Tuberculosis Of The Lumbar Spine: Outcomes After Combined Treatment With Short-Course Two-Drug Therapy And Surgery

O Karaeminogullari, U Aydinli, R Ozerdemoglu, C Ozturk

Citation

Abstract
The purpose was to evaluate complications and treatment results in patients with tuberculosis of the lumbar spine. Eighteen patients with active tuberculosis of the lumbar spine were treated surgically in the Department of Orthopedic Surgery at Uludag University School of Medicine between the years 1993 and 2000. All the patients received a short course of anti-tuberculosis combination drug therapy (isoniazid and rifampicin) for 9 months. The patients who underwent anterior radical debridement + anterior fusion and/or posterolateral debridement + posterior fusion + stabilization showed 5-8 degrees correction of local angulation after surgery; however, the number of patients was too small for statistical analysis. The mean loss of correction at final follow-up of meanly 5 years in cases of anterior or posterior surgery alone was 45-50%, whereas the corresponding finding for the combined approach was 12%. The combination of short-term two-drug chemotherapy (daily isoniazid plus rifampicin for 9 months) and surgery is effective for tuberculosis of the lumbar spine.

INTRODUCTION
Tuberculosis (TB) is the most common granulomatous bacterial infection of the spine. The goals of management are to eradicate the infection and prevent or treat neurological deficits and/or spinal deformities. Short-course (6- or 9-month) regimens of chemotherapy with daily isoniazid and rifampicin are highly effective for treating TB cases with positive bronchoalveolar smears [1]. The same regimen is expected to be effective in spinal TB based on its paucibacillary nature.

The literature reports different treatment outcomes for spinal TB relative to duration of anti-tuberculosis treatment (6-18 months), the number of drugs used (two to four per regimen), and frequency of drug administration (daily, or twice or three times weekly). In a meta-analysis from Turkey [2], the duration of drug usage ranged from 6-18 months and four-drug chemotherapy was used by most centers. Parthasarathy et al. [3] found that two-drug chemotherapy (daily isoniazid + rifampicin) for 9 months yielded the most favorable results. Resistance to first-line drugs is not a major problem in osteoarticular TB due to the small load of microorganisms present and the absence of closed caseous lesions. Also, two-drug chemotherapy is advantageous with respect to lower toxicity. Isoniazid + rifampicin is the most effective drug combination from a bacteriological perspective.

In recent years, numerous studies [4-20] have advocated radical anterior surgery (debridement and grafting) for correction and prevention of kyphosis in cases of spinal TB. The reason is that debridement alone may result in development of a kyphotic deformity, particularly in cases with multi-segmental involvement [20]. However, even this radical surgery is not always sufficient for preventing progressive kyphosis, because lack of stability is common in these cases, as is graft failure due to fracture, absorption, or slippage [20]. External support or prolonged bed rest with surgery and drugs do not seem to be adequate for treating spinal TB. These approaches are not comfortable, and are sometimes intolerable for patients. Use of internal fixation devices in the surgery seems to be the best choice for stabilizing the spine, for early return to daily life activities and normal comfort levels, and for maintaining the degree of correction.

In this report, we present the clinical results for cases of lumbar TB at our center that were treated with the combination of surgery and a 9-month course of daily...
isoniazid + rifampcin chemotherapy.

**PATIENTS AND METHODS**

The patients were 18 individuals (7 males, 11 females) with active TB of the lumbar spine who were treated in the Department of Orthopedic Surgery at Uludag University School of Medicine between 1993 and 2000 (Table I). Each underwent surgery while on short-course (9-month) two-drug anti-tuberculosis therapy (isoniazid 5 mg/kg and rifampcin 10 mg/kg once daily)

**Figure 1**

Table I: The data for the 18 cases of lumbar tuberculosis.

