Anterior spinal decompression in HIV-positive patients with tuberculosis

A PROSPECTIVE STUDY

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A total of 39 HIV-infected adults with spinal tuberculosis underwent anterior spinal decompression for neurological deficit. Fresh-frozen allografts were used in 38 patients. Antituberculous drugs were prescribed for 18 months, but antiretroviral therapy was not used. Six patients died within two years of surgery. Neurological recovery and allograft incorporation were observed at follow-up at a mean of 38 months, although the CD4/CD8 ratios were reversed in all patients. Adequate preoperative nutritional support and compliance with antituberculous treatment are essential in ensuring a satisfactory outcome.

Patients and Methods

Between 1994 and 1997, 39 HIV-positive adults (27 women and 12 men of mean age 28.5 years (17 to 43)) with spinal tuberculosis were evaluated for neurological deficit after anterior spinal decompression. Informed consent was obtained before HIV testing and counselling was provided for all patients. The duration of paralysis was eight weeks (3 to 14) and the Frankel classification was used to grade the neurological state (Table I). Two contiguous vertebral bodies were affected in all patients, in the thoracic spine (Fig. 1a) in 33, the lumbar spine in five, and the cervical spine in one. The mean preoperative kyphosis was 42° (19 to 65). Generalised lymphadenopathy, skin lesions and oral candidiasis were not observed.

A total of 19 patients had been treated for pulmonary tuberculosis in the past; three were having treatment when first seen and 11 had a family history of the disease. The nutritional status was poor in this study group with a mean haemoglobin of 88 g/l (56 to 94) and a serum albumin of 230 g/l (180 to 280). The ESR was elevated in all patients with a mean of 91mm/hour Westergren (74 to 109). Preoperative nutritional support was provided for all patients and, in addition, six required blood transfusion. The duration of nutritional supplement to achieve a safe level (haemoglobin >100 g/l, albumin >300 g/l) ranged for between five and nine weeks. The CD4/CD8 ratios were reversed (mean value 0.55 ± 0.4) (Table II).

A left thoracotomy was used to expose thoracic lesions and the lumbar spine was approached retroperitoneally. Exuberant extradural granulation tissue and extensive para-

Table I. Neurological status of patients at admission and after surgery

<table>
<thead>
<tr>
<th>Frankel grade*</th>
<th>Before operation</th>
<th>At one-year follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>B</td>
<td>13</td>
<td>3</td>
</tr>
<tr>
<td>C</td>
<td>23</td>
<td>5</td>
</tr>
<tr>
<td>D</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>E</td>
<td>12</td>
<td>22</td>
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* A, complete motor and sensory loss below the lesion; B, complete motor loss but sensation intact; C, some motor power distal to the lesion; D, useful motor power and patients able to walk with or without aids; E, no neurological symptoms
vertebral abscess formation were a characteristic feature in all cases. The diseased vertebral bodies were excised and the spinal cord decompressed by removing the granulation tissue from the medial, lateral and ventral aspects. Gentle pressure was applied over the gibbus to assess the degree of correction and tension in the spinal cord. An appropriate length of fresh-frozen femoral allograft was thoroughly cleaned and compacted with morsellised rib autograft, which was harvested during the thoracotomy. The autograft/allograft composite (33 patients) and allografts (5 patients) were positioned by interference fit. The harvesting and preparation of the allografts were described in a previous study.\(^8\)

The cervical lesion was treated by a tricortical iliac autograft. In nine patients anterior spinal instrumentation was utilised to provide additional stability (Fig. 1b). Intraoperative imaging was used to confirm the appropriate placement of the graft. Antituberculous medication, with a daily dose of rifampicin 600 mg, isoniazid 400 mg, pyrazinamide 1500 mg and ethambutol 1200 mg, was prescribed for 18 months.

The Mann-Whitney, unpaired, non-parametric Z-test was used to compare lymphocyte subsets between the six patients who died and the rest of the study population, and \(p < 0.05\) was considered to be statistically significant.

**Results**

Patients were initially monitored monthly for six months to ensure compliance with antituberculous treatment and thereafter at three-monthly intervals. The mean period of follow-up was for 38 months (26 to 60). Three patients (7.7%) had superficial wound sepsis, *Staphylococcus aureus* in one and no growth in two, which resolved without any sequelae. Seven patients (18%) who developed pulmonary complications after surgery as a result of adhesions after previous pulmonary tuberculosis improved after physiotherapy and nebulisation.

