Clinical and Radiological Features of South African Patients with Tuberculomas of the Brain

Intracranial tuberculomas are a rare complication of tuberculosis that typically occurs in immunocompromised patients not treated previously for tuberculosis. We identified tuberculomas in 12 patients (11 of whom were infected with human immunodeficiency virus) at a hospital in Johannesburg, South Africa. Responses to antituberculous therapy were good, often despite the presence of large lesions, and surgery was not considered necessary in any of the patients.

Extrapulmonary tuberculosis (TB) involving the CNS occurs frequently in patients infected with HIV [1]. However, the incidence of intracranial tuberculomas in HIV-infected patients is not well documented [2-4]. A bacteriological diagnosis of the lesions requires invasive techniques and is rarely justified unless empiric therapy fails. With this limitation in mind, we investigated tuberculomas diagnosed on radiological grounds, excluding other causes of space-occupying lesions, such as pyogenic abscess, toxoplasmosis, cysticercosis, lymphoma, and syphilitic gummas. CT is a valuable diagnostic tool [5] that is also helpful in monitoring responses to treatment and in avoiding the need for invasive procedures [6]. Rarely, tuberculomas enlarge with anti-TB treatment [7] or antiretroviral therapy [8], and new lesions have been reported to develop during the treatment of patients with miliary TB or tuberculous meningitis [9].

Bearing in mind the diagnostic difficulties, the spectrum of responses to therapy, and the unknown influence of underlying HIV infection on tuberculomas of the brain, we reviewed all clinical cases of this condition identified at Sizwe Tropical Disease Hospital in Johannesburg, South Africa, from September 1996 through March 1998, in an attempt to improve our understanding of this complex pathology.

The hospital serves as a referral center for patients in the Johannesburg metropolitan area who have TB and other infectious diseases. Approximately 60% of all admitted patients are infected with HIV. A hospital database that recorded, from September 1996 through March 1998, all adult (>14 years of age) admissions with a clinical diagnosis of TB was reviewed for cases of tuberculoma of the brain. The diagnosis was based on the presence of a neurological abnormality not explained by another pathological process, a consistent lesion on CT scan, and supportive findings suggesting TB elsewhere in the body. A total of 474 adult admissions for TB were identified during the study period.

Among these, 13 adult patients with clinical and radiological features suggestive of intracranial tuberculomas were identified. One was rejected because a sputum culture revealed Mycobacterium kansasii and not Mycobacterium tuberculosis. Thus, cerebral tuberculomas were found in 2.5% of this population.

The 12 patients with tuberculomas (10 men and 2 women) were aged 18–54 years (mean, 32 years). Eleven were infected with HIV, with a mean CD4 cell count of 168 cells/μL (range, 6–496 cells/μL). Chest radiographs were performed on admission, and all 12 patients had infiltrates that were consistent with pulmonary TB. M. tuberculosis was isolated from the sputum of 3 patients, and from the CSF of 1. Sputum could not be obtained from 6 patients. In 2 patients, lymph-node aspirates showed necrotic material with epithelioid giant cells and granulomas, suggesting TB.

CSF obtained from 10 patients showed elevated protein in all samples and pleocytoses in 7. The mean CSF protein was 1.4 g/L (range, 0.7–2.6 g/L); the mean lymphocyte count was 59 × 10^3 cells/mL (range, 1–375 × 10^3 cells/mL); the mean neutrophil count was 66 × 10^3 cells/mL (range, 0–400 × 10^3 cells/mL); the mean glucose level was 1.8 mmol/L (range, 1–2.9 mmol/L); and the mean chloride level was 114 mmol/L (range, 85–127 mmol/L). One of the 6 CSF samples that was cultured was positive for M. tuberculosis.

All 10 CSF specimens were negative for bacterial culture, cryptococcal antigen, and Venereal Disease Research Laboratory (VDRL) tests. CSF toxoplasma antibodies were tested in 4 patients and were negative. One of 9 patients tested had positive serum IgG but had negative IgM antibodies to toxoplasmosis; however, this patient was not treated for this condition and responded to treatment for TB.