<table>
<thead>
<tr>
<th>Patient ID</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>Location</th>
<th>Disease of infection (anteroposterior)</th>
<th>Neurological deficit</th>
<th>Surgery</th>
<th>Infective source</th>
<th>Histologic diagnosis</th>
<th>Clinical follow-up</th>
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<td>5 years</td>
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*At: Anterior radical debridement + fusion
P: Posterior lateral debridement, fusion, and instrumentation
A-P: Anterior and posterior instrumentation and fusion

The diagnosis of tuberculosis was based on clinical presentation, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) levels, a positive proteinase derivate reaction, and findings on plain radiography, computed tomography and/or magnetic resonance imaging. In the cases treated between 1997 and 2000, we also performed percutaneous transpedicular biopsy under local anesthesia and fluoroscopic guidance prior to starting anti-tuberculosis drug treatment. In all cases, the infection was localized to the lumbar region.

In choosing the surgical treatment method for each case, we considered the local kyphotic angle, the patient’s neurological status, the amount of bony destruction at the infected site, and the amount of abscess formation. Seven patients underwent anterior radical debridement + fusion (Figure I), five underwent posterolateral debridement + fusion + instrumentation, and six underwent anterior radical debridement + fusion combined with posterior instrumentation + fusion (Figure II). If the defect after radical debridement was less than 5 cm, a tri-cortical iliac bone graft or allograft was used for anterior column support.

If the defect was larger, a titanium mesh cage was used. In cases that were not treated with instrumentation, an external support with a thoracolumbosacral orthosis (TLSO) was used for approximately 5 months. Other patients were allowed to mobilize without any support in the early-postoperative period.

**Figure 2**

Figure I: A 42-year-old male with the diagnosis of Pott’s disease involving L4-L5. Anteroposterior and lateral radiographs showed moderate involvement of the vertebral bodies but magnetic resonance imaging demonstrated anterior and posterior abscess formation with epidural involvement. The patient underwent anterior radical debridement and fusion without instrumentation. At 5 years post-surgery the patient was symptom-free.
Figure 6

Figure 7
Figure 8
Figure II: A 65-year-old female with Pott's disease involving L2-L3. Anterior radical debridement + fusion and posterior instrumentation + fusion were performed. A combination of a femoral shaft allograft and an autograft was used for anterior fusion. Plain radiographs taken at 6.5 years post-surgery showed fusion.
Treatment results were assessed on the basis of clinical, laboratory and radiological findings. For each patient, we recorded data from re-check exams done 1, 3, 6, 9, 12, 18, and 24 months after surgery, and from the final follow-up visit. At each of these time points, ESR and serum CRP were recorded to evaluate disease status. Liver enzyme levels, BUN, creatinine testing were also done every 2 months during anti-tuberculosis drug treatment. Radiological assessments were done preoperatively, immediately after surgery, and at the last follow-up check. At each assessment, we recorded local kyphotic angulation, as measured from the superior end-plate of the proximal healthy vertebra to the inferior end-plate of the distal healthy vertebra on lateral spinal X-ray \[1\]. The status of the graft and evidence of fusion were also evaluated. The graft was considered incorporated if there was no graft resorption, and if there was visible graft remodeling (trabecular rearrangement) and graft hypertrophy.

RESULTS
The patients’ ages ranged from 31 to 72 years (mean, 58.5 years). The presenting signs were mostly low-back pain and difficulty in walking. The mean duration of prodromal symptoms before admission was 13 months. Six patients had neurological deficits at the time of presentation.

In the 18 cases, pain relief was achieved at an average of 3 months after start of drug treatment. The neurological deficits that were present preoperatively in six patients all resolved during follow-up. All patients had elevated ESR and serum CRP were high (mean 64.5 mm/hr and 6.3 mg/dL, respectively). At the final follow-up exam, the mean results for ESR and CRP were 20.5 mm/hr and 0.4 mg/dL, respectively.

The infection was localized to a single vertebra in 2 cases, involved one adjacent vertebra in 14 cases, and affected more than two vertebrae in 2 cases. The average preoperative local angulation was -6.5 degrees. The average amount of correction of local angulation immediately post-surgery was 9.6 degrees. The mean percentage of angle loss of correction at final follow-up was 34.7%.

