr>
<td>Normal</td>
<td>4</td>
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</tbody>
</table>

Some patients had more than one abnormality on computerized tomography scan