Neurological findings included seizures (3 patients), headaches (2 patients), limb weakness (8 patients), and vomiting, dizziness, and diplopia (1 each). Four patients had cognitive impairment (Glasgow Coma Scale score, <12) and 1 had expressive aphasia. Meningismus was present in 5 patients. One patient had an upper motor neuron lesion of the seventh cranial nerve, and another had cerebellar ataxia.

All patients received isoniazid, rifampicin, pyrazinamide, and ethambutol. Seven received either prednisone or dexamethasone for ≥1 week after admission. Those with CD4 cell counts <200 cells/mL were given cotrimoxazole. None of the patients received antiretroviral therapy.

Analysis of CT scans indicated that 8 patients had single hemispheric lesions. Of these lesions, 5 were irregular and 3 were rounded; 4 were surrounded by edema. Four patients had bilateral lesions. All were hemispheric, with the exception of one that was situated in the brain stem; 3 were surrounded by edema. All lesions enhanced with contrast.

Of the 12 patients, 2 died; one died in the hospital after 3 weeks, and the other died at home one year later. The former
A comparison of patients with tuberculomas and other hospitalized patients with tuberculosis (TB).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patients with tuberculomas (n = 12)</th>
<th>Control patients with TB (n = 461)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, years (range)</td>
<td>32 (18–54)</td>
<td>35 (14–80)</td>
<td>.3</td>
</tr>
<tr>
<td>Mean CD4 cell count, cells/µL (range)</td>
<td>168 (6–496)</td>
<td>270 (0–2182)</td>
<td>.3</td>
</tr>
<tr>
<td>Previously treated, %</td>
<td>0</td>
<td>39</td>
<td>.005</td>
</tr>
<tr>
<td>HIV infected, %</td>
<td>92</td>
<td>64</td>
<td>.04</td>
</tr>
</tbody>
</table>

* Calculated using Epi-info, version 6 (Centers for Disease Control, Atlanta). P values are 2-tailed.

HIV-infected patients.

The size of the radiological lesions was normalized by use of a ratio between the maximal horizontal measurement of the lesion and the maximal horizontal measurement of the skull. A corresponding ratio was calculated for the largest lesion. If >1 lesion was present, the change was reported for the largest lesion.)

The mean time between the initial CT scan and the follow-up CT scan was 75 days (range, 25–196 days). Among the 5 patients (all HIV-infected) for whom follow-up CT scans were available, the percentage reduction in lesion size varied from 6% over 3 weeks to an 81% reduction in 5 weeks.

Clinical responses to therapy were rapid, even in the presence of very large lesions. One patient, aged 18 years, who presented in a semicomatose state and who had a lesion with a diameter that was 32% of the diameter of the skull, was ambulant within 7 days of initiation of TB therapy and ancillary steroids and had made a complete neurological recovery at the time of hospital discharge. Five other patients who had been admitted with significant impairments of consciousness were discharged without residual neurological deficits. Limb weakness improved in all 8 patients who presented with this problem.

Of the 7 patients who received steroids, 4 were comatose. Three responded to TB therapy and steroids, whereas 1 remained comatose and died after 3 weeks. Of the 5 patients who received only TB treatment and no steroids, 2 were comatose. All 5 patients responded well to therapy, but 1 died a year later.

The clinical features of the most recent 461 adult admissions for TB without tuberculomas were available from the hospital TB database and were compared with those of the 12 tuberculoma patients (table 1).

On the basis of data on this small series, tuberculomas appeared to be a rare complication of TB, typically occurring in immunocompromised patients not treated previously for TB. CSF findings showed inflammation in all case patients that were tested and resembled those of tuberculous meningitis, with increased protein levels and lymphocyte counts. The CT appearance of the lesions was variable, although most were single lesions in the cerebral hemispheres that were enhanced with intravenous contrast. Responses to antituberculous therapy were good, often despite the presence of very large lesions. Although clinical recovery appeared to be hastened by the ancillary use of corticosteroids in some patients, the clinical value of steroids could not be determined in this limited study. Surgery was not regarded as necessary in any of the patients. The impact of antiretroviral therapy was not explored, and our findings may differ from those in patients fortunate enough to receive such treatment.

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References