At a mean follow-up period of 60.6 months (range, 40 to 112 months), none of the 18 cases had shown TB recurrence. In addition, we observed no pseudoarthrosis or complications (fracture, slippage or subsidence) related to the grafts used.

DISCUSSION

LOCALIZATION OF SPINAL TB

Approximately half of all forms of skeletal TB affect the spinal column, and the dorsal and dorsolumbar regions are the primary sites of infection. In contrast, involvement of lumbar vertebrae and the lumbosacral junction is relatively rare [19,23]. Tuberculosis in lumbar region behaves different from TB in other areas of the spine. A capacious spinal canal with floating nerve roots is usually relatively tolerant to compression by an abscess or by granulation tissue, which may develop slowly. Normal lordosis helps block the tendency of anterior disease to cause kyphosis, so extensive destruction of a vertebral body is required before kyphosis occurs. Thus, cosmetic deformity is less common in this region of the spine compared to the thoracic spine.

PRESENTING SIGNS, CONSEQUENCES OF DELAYED TREATMENT

The duration of prodromal symptoms is extremely long in most case of lumbar TB (mean 13 months in our series). Since the symptoms are non-specific and there are no obvious radiographic findings in the early stage of lumbar TB, these cases are often misdiagnosed or go undetected for a very long time. Consequently, the disease is usually at an advanced stage before the patient seeks medical attention. This is one reason why it is important to keep the diagnosis of TB in mind for any patient with back pain or low-back pain, and to do a laboratory work-up for TB. Magnetic resonance imaging should also be performed if there is suspicion of this infection. Once a case of spinal TB is diagnosed, percutaneous transpedicular biopsy should be carried out under local anesthesia and fluoroscopic guidance.

To minimize treatment time and costs, and to avoid surgical complications, it is better to spend time and money on diagnosis when a patient first presents with symptoms. Delay of diagnosis leads to more severe bone destruction, which can result in kyphosis, cord compression, and even neurological deficits.

In our series of lumbar spine TB, 33.3% of the patients showed neurological symptoms at presentation. However, none of these six individuals had severe kyphotic deformity. Most of the 18 patients exhibited hypolordosis or flattening of normal lordosis at presentation. This is in accordance with the study of Rajasekaran and Soundarapandian [20]. These authors showed that lumbar spine TB leads to a phenomenon of subsidence, in which the superior vertebra gradually descends resulting in a loss of normal lordosis but no kyphosis. Similarly Puig Guri [18] reported that destruction of thoracic vertebrae by TB results in posterior displacement of the center of motion, subluxation at the level of the facets, and increased weight borne by the anterior part of the vertebral body, all resulting in aggravation of kyphosis if kyphosis is present. In contrast, in the lumbar spine the large vertebral bodies and the vertical articular facets allow the collapse to occur in a more telescopic way rather than by angulation [18]. All these observations support the conclusion that normal lordosis, lumbar regional anatomy, and the specific biomechanics of the lumbar region are major factors that affect the pattern of progress of lumbar spine TB and development of deformity.

TREATMENT

The goals of management of spinal TB are to eradicate the infection, to prevent or treat neurological deficits, to correct spinal deformities, to achieve normal sagittal contours of the spinal column, and to achieve unrestricted mobilization and normalization of patients’ daily activities as soon as possible. In 1985, the Medical Research Council’s Working Party on
Tuberculosis of the Spine began to investigate the different forms of treatment used throughout the world [12]. Randomized clinical trials were done to assess various treatment modalities:

1. Chemotherapy with immobilization via strict bed rest or body cast
2. Outpatient chemotherapy with ambulation
3. Chemotherapy and debridement of infected bone without fusion
4. Radical surgery involving anterior resection and debridement with autologous bone-strut grafting