At one year 30 patients (77%) had made a useful neurological recovery (Frankel\(^7\) grades D, E) and walked without aids, five recovered partially (Frankel grade C), and four made no improvement (Table I). Six patients (15.4%), who died between 15 and 23 months after surgery, had a mean CD4-lymphocyte count of 325 (140 to 445). There was no

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**Table II.** Preoperative lymphocyte subset analysis in peripheral blood of HIV-positive patients with spinal tuberculosis (values are means ± sd and range)

<table>
<thead>
<tr>
<th>Lymphocyte Subset</th>
<th>Mean ± SD (Range)</th>
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<tbody>
<tr>
<td>Total lymphocyte count</td>
<td>2.98 ± 2.3 (1.0 to 3.0)</td>
</tr>
<tr>
<td>T-helper cells (CD4 count*)</td>
<td>453 ± 216 (140 to 1625)</td>
</tr>
<tr>
<td>T cytotoxic cells (CD8 count*)</td>
<td>897 ± 489 (477 to 3390)</td>
</tr>
<tr>
<td>CD4:CD8 ratio</td>
<td>0.55 ± 0.4 (0.19 to 0.97)</td>
</tr>
<tr>
<td>Total T-cells (CD3*)</td>
<td>1451 ± 501 (652 to 3500)</td>
</tr>
<tr>
<td>Natural killer cells (CD56*)</td>
<td>259 ± 122 (98 to 604)</td>
</tr>
<tr>
<td>B-cells (CD19*)</td>
<td>186 ± 104 (16 to 843)</td>
</tr>
<tr>
<td>Naïve cells (CD45RA*)</td>
<td>1042 ± 533 (582 to 4106)</td>
</tr>
<tr>
<td>Memory cells (CD29*)</td>
<td>1393 ± 471 (709 to 3232)</td>
</tr>
</tbody>
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* per μl of blood
statistical difference between the CD4 counts of these six patients and the rest of the study cohort (p = 0.6), but there was a statistically significant decrease in their CD8 counts (p < 0.05). Two of these six patients (33%) had not complied with the antituberculous treatment, and, apart from weight loss, had no other manifestation of AIDS, as defined by the guidelines of the Centre for Disease Control (CDC).\(^9\)

The neurological status before death was Frankel grade A in one, B in one and C in four. Cervical fusion had occurred by four months after operation. Incorporation of the allograft was evaluated by flexion/extension radiographs using a modification of the criteria of Bridwell et al\(^{10}\) as follows: grade 1, fusion with remodelling; grade 2, graft intact, fully incorporated and not completely remodelled; grade 3, graft intact with potential lucency at the graft-body interphase; and grade 4, no fusion, with collapse and resorption of graft. At a follow-up of between three and five years, 32 patients showed evidence of incorporation, but remodelling was incomplete (grade 2, Fig. 1c), and there were no differences between the nine patients who were instrumented and those who were not. At the final review the average kyphosis was 26° (11 to 42).

A total of 21 patients had no back pain, seven had pain following strenuous activity and four required analgesics. There were no cases of late sepsis or collapse of the allografts. Histological examination revealed caseative granuloma in 31 patients and acid-fast bacilli in five. In the remaining eight patients, the histological features were those of chronic non-specific infection, and the cultures were negative for fungal studies.

**Discussion**

*Mycobacterium tuberculosis* is estimated to infect 1.6 billion people worldwide.\(^9\) In approximately 2% of cases of tuberculosis the skeletal system is affected and of these 60% localise to the vertebral column. The main reasons for the global increase in tuberculosis are poverty, insufficient and inadequate health resources, and the impact of the HIV epidemic, especially in Africa and Asia.\(^2\) HIV and tuberculosis form a lethal combination and one-third of the increase in the incidence of tuberculosis has been attributed to HIV. Several clinical and laboratory studies have shown that HIV-positive patients with active tuberculosis have an increased viral load compared with similar patients without this disease.\(^11,12\) Cellular activation increases the pro-inflammatory cytokines (interleukin-6 and tumour necrosis factor-α), which, in turn, enhance HIV replication, both in monocytes and lymphocytes.\(^13\) The increase in viraemia has been associated with declining CD4-lymphocyte numbers. We did not evaluate the viral loads, and antiretroviral therapy was not prescribed because of economic constraints.