Conservative Treatment: The advent of anti-tuberculosis drugs led to great success in treating this disease [14]. We concur with Hamzaoglu [6] and Moon et al. [14], who stated that, if diagnosed early, Pott's disease (particularly lumbar localization) is medically treatable. Moon et al. [14] reported that, in patients treated with long-term (12-18 months) triple chemotherapy, the disease is inactivated at 6 months on average, and that fusion occurs by 36 months in 87.5% of cases. However, there is still some controversy about the optimal duration of anti-tuberculosis drug regimens for management of spinal TB when medical treatment is combined with radical surgery [17, 21]. A number of authors have advocated short-term chemotherapy. Griffith [4] reported results with a 6- or 9-month course of rifampin and isoniazid. After 3-4 years of follow-up, the author found that this protocol was at least as effective as an 18-month course of isoniazid and paraaminosalicylic acid. Upadhyay et al. [15] reported that 6 months of triple-drug chemotherapy in conjunction with radical surgery was adequate for managing TB of the spine, as this produced results comparable with 9-month and 18-month chemotherapeutic regimens.

In addition to shorter courses of medical treatment, researchers have studied the effectiveness of two or three times weekly drug administration as opposed to daily administration. The former has many advantages. The regimen can be supervised by Shembaker and Babhulkar and this improves patient compliance, which is the most important determinant of treatment outcome in spinal TB cases only with medicine [31].

Chemotherapy is the most critical factor in managing TB of the spine, and it is vital to ensure that appropriate regimens are given under adequate supervision [15]. However, isolated cases of drug resistance have been reported [12, 16]. In our series, the drug portion of the treatment was a 9-month course of isoniazid and rifampcin, as advocated by the Medical Research Council's Working Party on Tuberculosis of the Spine [11, 12, 13].

Surgical Treatment: A wide variety of surgical treatments for TB of the spine have been reported in the literature, including anterior or posterior surgery alone, and combined anterior and posterior surgery. Different published series also describe the use of instrumentation systems and varied amounts and types of bone grafts.

Radical surgery, or combined posterior instrumentation + anterior radical surgery combined with anti-tuberculosis chemotherapy is indicated only for patients with advanced disease who already have spinal deformity, or patients who will eventually develop kyphosis [16].

Kim et al. [7] reported 140 patients who were treated with radical anterior surgery in 1993. They obtained 51% initial correction of kyphosis, but the rate of correction dropped to 7.5% by two years of follow-up. Others have reported similar results with radical anterior surgery [6, 20].

Moon et al. [14] and Chen et al. [4] reported 44 and 29 patients with TB of the spine, respectively, who were treated by anterior radical surgery combined with posterior instrumentation and fusion. They achieved remarkable correction of the kyphotic deformity, and loss of correction after surgery was negligible (1 to 3 degrees). The number of patients in our series was not quite large enough to statistically compare outcomes with different surgical methods. However, our results indicate that combined surgery yields better end results from a radiological point of view. Although we noted some differences among the three surgical approaches with respect to certain radiological measurements, the overall levels of patient satisfaction at the end of treatment were similar.

COMPLICATIONS/FOLLOW-UP

The main problem in the treatment of spinal TB is progression of spinal deformities such as kyphosis, and this issue is even more prevalent in cases treated with conservative treatment only [4]. The results from two long-term follow-up studies have shown that all patients who show kyphotic angle increase greater than 30 degrees have lesions in the dorsal spine [11, 23]. This can be attributed to
the normal kyphotic curve of the dorsal spine, which combines with gravity and leads to progression of the deformity. As mentioned above, compared to disease in the thoracic spine, TB of the lumbar spine seems to carry less risk for kyphotic deformity.

The literature contains a high number of complications with graft use in surgery for spinal TB particularly in cases of multi-segment involvement [17, 18]. Only 2 of the 18 patients in our series had involvement of more than two vertebrae, and we observed no graft or cage problems in either case.

In our series of lumbar TB cases, all the patients presented at an advanced stage of disease, and therefore required more extensive surgery. The serious problem of delayed diagnosis of spinal TB underlines the need for preventive health care practitioners and orthopedic surgeons to keep a high index of suspicion for this disease. The clinical results in our 18 cases suggest that surgical debridement combined with a 9-month regime of daily isoniazid + rifampicin is an appropriate mode of treatment for lumbar TB.

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