Extrapulmonary manifestations of tuberculosis are particularly common in patients with HIV infection, but there have been few studies on the treatment and outcome of spinal tuberculosis. In a report\(^14\) on seven HIV-positive patients with spinal tuberculosis, the CD4-lymphocyte counts performed on four patients were between 22 and 620. The mean age was 43 years (24 to 63), 71% were men, and most were homeless with a history of drug abuse. The development of spinal tuberculosis was not related to the degree of immunosuppression, as two patients had a normal CD4-lymphocyte count. One patient had a successful anterior decompression of the spine for neurological deficit. There was no difference in the presentation and outcome after antituberculous treatment between the HIV-negative patients (19) and those who were HIV-positive (7) but there was no mention of antiretroviral therapy. There were several differences between that study and ours. Our patients were younger, mostly female, with a history of contact with tuberculosis in 27 patients, and no record of substance abuse; the predominant mode of HIV transmission in Sub-Saharan Africa is by heterosexual practice.

The literature on surgical complications in HIV-infected patients is retrospective and inconsistent, with reports documenting both favourable and unfavourable outcomes.\(^3,14,15\) A review by Rose et al\(^9\) found that the complications after surgery were higher in patients with the late stages of the disease and in those with other risk factors. Postoperative complications have been associated with emergency procedures in patients with malnutrition, uncontrolled diabetes and neutropenia. Protein-calorie malnutrition is associated with poor wound healing, increased postoperative infection and immunosuppression: a serum albumin level of less than 350 g/l and a total lymphocyte count of less than 1500 cells/l are considered to represent clinical malnutrition.\(^16\) Five reports on HIV-positive patients\(^3,5,13,17\) describe complications after 145 orthopaedic operations in 138 patients, and the median complication rate was 23% (0 to 50). In a retrospective review of 476 orthopaedic trauma patients who underwent surgery, the postoperative complications in the asymptomatic seropositive group was 16.7%, and 5.4% in the seronegative group. When open fractures were considered separately, the seropositive group had an infection rate of 55.6% compared with 11.3% in the seronegative group. A study of postoperative infection after open reduction of fractures in 26 asymptomatic and 17 symptomatic HIV-infected patients found none in the asymptomatic group and four cases (24%) in the symptomatic group. The immediate postoperative complications in our study were similar to a group of HIV-negative patients with spinal tuberculosis described previously.\(^8\) The low incidence of postoperative wound sepsis in our patients may be attributed to the nutritional support provided before elective surgical treatment.

Extrapulmonary tuberculosis is an AIDS-defining disease according to the CDC classification.\(^9\) Although the CD4/CD8 ratios were reversed, the relative lymphocytosis in most of our patients suggested early-stage disease. The significantly decreased CD8 counts (p < 0.05) in the six
patients who died indicated a more advanced stage. Active tuberculosis decreases the number of circulating CD4 T-lymphocytes and the CD4 count may be the only independent predictor of survival.\(^1\) The number of CD4 lymphocytes is not an absolute indication of their functional capacity in HIV-infected patients, and variations in the CD4-lymphocyte count have been noted when the test was performed frequently. Greene et al\(^3\) found no increase in the rates of postoperative infection in HIV-positive patients when compared with HIV-negative haemophiliacs undergoing similar elective orthopaedic procedures, suggesting that the preoperative CD4-lymphocyte count could be used as a guideline to evaluate outcome.\(^3\)

The rationale for the use of structural allografts in spinal tuberculosis was based on our previous study\(^1\) of 117 patients who had been treated with a rib autograft. We noted a progressive increase in kyphosis (5° to 25°) owing to slippage, fracture of the graft and subsidence, between one and four years after surgery, with lesions involving the lower dorsal spine. The weakness of the rib grafts can be attributed to the unfavourable length-to-width ratio and the small surface area of contact with the adjacent vertebral end plates.\(^2\) The increased compressive strength of the allografts and the large surface area of contact between the allograft/autograft composite and the vertebral body resulted in a stable construct allowing immediate loading. The duration of biological incorporation of fresh-frozen cortical allografts in adults is frequently slow and unpredictable. Bony incorporation may be mediated immunologically, since measurable humeral responses to donor antigens have been noted in patients.\(^20\)-\(^22\) The delayed fusion may also be due to an unhealthy graft bed as a result of the infection. It is remarkable that there were no cases of graft rejection or late sepsis, which may be because the disease was in its early stages and there may have been diminished adherence of acid-fast bacilli to foreign material.\(^23\)

Orthopaedic surgeons should be aware of the increasing prevalence of HIV infection and the worldwide resurgence of spinal tuberculosis. The ultimate outcome of surgery in HIV-infected patients depends on a number of factors including whether it is an emergency or elective procedure, coexisting medical problems, the nutritional status, and the stage of the disease.

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

References